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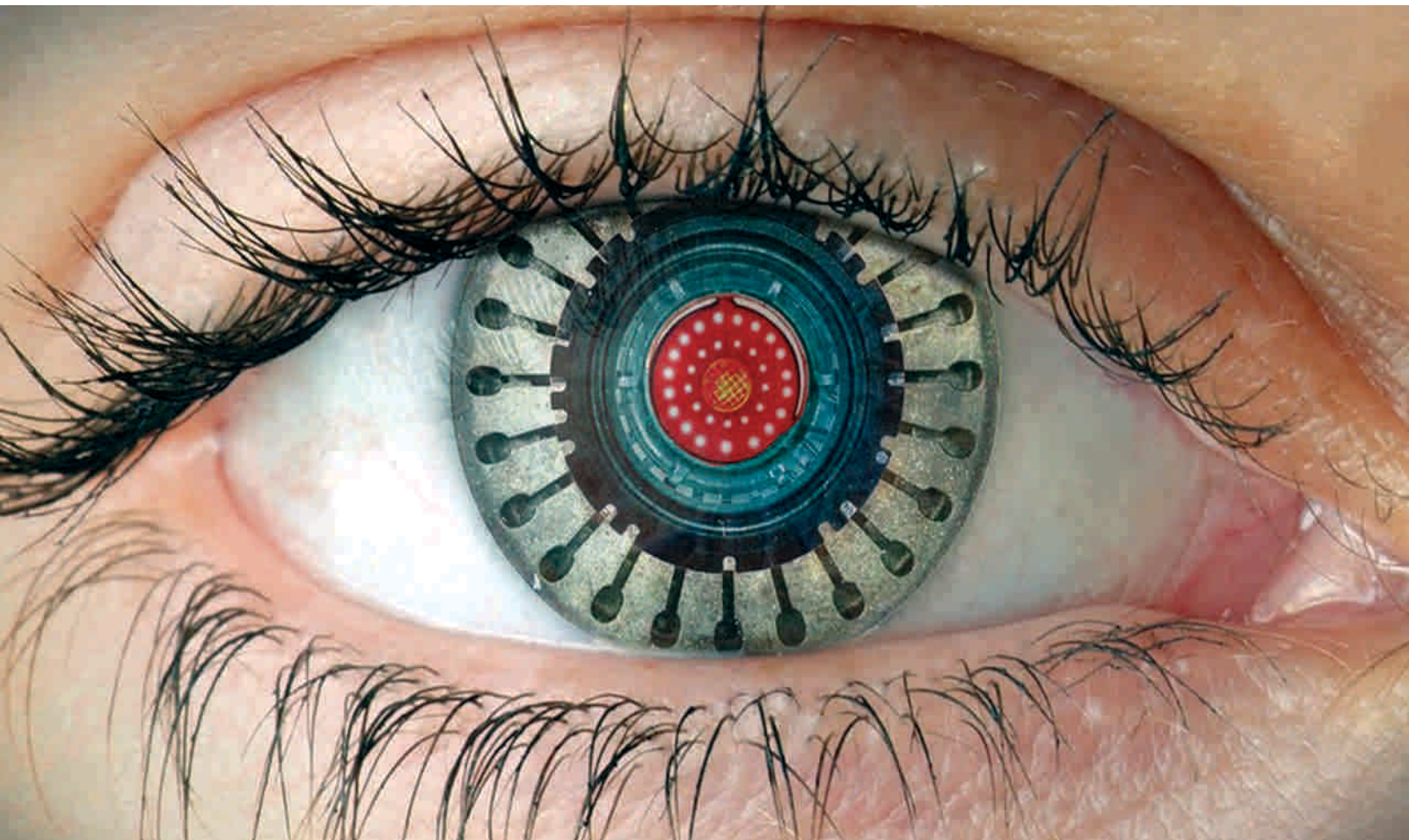
HARYANA JOURNAL OF OPHTHALMOLOGY

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June, 2019

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Journal of Haryana Ophthalmological Society



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गायत्री मंत्र

ॐ भूर्भुवः स्वः
तत्सवितुर्वरेण्यं भर्गो देवस्य
धीमहि धियो यो नः प्रचोदयात्



हे ईश्वर! आप हमारे दुखों को दूर करने वाले और सब जगह रहने वाले हैं। हम सब आपके पाप नाशक तेज का ध्यान करते हैं और आपसे प्रार्थना है कि हमारी बुद्धि को हमेशा अच्छे मार्ग और सत्कर्मों के लिए प्रेरित करें।

भावानुवाद

तूने हमें उत्पन्न किया, पालन कर रहा है तू,
तुझसे ही पाते प्राण हम, दुखियों के कष्ट हरता तू।
तेरा महान तेज है, छाया हुआ सभी स्थान,
सृष्टि की वस्तु-वस्तु में, तू हो रहा है विद्यमान।
तेरा ही धरते ध्यान हम, प्रभु माँगते तेरी दया,
ईश्वर हमारी बुद्धि को, श्रेष्ठ मार्ग पर चला।



JACK J KANSKI

FRCS, FRCOphth

(August 5, 1939 - January 5, 2019)



Haryana Ophthalmological Society's

Tribute to The Legend

The great American philosopher and psychologist William James once said, “The great use of life is to spend it for something that will outlast it.” These words were perhaps written for Jack J. Kanski.

Clinical Ophthalmology by KANSKI is the first book that every budding ophthalmologist starts reading and continues to read it with joy. World-renowned ophthalmologist Jacek Jerzy Kanski (better known as Jack J. Kanski) was born on August 5, 1939 in Warsaw, Poland, to Jerzy Jordan and Adela Jozefa Kanski. Mr. Kanski obtained his Bachelor of Medicine and Bachelor of Science degrees from London Hospital Medical School in England in 1963. His professional journey was remarkable. He worked as house officer at London Hospital from 1963 to 1964, senior house officer at Western Ophthalmic Hospital in London in 1965, registrar at Westminster Hospital in London from 1965 to 1966, resident at Moorfields Eye Hospital in London from 1966 to 1970, senior registrar at London Hospital from 1970 to 1973, and consultant surgeon at King Edward VII Hospital in Windsor, England, from 1974 to 2000. King Edward VII Hospital in Windsor has developed into a world-class teaching venue under his leadership and today attracts trainees from far and wide.

As a resident, he had started to collect a series of interesting cases with clinical photos which were the inspiration for his books and the basis for his first book Clinical Ophthalmology, in 1984. He was helped by his wife Valerie Ann Shannan and what followed in over the next 25 years was more than 30 books covering all aspects of ophthalmology.

He created ophthalmic textbooks, illustrations, and photography of exceptional quality. Residents the world over consider Mr. Kanski's, “Clinical Ophthalmology: A Systematic Approach” to be a Bible of ophthalmology, and it has been translated into several languages. The ninth edition of Kanski's Clinical Ophthalmology is scheduled to be published in April, 2020. Besides his books on ophthalmology he also produced several books on world history.

Mr. Kanski passed away on January 5, 2019 leaving behind a rich legacy. Haryana Ophthalmological Society bows down in all humility to this great man whose dedication and work in teaching and training generations of ophthalmologists world-wide epitomises the essence of a true Professor and will echo in eternity.

Compiled by -
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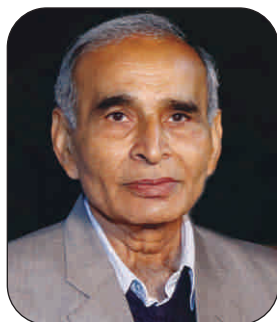
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Message from the President



Dear Friends,

Greetings from HOS executives .

Publication of a scientific journal is an important activity and Haryana Journal of Ophthalmology (HJO) is our showcase where members present their work and add to the existing knowledge. Haryana Ophthalmological society has always been striving hard for raising the levels of CMEs , conferences, AIOS-ARC Symposia and other scientific and social activities. Prof. Dr. Manisha Nada who is the Chief Editor of HJO has put in a lot of effort to raise the bar. I am sure that her enthusiasm and energy as an active ophthalmologist will bring an excellent issue of HJO both in terms of quality and contents.

HOS executives are always working to make the society stronger and are well recognized across India. HOS conferences have always been very successful and now we have the mammoth responsibility to host “AIOC 2020” which happens to be the first ever to be hosted by HOS. We should all work as a team to make it a successful and most memorable conference ever.

On behalf of HOS, I would like to congratulate and extend my best wishes and full support to Dr. Manisha Nada for making this issue of HJO a huge success.

Regards!

Dr. Ajay Sharma

President, HOS

Secretary's Report



Respected Seniors and Dear Colleagues,

Warm greetings from the desk of honorary general secretary,

I am feeling elated that Haryana journal of Ophthalmological Society is being published. Congratulations to Prof. Manisha Nada, Chief Editor for splendidly carrying out this arduous work.

Haryana ophthalmological society's membership has grown to 858 thanks to untiring efforts of Dr. Narinder Taneja and Dr Rajan Gupta. The society has been very active in academic and social activities and has successfully conducted Gurugram refractive mela at Gurugram, AIOS-ARC symposium on Crusade against Diabetic Retinopathy at Rohtak, Glaucoma and Cataract symposium at Gurugram, Glaucoma week and Glaucoma awareness walk at Gurugram, Installation of Haryana Chapter of ACOIN to name a few. All the events were well attended and recognized by Haryana Medical Council by allotting credit hours and Dr. Jagdeep Basur is our man for all HMC credit points and needs special mention here .

Annual conference of our society, “Ophthalmic Rainbow” was organized by Gurugram Ophthalmological Society Gurugram on November 24th & 25th, 2018 under the Chairmanship of Dr. Ajay Sharma. He took over as President and Prof. (Dr.) Narinder Taneja as Vice President of HOS . The conference was a big success and was allotted 12 credit hours by Haryana Medical Council. Life time achievement awards were conferred upon Dr. Praveen Arora from Sirsa, Dr. S.L. Bansal from Yamunanagar, Dr. P.C. Sharma from Ambala and Dr. M.S.Boparai from Gurugram. Iron man HOS Sardar Patel award of excellence was conferred upon Prof. Narinder Taneja.

HOS has been entrusted with a big responsibility of hosting annual conference of AIOS i.e. AIOC-2020 in February, 2020 at Gurugram. Under the able guidance of Prof A.K. Khurana and Dr Ajay Sharma the organizing team is putting all possible efforts to make this event a memorable one. Myself has been entrusted upon the job of chief organizing secretary and being assisted by the ever ready pen friendly Dr. Narender Taneja as organizing secretary . Dr. Dheeraj Gupta, a personality full of energy and positive critic from GOS would be looking after the affairs of treasurer of AIOC-2020. This is going to be an International event and all the members of HOS should come forward to support to take this responsibility to make this conference a splendid show . So be ready for this responsibility and have the Josh. I need blessings from all seniors, mentors, ex-presidents of HOS, unsung heroes of the society from all District societies and support of all colleagues, energy of my juniors to make this event unforgettable for the rest of the ophthalmic world.

Finally, I would like to extend my thanks to all my friends, well wishers, my senior colleagues, family members for their love and selfless moral support towards HOS concerned activities .

God bless you, God bless HOS to live long.

Jai Hind!

Prof. Dr. Inder Mohan Rustagi

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Editorial



Dear Colleagues,

Warm Greetings!

I start my sojourn as Editor of Haryana Journal of Ophthalmology with great enthusiasm and your best wishes. At the very outset I thank all the contributors for providing brilliant scientific material.

Ophthalmology has progressed by leaps and bounds. Starting ocular examination with a torch to direct and indirect ophthalmoscopy to slit lamp examination to various lenses for improved optics, now we talk of smartphone-based imaging, robotics, bionic eye and artificial intelligence-based screening programmes. Continuously updating oneself is mandatory to keep abreast with latest developments and this precisely is the aim of publishing this journal. The focus will always be to provide you with “must know” updated material of the common ophthalmological conditions.

There is a global diabetes epidemic and India has been called the Diabetic Capital of the world with up to 65 million diabetics. Whilst improved diabetic care has substantially improved diabetes outcomes, the disease remains a common cause of working age adult-onset blindness. Diabetes tends to occur at a younger age in Indians than Caucasians, and the improving life expectancy in India means that individuals will now live longer with diabetes than ever before. Diabetic retinopathy is going to be a major health issue in future. Screening for diabetic retinopathy can facilitate early detection and hence provide an opportunity for treatment at an early stage. India has 1 ophthalmologist per 100,000 population and this ratio is even more dismal for rural settings. The big question is who will do the screening and how?

Screening for diabetic retinopathy can be either ophthalmologist-based or ophthalmologist-led. Given the ophthalmologist/population ratio, the ophthalmologist-based approach is not possible. Teleophthalmology, an ophthalmologist-led screening model, may offer a cost-effective and feasible model for screening large groups of people in remote and often poor areas. Here the screening is done at the grassroot level by trained optometrists using latest imaging tools and images are transmitted to a designated ophthalmologist who guides further action.

Artificial intelligence (AI) assisted automated screening models have been developed world over. AI platforms for capturing retinal images are placed in areas where an ophthalmologist is not available and these can be used by patients at their comfort. The images of retina are interpreted by the computer interface by comparing them with a library of images and patients with suspicious lesions are informed and are further investigated. One such system has been approved by FDA and AI-assisted automated screening models have potential to relieve the overburdened healthcare system's problems.

The screening programmes practically do not exist in India where they are most needed. This is vital to understand that planning for effective interventions needs to start much before the “epidemic” sets in. As ophthalmologists the onus is on us to develop local models to screen the diabetic population and this also means an effective interaction between practicing physicians/endocrinologists.

The doctor-patient relationship and inter-personal relations amongst fraternity need to be maintained at the highest levels. The recent incidences of violence against doctors are of great concern and we need to sit down and think why this is happening and what is wrong with our noble profession? Society and media is quite sceptical today towards doctors. Access to information is just a screen touch away and a well informed (albeit partially) patient with high expectations comes to us in this atmosphere of uncertainty. The nuances of medical profession are not known to him/her and this is our responsibility to clarify the doubts and give a scientifically correct advice. This is possible only if we believe and practice evidence-based medicine and avoid personal preferences and whims.

I would like to express my appreciation for the efforts of the editorial team members who showed sincere willingness and contributed their work and time for this scientific endeavour.

The facility of the "Online submission of manuscript" is very useful and has helped the editorial team in getting good quality articles from far and wide. We encourage the use of this facility by future authors to further raise the standards of the journal.

The blessings of elders are precious and always solicited. I sincerely thank my seniors Dr. Ishwar Singh, Dr. R.C. Nagpal, Dr. C. S. Dhull, Dr. A. K. Khurana, Dr. S.V. Singh, Dr. Sunandan Sood, Dr. J. P. Chugh for their guidance and constant motivation. My heartfelt thanks to the President Dr. Ajay Sharma, Vice-President Dr. Narinder Taneja, young and energetic Secretary Dr. Inder Mohan Rustagi, Treasurer Dr. Rajan Gupta and Joint Secretary Dr. Neeraj Sanduja.

Thanks are also due to the past editors Dr. A. K. Khurana, Dr. Ashok Garg and Dr. Urmil Chawla for their ever available help. RIO family has always been a source of strength and I sincerely thank one and all for the same.

The journal is ours and we should all strive to make it a high impact journal for all the specialities in ophthalmology. This is the vision of Haryana Journal of Ophthalmology. I would eagerly look forward to your feedback regarding the contents and their quality. Any suggestions to improve forthcoming issues will always be solicited.

Beyond the horizons HJO would live.

Happy reading !!



Dr. Manisha Nada

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Rashtriya Arogya Nidhi

Introduction

The Scheme provides for financial assistance to patients, living below poverty line who are suffering from major life threatening diseases as listed in the annexure to this guidelines, to receive medical treatment at any of the super specialty Govt. hospitals / institutes or other Govt. hospitals. The financial assistance to such patients is released in the form of 'one time grant' to the Medical Superintendent/Director of the hospital in which the treatment is being received.

Setting up of Revolving Fund

In a bid to speed up the assistance to the needy patients, the Scheme has been modified and Revolving Funds have been set up at the following Hospitals/Institutes and funds upto Rs. 50 lakh (upto Rs. 90 lakh in respect of AIIMS) will be placed at the disposal of the Medical Superintendent/Director of the Hospital/Institute concerned:

- I. AIIMS, New Delhi
- II. Dr. RML Hospital, New Delhi
- III. Safdarjung Hospital, New Delhi
- IV. Lady Hardinge Medical College and Smt. SK Hospital, New Delhi
- V. PGI, Chandigarh
- VI. JIPMER, Pudducherry
- VII. NIMHANS, Bangalore
- VIII. SGPGIMS, Lucknow
- IX. CNCI, Kolkata
- X. KGMC, Lucknow
- XI. NEIGRIHMS, Shillong
- XII. RIMS, Imphal.
- XIII. SKIMS, Srinagar

Financial powers have also been delegated to the Medical Superintendents/Directors of hospitals/institutes to sanction financial assistance up to Rs. 2,00,000/- in each eligible case reporting for treatment in their respective Hospital/Institute and upto Rs. 5,00,000/-in emergency cases.

Setting up of State Illness Assistance Fund

The Grant-in-aid to States/UTs would be to the extent of 50% of the contributions made by the State Governments/UTs to the State Fund/Society subject to a maximum of Rs. 5 crore to States with larger number and percentage of population below poverty line viz. Andhra Pradesh, Bihar, Madhya Pradesh, Karnataka, Maharashtra, Orissa, Rajasthan, Tamil nadu, Uttar Pradesh and West Bengal and Rs. 2 crore to other States/UTs.

Eligibility for Assistance under Rashtriya Arogya Nidhi (RAN)

- (i) Only for persons below the poverty line suffering from specified life threatening disease.
- (ii) Assistance admissible for treatment in Government Hospital only.
- (iii) Central Government/State Government/PSU employees not eligible.
- (iv) Re-imburement of Medical Expenditure already incurred by the patient shall not be permissible.
- (v) Diseases of common nature and disease for which treatment is available free of cost under other health programmes/schemes are not eligible for grant.
- (vi) Patient taking treatment in his/her State should preferentially avail assistance from State Illness Fund (where such fund has been set up) provided medical estimate does not exceed Rs. 1.50 lakh.
- (vii) Cases of estimates above Rs.1.50 lakh to be referred by States for assistance from Rashtriya Arogya Nidhi (Central Fund) of the Ministry of Health & Family Welfare.

Annexure- I

Illustrative list of categories of treatment to be Provided Grant from the fund is as follows
(This list is reviewed by the Technical Committee from time to time)

- | | |
|--|------------------|
| 1. Cardiology & Cardiac Surgery | 2. Cancer |
| 3. Urology /Nephrology/(Gastroenterology/GI Surgery) | 4. Orthopedics |
| 5. Neurosurgery — Neurology | 6. Endocrinology |
| 7. Mental Illness | 8. Gynecology |
| 9. Miscellaneous : | |

Any life saving procedure any other major illness/treatment intervention considered appropriate for financial assistance by Medical Superintendent/Committee of Doctors could be considered for grant.

Annexure-II

How to Apply for availing of Financial Assistance under RAN:

The following information /documents are required to be sent to this Ministry in original to process request for financial assistance under RAN :-

1. An application in the enclosed format with medical report on the Page no. 2 of the attached proforma duly signed /stamped by the treating Doctor/ Head of Department and Countersigned by Medical Superintendent in original from the Government Hospital where you receive the treatment and Page 1 of the proforma should be filled in respect of all columns.
2. Monthly Income Certificate (in original) of the patient/parents/other major earning members of the family duly certified by the Block/Mandal Development Officer/ Tehsildar/ S.D.M/ Administrator/ Special Officer of Municipal Boards/District Officer stating that the beneficiary belongs to a family living below poverty line in the area of their jurisdiction and including the source of income.
3. A copy of the entire ration card along with its cover page, covering details of all the family members, issued by the Food and Supply Department of the State Government duly attested by a Gazetted Officer with seal bearing the name and designation of the Officer and Department where working.
4. It may be noted that re-imburement of medical expenditure already incurred by the patient for treatment /operation is not admissible under Rashtriya Arogya Nidhi.
5. Cases for treatment in private hospital are not entertained. 6. All the columns of the application form may be filled properly. 7. The request for financial assistance will be considered immediately on receipt of above said information/papers in original.

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Eye care system - The future scenario

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Abstract

Electronic health record (EHR) has become almost mandatory all over the world. Its advantages include readily availability of patient's data base, clearly organized standardized examination template, telemedicine and facilitation of research activities. Further, the EHR has the potential to empower the patient to become more involved and become engaged in their own care. Despite the clear advantages there are some disadvantages of EHR as well, namely significant cost and need of trained man power. Further many healthcare providers feel that use of EHR have added hours to the workday and distracted from the doctor-patient interaction during follow up visits.

Keywords : *Electronic health record, smart phone, retinal prosthetics.*

Introduction

The eye care system is constantly evolving. In future health care system the ophthalmology practice will be radically different. So, it is vital that eye care providers should anticipate, contemplate and plan for the change to keep pace with the fast evolving health care system.

Potential areas of evolution in eye care system

System to improve the initial diagnostic of eye care providers will become a new area of focus for the individuals and organizations involved in eye care services. Improvement in eye care with reduction in cost will be a major challenge in the competitive future. Expanding the role of optometrists and technicians and even persons with skill in eye care delivery system is likely to become the important component of the redesigned eye care system all over the world in future. Though it is the need of the day and will add to quality practice; it may come as a menace for ophthalmologists because of malpractice by the uncontrolled personnel. Role of non human systems in achieving the highest levels of accuracy and reliability are going to be the game changers in the eye care delivery, as evidenced by work on automated analyzers of retinopathy of prematurity (ROP).

Electronic Health Record

Electronic health record (EHR) has become almost mandatory all over the world. Its advantages include

readily available of patient's data base, clearly organized standardized examination template, telemedicine and facilitation of research activities. Further, the EHR has the potential to empower the patient to become more involved and become engaged in their own care. Despite the clear advantages there are some disadvantages of EHR as well, namely significant cost and need of trained man power. Further many healthcare providers feel that use of EHR have added hours to the workday and distracted from the doctor-patient interaction during follow up visits.

Future Trends in Ophthalmology

1. Smart phones in ophthalmology A smart phone is a multifunctional electronic device – a mobile phone with advanced computing capability and connectivity. In last few years, clinicians, including ophthalmologists have started adopting smart phone technology with some innovative modification in their routine clinical practice.

Operating system platforms are:

- Android operating system by Google
- iOS by apple
- Blackberry by RIM
- Symbian
- Window mobile and windows phone

Some useful applications for ophthalmic practices are

- The EHB
- Eye Route ophthalmic image management system
- Pubmed on tap
- Dragon dictation
- Flash card
- Skyscape medical resources
- IKONION
- Personalized physician apps

Uses of smart phones in ophthalmology can be classified as follows :

- Patient assessment tools
- Smartphone ophthalmic imaging
- Patient education tools
- Education and reference tools for ophthalmologists
- Smartphone based calculators in ophthalmology
- Office tools for patient record and administration
- Tools for the vision researchers

2. Predictive Analytics Recently one of the world's leading cancer centres “hired” Watson, IBM's powerful supercomputer, to help diagnose cancer faster, more affordably and more accurately. In the near future, similar tools may help in diagnosing patients with various eye-related ailments. “Big Data” and predictive analytics may also help identify patients most at risk for not taking their medication properly—a problem hindering care of patients . Once identified, however, ophthalmologists and other healthcare professionals will be able to take targeted action to help these at-risk individuals better adhere to their drug regiments.

3. Pharmaceutical Advances Quite a good number of eye-related pharmaceutical clinical trials are currently under review. Many of these treatments may ultimately prove ineffective but if just a small percentage is successful they could be “game changers.” Pharmaceutical solutions for presbyopia, dry-eye and myopia are real possibilities.

4. Robotics Femtosecond laser assisted cataract surgery (FLACS) is already here. The technology will only become better and more affordable in the future. Robotics may soon be used in vitreo-retinal surgery and various other procedures. Startling advances by entrepreneurial ophthalmologists using open-source methodologies and off-the-shelf technology to create sophisticated, low-cost surgical robots such as Raven may even point to an affordable robotic future.

5. Longer term, advances in microsurgical devices point toward a bolder-and far less invasive-future for eye surgery.

6. Gene Therapy The cost of sequencing the human genome is plummeting. As it does, society will come to a better understanding of the roles various genes play in the development of diseases such as diabetes and retinal degeneration. This new understanding may lead to earlier and better treatment of eye-related ailments like diabetic retinopathy and retinitis pigmentosa.

7. Retinal Prosthetics The Food and Drug Administration (FDA) has approved the use of Argus II a bionic eye; and in September, European regulators approved the use of the Atlas IMS-the first fully implantable, wirelessly controlled retinal prosthetic. At the present time both devices are very costly and allow patients with retinitis pigmentosa to see in black-and-white. In the near future, as ever-more electrodes are packed into the device, the technology may allow the users-including those suffering from age-related macular degeneration-to see more clearly and in colour at an affordable price.

8. Biosynthetic Cornea The first successful transplant of a biosynthetic cornea occurred in 2010. Since that time, breakthroughs in biotechnology, material science and 3D printing have accelerated the field and, in the not-too-distant future, biosynthetic corneas could help restore sight to the vast number of people who are currently waiting for a donated human cornea for transplantation.

9. Nanotechnology Researchers have recently created “fuzzy fiber” nanotubes. This could be a significant breakthrough for the treatment of glaucoma because the “fuzzy fibres” are biocompatible and can help

prevent the build-up of fibroblasts. Other breakthroughs in nanotechnology include using nanoparticles for gene therapy-such as the one for the treatment of macular degeneration-and are quite exciting.

10. Stem Cell Therapy Advances in stem cells therapy for cornea and ocular surface disorders as well as retinal disorders such as retinitis pigmentosa and Stargardt's macular dystrophy are going to be real breakthrough for non treatable disorders.

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Reliability of measurement of intraocular pressure with i-care rebound tonometer

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Abstract

Objective: To compare rebound I-care tonometer with Goldman applanation tonometer (GAT) for correlation and agreement and study the influence of pachymetry (CCT) on the intraocular pressure (IOP) measurements using each of the instruments. *Design:* Prospective non randomized observational case series. *Participants:* Two hundred and three eyes of 102 patients (> 16 years of age) attending a general ophthalmology clinic at a tertiary eye care centre. Eyes with IOP < 10 mmHg and > 23 mmHg were excluded and 192 eyes were finally analyzed. *Methods:* A single observer measured the IOP (using the GAT and I-care tonometers) and the pachymetry. Correlation coefficient of Pearson was calculated for the two tonometers. The correlation of I-care and GAT readings to CCT was also studied by linear regression model (r^2). Bland Altman analysis was done to look for any bias and limits of agreement between the two tonometers. *Results:* Pearson correlation between two methods showed an $r = 0.78$ (95% confidence interval of 0.71-0.83; p -value < 0.0001). The Bland Altman analysis showed a bias of -0.21 with 95% confidence interval of -0.60 to 0.17 (p -value 0.2783) with 95% limits of agreement ranging from -5.51 to 5.08 mmHg. The association between CCT and IOP measurements with I-care ($r^2 = 0.14$) and GAT ($r^2 = 0.05$) were clinically insignificant. *Conclusion:* The correlation between I-care tonometer with Goldman applanation tonometer is good, but the limits of agreement are wide. Hence it is evident that I-care tonometer cannot replace the Goldman applanation tonometer.

Keywords: Intraocular pressure, applanation tonometer, pachymetry, rebound tonometer.

Introduction and literature review

It is well known that the major risk factors in the progression of glaucoma include increased intraocular pressure (IOP) levels and increased variation in IOP.¹ Although the role of IOP in glaucoma is not fully understood, there is sufficient evidence to suggest that lowering it may halt or delay the progression of the disease.²

During the search for the ideal device for measurement of IOP various new instruments were developed. However the ideal tonometer that must make accurate and repeatable measurements of IOP without harming the eye but at the same time be patient and observer friendly is still illusive.

Goldmann applanation tonometry (GAT) is internationally accepted as the gold standard for IOP measurements.³ Introduced in 1957, GAT is the most commonly used method by ophthalmologists and glaucoma specialists till date. This is because it has proved to be accurate, precise and easy to use with a low intra- and inter-observer variability.⁴ However, the accuracy of GAT measurements is dependent on many factors including the central corneal thickness

(CCT), curvature and structure of the cornea, and the axial length.⁵ CCT has been shown to have a substantial effect on IOP readings obtained by GAT. A standard CCT measurement of 520 micrometers was originally considered in the calibration of the Goldmann tonometer,⁶ thus causing a possible underestimation of IOP in eyes with thin corneas and an overestimation of IOP in eyes with thick corneas.⁷ Apart from these factors, GAT also has the disadvantages of requiring slit lamp, topical anaesthesia, fluorescein staining, significant amount of cooperation from the subject and a certain degree of skill by the observer which limits its use in conditions requiring rapid but reliable assessment of IOP.

Several different methods have been proposed to overcome the disadvantages of GAT. These alternative methods include new electronic applanation tonometers, noncontact tonometers, rebound tonometry, and dynamic contour tonometry. Most of the new electronic applanation tonometers available, such as the Tonopen⁸ also require the administration of a local anaesthetic. Noncontact tonometers⁹ have the advantage of not requiring

corneal anaesthesia; however, the disadvantages are the variability of the readings based on cardiac cycle and the cost of the equipment. On the other hand the Rebound tonometer^{10, 11} has been reported for its simplicity in usage, becoming cost effective and not requiring the use of a local anaesthetic agent.

Induction-based impact tonometry, first proposed in 2000 by Kontiola,¹² gave rise to an interesting modification of rebound tonometry (RT). The I-Care tonometer is the first commercially available instrument based on this principle. The advantages this device offers in comparison to other methods are that the device is small, lightweight and portable; a slit lamp is not required; it is easy to use; IOP is taken with the patient in a comfortable sitting position; an anaesthetic or sedation is not required; and the rapid measurement enables monitoring in noncompliant individuals.

In last few years there have been several studies comparing RT with the gold standard GAT. Most of these studies have found that IOP measurement by RT shows good correlation with GAT^{13, 14} having a high intra & inter-observer correlation¹⁵. On the basis of the statistical analysis some researchers have concluded that RT is a reliable alternative to GAT especially for screening purpose.¹⁶

Whenever a new method of measurement is developed, clinicians need to compare this new method with the established one to determine whether these two methods can be used interchangeably or the new method can replace the established one. In a series of articles, Bland and Altman¹⁷⁻¹⁹ advocated the use of a graphical method to plot the difference scores of two measurements against the mean for each subject and argued that if the new method agrees sufficiently well with the old, the old may be replaced. Here the idea of agreement plays a crucial role in comparison studies. There are numerous published clinical and laboratory studies evaluating agreement between two measurement methods using Bland–Altman analysis. The Bland–Altman method calculates the mean difference between two methods of measurement i.e. the 'bias', and 95% limits of agreement as the mean difference (2 Standard Deviations or more precisely 1.96 SD). It is expected that the 95% limits include 95% of differences between the two measurement methods. The plot is commonly called a Bland–Altman plot and the associated method is usually called the

Bland–Altman method. The presentation of the 95% limits of agreement is for visual judgement of how well two methods of measurement agree. The smaller the range between these two limits the agreement is considered to be better. The question of how small is small, depends on the clinical context that is whether a difference between measurement methods as extreme as that described by the 95% limits of agreement would meaningfully affect the interpretation of the results. This question is particularly relevant to the measurement of IOP. The newer tonometers are being compared with the gold standard that is GAT, and are reported to be accurate or in accurate based on their correlation and agreement with GAT. The purpose of our study was to compare the accuracy of IOP measurement by I-care impact tonometry with that of GAT in a subset of Indian population.

Methodology

This prospective observational study included patients visiting the glaucoma clinic of a tertiary eye care centre. Informed consent was obtained from each participant. The research was conducted according to the guidelines of the Tenets of the Declaration of Helsinki. Patient willing to participate with age range 18-70 years and IOP range of 10 – 23 mmHg were included.

All patients underwent a complete ophthalmologic examination, including best-corrected visual acuity evaluation, slit-lamp examination, gonioscopy, and fundus biomicroscopy with a 90-diopter lens.

Eyes with corneal pathology (for example, epithelial lesions, edema, scarring, grafts) as well as blind eyes and eyes with ocular hypotony (IOP <5 mmHg) were excluded from the study. Other exclusion criteria were a refractive error more than 6.0 D myopia, +4.0 D hyperopia, or 2.0 D astigmatism.

The central corneal thickness (CCT) was measured with central ultrasonic pachymetry. The pachymeter probe was placed on the center of the cornea, and the mean of 3 readings was calculated for each eye.

All measurements with GAT & I-care tonometer were taken by single independent observer. IOP was measured first with I care and then with GAT with minimum 15 minutes time interval between readings taken with each tonometer.

The GAT (Haag Streit, Koeniz, Switzerland) was performed on a slit lamp after instillation of 1 drop of a local anesthetic (0.5% Proparacaine) and after

staining the tear film with sterile Fluorescein sodium strips. GAT was calibrated according to the manufacturer's guidelines. The mean of 3 consecutive readings was recorded.

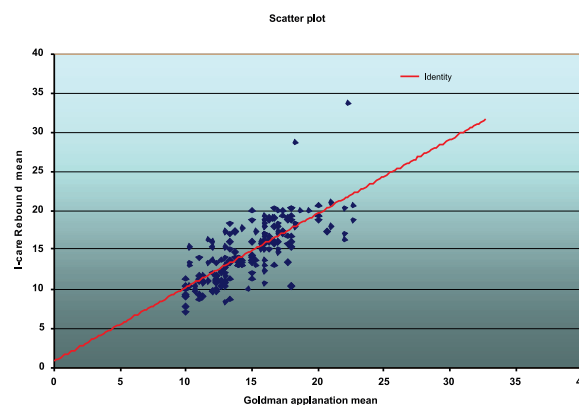
To obtain a measurement with the rebound tonometer, single-use probes were fitted into the apparatus. Subjects were instructed to fixate on a distant target while the probe of the I-care was held at a distance of 4 to 8 mm, and perpendicular to the central cornea. The measurement was initiated by the operator, with the probe being propelled against the central cornea. Individual measurements are displayed digitally in mm Hg. Six rapidly consecutive measurements are obtained in each eye, yielding a mean reading with a SD (standard deviation) on the LCD screen. As per manufacturer instructions, a mean reading displayed with a static P and no error bars (P) indicates a low SD of the 6 measurements. A mean with a flashing P and error bar indicates a less than optimal SD. An inferior error bar (P_) implies that the different measurements have a SD slightly larger than normal (judged acceptable according to the manufacturer); a mean with a middle error bar (P_) indicates a SD clearly greater than normal (a new measurement is recommended); and a mean with a superior error bar (P_) signifies that the SD is too large and a new measurement is required. In our study, consecutive measurements were obtained from each eye until either a mean reading displaying a P with no bar (P) was acquired,

Correlation co-efficient (r) of Pearson correlation between two methods and co-efficient of linear regression model for association with CCT (r^2) was calculated. The agreement between the GAT and I-care tonometry values was assessed by the Bland-Altman method, which included the bias and limits of agreement between two methods. Here the mean difference between measurements (I-care tonometry minus GAT values), the SD, and the 95% confidence interval (CI) of the differences was calculated. Statistical analysis was performed with the Analyze-it statistical software.

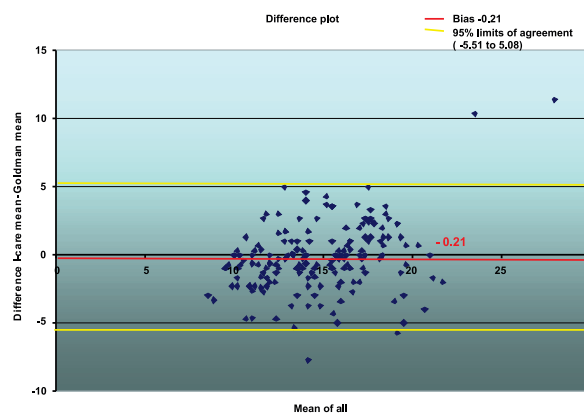
Results

Two hundred and three eyes of 102 patients were examined. Mean age of the patients was 46.4 years (range: 16-82 years), 37 were females and 65 were males. Of these, the eyes with IOP less than 10 and more than 23 on GAT were excluded and 192 eyes

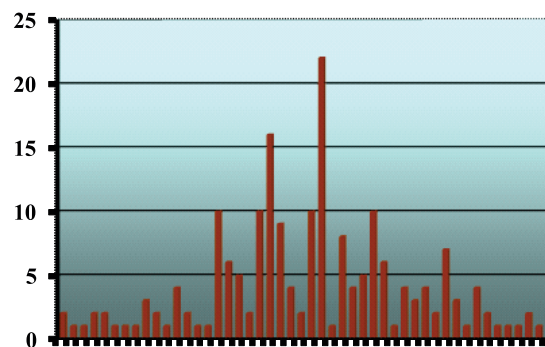
were finally analysed. Pearson correlation between two methods showed an $r = 0.78$ (95% confidence interval of 0.71-0.83; p-value < 0.0001). The Bland Altman analysis showed a bias of -0.21 with 95% confidence interval of -0.60 to 0.17. The standard error was 0.195 and t-statistic was -1.09 (p-value 0.2783). Lower and Upper 95% limits of agreement were ranging from -5.51 (95% CI -6.16 to -4.85) to 5.08 (95% CI 4.42 to 5.74) mmHg. (Graphs 1, 2 and 3)



Graph 1: Correlation between Goldman tonometer and Rebound tonometer

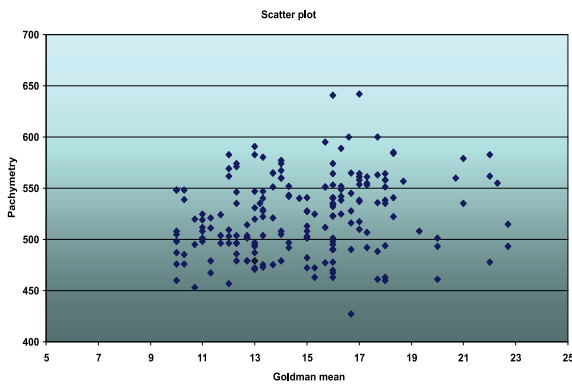


Graph 2: Agreement between Goldman Applanation and Rebound tonometer

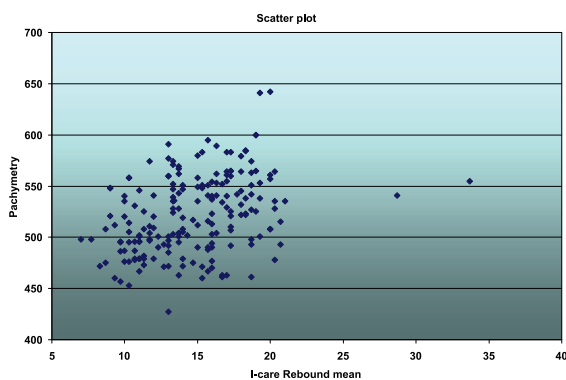


Graph 3: Histogram of differences between two tonometers

The association between CCT and IOP measurements with RT ($r^2 = 0.14$) and GAT ($r^2 = 0.05$) was clinically insignificant. (Graphs 4&5)



Graph 4: Correlation between GAT and CC



Graph 5: Correlation between RT and CCT

The results clearly demonstrate that the correlation between the two tonometers is good with statistically significant p values but agreement is poor. Test-retest variability and inter-observer that is permissible for the tonometer is ± 2 mmHg whereas, the limits of agreement between rebound and Goldman tonometer were found to be much more than that.

Discussion

The aim of this study was to assess the reliability and repeatability of the I-care rebound tonometer by examining its agreement with a Goldman applanation tonometer in normal and healthy subjects.

The first studies conducted with the rebound tonometer I-care were performed in animals by Kontiola. They concluded that the rebound tonometer is a reliable and accurate instrument for non-invasive IOP measurements in rat eyes¹²

True accuracy of the IOP measured by a tonometer can only be assessed by comparison to an invasive manometry. Due to the obvious limitations in human investigation, however, this study quantified the

reliability and repeatability of I-care IOP measurements by comparing them with those taken by the current clinical gold standard, namely, Goldman applanation tonometry.

In our study 113 eyes of 83 patients were studied with IOP range of 10 mmHg to 20 mmHg as recorded by GAT. The coefficient of correlation (r) was 0.7175 ($p < 0.0001$) and the 95% confidence interval for r was 0.6142 to 0.7967. This finding is comparable with the results obtained by Kontiola ($r=0.82$)¹² and Poostchi et al ($r=0.726$).²⁰ Rehnman and Martin²¹ found an overestimation of the I-care of 1.5 ± 3 mmHg (mean \pm S.D) when compared with GAT while Martinez de la casa et al²² found I-care to overestimate the IOP in the range of 1.4 ± 2.7 mmHg. In accordance with previous studies, our study confirms the tendency for an overestimation of IOP by I-care as compared to GAT. The average difference found is 0.34 mmHg with the standard deviation being 0.3 -3.3. The intraclass correlation coefficients for GAT & I-care were 0.9473 and 0.9416 respectively showing high reliability of the measurements by both instruments comparable with the values obtained by Kyoung Nam Kim et al.¹³

ANOVA repeated measurements for GAT was 0.76, whereas with I-care was 0.904 showing better repeatability of I care; intra-observer coefficients of correlation between 0.73 and 0.82 Martinez-de-la-Casa et al.⁴

We accept our limitations that we studied the comparison in normal IOPs. The population with increased IOP was not included and also the influence of corneal biomechanical properties on the IOP measurements was not studied. Kim et al²³ have studied effect of axial length, CCT and refractive error on I care PRO tonometer and reported good agreement but the limits of agreement are found to be wider than our study that is -4.5 to 8.4.

The agreement between two methods of measurement can be determined by various methods like Bland Altman analysis, calculating the coefficient of correlation R , regression analysis. However, r measures the strength of a relation between two variables, not the true agreement between them. The Bland Altman analysis, on the other hand, calculates mean difference between two methods of measurement (the bias) and 95% confidence intervals, also known as the limits of agreement. The smaller the range between these two limits the better the agreement. In clinical studies, two methods of

measurement showing good correlation may have wider limits of agreement which in relation to the measurement of IOP may not be acceptable clinically. As each of the methods has its own flaws, hence it is crucial to analyse the data by more than one method and reach a logical conclusion.

Conclusion

This study demonstrates a good correlation between the new I-care tonometer and the gold standard GAT in normal IOP range with the I care showing a higher reading than GAT however limits of agreement are much wider than the inter observer variability, hence both the instruments cannot be used interchangeably.

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Surgical results in congenital ptosis with Marcus-Gunn phenomenon

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Abstract

Various surgical techniques have been proposed for the correction of jaw-winking ptosis but their comparative success rates are not available. This study assesses the success of various surgical options in correcting the ptosis as well as the jaw-winking phenomenon.

Purpose: To report the results of various surgical modalities described for correction of Marcus-Gunn ptosis. **Methods:** Surgical results in 32 patients with Marcus-Gunn jaw-winking ptosis were reviewed. Postoperatively, a difference of 1mm or less between palpebral fissure heights of two eyes was considered a success. Various surgeries done were levator excision with frontalis sling, levator resection, transposition and Fasanella Servat. **Statistical tools:** 2-proportions test (Z test) **Results:** Maximum success rate was seen with levator resection (57.15%) followed by levator excision and frontalis sling (55.5%). Overall undercorrection rate was 53.12%. Marcus-Gunn phenomenon was abolished or a flicker remained in 90.65% of cases. **Conclusion:** Management of Marcus-Gunn ptosis remains a challenge. Levator excision and levator resection are able to correct the ptosis component equally well yet the undercorrection rate is high. All the procedures are able to control the jaw-winking phenomenon to a good extent.

Keywords: Marcus-Gunn ptosis, jaw winking ptosis.

Introduction

Blepharoptosis associated with Marcus-Gunn jaw-winking phenomenon holds a unique place amongst all types of ptosis because of the peculiarity of lid movements, which may remain, even after surgery (Figure 1). It is a significant cosmetic and functional defect.

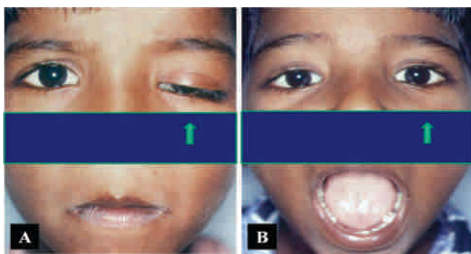


Fig 1: Marcus Gunn jaw winking ptosis. A: ptosis of left eye when mouth is closed. B: eyelid elevates on opening mouth.

Several surgical modalities have been reported for the correction of jaw-winking phenomenon, but few studies have reported the outcome of these operations with respect to the correction of ptosis and their comparative success rates are not available.¹ This study was done with an objective of assessing the success of various surgical options in correcting the ptosis as well as the jaw-winking phenomenon.

Patients and Methods

The records of all patients who presented to the out patient department of our hospital over a ten-year period from 2007 till 2017 with ptosis associated with Marcus-Gunn phenomenon were reviewed retrospectively. Each patient underwent complete preoperative ophthalmological checkup including the amount of ptosis, lid excursion and status of Bells phenomenon. The grading of ptosis and levator action had been done as proposed by Beard.² Strabismus if any, had been dealt with before ptosis surgery.

The ptosis and the jaw-winking phenomenon had been treated individually with levator excision with frontalis sling, levator resection, levator transposition or Fasanella Servat surgeries. The surgical method adopted was based on severity of ptosis as well as Marcus-Gunn phenomenon and also upon the patient's individual decision after detailed discussion. Levator resection or Fasanella Servat was done in patients in whom the Marcus-Gunn phenomenon was not bothersome. In other patients, levator excision or transposition was done to deal with jaw-winking phenomenon also. Levator resection was done by skin approach in all the patients. Levator excision involved excising 18-20

mm of aponeurosis-muscle complex. Frontalis sling was done by fox's pentagon method using silicone rod (Aurolab, Madurai) as sling material. Levator transposition was done by attaching the part of levator distal to Whitnall's ligament to the Frontalis muscle via a sub-brow tunnel.

Follow up data included the measurements of residual ptosis and residual jaw winking, if any. Residual ptosis and patient's satisfaction level had been taken into consideration while deciding about repeat surgery.

For the study purpose a difference of 1mm or less in palpebral heights between the two eyes was considered a success. The statistical analysis, wherever the sample size permitted, was done by 2-proportions test. It is a test which equates the denominator of the proportions and then predicts how the difference will be if the sample sizes were equal.

Results

A total of 32 patients were included in the study. This comprised 18 males and 14 females. All cases had unilateral ptosis (OD=18 eyes, OS=14 eyes). Mean age at presentation was 14.8 years (range = 2.5 years-31 years). Eighteen of 32 (56.25%) patients had severe ptosis (Table 1). Associated findings were double elevator palsy in 6 patients (18.75%), hypotropia with superior rectus underaction in 4 cases

	Number Of Cases (n=32)	Percentage (%)
Amount Of Ptosis		
Mild	4	12.5
Moderate	10	31.25
Severe	18	56.25
Levator Action		
Excellent	0	0
Good	9	28.1
Fair	8	25
Poor	15	46.8

Table 1: Severity Of Ptosis And Levator Action

(12.5%) and amblyopia in 6 (18.75%) cases.

Results of individual surgical method have been analyzed in Figures 2-6. The overall success seen was 46.85%. The difference in overall success rates of levator resection and levator excision with frontalis sling was not statistically significant (2-proportions test, Z= 0.07, P=0.47). Levator excision with frontalis sling was done unilaterally in all the patients. It was done in patients with significant Marcus-Gunn phenomenon associated with ptosis. Of these, 94.4% were done in two sittings with a mean gap of 2.65 months between the two surgeries.

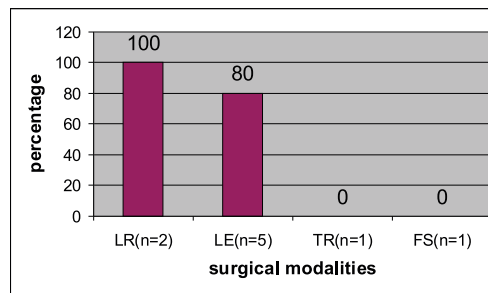


Fig 2: Surgical success rates according to severity of ptosis

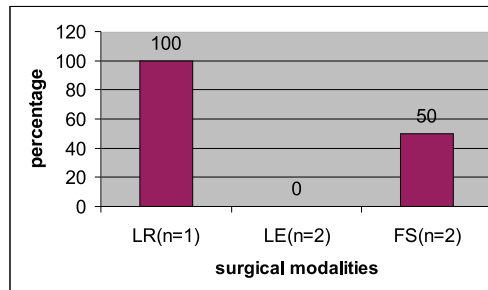


Fig. 3: Success rates of each surgery in mild ptosis (LR=levator resection, LE= levator excision with frontalis sling, FS= Fasanella Servat)

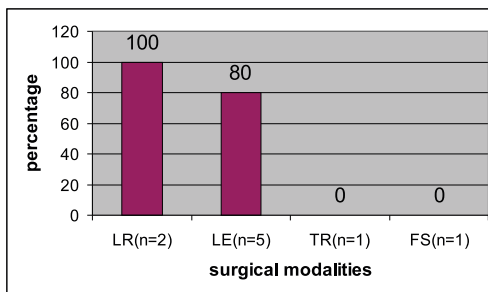


Fig. 4: Success rates of each surgery in moderate ptosis (LR=levator resection, LE= levator excision with frontalis sling, TR= levator transposition, FS= Fasanella Servat)

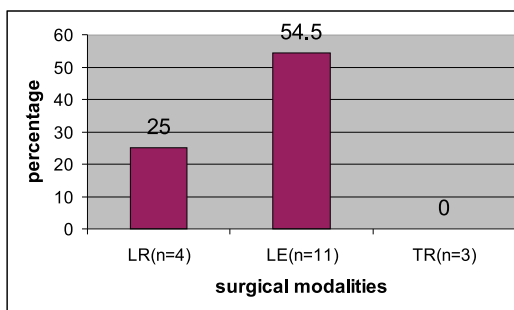


Fig. 5: Success rates of each surgery in severe ptosis (LR=levator resection, LE= levator excision with frontalis sling, TR= levator transposition)

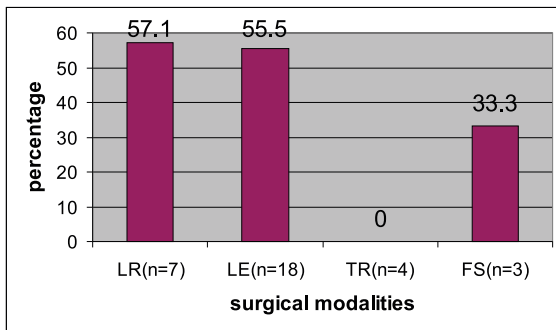


Fig. 6: Comparative overall success of each surgery (LR=levator resection, LE=levator excision with frontalis sling, TR= levator transposition, FS=Fasanella Servat)

Resurgery was done in 8 out of 32 cases (25%) after a mean gap of 5.2 months. Overall the Marcus-Gunn phenomenon was totally abolished or brought down to a mild acceptable flicker in 90.65% of cases.

Discussion

Though more than 100 years have elapsed since Marcus Gunn first described the jaw winking phenomenon, consensus has not evolved on various aspects like etiology, optimal management and timing of surgery.

It is believed that jaw-winking ptosis is rare after 25 years of age as it reduces with age.³ Doucet et al showed that decrease in magnitude is because of masking by the patients.⁴ The maximum age at presentation seen in our study was 31 years with average age being 14.8 years.

Marcus-Gunn jaw-winking is associated with variable amount of ptosis.⁵ Doucet et al believe that amount of ptosis is directly proportional to the severity of jaw-winking.⁴ Wong also noticed more number of severe ptosis cases.⁶ Most of the cases in our study had severe ptosis (56.25%) with poor levator action (46.8%) though the jaw-winking was not bothersome in 11 of 32 (34.37%) cases.

It is universally accepted that the surgical management of jaw-winking ptosis is tailored according to the severity of jaw-winking and amount of ptosis. Levator resection is done when ptosis is more bothersome than the jaw-winking.⁴ Levator resection is not advisable for significant jaw-winking because then the lid excursion begins at a higher level thereby increasing the superior scleral show.⁴ In our study levator resection gave excellent results in mild to moderate ptosis with insignificant jaw-winking

(100%). Its success rate fell to 25% in severe ptosis group. Post-operatively unacceptable jaw winking was seen in 1 out of the 7 (14.28%) patients who underwent levator resection. The overall undercorrection rate for levator resection was 42.9%. In comparison, undercorrection following levator resection was seen in 37.5% of cases by Doucet et al.⁴ Higher percentage of undercorrection seen in our series could be attributed to the stringent criteria we adopted for defining success as well as due to high number of patients having severe ptosis. Apart from that undercorrection following levator resection is common because of preoperative underestimation due to control of eyelid position by the patient.⁶ Jaw winking ptosis requires a larger amount of levator resection as compared to that in simple congenital ptosis.²

Unilateral or bilateral levator excision with bilateral frontalis sling is the recommended procedure in ptosis associated with jaw-winking because it is highly effective and gives more functionally and cosmetically acceptable results.^{1,4,5,6} During the preoperative discussion, none of the patients or their parents preferred to have bilateral sling surgery so we had to resort to unilateral excision and sling on the involved side. We used silicone rod as the sling material in all of our patients as it is non-reactive, surgery is easier and revision also is easier. In our series it was most successful in correcting ptosis in moderate ptosis group (80%). In severe ptosis group it was successful in only 54.5% of the cases yet its results were better than levator resection (25%), however this difference was not statistically significant (2-proportions test, $Z= 1.01$, $P= 0.16$). Residual unacceptable jaw-winking was seen in 5.55% of the patients after excision and sling. Undercorrection after levator excision as reported in other series ranges from 20.8% to 30%.^{1,4} Effect of excision is incomplete in some patients because of reformation of fibrous connections and incomplete division of all connections of levator muscle.¹ Another factor is that in unilateral cases with frontalis suspension, habitual use of frontalis is negligible as the patient manages with the other eye thereby leading to underaction of the sling and undercorrection.

Fasanella Servat was successful in 1 of the 3 (33.3%) cases in which it was done. Putterman has reported 100% success with this procedure. It relieves ptosis without strengthening the abnormally innervated levator muscle therefore it brings down the jaw-

winking.³ Fasanella Servat procedure is recommended for smaller amount of ptosis.⁴

Levator transposition was not able to correct ptosis to within 1mm level in any patient hence it was performed in a limited number of patients only. It was able to bring down the jaw-winking to unnoticeable level in all the patients in whom it was done. Advantages associated with levator transposition and its use as a sling are good strength, viability of the sling as it has got its own blood supply from palpebral arcades and good maintenance of contour.⁵ Out of the 8 reoperated cases, surgical success was seen in 6 (75%) patients. The overall undercorrection rate was 59.3%, which underlines the problems associated with the surgical correction of ptosis component even though all the methods were able to control the jaw-winking to a good extent. Statistical analysis could only be performed overall and not in each group as the sample size was inadequate and that is a limitation noted in this study.

Conclusion

To summarize, surgical management of the ptosis component in Marcus-Gunn ptosis remains unsatisfactory. Severe ptosis is more commonly seen and presentation is often unilateral. Levator resection gives good results in mild and moderate ptosis with insignificant Marcus-Gunn phenomenon whereas levator excision with sling gives good results in moderate or severe ptosis. Fasanella Servat is reserved for mild ptosis with insignificant jaw-winking only. Levator excision with frontalis sling is the preferred modality for correction of severe ptosis and severe jaw-winking because it is better able to control the jaw-winking and the ptosis. Undercorrection is common and is seen more in severe ptosis cases.

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Fourth Industrial Revolution: Why it is important for Indian Ophthalmology and Ophthalmic Professionals?

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Abstract

The fourth industrial revolution refers to a fusion of technologies which blend the physical, digital and biological worlds. It can mitigate miseries of the teeming masses. However, India faces the unique challenge. It is both the creator of enormous amount of data required for this revolution as well as largest potential market for those innovations in the coming future. This article traces the challenges and draws parallels with the past experiences. The first transformation is expected to hit healthcare sector much sooner than projected earlier. It outlines the call to action required of our thought leaders today.

Keywords: Fourth Industrial Revolution, deep learning, healthcare, machine learning, diabetic retinopathy.

Introduction

Columbus had sailed to find a new route to India. The lure of trading with the Mistress of Spices was so strong that people put their lives at stake in those days. Indian weavers produced the world's most exquisite and prized handloom fabrics. The mysteries and finery of India and China were spun into stories and altogether created a mystical charm of the Orient. However, India missed the First Industrial Revolution. In 1750 AD, India's share of global industrial output was 25 percent which declined to two percent by 1900. This revolution saw the invention of the steam engine and powered looms which made handlooms of India uncompetitive. The British East India Company forcefully colonized India. India started exporting stock cotton and became a consumer of mill cloth from Manchester. India's handloom industry was decimated. The bulk of the nation got marginalized and deindustrialized.¹ Today we are trying to revive the few remaining traditions like the Benares silk saree and Kanjivaram silk using modern methods and designs to create employment and a bid to resell our fineries to the world.

Cut to the modern times, and we find that certain recent advances in medical circles have created a buzz about artificial intelligence (AI) and machine learning. Artificial intelligence refers to the ability of a digital machine or computer to accomplish tasks that traditionally have required human intelligence. Machine learning refers to a computing machine or system's ability to teach or improve itself using

experience, without explicit programming for each improvement using methods of forward chaining of algorithms derived from backward chaining of algorithm deduction from data. Deep learning is a subsection within machine learning focused on using artificial neural networks to address highly abstract problems. Cardiology with its automated electrocardiographic analysis and ophthalmology with wavefront analysis have used limited expert systems with success.

Premise

The increased computing power has allowed a more complex algorithm development methodology with driverless cars becoming a distinct business opportunity. There are other vistas that have been opened by these developments. One such area is interpretation of complex images in ophthalmology.² In 2009, Retinopathy Online Challenge used competition fundus photographic sets from 17,877 patient visits of 17,877 people with diabetes who had not previously been diagnosed with DR consisting of two fundus images from each eye. These were compared using a single rater to that of a large computer-aided early DR detection project EyeCheck. The fundus photograph set of every visit was analyzed by single retinal expert. 792 out of these 17,877 sets were classified as containing more than minimal DR which was the threshold for patient referral. Two algorithmic lesion detectors were used on the datasets separately and compared by standard statistical measures (area under the ROC curve as the main performance indicator). The two computerized

lesion detectors demonstrated high agreement. At 90% sensitivity, the specificity of the EyeCheck algorithm was 47.7%. The specificity of the ROC-2009 winner algorithm was 43.6%. On comparing this with interobserver variability of the employed experts it was concluded that DR detection algorithms demonstrated maturity and the detection performance was not too different from the prevailing best clinical practices having reached the human intrareader variability limit. Similar trials in the U.S., U.K., and the Netherlands showed promising results. It is universally agreed that a combination of blood vessel parameters, microaneurysm detection, exudates, texture and distance between the exudates and fovea are among the most important features to detect the different stages of diabetic retinopathy.³ In 2008 Nayak et al used area of the exudates, blood vessels and texture parameters analyzed through neural network to classify the fundus image into normal, nonproliferative DR (NPDR) and proliferative DR (PDR).⁴ The detection accuracy of 93% with sensitivity of 90% and specificity of 100% were reported. Support vector machine (SVM) classifier classified fundus images into normal, mild, moderate, severe and prolific DR classes with detection accuracy of 82% and sensitivity of 82% and specificity of 88%. Lee et al described a software to grade the severity of hemorrhages and microaneurysms, hard exudates and cotton-wool spots of DR to classify NPDR. They were able to identify 85.3%, 87.5%, and 93.1% hemorrhages and microaneurysms, hard exudates, and cotton wool spots.⁵

Discussion

Development of complex algorithms is laborious and requires skilled resources. However, once developed, these algorithms can be used in simple devices with standard hardware like face recognition was used on mobiles. These algorithms can bring down the costs of the screening programs immensely. Though in its nascent stages the potential of this deep learning for use in diabetic retinopathy (DR) screening programs has been recognized and efforts over the last twenty five years have now reached a level of refinement that such attempts are now in the realms of clinical practice over the next few years. The latest results from Google's recent attempt are very encouraging. However, they must be evaluated with a sense of urgency by nations like India which have lot to gain

being a software developer and ophthalmology hub as well as a potential market for diabetes care products having already earned the dubious eponym of Diabetic Capital of the World. According to the International Diabetes Federation calculation in 2015 roughly 415 million adults worldwide had diabetes mellitus which was estimated become more than 640 million individuals expected by 2040.⁶ As 35 to 50 percent may be afflicted with retinopathy and of those about 10 percent are at risk of vision loss, more than 20 m people are currently at higher risk of significant visual impairment due to diabetic retinopathy. This figure at current exposure rates will become 32 million by 2040.

The fourth industrial revolution is a conceptual upgrade on the third industrial revolution. It encompasses a fusion of technologies which blend the physical, digital and biological worlds. The potential for mitigating miseries for the masses is huge. But then this may require sagacious planning and strict implementation to ensure that the benefits reach the needy. Herein lies the threat for the developing world. The previous colonization drives were motivated by profits and managed by countries. The profit motive of the East India Company became subservient to suzerainty of the Crown in 1857. The current profit motive involves markets and technological transformation. Technology drives the big transnational tech companies like Amazon, Google, Facebook, Uber or AirBnB. These companies are the colonizers of today. They have been using technology and new business models to reengineer industry after industry across the world without even setting a foot in the nation. If not properly managed, they have left behind a swathe of destruction like the empty factories of the US when all production moved to the Chinese mainland. These companies are bringing similar destruction to smaller businesses like the hotels and your neighbourhood taxi stand. The new business models have delighted consumers, generated great wealth for their shareholders and employees. They have lowered costs, smoothed distribution channels and helped greater penetration of services at more affordable costs. That they have been useful to the society is well established and cannot be denied. In doing so they have gained access to intimate details of our lives at a level of magnitude never seen before and they have resulted in loss of middle and lower income jobs. The first industrial revolution created wealth for Britain and some parts of Europe. It impoverished

hundreds of millions of people in China and India. The British East India Company was a global monopoly which managed to extract and redistribute wealth. The fourth industrial revolution may also portend a new era of exploitation, not by countries but by companies. The Facebook experience has a lot of lessons in it especially for the advocates of laissez faire and mindless disruptive innovation at the cost of the liberty and privacy of the citizens. Protectionism and deprecation of technology-driven innovation is not the answer. The productivity revolution of new technology is required for the developing world for a better lifestyle for its citizens. We require global reach, foreign capital, technology and skills. However, a thoughtful health technology policy and regulations that encourage innovation are a must. But we need to put into place controls that safeguard the interests of our citizens. Currently, the screening for DR is a labour intensive exercise. It requires resources and trained manpower. The AI algorithms can make it cheap and reproducible. The same may apply to other specialties soon. Application of deep learning principles to create an algorithm for automated detection of DR and diabetic macular edema (DME) can cut back on costs and improve efficiency. The spinoffs from this drastic change in the management of patients must be converted into savings by early intervention on treatment costs rather than profits for transnational corporations and their shareholders. It is also imperative to ensure that India does not become 'a digital colony' of US or Chinese firms.

Our experience in technology use in ophthalmology has shown that we desperately need a strategy to moderate the behaviour of foreign companies so that the relationship between provider and user is not exploitative but genuinely symbiotic. We need a policy for this at the national level, more so, for platform companies like Uber and Amazon, machine providers like Zeiss and AMO, and software giants like Microsoft and Google that are near monopolies. No individual or company has the might to stand up against such behemoths. The actions of such behemoths need to be monitored and sometimes moderated to safeguard the interest of India and Indian citizens.

Indian standards for healthcare data interexchange, healthcare privacy and a unified national data strategy are necessary to ensure that the big data generated in our country is used to empower our people and provide them services rather than to exploit them for

commercial gains. A data and privacy protection law is an initial step which must not brook any delay. Srikrishna Committee is already drafting a data protection law.⁷ GDPR already has such a law. Europe has taken a lead in ensuring that transnationals do not hinder competition or become cartels working against the needs of its citizens. Such statutes need to strike a balance between regulation and innovation without hindering either. However, being a large market with low cost production capabilities India must emulate the Chinese strategy of trading market access for investments in building indigenous capability in new technologies. An example of this already exists. India successfully used open source software and open source standards to moderate the pricing of Microsoft products in India. Today many of the same Microsoft products are developed in India in addition to the India-specific products that the corporation and other companies then developed. In fact, Microsoft set up a local data centre and research lab in Chennai and Bangalore. The low cost strategy has worked for Microsoft as well resulting in a win-win outcome for both parties. Global companies need Indian markets just like we need their products. It has been seen in the past that the intangible knowledge from healthcare was used to develop a hospital information system using the resources of Indian hospitals. Later the same hospitals got locked out of the products they helped develop and were coerced into buying the licenses for the next versions of the same or similar products. We need to move in to ensure that this is not repeated.

Our own regulation must make our own local ecosystem of companies excel on a global level and be competitive. We need to encourage innovators to become leaders in the technologies of the fourth industrial revolution. While we are leaders in many aspects of healthcare delivery at rather competitive costs we lack in processes and quality control. We have bright patches and dark patches. The aspect of consistency and cutting research is often overlooked by a system that celebrates bureaucratism and archaic rules over scientific temper and innovation. China has been a late entrant but has effectively leveraged its young population and market to get favorable deals from the current market leaders. The tools and technologies of the fourth industrial revolution are dominated by American and Chinese companies. We have had some success but that is also a pyrrhic victory because Indian innovation platform's navratnas like Ola, Flipkart and Paytm are actually

owned by Alibaba, Tencent and Softbank.

We have been consuming technology and tech based products in ophthalmology for a long time now. However, our models like the Aravind Eyecare System and several product manufacturers have won accolades for the efficiency improvement demonstrated by them. We have managed to make intraocular lenses at less than a dollar apiece and the phacoemulsification platforms at a fraction of the cost that it costs in the west.⁸ However, in the near foreseeable future the trends will require greater use of data science systems, wearable technologies, always on sensors and interacting algorithms. Here we are emulating the west. Slowly artificial intelligence is getting built into our machines. We are giving major inputs and large amounts of data for rule induction and forward chaining but unfortunately we may be like the builders' labour who will be forced to leave the site once the building is ready. The irony of the situation is that we will also be buying flats from the same builders. We will be purchasing these same machines for our healthcare delivery. In doing so, we will be paying large sums of money as royalty expenses and profits to people who did not really contribute in the entire chain. This will leave behind an impoverished society not only in terms of money but also in ideas. The purpose of this article is to generate awareness to start a meaningful public discourse on this professional platform on these issues so that we progress with awareness rather than wake up with regret. Our thought leaders are today entrusted with the task of guiding this informed and intelligent dialogue between key stakeholders including but not limited to practitioners, innovators, patients, policymakers, scientists, civil society and business leaders before a real technology strategy is formulated so that these aspects can be taken care of. We have already tasted success by such mission approaches in eradicating polio, atomic energy and our space programme. In November 1954, it was Homi J Bhabha who enunciated a three-stage plan for national development in atomic Energy for Peaceful Purposes. Four years later the Government of India formally adopted the three-stage plan. Today, it is the fifth-largest source of electricity in India after coal, gas, hydroelectricity and wind power. India has 22 nuclear operational reactors in 7 nuclear power plants with a total installed capacity of 6,780 MW and operationally produced a total of 35 TWh of electricity.⁹ In 1962, it was through the efforts of

Vikram Sarabhai that the Indian National Committee for Space Research (INCOSPAR) established. It finally became the Indian Space Research Organization or ISRO with its headquarters in Bangalore. Our success in rockets and missile development is as famous as our own Mangalyaan whose cost per kilometer was less than the cost of an autorickshaw in Delhi at that moment in time and the entire mission cost one tenth of that accomplished by its US counterpart NASA(National Aeronautical Space Association).^{10,11} We have shown that we can achieve extremely good results in healthcare at very low costs through our Pulse Polio immunization program started in 1995 which aimed at 100% coverage . The polio free status was achieved in 2011.¹²

Conclusion

The fourth industrial revolution is the biggest opportunity and the largest threat to a prosperous India. We need our leaders today. Not only the ophthalmologists, rather the healthcare professionals must all become thought leaders because as subject matter experts it is our bounden duty to do this for our beloved country and its people. The need for guided expert regulation and support for computing ethics is the need of the hour. This will create advancements that outlive our mortal lifetimes. We can look towards no one else to do it for us. As developers and as a big market, the opportunities before India are as big as the challenges. We need to ensure that there is a favorable distribution of the benefits of the Fourth Revolution as well as prevent colonization by other agencies. This is what the nation needs us to do in the interest of our future generations.

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Endoscopic Revision Dacryocystorhinostomy

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Abstract

Primary Dacryocystorhinostomy (DCR) is gold standard for the treatment of nasolacrimal duct obstructions. However, failure can occur in 5-10% cases. Both external and endoscopic approach are now considered equally effective but some cases may need revision. Endoscopic approach for repeat surgery has advantages over external approach and aim is to highlight its role in management of failed DCRs.

Keywords: Dacryocystorhinostomy, nasolacrimal duct obstruction, epiphora, endoscopic dacryocystorhinostomy.

Introduction

Both external dacryocystorhinostomy (DCR) and endoscopic DCR are highly successful procedures for primary nasolacrimal duct obstruction (PANDO) with success rate over 90-95%.^{1,2,3} However, persistent epiphora after DCR can be seen in few patients. Causes of failure of DCR includes complete/incomplete cicatricial closure of ostium, canalicular obstructions, improper ostium position, inadequate opening of sac, failure to clear superior bone sufficiently, concomitant nasal pathology, synechiae in nose and extensive post-operative granulation around the ostium. Whenever, revision DCR is planned it is important to identify and manage the cause(s) of failure appropriately.^{3,4} The purpose of the present review is to discuss the concepts, steps and advantages of Endoscopic-revision DCR in addressing the failed sac surgery.

Approach to Endoscopic Revision DCR

Preoperative nasal endoscopy

A thorough evaluation of nasal cavity is done to rule out deviated nasal septum, turbino-septal synechiae, adhesion between middle turbinate, concha bullosa and status/location of the ostium (Figure 1 A-C). Figure 1 C shows an example of enlarged pneumatized middle turbinate (concha bullosa). Figure 2 shows complete cicatricial closure of the ostium.



Fig. 1: Endoscopic nasal anatomy

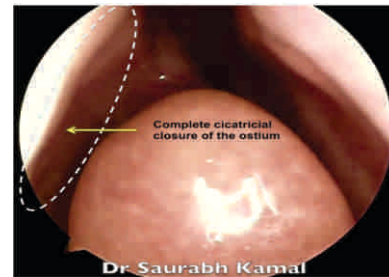


Fig. 2 : Cicatricial closure of ostium

Anesthesia

General anesthesia is preferable because of increase patient comfort and also hypotensive anesthesia reduces bleeding. Total intravenous anesthesia (TIVA) with Propofol and Fentanyl along with Laryngeal mask airway is also suitable for cases requiring short operative time.

Surgical technique

After induction, nasal mucosa is infiltrated with lignocaine mixed with adrenaline (1:80000) at previous ostium site (figure 1 D & E) guided by axilla of middle of turbinate. Nasal packing is then done and kept for 10 minutes to achieve hemostasis (Figure 1 F). After decongestion area of cicatricial closure is assessed to note if any miniature ostium is present or not (Figure 3 A & B). Bowman probe is passed then (Figure 3 C & D). Next nasal mucosal incision is given over cicatrix at ostium site and dissection done with no.15 Bard Parker blade to lift up the cicatrix (Figure 3 E & F, Figure 4 A).

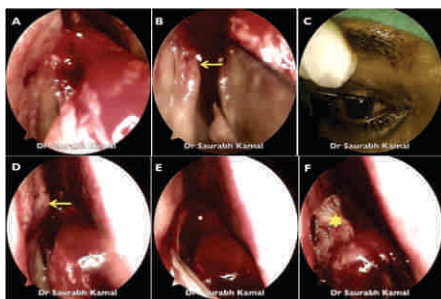


Fig.3: Surgical steps

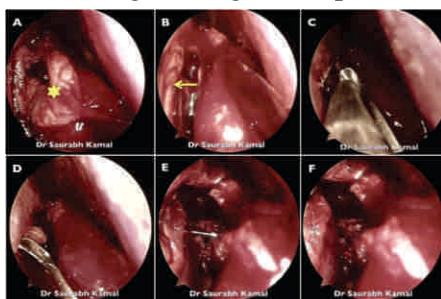


Fig.4: Surgical steps

Usually sac mucosa can be identified at this step and can be confirmed with Bowman's probe passed through one of the canaliculi (Figure 4 B). All cicatrix and adhesion are released. Next step is to assess surrounding bone and whether sac has been exposed completely or not. Osteotomy is enlarged with Hajek-Kofler bone punch (Figure 4 C & D). Once the osteotomy and all cicatrix is released, sometimes a small opening in sac can be identified indicative of previous sac-nasal mucosa adhesion through which probe will be visualized (Figure 4 E). Next is to push the medial wall of the sac with probe (Figure 4 F) for fashioning of anterior and posterior lacrimal sac flaps (Figure 5 A & B). Any intrasac synechia should be examined and released adequately (Figure 5 C-E). Sac flaps are then repositioned with ball probe (Figure 5 F). Mitomycin-C (MMC) 0.02% is then applied (Figure 6 A) and also injected into nasal mucosa around the newly created ostium (this is called circumostial injection of MMC)^{5,6} (Figure 6 B). Next bicanalicular silicone intubation is done (Figure 6 C-E). Figure 6 F shows the sac opened completely in a book like fashion with silicone tube in situ.

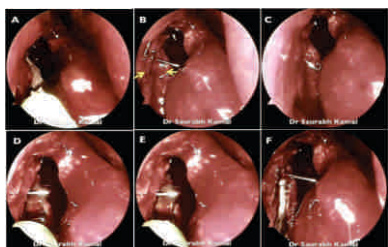


Fig.5: Surgical steps

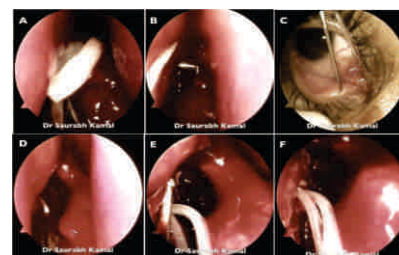


Fig.6: Surgical steps

Postoperative care

1. Topical antibiotic-steroid eye drops are tapered over 4 weeks and nasal decongestants and nasal steroid spray are advised for a period of 2 weeks.
2. Silicone tube is removed at 4-6 weeks after nasal endoscopy demonstrates that the ostium is healed completely. It is important to identify and manage any granuloma, if present.

Discussion

There have been many studies published in the literature describing the role of revision endoscopic DCR and its success rate for failed cases with success rate ranging from 76.5%-94%.^{1-3,7-12} Approach to a failed DCR case involves a thorough preoperative examination including irrigation and probing of lacrimal drainage system and nasal endoscopy to evaluate any pathology. Either of the two, external or endoscopic approach can be performed for failed cases. Endoscopic revision DCR offers advantage of avoiding cutaneous incision (particularly if previous external scar is evident), recognition/correction of intranasal abnormality, achieving mucosal-mucosal approximation, easy enlargement of ostium and less to minimal bleeding.^{3,4,7,8} More importantly endoscopic approach allows easy recognition of factors responsible for failure and thus appropriate management because of better visualization.^{7,8,9}

The following factors were identified as a cause of failure during the repeat endo-revision DCR in the present case: Concha bullosa, improper and small bony ostium, posteriorly located ostium, incomplete opening of lacrimal sac and intrasac synechia. There may be other factors for failures such as large agger nasi cell, turbinate adhesion to ostium, nasal synechia, paradoxical middle turbinate, deviated nasal septum, ostium granulomas, sac in sinus syndrome (lacrimal sac located in ethmoids), high internal common opening etc, and these can be identified and managed with endoscopic approach only. So spectrum of possibilities endoscopic

approach offers in revision cases is far more than that with external approach.

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Diabetic Macular Edema- A Review

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Abstract

Diabetic macular edema(DME)is the leading cause of vision loss all over the world. It occurs when there is abnormal leakage and accumulation of fluid in the macula from retinal blood vessels damaged due to diabetic retinopathy. The increasing number of individuals with diabetes worldwide suggests that diabetic retinopathy (DR) and DME will continue to be the major contributors to vision loss and associated functional impairment for the years to come. Early detection of retinopathy in individuals with diabetes and timely treatment is critical in preventing visual loss. This article reviews the etiology and the available modes of treatment for systematic management of DME.

Keywords: Diabetic retinopathy, macular edema, VEGF, OCT, FFA.

Introduction

The burden of diabetes is estimated as 642 million people by 2040 according to International federation of diabetes. The young and elderly population is more likely to suffer. The prevalence of DR increases with the duration of diabetes. It has an overall rate of up to 30% and a high risk of severe visual impairment in 10% of subjects^{1,2}. Diabetic macular edema (DME) is more frequent in type 2 diabetes. It involves about 7.5% of diabetic patients, and is the main cause of blindness in middle aged adults in industrialized countries. Survey conducted in north India in 2016 stated prevalence of DR as 21.7% with male preponderance. Sankara Nethralaya DR epidemiology and molecular genetics study report1 estimated incidence of vision threatening diabetic retinopathy as 5%².

Pathology

DME is defined as the retinal thickening within one disk diameter of the center of the macula or definite hard exudates in this region. This is due to the increased extracellular fluid derived from hyperpermeable retinal capillaries. Prolonged hyperglycemia leads to reduced inner retinal oxygen tension, venous dilation and increased VEGF concentration within the retina. This is associated with increased exudation of serum out of the retinal vasculature and into the extracellular space. The RPE pump is overwhelmed by the exudation of serum leading to macular edema^{3,4}.

Decrease in subfoveal choroidal blood flow in type 2 diabetic patients with retinopathy may be relevant in

the pathophysiology of DME. Eyes with DME have a lower choroidal blood flow than eyes without DME, suggesting relative hypoxia of the RPE and outer retina, and consequent increased permeability of the outer blood retinal barrier².

Cross-linking and protein glycation are increased in the diabetic vitreous, which may explain instances of tangential macular traction that may induce DME. Besides the direct effect of traction causing leakage from blood vessels or macular elevation with subretinal fluid, vitreous adherent to the macula may loculate mediators of vessel permeability in proximity to macular capillaries and may impede oxygenation of the retina, thereby causing venous dilation and increased edema via Starling's law or by upregulation of VEGF⁴.

	Definition
Center-involved diabetic macular edema	DME in which the fovea is involved.
Clinically significant macular edema	a. Retinal thickening within 500 µm of the center of the macula or
	b. Hard exudates within 500 µm of the center of the macula with adjacent retinal thickening or
	c. One disk area of retinal thickening any part of which is within one disk diameter of the center of the macula

Focal and diffuse diabetic macular edema

Focal edema is believed to arise from microaneurysms, whereas diffuse edema is said to arise from generally dilated and hyper-permeable capillaries in macula. Focal DME has been reported to be more common than diffuse DME.

Clinical features

Focal macular edema.

- Clusters of microaneurysms usually are found within areas of focal retinal edema.
- Fluorescein angiography clearly demonstrates that microaneurysms on the retinal capillaries which leak.
- Hard exudate rings may surround foci of retinal edema.
- Circinate rings develop around cottonwool spots
- Leaky microaneurysms and dilated capillaries often form in the capillary bed surrounding the occluded terminal arteriole that produces the cotton-wool spot.
- Focal leakage from microaneurysms causing focal edema is important to recognize, because it can be treated by focal laser.

Diffuse macular edema.

- Diffuse macular edema results from a generalized breakdown of the inner blood-retinal barrier, in which microaneurysms, retinal capillaries and arterioles leak diffusely.
- The capillary bed is diffusely dilated and may show widened intercapillary spaces in fluorescein angiograms, corresponding histologically to dilated hypercellular capillaries and numerous acellular occluded capillaries.
- Hard exudate is usually absent in eyes with diffuse edema, suggesting that the generalized defect in the inner BRB is insufficient to allow larger lipoprotein molecules to pass into the extravascular space.
- The retinal pigment epithelium (RPE), forming the outer BRB, contributes to normal fluid dynamics in the retinal extracellular and subretinal space^{6,7}.

Subclinical diabetic macular edema (SCDME)

The term subclinical DME has been used to define classes of DME that are less severe than clinically significant DME.

1. Persistent diabetic macular edema
DME that has been treated without complete resolution is defined as persistent.
2. Recurrent diabetic macular edema
DME can resolve spontaneously without treatment, and then recur, the term recurrent

DME is used with reference to treated eyes with recurrences.

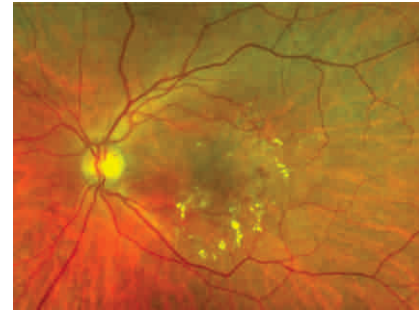


Fig.1: Image showing non proliferative diabetic retinopathy with diabetic macular edema



Fig.2: Fundus picture of right eye showing center involving DME



Fig.3 : Fundus picture of Left eye showing diffuse DME.

Specific diagnostic tools for DME

1. Optical Coherence Tomography(OCT)

It provides high-resolution images of the retinal layers, choroid, vitreous gel, and the vitreoretinal interface. The presence, location and morphology of macular edema can be determined. It can also quantify the retinal thickening (Figure 4, 5, 6, 7). Hence OCT is the gold standard investigation for the diagnosis, treatment approach, prognosis, assessment of treatment response in patients with DME. It has the advantage of the speed and ease of image acquisition^{6,8}.

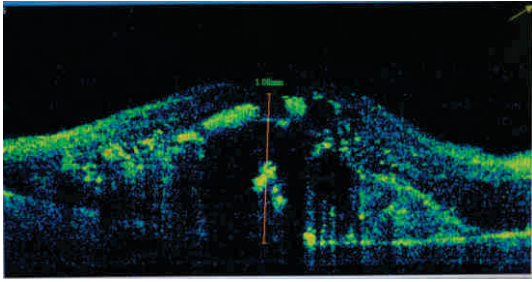


Fig. 4: OCT of macula showing diabetic macular edema with distortion of ellipsoid zone

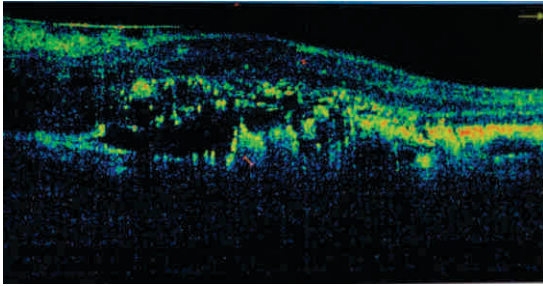


Fig. 5: OCT of macula showing diffuse DME with distortion of ellipsoid zone

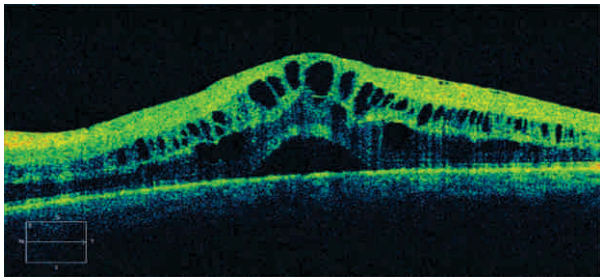


Fig. 6: OCT Image showing diabetic macular edema with neurosensory detachment

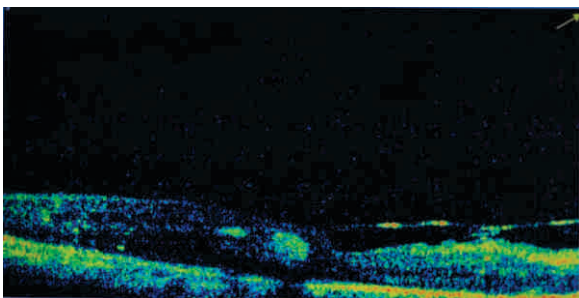


Fig. 7: OCT image in non proliferative diabetic retinopathy with macular edema

OCT classification of macular edema.

Type1	Focal macular thickening
Type2	Diffuse non-cystoid macular thickening
Type 3	Diffuse cystoid macular thickening
Type 4a	Tractional macular edema due to posterior hyaloid traction
Type 4b	Tractional macular edema due to epiretinal membrane
Type 5	Serous retinal detachment

2. Fluorescein angiography (FFA)

It is an invasive and a sensitive method to detect vascular changes due to rupture of the inner and outer blood retinal barrier in the course of an established DR. Routine FFA is not recommended in DR due to its adverse effects like anaphylaxis and dehydration⁵.

Indications of FFA

- To differentiate IRMA from neovascularisation.
- To determine the cause of unexplained visual loss in macular ischaemia.
- To differentiate tractional macular edema from cystoid macular edema.
- To confirm suspicious neovascularisation.
- To identify areas of untreated capillary non-perfusion in eyes with persistent or recurrent neovascularisation post laser therapy.
- To evaluate retinopathy status in dense asteroid hyalosis¹⁰.

Limitations

- Invasive procedure
- Adverse effects are numerous
- Time consuming
- Does not provide depth resolved images

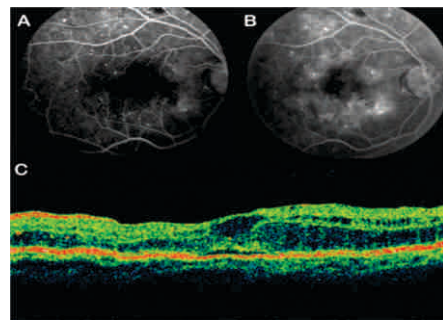


Fig. 8: (A and B) Fluorescein angiography shows diffused diabetic macular edema. (C) optical coherence tomography illustrates diffuse retinal thickening and cystic spaces, consistent with cystoid macular edema.

3. OCT angiography (OCTA)

It is a new non-invasive imaging technique that employs motion contrast imaging to high resolution volumetric blood flow information generating images similar to angiographic images. It provides a highly detailed view of the retinal vasculature, which allows for accurate delineation of the foveal avascular zone (FAZ) and detection of subtle microvascular abnormalities, including FAZ enlargement, areas of

capillary nonperfusion, and intraretinal cystic spaces. The possibility of detecting microvascular changes in diabetic eyes before the presence of visible microaneurysms may have important implications in the future. OCTA is a sensitive method for detecting early changes in DR. It is a very promising technique for early diagnosis and control of treatment in patients with DR.

Treatment

Maintaining proper parameters of modifiable risk factors of DR is important. They have a significant positive impact on long term outcome.

Current treatment thresholds are based on the presence of center involved DME (CIDME), or edema affecting the 1 mm in diameter retinal central subfield, rather than the presence of clinically significant macular edema (CSME)⁹.

Classification of DME according to International Council of Ophthalmology

- No DME- no exudates/hard exudates near macula
- Non-center involved DME (NCIDME)-retinal thickening in the macula that does not involve the central subfield zone 1mm in diameter
- Center involved DME (CIDME)- retinal thickening in macula that does involve the central subfield zone that is 1mm in diameter

The basic available options for medical treatment for DME are;

1. Laser photocoagulation⁷
2. Intravitreal anti-VEGF
3. Intravitreal steroid treatment
4. Combination therapy

Focal/grid laser photocoagulation

The ETDRS demonstrated superior visual outcomes with focal/grid laser for CSME compared with natural outcome. Laser thus became the standard of care over the next 30 years. Treatments were repeated at 4-month intervals if CSME persisted with or without thickened, and non-perfused retina.

This ETDRS style focal/grid photocoagulation for DME has potential side effects including paracentral scotomas, subretinal fibrosis, and secondary choroidal neovascularization. The technique of focal/grid argon laser treatment has been modified over time.

The most significant changes are mentioned in the DRCR.net protocols that employ focal/grid

photocoagulation. Burns can vary from 50 to 200 μm but all contemporary burns are 50 μm and less intense⁷.

Yellow wavelength laser is acceptable in addition to green, but blue-green is not used because of over-absorption by macular luteal pigment. Use of a guiding fluorescein angiogram is optional¹⁰.

For mild CIDME with central macular thickness in the range of 300–350 μm , focal/grid laser will produce ~25 μm of macular thinning at the first followup at 3-4months. For every 100 μm of additional baseline macular thickening above this threshold, approximately 10 μm of additional macular thinning is expected at the 3-to 4-month follow-up visit.

Visual acuity at 3-4month follow-up visit is average or unchanged from baseline. Subthreshold Laser Photocoagulation besides focal/grid suprathreshold laser treatment, diode laser micropulse laser can also be used.

Its advantages are absence of RPE scarring, subsequent choroidal neovascularization, and elimination of paracentral visual field scotomas. The disadvantages are that there is no visible endpoint for treatment. It makes it difficult to determine where treatment has and has not been given. There is no standardized, consensus set of treatment parameters or guidelines with respect to treatment within the foveal avascular zone⁸.

Intravitreal anti-VEGF agents

Intravitreal therapy with agents that neutralize VEGF is currently the standard of care in the management of eyes with CIDME according to the protocol T in DRCR study.

Studies have shown that monotherapy or even combination therapy with laser are equally potent. Currently three anti-VEGF agents are commonly used to treat eyes with CIDME. They are bevacizumab, ranibizumab, and aflibercept. Of these anti-VEGF agents, recent data from the Diabetic Retinopathy Clinical Research Network (DRCRN) suggest that for eyes with CIDME and good levels of acuity (20/40 or better), any agent effectively improves visual acuity. In eyes with CIDME and lower levels of acuity, 20/50 or worse, aflibercept appears to be most the effective at improving visual acuity. With the use of intravitreal anti-VEGFs the need for vitrectomy has come down.

Most patients require near-monthly administration of intravitreal anti-VEGF agents during the first 12 months of treatment, with fewer injections in subsequent years to maintain remission from CIDME. However, widespread observations that rapid regression of retinal neovascularization occurs in eyes receiving intravitreal anti-VEGF therapy for CIDME has made these agents a potentially viable treatment for PDR. In a study Intravitreal ranibizumab was compared to PRP for visual acuity outcomes in patients with PDR. There was no statistically significant visual acuity difference between the ranibizumab and PRP groups at 2 years.

Agent	Structure	Target	Half life in vitreous in days	Dose
Bevacizumab	Humanised IgG monoclonal antibody	VEGF-A	6.7-10	1.25mg/0.05ml
Ranibizumab	Fab fragment of humanised IgG monoclonal antibody	VEGF-A	7.1	0.3mg/0.03ml
aflibercept	2 nd Ig domain of VEGFR1 and 3 rd Ig domain of VEGFR2 fused to Fc portion of humanized IgG	VEGF-A VEGF-B PLGF	9	2mg/0.05ml

Intravitreal Steroids

It has been reported that there is role of inflammation in the formation of DME. The leukostasis on the retinal surface capillaries is thought to be the major culprit. Upregulation of intracellular adhesion molecule ICAM-1 enhances the vascular permeability leading to breakdown of blood retinal barrier. This is the main cause for development of DME.

Corticosteroids produce anti-inflammatory effect by decreasing the inflammatory mediators and VEGF formation. Intravitreal treatment with corticosteroids have significantly reduced inflammation and improved blood retinal barrier functioning³.

Based on the results of the studies available, intravitreal steroids are the second line of therapy in DME due to the risk of developing cataract and glaucoma. They can be used in cases which are resistant to anti-VEGF therapy. First line steroids can be considered in patients who have had a major cardiovascular event or in patients who demand for less frequent intravitreal injections⁸.

Dexamethasone is used as the first choice followed by flucinolone. These are appropriate for non-steroid responders and pseudophakes with DME. Still

intraocular pressure has to be monitored regularly. Retreatment can be considered if there is recurrence after 6 months-1 year³.

Role of surgery in DME

DME/macular thickening is the major cause of visual impairment in patients with DR. Vitreous may contribute to the development of DME. Several studies have shown that DME is more likely to resolve after spontaneous vitreomacular separation. Pars plana vitrectomy (PPV) has proved better results in resolving DME especially when there is presence of taut posterior hyaloid membrane and macular traction. The removal of vitreous cortex with or without peeling internal limiting membrane releases vitreomacular traction.

Indications for Vitrectomy

- Severe vitreous hemorrhage of 1–3 months duration or longer that does not clear spontaneously.
- Advanced active proliferative DR that persists despite extensive PRP. Surgery is reasonable in eyes with recurrent episodes of vitreous haemorrhage from PDR due to persistent vessels despite PRP or mechanical traction on NV.
- Traction macular detachment of recent onset. Fovea-threatening or progressive macula-involving traction detachments benefit from surgical management.
- Combined traction-rhegmatogenous retinal detachment.
- Tractional macular edema or epiretinal membrane involving the macula. This includes vitreomacular traction.

Conclusion

There have been significant advances in DME and its treatment aspects. Intravitreal anti-Vegfs are used as first line of therapy. In non center involved DME however, laser photocoagulation can be considered. In non responding or recalcitrant DME switch over therapy can be tried. Switching over to other anti-Vegfs or intravitreal steroids is done nowadays. Vitrectomy is carried out if vitreomacular traction is present.

DME is a preventable complication if the systemic and metabolic factors are well-controlled. Collaborative efforts of the patient, physician and the resource personnel are required for the effective

treatment. Pharmacotherapy advancements in last decade have been responsible for the changing paradigms in the management of DME.

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DropleSS Cataract Surgery: New Frontiers of Drug Delivery Innovation

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Abstract

Cataract surgery is continuously evolving with innovative techniques, devices and drug formulations introduced every year. Postoperatively instillation of antibiotic and steroid eyedrops is required for a long period. Correct and timely instillation of drops with proper hygiene has its own problems and is not always possible. Problem with compliance of topical eye drop application led researchers to find out some alternative applications. Newly introduced clinical technique of transzonular injection of antibiotic and steroid (described as dropleSS cataract surgery) that is an advancement to limit or perhaps eliminate the post-operative medication regime.

Keywords: DropleSS cataract surgery, transzonular injection, intracameral injection.

Introduction

Cataract-intraocular lens (IOL) surgery is the most common procedure performed by ophthalmic surgeons worldwide. Currently topical administration is the most common route of ocular drug delivery during cataract surgery. Despite its apparent easy accessibility, the eye is well protected from foreign materials and drugs by a number of very efficient mechanisms such as blinking, induced lacrimation, tear turnover, nasolacrimal drainage, which cause rapid removal of substances from the eye surface and by the cornea, which forms the physical-biological barrier. Most of the eye drop used during cataract surgery is not properly utilized in topical drug delivery system. Under normal condition the human eye can retain about 25–30 μl of an ophthalmic solution; however after a single blink the volume is reduced to 7–10 μl through nasolacrimal drainage which cause the drug to be systemically absorbed across the nasal mucosa or the gastrointestinal tract. A significant systemic loss from topically applied drugs also occurs from conjunctival absorption into the local circulation. Tear turnover, which can also be stimulated by factors such as pH and tonicity of the formulation, remove drug solution from the conjunctival cul-de-sac in a few minutes.

Problem with compliance of topical eye drop application led researchers to find out some alternative applications. Cataract surgery is continuously evolving with innovative techniques, devices and drug formulations introduced every year.¹

Drug delivery innovations for cataract surgery

At present drug administration options during the cataract surgery include topical application (most common). Subconjunctival application is not used now. Intracameral Injection is reserved for antibiotic supplement. Biodegradable implant had shown considerable utility management of retinal disorders (refractory macular edema). After the success of sustained-release drug delivery systems such as Retisert (fluocinolone acetonide intravitreal implant 0.59 mg, Bausch + Lomb, USA,) and Ozurdex (dexamethasone intravitreal implant 0.7 mg, Allergan, USA), various drug delivery technologies are being developed to treat diseases of the eye. Encouraged by these, different ophthalmic issue spaces to implant these reservoir-based drug delivery systems are also being explored. Subcutaneous, subconjunctival, intracanalicular, intracapsular, transzonular and even suprachoroidal spaces have been researched at as potential sites for drug reservoirs or delivery system. Intravitreal inserts of brimonidine are being developed on the lines of the sustained-release dexamethasone PLGA platform for the management of geographic atrophy due to age-related macular degeneration and also as a neuroprotective modality in the management of glaucoma.

Intracameral injections are increasing in use by ophthalmologists worldwide, several manufacturers are working on developing unique direct-delivery systems or devices (containing antibiotics& steroids)

that can be used for cataract surgery cases during the postoperative period. A clinical trial of a punctal plug delivery system that elutes moxifloxacin (Ocular Therapeutix Inc, USA) exhibited a favorable safety and tolerability profile.² PolyActiva (Melbourne, Australia) had developed a biodegradable implant that releases levofloxacin over a 30-day period. These experimental procedures are currently being explored in animal/clinical studies.

Dropleess cataract surgery

At present preservative free triamcinolone acetonide is available in India (Aurocort from Aurolab, Madurai, India). Indian pharmaceutical companies are working on combination of antibiotics and steroid formulation (for intracameral or transzonular application) and this formulation will be available in near future. In this article, the authors will focus about the newly introduced clinical technique of transzonular injection of antibiotic and steroid (described as dropleess cataract surgery) that is an advancement to limit or perhaps eliminate the post-operative medication regime.

Technique: Transzonular injection

The technique of transzonular injection of moxifloxacin hydrochloride and triamcinolone acetonide is simple. It is done intraoperatively by injecting 0.2 cc of the TriMoxiVanc or Tri-Moxi (Dropleess™; Imprimis Pharmaceuticals, San Diego, USA) formulation into the anterior vitreous space using a 27-gauge blunt curved cannula. With the capsular bag and anterior chamber filled with ophthalmic viscoelastic substance (OVD), the 27 gauge cannula is carefully introduced through the temporal clear corneal incision, and then directed by the operating surgeon beneath the iris nasally and over the peripheral edge of the anterior lens capsule. The tip of the cannula then passes between the zonular fibers, where the medication is then slowly injected by the surgeon. The medication in most cases can be visualized as it enters the anterior vitreous space posterior to the IOL implant. Once injected, the medication remains sequestered in the anterior vitreous space, even as viscoelastic is subsequently removed from the capsular bag and anterior chamber. Intracameral injection of 0.15 cc of combination of 0.5 percent moxifloxacin and 0.1 percent dexamethasone (manufactured by Ocular Science, Manhattan Beach, CA, USA) is also being used by some surgeons in USA. Advantage of this

clear solution is lack of transient blurring of vision associated with triamcinolone solution.

Transzonular injection of antibiotics and steroids (dropleess cataract surgery) technique is being utilized more and more by cataract surgeons around the globe. With manufacturers working to formulate optimum drug delivery system, it may be one of the significant developments for cataract surgery patients but is it really required, feasible, effective and safe?

Is dropleess cataract surgery really needed?

The usual cataract surgery medication schedule can be confusing and expensive for the elderly patients since it requires them to purchase and instill various eye drops, a number of times every day, for four to six weeks post-surgery. The main aim of these postoperative medications is the prevention of infection and inflammation after cataract surgery. Utilizing anti-inflammatory agents and antibiotics post cataract surgery has proven to be highly effective to minimize inflammation (leading to cystoid macular edema) and infection (endophthalmitis). Until recently, this had been considered an inconvenient, yet acceptable method since there were no alternatives. In a recently published study, An and associates³ reported that 92.6% cataract patients have an improper eye drop administration technique, including missing the eye (31.5%), instilling an incorrect amount of eye drops (64.0%), contaminating the bottle tip (57.4%), or failing to wash hands before drop instillation (78.0%). These authors concluded that postoperative cataract patients inexperienced with eye drop use showed a poor instillation technique by failing to wash hands, contaminating bottle tips, missing the eye, and using an incorrect amount of drops.² This study has indicated that due to non-compliance, the patients' risk of endophthalmitis development as well as other complications drastically increases. In India, this issue can be more serious in high volume eye camp setting as lesser number of ophthalmic assistant/healthcare workers to educate these patients about after care and proper application of eye drops with few incidence of contamination of eye drops as a result patients using pin/needle to open them.

With dropleess cataract surgery, the ophthalmologist performs transzonular injection of a combination of antibiotic and steroid intra-operatively during the cataract surgery. This technique only needs one administration and the patient is not required to

purchase a number of eye drops for prophylaxis against inflammation and infection after being discharged.⁴ This drastically decreases the compliance issues on part of patients.⁵ Transzonular injection of antibiotic and steroid was initiated in the United States and since its introduction, about 80,000 cataract operations have been performed using this adjunctive technique.⁶ Published reports indicated that cataract surgery completed with the use of prophylactic anti-infective and anti-inflammatory drugs delivered transzonularly into the vitreous or topically provided similar safety in terms of intraocular pressure and corneal and macular edema, as well as similar effectiveness in terms of inflammation control, visual acuity, and patient comfort.^{7,8,9}

The best option of performing dropless cataract surgery is by using one injection of anti-inflammatory and anti-infective drugs (manufactured by Imprimis Pharmaceuticals and currently available in USA). A solution of three drugs approved by U.S. Food and Drug Administration is also utilized for isotonicity at a pH level, which is best compatible with the patient's eye. The compound includes vancomycin hydrochloride, moxifloxacin hydrochloride ophthalmic solution, and triamcinolone acetonide injectable suspension.⁸ This compound solution eliminates the need to administer three or more eye drops after surgery to prevent/minimize infection and inflammation. Moreover, it also reduces the requirement of administering those eye drops repetitively for a course of four to six weeks as required with the drop current regime.⁹

Pros and Cons of Dropless Cataract Surgery

Let's have a look at the pros of transzonular drug delivery approach of, especially in terms of the high volume cataract surgery done in the developing world setting:

1. Minimal or no eye drops needed in majority of the cases after cataract surgery.
2. Post-op regimen is simplified with no need for doctors to worry about patients wrongly using the eye drops. There is a decrease in compliance issues.
3. The risk of application issues reduces with dropless surgery.
4. Patients don't have to worry about purchasing prescription eye drops after cataract surgery.
5. The overall cost is reduced.

According to reports on dropless cataract surgeries, as little as 5% of the patients needed drops with the Tri-Moxi experience, while the rest of the patients didn't experience any problem.¹⁰ It is a known fact that compliance of eye drops as well as poor adherence to medication after surgery, are major issues. Moreover, the patients are also less likely to admit their poor adherence in hopes of not disappointing their doctors, which results in worsening the problem. Therefore, transzonular drug delivery system is highly beneficial in these cases.

While there are various benefits of dropless cataract surgery, it also comes with a few cons that must be considered by the ophthalmic surgeons and patients before opting for this technique:

1. Floaters and cloudy vision have been reported by some patients a few days after surgery. This typically occurs because of opaque nature of the combination of drugs (moxifloxacin and triamcinolone acetonide) used. Cloudy vision is not reported with moxifloxacin dexamethasone combination preparation.
2. There are potential risks of retinal detachment and vitreous hemorrhage. However, such cases haven't been reported as yet.¹¹ The Tri-Moxi outcomes have not been researched enough.

Contraindications

It is too early to clearly determine the cons associated with dropless cataract surgery. There are of course some contradictions. It is best to avoid transzonular drug injection in cataract patients:

1. Who underwent vitrectomy in the past?
2. With capsular bag/zonular support system are unstable.
3. Who are steroid responders?
4. Who have glaucoma or are allergic to any component of the injection?

Our Experience

The authors are using preservative free triamcinolone acetonide (Aurocort, Aurolab, 2 mg 0.05 CC, intracameral or transzonular application) in routine and complex cataract cases. Most of these cases have clear cornea and quiet eye on post op day 1. We use antibiotic steroid combination two times for 3 weeks period.

At present preservative free triamcinolone acetonide is available in India (Aurocort from Aurolab, Madurai, India). Indian pharmaceutical companies

are working on combination of antibiotics and steroid formulation (for intracameral or transzonular application) and this formulation will be available in near future.

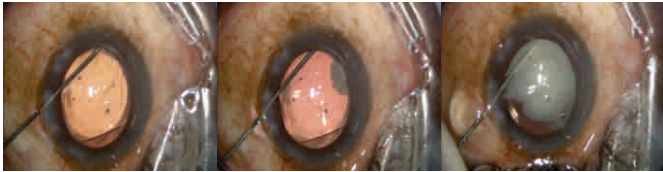


Fig.1 : Transzonular application of triamcinolone acetonide

Conclusion

Although not available in India at present, latest transzonular injection of antibiotics and steroids can be suitable for numerous cataract patients, especially in developing countries where there are a vast number of patients for cataract surgery and there are lesser number of ophthalmic assistant/healthcare workers to educate them about after care and application of eye drops post cataract surgery.^{11,12,13} In a typical cataract surgery, the patients are supposed to use at least three eye drops that are instilled for four-six weeks postoperatively. The instillation schedule of prescribed eye drops can be more challenging in cases with intra-operative complications or pre-existing ocular (e.g. glaucoma patients with 2 or 3 anti-glaucoma medications) or systemic conditions (e.g. difficulty in eye drop instillation by patients with rheumatoid arthritis). Nevertheless, this creates confusion amongst the patients as they are unable to keep up with the directions since various drops require differing times. Also there is also concern about cost, compliance and preservative induced corneal toxicity.

Dropless cataract surgery is also more beneficial for patients who get medication anxiety. Since majority of the patients undergoing cataract surgery are elderly, instilling three to four eye drops at different times every day can get rather challenging for them and their attendants. Many of these patients give up and don't take those prescribed medications and many simply forget to take them. With dropless cataract surgery, the patients need to put eye drop less frequently and can focus on their recovery instead. With no or minimal medications to purchase, the patients can save money. This eliminates the financial burden of buying medications for patients, especially the ones who have

financial constraints. Clinical trials are under way to address the efficacy of transzonular drug delivery system. Indian pharmaceuticals are currently working to formulate a triamcinolone and moxifloxacin combination that can be used intra-operatively during cataract surgery.

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Eye Banking

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Abstract

Corneal blindness is one of the commonest causes of curable blindness. Eye banks serve to procure, process and distribute corneal tissue of the highest quality for transplantation. Development of an eye banking system requires awareness among the general public, infrastructure and motivated trained personnel to dispel social and religious taboos. A well defined organizational structural system is followed for efficiently starting and managing an eye bank.

Keywords: Eye banking, corneal blindness, keratoplasty.

Introduction

Eye bank is an institution that should provide a round-the-clock public response system over the telephone and conduct public awareness programmes on eye donation and Co-ordinate with donor families and hospitals to motivate eye donation. Eye banks serve to procure, process and distribute corneal tissue of the highest quality for transplantation, to distribute tissue in an equitable manner, to ensure safe transportation of tissue and promote public relation activities. Diseases affecting the cornea are a major cause of blindness worldwide second only to cataract. The epidemiology of corneal blindness is complicated and encompasses a wide variety of infectious and inflammatory eye diseases that cause corneal scarring, which ultimately leads to functional blindness. Ocular trauma and corneal ulceration are also causes of corneal blindness and may be responsible for 1.5 to 2.0 million new cases of unocular blindness every year. Infectious conditions (eg, trachoma and corneal ulcer) are common in the developing world, whereas noninfectious entities (e.g. Corneal dystrophies and pseudophakic bullous keratopathy) are more common causes in developed countries.¹⁻⁴ Trachoma is the world's leading preventable and infectious cause of blindness and the foremost cause of ocular morbidity.⁵

History of Eye Banking

The first eye bank was founded in 1944 by two physicians, Dr. Townley Paton and Dr. John MacLean.⁶ Currently, in the United States, eye banks provide tissue for about 46,000 cornea transplants each year⁷ to treat conditions such as keratoconus⁸ and corneal scarring. In some cases, the white of the eye

(sclera) is used to surgically repair recipient eyes. In 1953 Stockler revealed the vital role endothelial cells play in corneal transparency. Harris and Nordquist, continuing Filatov's and Stocker's efforts and published a paper in 1955 that showed endothelium maintain function at 4°C. Eye bank association of America was established in 1961 as a nonprofit organization dedicated to the restoration of sight through the promotion and advances of Eye Banking. In 1974 McKarey and Kaufman developed M-K Medium which allowed the excised Corneal- sclera rim to be preserved for up to 4 days at 4°C. Kaufman et al presented K sol as a storage method viable for up to 10 days in 1985. In 1991 Optisol was developed as a storage medium that lasts up to 14 days. In India the first eye bank was established in 1943 at Madras, the first corneal transplantation was done in Dhanda, Indore in 1960. Till Oct 10, 2013 there are total No. of EBTC/EB/EDC (Registered) = 749 Eye Banks collecting eyes till Oct 10, 2013. In Himachal Pradesh the Eye bank was opened on 28th August, 2010.

Magnitude of corneal blindness worldwide

145 million people worldwide are bilaterally blind, of which 6 to 8 million are blind due to corneal disease. In some African areas, nearly 90% of the total blindness is due to corneal pathology. The prevalence of corneal disease varies from country to country and even from one population to another depending on factors including availability and general standards of eye care. At present, there are 146 million people worldwide with trachoma; 10 million suffer from trichiasis and need surgery to prevent corneal blindness, and another 4.9 million totally blind from trachomatous corneal scarring.^{9,10} In children, the

causes of corneal blindness include keratomalacia,¹¹ ophthalmia neonatorum, accidental ocular trauma¹² that may be mechanical or chemical,¹³ and less frequently, ocular diseases such as herpes simplex virus infections and vernal keratoconjunctivitis.¹⁴ Although herpes virus is the most common cause of corneal ulcer in developed countries, bacterial and fungal infections are more common in developing countries.

Magnitude of corneal blindness in India

There are approximately 25 million blind people in India, which is about one fourth of the total blind population of the world. This means 25 out of every 1000 people in India are blind compared to just 3 per 1000 in the developed countries. Blindness in most cases is avoidable and curable. Out of the 25 million, approximately 5 million are blind due to defective cornea. A good majority of these blind are children in their early childhood. Gonzales et al¹⁵ found that the annual incidence of corneal ulceration in the Madurai District in South India was 113 per 100,000 people, 10 times the annual incidence of 11 per 100,000 reported from Olmsted County, Minnesota, in the United States.¹⁶ This condition is potentially treatable it is a sad fact that due to non-availability of healthy cornea tissue, many people continue to live in a world of darkness. In India, there are approximately 6.8 million people who have corneal blindness with vision <6/60 in at least one eye, and of these, about 1 million have bilateral corneal blindness.⁹ If the present trend continues, it is expected that the number of corneal blind individuals in India will increase to 8.4 million in 2010 and 10.6 million by 2020.¹⁷

State of Eye Bank in Himachal Pradesh

Eye banking in Himachal Pradesh is in its budding stage. The First Eye bank of Himachal Pradesh was opened on August 28th, 2010 in IGMC, Shimla, and second Eye Bank is functioning in RPGMC Kangra at Tanda. First EDC was opened at Regional Hospital Nahan which is now upgraded as Medical College and second EDC at Dharmshala. Opening of Eye collection Centre in other district hospitals are also in the pipe line. Eye bank IGMC Shimla and Eye bank RPGMC providing round-the-clock public response system over the telephone and conducting public awareness programs on eye donation. Voluntary donation and Hospital cornea retrieval programs (HCRP) are the two sources of eye donation in eye bank at IGMC, Shimla .The eye bank of IGMC, Shimla is conducting public awareness programs on

eye donation and people of Himachal Pradesh are also filling the pledge form for donation of eyes after death.

The prevalence of corneal blindness in Himachal is less than India. Richa et al.¹⁸ examined 256 patients of corneal disease and found the pattern of corneal disease are depicted in Table 1

Disease	Number of eyes
Corneal opacity	64
Infective keratitis	69
Peripheral ulcerative keratitis	17
Degeneration/ Dystrophy	21
Keratoconus	12
Vernal Keratoconjunctivitis	14
Dry Eye Syndrome	8
Pseudophakic bullous keratopathy	33

Table1: Pattern of corneal diseases

Eye Banking System

Organization

For an efficient eye banking system, a three tier organization structure has been recommended. An integrated system involving a three tier community eye banking system based on the infrastructure and manpower at all levels. The three tiers proposed were eye donation center, eye bank and eye bank training centers (EBTC) which would be responsible for tissue harvesting, processing, and distribution, creating public awareness as well as training and skill up gradation of eye banking personnel. The middle tier should comply with all the regulations stipulated by govt. of India/Eye bank Association of India EBAI and these should cater to a population of 20 million each. These eye banks should be closely linked with 2,000 Eye donation centers(EDC- ratio 1:500) each would cater to a population ranging from 50,00 to 100,000. The Eye donation centers would be regulated and funded by the eye banks themselves.



Donation Center is affiliated to a registered eye bank, which should provide: (1) public and professional

awareness of eye donation (2) co-ordinate with donor families and hospitals to motivate eye donation (3) to harvest corneal tissue and collect blood for serology (4) to ensure safe transportation of tissue to the parent eye bank.

Eye donation – problems and solutions

There is severe lack of donor eyes in India and only about 20,000 operations are being performed every year, while 30,000 new victims are added each year to the long list of blind people waiting to be cured. In India, the need for corneas for sight restoring surgeries is one lakh per year. According to the Eye Bank Association of India, the number of eyes collected in 2010 is 41,549. And more important is the fact that of this total, only a little more than 10,000 meet all the criteria of medical standards as per the requirement for quality control of eye banks. Although there are enough qualified surgeons and plenty of potential patients corneal transplantation is rather scarce for want of donor eyes. Nearly 10 million people die in India, every year. Sadly the corneal donation does not exceed more than a few thousand. The reasons for the very low number of eye donation in India are manifold.

- Lack of awareness among the general public.
- Improper development of infrastructure.
- Absence of motivation among trained personnel.
- Social and religious taboos.

Following steps have been taken to create awareness for organ donation :

1. Indian Organ Donation Day is celebrated every year since the year 2010.
2. Programs on Organ donation are through various TV Channels.
3. Awareness activities are carried out in India International Trade fair to spread the message of Deceased Organ Donation among the public.
4. Regional "Organ Donation Awareness workshops" are organized in various cities with coordination of State Governments for increasing the awareness among public for organ donation.
5. Organ Retrieval Banking Organization at AIIMS has been registering the persons who pledge to donate their organs after death.
6. National Organ Transplant Program has been approved with main component of Information, Education and Communication activities to promote organ donation from deceased donors.

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Recent Advances in Diagnosis and Surgical Management of Mycotic Keratitis

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Abstract

Mycotic keratitis is a major cause of corneal blindness. The prognosis is markedly worse compared to bacterial keratitis. Delayed diagnosis, scarcity of effective antifungal agents and poor penetration of antifungal drugs are the major factors for poor outcome. Over the last decade, considerable progress has been made to rapidly diagnose cases with mycotic keratitis and increase the efficacy of treatment. This review article discusses the recent advances in diagnosis and surgical management of mycotic keratitis.

Keywords: Antimicrobial peptides, confocal microscopy, mycotic keratitis, polymerase chain reaction.

Introduction

Mycotic keratitis, commonly known as fungal keratitis, accounts for approximately 1-44% of all cases of microbial keratitis, depending upon the geographic location.^{1,2} Overall, it is more common in tropical and subtropical areas. The genera that commonly cause infection of the cornea include *Fusarium*, *Aspergillus*, *Curvularia*, *Bipolaris*, and *Candida*.^{1,2,3} Most of the currently available antifungal medications have limitations, such as poor bioavailability and limited ocular penetration, especially in cases with deep-seated lesions.^{4,5,6} These factors, especially in cases of severe fungal keratitis, account for the slow resolution of fungal infections, with most cases finally requiring a therapeutic penetrating keratoplasty.⁶

Epidemiology and risk factors

In developing countries most common risk factor for fungal keratitis is trauma with vegetative matter or objects contaminated with soil.^{1,2} While in developed countries, use of contact lenses (CL) has emerged as an important risk factor for the occurrence of fungal keratitis. In addition to CL wear and ocular trauma, ocular surface disease (OSD) is the third most common risk factor accounting for approximately 29% of cases.^{6,7}

Fungal Pathogens

Common organisms involved in mycotic keratitis include species of *Aspergillus*, *Fusarium*, *Candida*, *Curvularia* and *Penicillium*. Most of these species are saprobes. The rarely reported fungal pathogens include *Fonsecaea pedrosoi*, *Cylindrocarpon* species,

Scedosporium prolificans.

Clinical Features

Patient with mycotic keratitis usually have less symptoms and more signs clinically. Presentation is with gradual onset of pain, grittiness, photophobia, blurred vision and watery or mucopurulent discharge. A fungal corneal ulcer classically presents as a dry, raised lesion with crenate or feathery borders, presence of satellite lesions and a thick convex immobile hypopyon.



Fig. 1: Recalcitrant fungal keratitis showing dense stromal infiltrate

Laboratory Diagnosis

Conventional Methods

Staining of tissue scrapings with Gram-stain, 10% potassium hydroxide (KOH) wet mount, lactophenol cotton blue, Giemsa, or calcofluor white.^{1,2,3}

Recent Advances

- Polymerase chain reaction

PCR has emerged as a sensitive and specific test for the diagnosis of fungal keratitis.^{8,9,10} The advantage of

PCR-based tests is that only a small clinical sample is needed for diagnosis and it is rapid. PCR assay takes 4-8 h, whereas positive fungal cultures require on an average of 2-7 days.

● Genotyping

DNA sequence-based methods are used for rapid species identification of an organism. Recent reports suggest that filamentous fungi harbor unique species-specific in vitro antifungal agent susceptibility profiles as well as clinical characteristics.^{11,12,13,14} Thus genotyping may yield important prognostic and therapeutic information that could improve the management of fungal ocular infections. At present genotyping is performed only in selective cases and by few laboratories especially in countries like India.

● Confocal Microscopy

In vivo confocal microscopy (IVCM) uses a series of pinhole apertures to create optical sections of the cornea. It generates images from the cornea with a resolution of 1 μm , which is enough to yield instant imaging of organisms that are larger than a few micrometer such as *Acanthamoeba* cysts and fungal hyphae.¹⁵ The reported sensitivity of IVCM is between 80% and 94%.¹⁶

● Antifungal Susceptibility Testing

Unlike bacterial keratitis, susceptibility testing is not that frequently used in fungal keratitis. Although, a number of studies have reported the sensitivity of antifungals but these studies often suffer from the limitation of small sample size and nonuniformity of data reported on MIC or focus on one particular genus or species.¹⁷

● Smartphone-based digital imaging

Recently Agarwal et al. have reported on the use of smartphone-based digital imaging in diagnosis and follow-up of keratitis.¹⁸ Tissue samples obtained by conventional corneal scraping were stained and imaged using a smartphone coupled with a compact pocket magnifier and integrated light-emitting diode assembly.

Advances in Surgical Management

Recent advances have been made to ensure targeted drug delivery at the site of infection in the form of intrastromal injections, collagen cross-linking (CXL) and rose bengal (RB) aided photodynamic therapy (PDT).

Intrastromal Voriconazole

VCZ is a triazole antifungal agent, structurally related

to fluconazole but with a fluoropyrimidine group in place of triazole moiety.¹⁸ Similar to other triazole agents, it inhibits the enzyme 14-alpha-lanosterol demethylase leading to lower levels of ergosterol, which is an essential component of fungal cell wall.¹⁸

Various routes of administration of VCZ include oral, topical, intracameral, and intrastromal delivery. Intrastromal VCZ has also been shown effective in managing secondary lamellar interface infection for late-onset infectious keratitis after Descemet stripping automated endothelial keratoplasty, *Alternaria* keratitis, recalcitrant *Acremonium* fungal keratitis, and postphotorefractive keratectomy fungal keratitis. Thus, the role of intrastromal VCZ needs further research; however, at this point, it may be considered an alternative in selected recalcitrant cases of fungal keratitis.

Indications :

1. Not showing good response to topical natamycin (5%) and voriconazole (1%) drops.
2. More than half of stromal thickness involvement.

Procedure :

50 microgram/0.1 ml of voriconazole is constituted.

All aseptic precautions should be taken.

0.1ml injected with a 30G needle in midstroma, divided equally in all four quadrants.

Contraindications :

1. Impending or frank corneal perforation.
2. Scleral involvement.
3. Endophthalmitis.

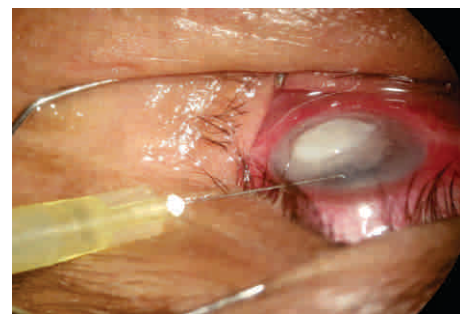


Fig. 2: Intrastromal voriconazole in recalcitrant fungal keratitis

Intracameral Amphotericin B (AMB)

AMB is a first-line treatment for keratitis caused by *Candida* species in many countries, and is used for the management of fungal keratitis in regions where natamycin is not available. AMB is also active against *Aspergillus* species but less effective against

Fusarium species. Intracameral AMB is another approach that is being utilized for targeted drug delivery. The concentration injected ranges between 5 and 10 µg/0.1 ml.

Corneal collagen cross-linking

Corneal CXL has been found successful in halting the progression of keratoconus. Over the last few years there has been much interest in the role of CXL in infectious keratitis. Recently, to distinguish the use of CXL for the treatment of infectious keratitis from CXL for keratoconus, the term photoactivated chromophore for infectious keratitis (PACK)-CXL was created at the ninth cross-linking congress in Dublin, Ireland, in 2013.¹⁹ CXL may act in cases of mycotic keratitis by a direct antifungal effect and by halting the ongoing melting, thus helping to avoid emergency keratoplasty.¹⁹ PACK-CXL has shown anti-fungal activity against pathogens such as *C. albicans*, *Fusarium* species, and *A. fumigatus*.

Rose Bengal Photodynamic Therapy

PDT has been used for numerous applications such as choroidal neovascularization in age-related macular degeneration, corneal neovascularization, for tumor treatment, *Acanthamoeba* keratitis, and to prevent lenticular epithelial cell proliferation.^{20,21} PDT involves the activation of photosensitizers using light of varying wavelengths. The photosensitizer is excited by the light and reacts with oxygen-generating ROS (Reactive Oxygen Species), which, in turn react with various intracellular components to cause cell death.²² Recently, in an experimental study, Arboleda et al. have demonstrated RB PDT to be successful in infectious keratitis.²³

Conclusion

Management of fungal keratitis remains a challenge to cornea specialists. Emerging fungal pathogens and resistance to existing antifungal drugs have further added to the reasons for poor prognosis in fungal keratitis. Newer investigative tools, such as PCR and IVCM (In Vivo Confocal Microscopy) can help in reducing the time gap between clinical suspicion and microbiological diagnosis. Newer antifungal agents and newer methods of targeted drug delivery system can be helpful in treating recalcitrant cases. Nanoparticles and AMPs (Anti Metabolite Products) have shown promise in experimental studies and offer hope for improving prognosis in cases of fungal keratitis in future.

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Recent Advances in Glaucoma Management

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Abstract

Over the last decade several novel medical and surgical treatment options and devices for glaucoma have been developed. The wide variety of topical effective antiglaucoma drugs that are available today, and a few others that are in the development stage, represent significant advancement in ocular therapeutics. This article highlights the recent advances in medical management and discusses newer pharmacotherapy including new molecules with novel mechanisms of action, novel target molecules/genes/tissues, and newer drug delivery systems.

Keywords: Glaucoma, drug delivery systems, gene therapy.

Introduction

Glaucoma is one of the blinding diseases affecting 60 million worldwide.¹ Glaucoma is characterized by slow progressive degeneration of the retinal ganglion cells (RGCs) and the optic nerve axons, leading to increasing deterioration of the visual field. If untreated, the condition can lead to irreversible blindness.² Glaucoma represents a common pathway for different eye conditions, many of which are associated with elevated intraocular pressure (IOP). Reduction of intraocular pressure (IOP) by medical or surgical means has been the standard treatment for glaucoma.

The involvement of excitatory and inhibitory nerve transmitters like glutamates, gamma-amino butyric acid (GABA), glycine and apoptosis can be implicated as a mechanism of progression of glaucoma. Early detection and treatment can slow, or even halt the progression of the disease. However, glaucoma often progresses despite lowering of the IOP to acceptable or normal levels.³

The current research in glaucoma management aims at the development of new drug formulations which have improved efficacy and duration of action, decreasing the need for multiple medications, thereby, decreasing side effect profile and improving adherence and overall quality of life.⁴

Newer Drug Delivery Systems

Surgical Implants

Surgical implants have the potential to deliver drugs for very long period in the eye. For neuroprotective

drugs, however, surgical implants may provide an attractive delivery option. They can facilitate the delivery of the neuroprotective drug to the retina for a prolonged period of time. For example, CNTF can be delivered from a rice-sized implant via encapsulated cell technology for up to a year.⁵ The implants has been studied in a Phase I trial for retinitis pigmentosa; the patients tolerated it well and some showed improvements in visual acuity.⁶

Using one or more of the existing IOP-lowering medications, such slow-release ocular delivery systems that circumvent patient adherence factors may offer an attractive alternative to traditional topical eye drops for many elderly patients.

Liposomes And Nanospheres

Newer Formulations

Although pilocarpine is no longer used commonly, it has been used in the development of novel drop formulations. It has been encapsulated in liposomes and delivered in solution as an eye drop.⁷ Monem *et al*⁷ studied the effect of the charge on the surface of the liposomes on IOP reduction in rabbits. Neutrally charged liposomes resulted in similar IOP reduction but lasted twice as long as the conventional eye drop, suggesting that the liposomes increased the residence time of the drug. This would reduce dosing of pilocarpine from four times daily to twice daily. However, prostaglandin analogs are still easier to use because of its once a day dosing.

The strategy of providing the drug with a carrier that allows it to stay longer on the surface of the cornea is an effective approach to reduce dosing frequency.

However, this technology does not eliminate the fundamental problems of patient adherence and proper administration of topical eye drops.

Contact Lenses as Delivery Vehicles

There has been a great deal of interest in using contact lenses as the delivery device because of its familiarity with clinical practices and patient experiences.⁸ Soft contact lenses are hydrogels, water-soluble polymers that are crosslinked to form networks. Hydrogels have a tremendous number of biomedical applications including drug delivery.⁹ One of the greatest challenges with using hydrogels for drug delivery is that water-soluble drugs, such as those likely to be used in glaucoma, tend to elute very quickly from the highly hydrated polymer networks.¹⁰ However, soft contact lenses, consisting of polymers of *N,N*-diethylacrylamide and methacrylic acid, have been shown to deliver timolol for longer periods (approximately 24 h).¹¹

Contact lenses may be an attractive alternative to eye drops for delivering drugs for glaucoma. One obvious limitation of contact lens delivery system is that it requires patients to wear the contact lens at all times. Another potential limitation is that lenses are generally stored in a hydrated state, which has the potential for the drug to leak out of the lens over time.

Injectable Systems

Injection of existing drugs into the subconjunctival space can lead to prolonged delivery compared with simple topical application, in the order of hours or days.¹² To achieve more prolonged delivery over weeks or months in the subconjunctival space, a delivery vehicle, based on a polymer, is an attractive alternative. Both degradable and nondegradable polymers have been studied for injectable systems for ocular delivery.¹³ Non-degradable polymers such as poly(ethylene-co-vinyl acetate) exhibit long term, constant rates of delivery for a number of drugs;¹⁴ however, their disadvantage is the continued presence of a foreign body with a resulting immune response. Degradable polymers such as poly(lactic acid) or poly(lactic-co-glycolic acid) are an appealing alternative. They can exhibit nonlinear release kinetics with a large initial burst of drug.¹⁵ The burst is particularly more pronounced for hydrophilic drugs because the drug interacts poorly with degradable polymers that tend to be hydrophobic.¹⁶ Fortunately, creative formulation using suitable excipients or additives can greatly reduce the burst effect and lead to greater polymer–drug interaction, resulting in drug

delivery at a rate that correlates with the polymer degradation.¹⁷ These polymers degrade by hydrolysis. The rate of degradation is controlled by the ratio of lactic acid to glycolic acid subunits, the molecular weight of the polymers, and, in the case of poly(-lactic acid), the crystallinity of the polymer. The FDA has approved a number of devices using these materials and much research has been carried out by evaluating these polymers for ocular use.¹⁷

Unfortunately, sustained delivery from degradable polymers have been more difficult to achieve for the traditional IOP-lowering glaucoma medications. One reason for this is the poor drug–polymer interaction. Another reason is that the injectable formulations typically contain particles with very high surface to volume ratios, and the large surface area results in rapid diffusion of the drug from the polymer.¹⁸

For large molecules that may offer neuroprotection (eg, growth factors), additional challenges remain beyond the polymer–drug interaction and high surface area of injectable formulations. The challenges include retaining the bioactivity of the drug once delivered and poor transport to target tissues, specifically the retina and optic nerve.¹⁹ However, intravitreal administration through a small gauge needle can overcome some of these issues.

Topical Medications

Rho and Rho-associated protein kinases

The Rho family consists of three small guanosine triphosphate (GTP)-binding proteins (RhoA, RhoB, RhoC), which regulate aspects of cell shape, motility, proliferation, and apoptosis throughout the body.²⁰ Rho GTPases were first hypothesized to function in aqueous humor outflow in 2001 because of their expression in TM, with the ability to induce calcium-sensitization in smooth muscle contraction in rabbit eyes.²¹

Among the farthest along in the clinical trial process is Ripasudil (K-115), developed by Kowa (Aichi, Japan). During Phase I trials, patients were treated with placebo or K-115 in concentrations of 0.05%, 0.1%, 0.2%, 0.4%, and 0.8% in a stepwise manner, either as a single instillation or repeated twice daily for 7 days. Mean IOP reduction of up to 4.3 mmHg for the highest concentration of treatment was observed 1–2 hours after instillation. Regarding adverse effects, more than half of participants treated with K-115 showed slight to mild conjunctival hyperemia, which spontaneously resolved for all cases within

several hours.²²

Netasurdil (AR 13324) (Aerie Pharmaceuticals, North Carolina, USA) has a dual action of being a ROCK inhibitor and norepinephrine transporter inhibitor. It facilitates uveoscleral outflow in addition to the trabecular outflow and decreases the episcleral venous pressure. Roclatan, fixed-dose combinations of netasurdil with latanoprost 0.005% for once daily night dosing, is in Phase III clinical trial.^{4,23} Although ROCK inhibitors seem very promising in the preliminary trials, many candidates have failed previously, as their selective inhibitory action is highly dose dependent. At higher concentrations, they tend to show unintended cross-reactivity with other protein kinase pathways, resulting in multitude of systemic side effects.⁴

Adenosine receptor agonists

Trabodenoson (INO 8875) (Inotek Pharmaceuticals, USA) is an adenosine A₁ receptor agonist currently in Phase III clinical trial. Phase II trials demonstrated a median IOP reduction of $-6.5 \text{ mmHg} \pm 2.5$ (standard deviation) mmHg at 500 mcg dose by day 28 of trial. It demonstrated a favorable safety profile including an unremarkable electrocardiogram and the conjunctival hyperemias produced were generally mild and transient.²⁴

Can-Fite Biopharma (CF-101) is an adenosine receptor A₃ agonist. When administered orally, in Phase II dry eye trial, a coincidental IOP reduction of 1.1 mmHg at week 12 was noted. This stimulated the idea for potential use of the drug for IOP-lowering therapy. The safety and efficacy of orally administered CF-101 in patients with elevated IOP and primary open-angle glaucoma (POAG) is currently in Phase II trial stage.²⁵

Gene therapy in glaucoma

Treatment of diseases with gene therapy is advancing rapidly. The use of gene therapy has expanded from the original concept of replacing the mutated gene causing the disease to the use of genes to control nonphysiological levels of expression or to modify pathways known to affect the disease.

After gene transfer studies using reporter genes provided proof of concept, a number of potential therapeutic genes have been inserted in viral vectors and delivered intracamerally to the TM of human perfused organ cultures and/or of living animals. To search for those genes whose delivery could result in lowering IOP, scientists have traditionally looked at 3

gene categories: a) genes with mutations associated with glaucoma, b) genes whose expression is altered under glaucomatous conditions, and c) genes that are known to be involved in pathways well-recognized as having an effect on IOP.²⁶ Large number of genes have been tested in animals but no human trials have been successful yet.

Although both adenoviral and lentiviral vectors have been used for RGC gene delivery, AAVs have become the vectors of choice. Adeno-associated vector 2 has a high tropism for RGCs, long-term expression, and low immunogenic profile. The high tropism might be due to the RGCs' high expression of heparin sulfate proteoglycan, which mediates attachment to the AAV2 virus. Adeno-associated viral vectors (AAV) have been used to deliver antiapoptotic genes to the retina in rodent glaucoma models. Intravitreal injections of AAV expressing brain-derived neurotrophic factor have resulted in RGC survival for a month in rodent models with induced OHT.²⁷

Significant challenges remain before gene therapy can be used to treat glaucoma. The tolerance to viral vectors seen in posterior segment applications has not been duplicated in the anterior segment. Continued research to screen specific genes and proteins, improve delivery vectors, and establish more suitable animal models will help realize the potential clinical applications of this promising new therapeutic strategy.

Conclusion

There are many effective topical medications currently available for treating glaucoma. However, their clinical efficacy is limited by inefficient delivery systems, resulting in poor target bioavailability, increased systemic absorption/side effects, and poor patient adherence. Novel, more efficient delivery systems are on the horizon with potential to improve patient care by eliminating patient adherence factor and reducing side effects. Ultimately, these novel delivery systems for both IOP-lowering and potential neuroprotective drugs can lead to better treatment options and preservation of vision in glaucoma.

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Basics of Ocular Surface Squamous Neoplasia

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Abstract

Ocular surface squamous neoplasia (OSSN) encompasses a broad spectrum of neoplastic squamous epithelial abnormalities, including squamous dysplasia, conjunctival intraepithelial neoplasia (CIN), and invasive squamous cell carcinoma (SCC). These neoplastic conditions can affect the conjunctiva and the corneal surface, and occasionally invade into the globe, orbit, and the nasolacrimal system. It can be managed by surgical excision with or without reconstruction, chemotherapy and immunotherapy.

Keywords: Feeder vessels, amniotic membrane transplantation, 5 Fluorouracil (5FU), mitomycin C (MMC), Interferon alfa-2b.

Introduction

Ocular surface squamous neoplasia (OSSN) is a term used to describe neoplastic epithelial abnormalities of conjunctiva and cornea, ranging from Squamous Dysplasia to Invasive Squamous Cell Carcinoma¹. (Figure 1)

Prevalence

OSSN is mostly unilateral and is seen in middle age and older patients. CIN accounts for 39% of all premalignant and malignant lesions of the conjunctiva and incidence of invasive SCC varies from 0.02 to 3.5 per 1,00,000 population². About 75% occur in men, 75% are diagnosed in older patients, 75% occur at the limbus³.

Etiology

Ultraviolet light (UV) exposure, especially in individuals with light skin pigmentation, is a known risk factor for OSSN, and the prevalence of OSSN is higher in equatorial regions of the world. UV-associated mutations in tumor suppressor genes such as *p53* have been demonstrated in OSSN, and hereditary deficiency of DNA repair such as in xeroderma pigmentosum increases the risk of OSSN formation⁴. OSSN is also associated with HPV infection, subtypes 16 and 18, as well as with human immunodeficiency virus (HIV) infection⁵. HIV-associated OSSN is especially common in sub-Saharan Africa, and HIV should be suspected in any patient with OSSN younger than 50 years. Non-HIV-related immunosuppression is also a risk factor for OSSN⁶. Other risk factors include older age

and smoking.



Fig.1: Lesion of OSSN.

Clinical features

Ocular surface squamous neoplasia (OSSN) typically arises adjacent to the limbus, over a pre-existing pinguecula, that is, over an area of solar elastosis, similar to actinic keratosis of the skin⁷. The presence of feeder vessels, intrinsic vascularity and a nodular lesion raise suspicion of invasive SCC. OSSN usually presents either as a fleshy, gelatinous, elevated lesion or as a sessile, papillomatous lesion mostly in the interpalpebral region. Most often vision is not affected unless the lesion is encroaching onto the pupillary area. OSSN patients usually present with a swelling, redness and irritation and one can see large, dilated vessels (feeder vessels) surrounding the lesion⁸. Advanced cases can infiltrate the cornea and sclera and rarely the tumour may extend into the orbit causing proptosis.

Clinically OSSN has myriad presentations. It usually appears as a sessile, fleshy, elevated lesion adjacent to the limbus in the inter-palpebral region. Contrary to

general perception the thickness of the lesion is not always an indication of invasive SCC. Even reasonably thick tumours tend to be confined within the epithelium. The presentation of CIN and invasive SCC is very similar thus making clinical differentiation difficult⁹. Usually the tumour presents as a circumscribed, gelatin-like, sessile, papillomatous lesion with variable degrees of leukoplakia (Figure 2 A–D). One often finds dilated conjunctival blood vessels feeding and draining the lesion. SCC is locally invasive and metastasis is seen in <2% of cases. It can invade intraocular tissues and orbit. Some lesions can be diffuse, flat, and poorly-demarcated without an obvious tumour making early diagnosis difficult. Massive tumours infiltrating the deeper corneal stroma and covering the entire ocular surface are also seen. Infiltrative variants of OSSN masquerading as necrotizing scleritis may pose a challenge in early diagnosis. Rarely pigmented variants of OSSN may be seen making differentiation from conjunctival melanoma difficult⁶.

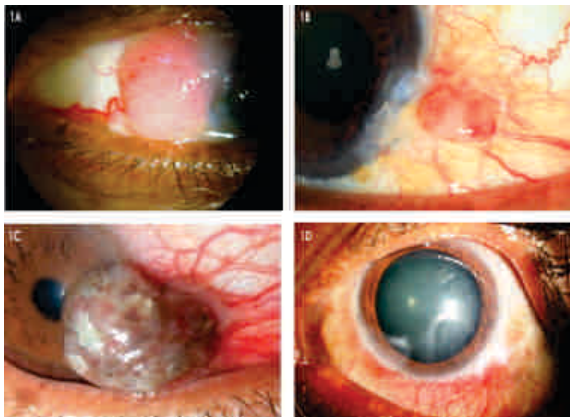


Fig. 2: Varied clinical presentations of OSSN

(A). Slit lamp photograph under diffuse illumination shows papillary ocular surface tumour with prominent feeder (B). Figure shows a globular pink-coloured lesion arising with large feeder vessels. The lesion seems to be overlying a pterygium and was clinically mistaken to be a pyogenic granuloma (C). Figure shows a pigmented OSSN with feeder vessels (D). Slit lamp photograph under diffuse illumination showing large leukoplakic lesions with abnormal vessels.

Diagnosis

The gold standard for the diagnosis of OSSN is the histopathological evaluation of the lesion after an incisional or excisional biopsy. Impression cytology has its limitations in differentiating carcinoma-in-situ from infiltrating carcinoma.

Anterior segment optical coherence tomography (OCT) allows morphologic and even histological characteristics of the tissue to be examined in vivo. The recent introduction of anterior segment OCT has enabled the assessment of the conjunctiva and cornea with high axial resolution of tissue planes. Time-domain, spectral domain and ultra-high resolution (UHR) OCT, axial resolutions of 2–3 microns allow an optical biopsy of ocular surface tissue.

Management

Management modalities in OSSN range from complete excision in well delineated tumours to chemotherapy in diffuse unresectable lesions. Surgical excision with adjunctive cryotherapy was previously considered the treatment of choice for OSSN. However, evidence suggests that microscopic signs of OSSN extend far beyond the macroscopic edges of the tumors, resulting in a relatively high risk of OSSN recurrence after surgery. Medical treatment alone or as an adjuvant has been used increasingly for these tumors. Possible advantages of medical therapy include the ability to treat the entire ocular surface and the potential to avoid the stem cell deficiency associated with extensive surgical excisions. Various topical agents have been advocated, including topical treatment with mitomycin C, 5-fluorouracil, and interferon γ -2b (IFN γ -2b).

Surgery

Complete tumor resection to avoid destructive local invasion, recurrence, and metastasis is an essential issue in the treatment of OSSN. Complete excision with adequate margins is the treatment of choice for most localised lesions. However, reconstruction of large excised areas ensuring both good functional and cosmetic results is as much important and can be very challenging. Surgical excision of OSSN larger than 10-mm base diameter might result in wide tissue defects that cannot be closed primarily. These defects require reconstruction with adjunctive methods such as amniotic membrane transplantation (AMT), transpositional¹⁰ or free flap conjunctival autografting, limbal transplantation and oral mucosa transplantation. The amniotic membrane (AMT) promotes epithelialization by functioning as a substrate for growth of epithelial cells. It also serves as an antiangiogenic, anti-inflammatory, and antifibrotic agent with the help of its structural and biochemical composition¹¹. Alcohol assisted keratoepitheliectomy and lamellar sclerokeratoconjunctivectomy are

indicated for the corneal and infiltrative components respectively.

Chemotherapy

Medical alternatives in the form of topical applications 5 Fluorouracil (5FU) and mitomycin C (MMC) have been extensively reported in the literature. Primary treatment with chemotherapeutic agents for OSSN is largely limited to localised OSSN. Both MMC and 5FU have also been used as adjuvant therapy for recurrent lesions¹². Extensive OSSN with a mean diameter of 40 mm have shown 57% reduction in tumour base after chemoreduction with MMC¹³.

Immunotherapy

In 1994, Maskin was the first to report the use of topical interferon (IFN α 2b) in a multi-focal limbal OSSN¹⁴. Karp reported complete response in five cases of OSSN measuring 4 clock hours of the limbus. Overall topical IFN α 2b is preferred for OSSN which are relatively thinner for complete tumour control (immunotherapy) while combination therapy with topical and injection IFN α 2b is reserved for partial reduction of thicker and extensive OSSN (immunoreduction)¹⁵.

Interferons are protein molecules that bind to cell receptors and trigger synthesis of effector proteins that can inhibit viruses, activate immunocompetent cells, and regulate oncogenes. They alphere a natural defense mechanism. Interferon alfa-2b is a recombinant form of interferon alfa that is approved by the US Food and Drug Administration for treatment of chronic hepatitis B and C, malignant melanoma, hairy cell leukemia, multiple myeloma, follicular lymphoma, condyloma acuminata, and AIDS-related Kaposi sarcoma.

Interferon alpha-2b has become an ideal topical chemotherapeutic agent to treat selective cases of ocular surface squamous neoplasia (OSSN) due to its efficacy and low toxicity. Interferon has been used effectively for CIN using intralesional/subconjunctival injection (3 million IU in 0.5 ml) combined with topical IFN α 2b (1 million IU/ml four times a day). Perilesional and subconjunctival interferon, similar to the intramuscular injections given to patients with hepatitis, can cause systemic side effects, including transient fevers and myalgias in some patients. Patients may feel like they are developing “flu-like” symptoms for 2 or 3 hours after the interferon injections. This is usually ameliorated by acetaminophen. Occasional flu-like symptoms and

ocular surface irritation are sometimes seen in patients after treatment with IFN α 2b. Cost of IFN α 2b remains to be a major disadvantage of IFN α 2b therapy especially in the developing world¹².

In conclusion, considering the difficulty of complete eradication and potential surgical complications associated with treating OSSN, we believe that topical IFN α 2b is effective as a single therapy in the management of primary OSSN with minimal selflimited adverse effects. It may provide the least invasive way of treating OSSN, and it appears to be a safe alternative to radiation, topical mitomycin C, intralesional IFN α 2b injection, and surgical excision with cryotherapy

Prognosis

The overall prognosis in OSSN is good. Modern treatment strategies are effective with local recurrence rates reported to be 5% and regional lymph node metastasis at <2%. Aggressive variants like muco-epidermoid and spindle cell carcinoma and OSSN in immunocompromised patients have a worse prognosis.

Conclusion

Histopathology is the gold standard in the diagnoses of various grades and types of OSSN, and gives a fair understanding of the disease prognosis. Conjunctival impression cytology could be a diagnostic aid or to confirm flat corneal–limbal lesions.

Future studies are needed to understand the pathogenesis of OSSN and the role of various carcinogens specifically HPV and HIV in varied manifestations of the disease process and their role in prognosis of disease. Further work is required in the diagnoses of OSSN with the aid of UHR, OCT and confocal microscopy. While complete excision with cryotherapy gives excellent results with localised lesions, newer modalities like immunotherapy hold a promise in the larger, unresectable and recurrent lesions.

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Malignant Glaucoma - An Overview

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Abstract

Malignant glaucoma is characterised by elevated IOP with a shallow or flat anterior chamber and patent iridotomy. It usually follows intraocular surgery. Shaffer proposed posterior segment pooling of aqueous due to a blockage of the normal anterior aqueous flow by an abnormal vitreo-ciliary relationship calling it ciliary block glaucoma. Women are three times more likely than men to develop malignant glaucoma. Examination reveals shallow or unequal anterior chamber, progressive shallowing of the anterior chamber, increasing myopia and elevated IOP. Choroidal detachment and suprachoroidal hemorrhage need to be ruled out. Treatment options include medical and surgical modalities. Malignant glaucoma is one of the most complex and difficult of all the glaucomas to treat, and it can progress to permanent blindness without prompt intervention. Hence, timely diagnosis and treatment are of utmost importance.

Keywords: UBM, malignant glaucoma, intraocular pressure.

Introduction

The term “malignant glaucoma” was coined by Von Graefe in 1869 to describe an aggressive form of postoperative glaucoma that was resistant to treatment and resulted in blindness. This rare form of glaucoma generally follows surgery for primary angle closure glaucoma and is characterised by elevated IOP with a shallow or flat anterior chamber and in the presence of a patent iridotomy. Malignant glaucoma is also known by aqueous misdirection, ciliary block and cilio-lenticular block glaucoma. It usually follows intraocular surgery but has also been described following laser iridotomy.^{1,2}

Mechanism

The exact mechanism behind its aetiology is still not clearly understood. Shaffer proposed posterior segment pooling of aqueous due to a blockage of the normal anterior aqueous flow by an abnormal vitreo-ciliary relationship calling it ciliary block glaucoma. This theory is backed up by the finding of anterior rotation of the ciliary body on ultrasound examination, and ciliary processes in direct contact with the lens equator.³ Epstein and colleagues proposed anterior displacement of the vitreous due to posterior diversion of aqueous. According to this theory, the accumulation of aqueous within the posterior segment forces the ciliary body and the anterior hyaloid face forward, shallowing the anterior chamber and causing secondary angle closure.⁴ Quigley and colleagues believe that the cause for

malignant glaucoma is the inability to generate sufficient fluid flow across the vitreous to compensate for aqueous outflow anteriorly under the higher pressure conditions generated by choroidal expansion. Choroidal expansion increases the eye pressure leading to increased anterior aqueous outflow. The ability to transmit fluid through the vitreous cavity is limited. When transvitreal flow is insufficient to equalize the pressure differential, the vitreous gel moves forward, carrying the lens and iris with it, which causes direct angle closure by physically pushing the iris against the trabecular meshwork with a shallow or flat anterior chamber.⁵ Hence, the shallowing of the anterior chamber is associated with forward displacement of the lens-iris diaphragm. Whether this anterior movement allows a change in the anatomical configuration of the structures involved thus allowing diversion of aqueous posteriorly, or whether the increase volume of the aqueous causes this forward displacement, is not clear.

Risk factors

Malignant glaucoma occurs in 2 to 4 percent of eyes undergoing surgery for angle-closure glaucoma.⁶ It may also occur after cataract extraction with or without IOL implantation, glaucoma drainage implantation, laser iridotomy, capsulotomy, laser suture lysis or argon laser photocoagulation, miotic therapy, needling of filtering blebs, viscoelastic use or intravitreal injection. Women are three times more

likely than men to develop malignant glaucoma. Other risk factors are hyperopia, chronic angle closure with plateau iris configuration, nanophthalmos or a history of malignant glaucoma in the fellow eye.

Diagnosis

Examination reveals shallow or unequal anterior chamber, progressive shallowing of the anterior chamber, increasing myopia and elevated IOP. Most cases occur in the presence of a patent peripheral iridotomy, though cases have been reported without an iridotomy. choroidal detachment and suprachoroidal hemorrhage to be ruled out. In the absence of a history of surgery other causes of secondary angle closure including intumescent lens, choroidal neoplasm, central retinal vein occlusion, and secondary pupil block must be excluded.

Imaging

UBM has documented anterior rotation of the ciliary body with forward rotation of the lens-iris diaphragm, relaxation of the zonular apparatus leading to angle closure. AS-OCT is similar to UBM although details behind the iris are not reliably seen in AS-OCT.

Management

Medical

This consists of cycloplegic drops (and/or subconjunctival Mydracaine), topical β blockers, aproclonidine, oral carbonic anhydrase inhibitors and, if necessary, oral glycerol or intravenous mannitol. This combination shrinks the vitreous, decreases aqueous production, and encourages backward displacement of the lens-iris diaphragm. The effect of medical therapy is often not immediate, but approximately 50 percent of cases will be relieved within five days³.

Laser

Direct argon laser through a peripheral iridectomy may be used in an attempt to shrink the ciliary processes and thus relieve cilio-lenticular block to anterior flow of aqueous. Nd-YAG laser may be used to perform posterior capsulotomy/hyaloidotomy.

Surgery

When laser therapy is not possible or is unsuccessful, posterior vitrectomy should be performed with disruption of the anterior hyaloid face. Once the anterior chamber deepens and the IOP has been normalized, medical treatment can be withdrawn gradually.

Conclusion

Malignant glaucoma is one of the most complex and difficult of all the glaucomas to treat. It can progress to permanent blindness without prompt and timely intervention. Hence diagnosis and treatment are of utmost importance.

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Endoscopic Pars Plana Vitrectomy

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Abstract

Endoscopic Pars Plana Vitrectomy (PPV) is more capable than routine PPV due to its two fundamental surgical advantages: (1) bypassing anterior segment opacities, and (2) visualizing anteriorly positioned structures such as the ciliary bodies and sub-iris space. In this article, the present state of the ophthalmic endoscope is reviewed along with its multitude of applications in glaucoma, vitreoretinal, and ocular trauma surgery. This review examines both the advantages and dis-advantages of application of endoscopic PPV.

Keywords: Pars plana vitrectomy, endoscopy, endocytphotocoagulation.

Introduction

The word “Endoscope” has been derived from the following two Greek words – endon, meaning inside, and skopin, meaning to view. In 1934, Thorpe described the ophthalmic application of endoscopy, and designed an instrument for removal of nonmagnetic intraocular foreign bodies (IOFB).¹ After combining a Galilean telescope and an illumination source within a 6.5 mm diameter shaft, Thorpe attached an eyepiece for direct monocular vision and the device was inserted into the globe through 8 mm scleral incisions. The ophthalmic endoscope was reviewed and improvised in 1978 by Norris and Cleasby, who introduced a 1.7 mm diameter (between 13 and 14 gauge) rigid shaft for endoscopic intraocular and orbital surgery.^{2,3,4,5} The popularization of pars plana vitrectomy (PPV) soon thereafter complimented this advancement. By 1990, Volkov et al developed flexible endoscopes^{6,7} and Eguchi and Arai coupled a flexible 20-gauge video-endoscope with a charge-coupled device (CCD) camera for remote visualization of real time images,⁸ similar to modern ophthalmic endoscopes. Laser units were implemented into endoscopy soon thereafter.^{9,10}

Literature on the use of endoscopy in vitreoretinal surgery is relatively limited, but has demonstrated the technique's usefulness in well-conducted case reports and small retrospective studies. Studies have reported indications including penetrating injuries,^{11,12,13,14,15} perforating injuries of the globe,¹⁶ intraocular foreign bodies, post-traumatic endophthalmitis,¹³ endogenous, post-cataract and bleb-related endophthalmitis,¹³ proliferative vitreoretinopathy (PVR), and even retinal assessment in forensic cases. During these procedures, the endoscope can bypass anterior segment opacities, or serve to enhance visualization while using other wide-angle microscopic viewing systems.

Advantages of Endoscopic PPV

The endoscopic view provides two fundamental advantages: (1) bypassing anterior segment opacities, and (2) visualizing anterior structures such as the ciliary bodies and sub-iris space.

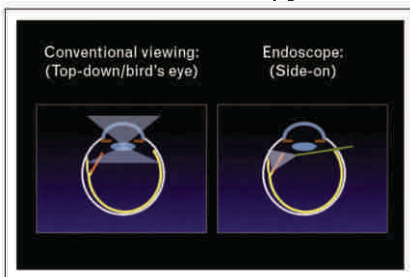


Fig. 1: Diagram showing difference in views of conventional and endoscopic approach

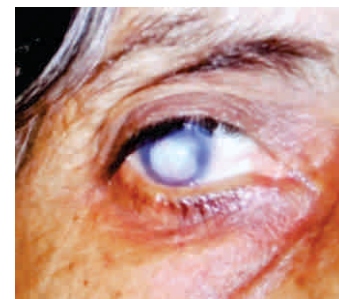


Fig. 2: Figure showing dense corneal opacity necessitating endoscopic PPV.

Endoscopic PPV is useful over Wide Angle contact or non contact lens PPV as follows-

- Bypassing media haze and/ or disorganised Anterior Segment – Severe traumatic eye leading to hazy cornea or endophthalmitis.
- PPV in micro cornea,
- Improves corneal graft survival by reducing endothelial cell loss.
- In patients where temporary keratoprosthesis (TKP) is not available or cannot be replaced by permanent keratoprosthesis (PKP), early intervention leads to less proliferative vitreoretinopathy (PVR).
- Visualizing anterior structures such as the ciliary body and sub-iris space
- Endoscopy is also an effective method for visualizing and manipulating anterior structures such as the posterior iris surface, ciliary body, pars plana, ora serrata and peripheral retina. Variable planes of visualization can facilitate anterior vitrectomy, membrane peeling and sclerotomy placement, and also enhance diagnostic visualization. It can be used for:
 - Difficult-to-access diseases
 - Undetected retinal breaks
 - Scleral Fixated PCIOL(SF PCIOL) in children
 - Endocyclophotocoagulation :

In a few cases if the iris is heavily pigmented, laser beam is set too high or probe is too close to the tissue; aqueous may evaporate and may be seen in the form of bubbles. This in particular can be corrected by moving the probe farther away or reducing the power of the laser.

The unique endoscopic view of sutured intraocular lenses, sub-iris and ciliary body abscesses, and anterior PVR precludes aggressive scleral depression, which is to be avoided in eyes with recent open globe surgery, unstable intraocular lenses and filtering blebs.

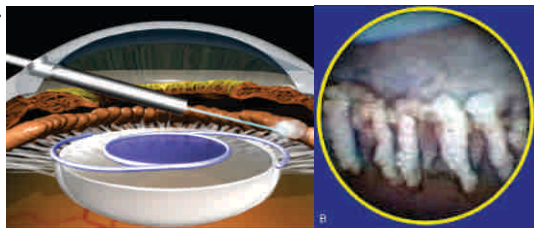


Fig. 3 : Diagram showing A) Endocyclophotocoagulation being performed on a pseudophakic patient B) Endoscopic view of ciliary processes.

Direct visualization of sclerotomy creation allows the maneuver to be performed atraumatically. In aphakic eyes, the endoscope can be initially inserted through a limbal incision, and sclerotomies can be created under transpupillary visualization.¹² The placement of sclerotomies may be complicated by ciliary and choroidal hemorrhage or anterior displacement of the vitreous base and retina; imprecise sclerotomies may result in subciliary, subchoroidal, or subretinal placement of the infusion line. The intraocular view of endoscopy can prevent such complications.

Limitations

Present model of ophthalmic endoscopy does not allow for bimanual instrumentation.

Anterior opacities can be overcome by endoscopy for PPV but post-op visualization of retina is not possible.

Increased rehabilitation period owing to secondary reconstructive surgery of the anterior segment(if performed).

Cautions

The endoscope has to be correctly inserted without forming a false track going behind retina or choroid.

This should always be ensured that endoscope is in the vitreous cavity before beginning vitrectomy.

It is advisable to begin being away from the retina to avoid pulling in the retina/ choroid inadvertently.

Curved endoscopy probe can avoid the touching of the crystalline lens by mistake.

Conclusion

Since its beginning- nearly 80 years ago, the ophthalmic endoscope has evolved to confer various advantages in surgical procedures. These include bypassing anterior segment opacities and permitting otherwise seemingly impossible vitreoretinal surgery. As of now, however it cannot replace the conventional method of PPV.

In future, the field may benefit further from 23-gauge endoscopic probes, which may also prove to be an effective vehicle for retinal vascular cannulation or for delivering cells or therapeutic agents subretinally.

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Lateral Rectus Palsy-Diagnosis and management

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Abstract

Lateral rectus palsy is the most common extra-ocular muscle paralysis. The abducens (sixth) cranial nerve controls the lateral rectus muscle. Because of its long tortuous course, and the location of the peripheral part of the nerve near the clivus as it enters the area of the cavernous sinus, elevated intracranial pressure due to any cause may tether the nerve. Esotropia in primary position is the chief complaint of the patient. There is a myriad of causes for sixth nerve palsy. In adults conservative treatment followed by surgery if needed is the management strategy employed while in pediatric age-group, prevention of amblyopia followed by maintenance of cosmesis is the sequence of priority usually followed. The following article presents the clinical presentation, causes, diagnosis and management of sixth nerve palsy through illustration of cases.

Keywords: Lateral rectus, esotropia, amblyopia.

Clinical Presentation

Patient presents with esotropia in primary position due to the unopposed action of the antagonistic medial rectus muscle and is proportional to loss of LR function (Fig1). The esotropia increases in the direction of the paralysed muscle. Later on, secondary MR contracture occurs which further limits weakened abduction function and esotropia occurs in contralateral gaze too. Patient usually has compensatory face turn to maintain fusion and avoid diplopia (Fig 2). Anomalous head posture should be recorded for both distance and near. Ocular deviation should be measured with face turn and with forced primary position and in lateral gaze and upgaze and down gaze for distance and near using prism bar cover test. V pattern may result from lessened abduction and unopposed action of MR in down gaze. There may be presence of vertical deviation less than 3 PD due to removal of inhibitory effect of LR on vertical movements. If hyperdeviation is larger than 5 pd, rule out 4th nerve Palsy too. Ocular motility examination should be done including ductions and versions to differentiate palsy from paresis.



Fig. 1 : Presence of esotropia in primary position in top image, the bottom image showing limitation of abduction in left eye.



Fig. 2 : Left face turn of a patient with left lateral rectus palsy

Symptoms

Diplopia- A patient with acquired sixth nerve palsy usually presents with complaint of binocular horizontal diplopia both for distance and near while a case of divergence paresis usually has diplopia for distance. Initially with near fixation equilibrium in convergence can occur without diplopia but later on with greater and older deviations and with secondary contractures permanent diplopia occurs for distance and near. Diplopia is more bothersome in acquired palsy while in congenital palsy (Fig 3), children usually adopt compensatory head posture. Their parents usually present as esotropia with apparent abduction limitation as the chief complaint and these category of patients have to be differentiated from esoduanes syndrome (Fig 3a) and infantile esotropia (Fig 3b). Doll's head maneuver helps to detect true abduction limitation from apparent one seen in infantile esotropia while in duanes syndrome the deviation in primary position is small as compared to amount of limitation. Ideally Diplopia charting should be done at distance of 1m and also Hess

charting should be done to look for underaction and overaction of extraocular muscles and also to prognosticate the case.



Fig. 3 : Congenital right sixth nerve palsy



Fig. 3a : Case of Esoduane's in right eye



Fig. 3b : Case of infantile esotropia with apparent abduction limitation

Causes of lateral rectus palsy

Children

- Infections-Meningitis due to viral infections like CMV, EBV, Influenza, Varicella zoster etc (Fig 4). Others being Lyme disease, streptococcus, brain abscesses etc.¹
- Trauma- head trauma, skull fracture (Fig 4a).
- Neoplasm- Primary neoplasm like pontine glioma, astrocytoma, chondrosarcoma etc and secondary neoplasm like neuroblastoma, small cell carcinoma and rhabdomyosarcoma.²
- Miscellaneous neurologic conditions like Arnold-Chiari malformation, demyelinating disease, hydrocephalous etc. Transient sixth nerve palsies in neonates may be caused by elevated intracranial pressure due to forceps or vacuum extraction, hypoxia or temporary edema caused by birth process.³



Fig. 4 : Bilateral lateral rectus palsy in child with meningitis



Fig. 4a : 7 years old child with traumatic right sixth nerve palsy

Adults

Most common age is 40 to 50 years, the cause being vasculopathies due to hypertension, diabetes, atherosclerosis and arteriovenous malformations,⁴ and in older age group giant cell arteritis can be a cause. Just like pediatric age group, infections (Fig 5), trauma, neoplasms² constitute other causes. Iatrogenically it can be caused in myelography, nerve blocks in head and neck and spinal or epidural anesthesia.⁵



Fig 5-Left lateral rectus palsy in case of chikungunya fever

Diagnosis

History

The history of the pattern of onset and associated symptoms can be very important in determining the etiology of an abducens nerve palsy. Sudden onset of abducens nerve palsy suggests a microvascular etiology.⁶ Conversely, slowly progressive onset suggests a compressive etiology. Subacute onset suggests a demyelinating process as a possible etiology. Associated pain suggests a microvascular etiology. If a patient has a lesion causing the abducens nerve palsy which affects other structures in the brain, other neurologic signs may be present. Recurrent episodes of lateral rectus palsy may be present in ophthalmologic migraine and aberrant antero-cerebellar artery.

Symptoms

Acute onset horizontal diplopia is usually the presenting symptom. The diplopia is also worse in the direction of the palsied muscle and gets better in the contralateral gaze (incomitant).

In cases of abducens nerve palsy due to raised intracranial pressure, patients may experience associated symptoms of headache, pain around the eyes, nausea, or vomiting. Associated pain suggests a microvascular etiology. If the etiology of the abducens nerve palsy is a brainstem lesion affecting the sixth cranial nerve fasciculus, there may be associated ipsilateral facial weakness, contralateral hemiparesis, or sensory abnormalities. In the involvement of the meninges, superior orbital fissure, orbital apex, or cavernous sinus, other ipsilateral cranial nerves are also involved.

Signs

There is esotropia of the involved eye in primary gaze, increasing on attempted abduction of the same eye. Compensatory face turn may be assumed if there is meaningful field of binocular single vision.

The diagnosis is fairly clinical, though investigations are needed to rule out the cause of the lateral rectus palsy. There should be emphasis on differentiating between paresis, palsy and restrictive cause for the impaired function of lateral rectus muscle because it guides the treatment modality for the same. In paresis saccadic velocity of LR is 175 degrees/s while it is less than 100 degrees/s in palsy. Forced generation test is reduced in paresis and absent in palsy. Abduction is restricted in on FDT in case MR is fibrosed secondary to contracture.

Investigations

Blood studies include a fasting blood glucose determination, complete blood cell count, ESR, ANA titres, rapid plasma regain test, fluorescent treponemal antibody test, thyroid function test and so on. Lumbar puncture test and edrophonium test may be required. Orbital USG may be obtained to rule out enlarged extraocular muscles.

Differential diagnosis

Differential diagnosis for unilateral lateral rectus palsy include congenital absence of lateral rectus, congenital fibrosis, disinsertion or dehiscence of lateral rectus muscle, excessive medial rectus resection or lateral rectus recession, medial orbital wall fracture, horizontal gaze palsy etc. Differential diagnosis for bilateral lateral rectus palsy are convergence spasm, divergence excess, infantile esotropia etc.⁷

Management

Non surgical

In children upto 4 years of age aim is to prevent amblyopia and preserve binocular fusion. There standard amblyopia therapy should be given. Alternate occlusion to prevent MR contracture can be applied. Fresnel add-on prisms may be given and reduced as the palsy improves. In adults with acute sixth nerve palsy, aim is to prevent secondary MR contracture and to create a meaningful area of binocular vision, any patients spontaneously recover especially if palsy is associated with diabetes (Fig 6). Recovery is the rule within 6 months. Botulinum toxin to weaken the MR might be used if diplopia is too incapacitating. Botox should be given in the first 2 months before the contracture of medial rectus

develops. 2.5 IU are given in the belly of medial rectus muscle 10 mm from the insertion. For residual esotropia prisms can be prescribed.⁸

Surgical

If recovery does not occur beyond 6 months, partial sixth nerve palsy or paresis can be managed with any one of the following depending on severity – MR recession, LR resection, both combined or the combination can be further supplemented with contralateral eye MR recession. Total sixth nerve palsy has to be managed with a transposition procedure combined with or without a botulinum toxin injection pre-operatively, intraoperatively or postoperatively depending on the surgeon. Recently superior rectus transposition with or without augmentation and with MR recession if FDT is positive due to contracture is recommended or other option is partial Vertical rectus transposition can be done.⁹

Prognosis

The prognosis for sixth nerve palsy depends on the underlying etiology. Rush and Younge reported a recovery rate of 49.6% in 419 nonselected sixth nerve palsy cases, and a higher rate of 71% in 419 patients with diabetes mellitus, hypertension, or atherosclerosis.¹⁰



Fig. 6 : Showing recovery in a patient with idiopathic sixth nerve palsy in left eye

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Fundus Autofluorescence in Retinal Imaging



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Abstract

Fundus autofluorescence (FAF) is a relatively new imaging technique which can be used to study retinal diseases. It provides information on retinal metabolism and health. Several retinal pathologies can be detected using this investigative modality. Peculiar AF alterations can help the clinician to monitor disease progression and to understand its pathogenesis in depth. In the present article, we review FAF principles and its clinical applications.

Keywords: Fundus autofluorescence, retinal imaging, fluorophores.

Introduction

Fundus autofluorescence (FAF) is a non-invasive imaging technique that detects fluorophores. Fluorophores are naturally occurring molecules that absorb and emit light of specified wavelengths. Hence this is a novel non-invasive imaging technique providing in-vivo information on retinal status. It is commonly employed in clinical practice to diagnose and study several retinal pathologies.¹

Methods

Lipofuscin (LF) and melanolipofuscin are the main fluorophores acting as sources of retinal AF. These fluorophores which exist endogenously are used to acquire FAF images. FAF can show changes in the integrity and metabolism of retinal cells by detecting pathological accumulation or depletion of fluorophores within the retinal pigment epithelium (RPE) cells.² Retinal pigment epithelium is a monolayer of approximately hexagonal cells located between the neurosensory retina and the choroid. Its functions include rod's outer segment (OS) phagocytosis.² Each RPE cell supports approximately 45 photoreceptors and phagocytes approximately 3 billion OS cells over a lifetime. The by products of this process are stored in lysosome residual bodies as LF.^{3,4}

LFs are ubiquitous lipoprotein pigments accumulating in post-mitotic cells in nervous, myocardial and retinal cells during ageing. LF occupies approximately one-third of the RPE cells cytoplasm over the age of 70. These emit AF when excited by specific wavelengths. N-retynilidene-N-retynilethanolamine (A2E) represents the LF's major fluorophore. It accumulates in the lysosomes due to non-recognition by lytic enzymes.⁵ Its chemical

structure is responsible for the detergent-like action on the RPE cells membranes. Its conjugated double bonds promote light absorption and fluorescence emission.

Autofluorescence Imaging Techniques

FAF was observed for the first time during vitreous fluorophotometry. Ruckmann et al introduced the confocal scanning laser ophthalmoscope (cSLO) that elicits retinal AF by scanning the retina with a low-powered laser beam. This technology adopts confocal optics and overcomes the interference of autofluorescent preretinal structures like the crystalline lens. Confocal optics ensure that the reflectance of the scanning laser and the retinal fluorescence are derived from the same optical plane. The exciting and emitting filters of standard confocal ophthalmoscopes are 488 nm (blue light), and 500–520 nm respectively. So c SLO-AF is also called blue-AF or short-wavelength (SW)-AF.^{4,6}

Confocal Scanning Laser Ophthalmoscope (cSLO)	Modified Fundus Camera (mFC)
One excitation wavelength (laser source) Large emission spectrum (cut-off filter)	Bandwidths filters for excitation and emission
Continuous scanning at low light in a raster pattern intensities	One single flash at maximum intensities
Confocal system	Entire cone of light
Laser power fixed by manufacture, gamma detector sensitivity	Flash light intensity, and gain of detector adjustable.
Automatic real time image processing with averaging of single frames and pixel normalization	Manual contrast and brightness

Table1: showing differences between cSLO and modified fundus camera (mFC)

Near infra-red (NIR)-AF also uses confocal optics, but with longer exciting wavelength (790 nm). The emission is above 800 nm and its signal is 60–100

times weaker than in blue light AF. Melanin is the main fluorophore in NIR-AF. Fluorescence is more intense in choroidal tissue and RPE cells due to higher melanin density.^{5,7}

Fundus cameras can also be adapted to provide FAF images projecting a single flashlight on the entire retina at one time. But they don't have a confocal optic system, so the AF gets elicited from pre-retinal structures, such as crystalline lens. Potential interferences may be overcome using specific filters with longer wavelength (excitation filter 535–580 nm, barrier filter 615–715 nm). This type of FAF is also called green AF.⁸

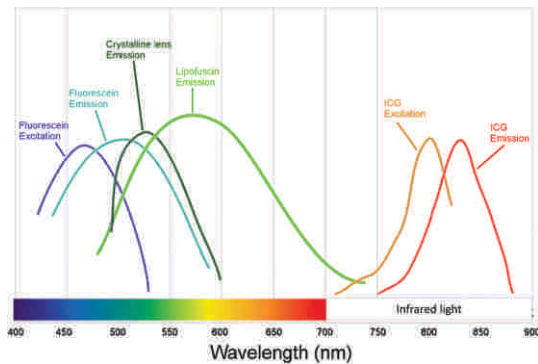


Fig. 1: showing wavelength emission in autofluorescence

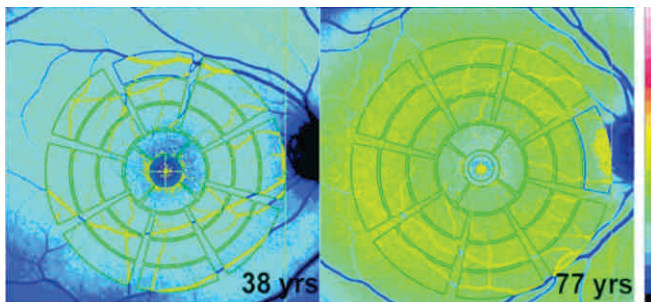


Fig. 2: Showing the difference in AF in younger and elderly age groups

Fundus autofluorescence in retinal disorders

AF in Age related macular degeneration (AMD) and Drusen

Fundus autofluorescence can exhibit topographic changes in intensity in the presence of retinal disease such as age related macular degeneration (AMD). Areas of markedly deficient or absent fundus autofluorescence, signals are recognized as regions of RPE and photoreceptor cell demise. Loss of the RPE cell monolayer have been confirmed by OCT (optical coherence tomography) in geographic atrophy(GA).⁸ These areas of atrophy have been observed to expand with time but rates may vary considerably among

individuals. In fundus autofluorescence images this junctional area is often marked by elevated levels of brightness. With time, outward enlargement of GA occurs, but outward extension of the band of elevated autofluorescence always precedes growth of the area of absent autofluorescence (atrophy).⁹⁻¹²

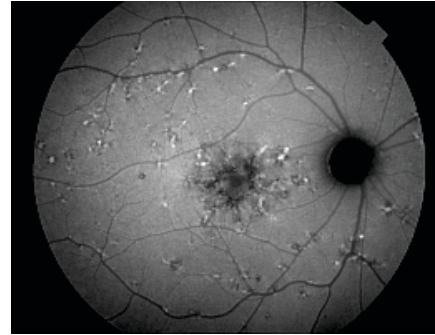


Fig. 3: Showing AF in AMD

Drusens have an extremely variable appearance on FAF depending on size, composition, and health of the overlying RPE and ellipsoid layer. Large drusens are more likely to result in FAF changes, while small drusen may be iso-autofluorescent and remain undetected.¹³

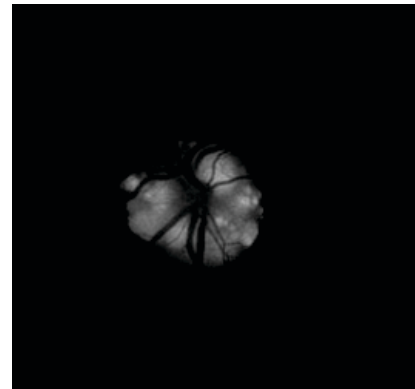


Fig.4: showing AF in optic nerve drusens

Neovascular AMD is defined by the presence of choroidal neovascularization, which is located either above, below the RPE or located intraretinally which originates from the deep retinal capillary plexus. Early choroidal neovascularization is not readily detectable on FAF due to intact RPE and photoreceptor layers. Classic choroidal neovascularization appears hypo-autofluorescent due to blockage of the RPE by the type 2 fibrovascular complex in the subretinal space. Occult neovascularization is hypo-autofluorescent due to associated atrophy of the overlying RPE.^{11,13}

Hemorrhages and exudates are initially hypo-autofluorescent due to excitation light absorption, but then may become hyper-autofluorescent after undergoing organization. Fundus autofluorescence

patterns in non-neovascular AMD may predict the development of choroidal neovascularization. Linear and reticular patterns are also associated with increased risk for choroidal neovascularization.¹²

RPE tears are a well-known complication of neovascular AMD. They are most commonly associated with large (greater than 600 microns in height) fibrovascular PEDs. RPE tears can occur spontaneously or following photodynamic therapy or anti-VEGF therapy due to accelerated contraction of the neovascular complex exerting traction on the RPE monolayer. RPE tears appear as a well-demarcated area of hypoautofluorescence due to absent RPE. Adjacent hyperautofluorescence is due to the rolled redundant RPE. Later, tears remodel and resurfacing occurs, with recovery of autofluorescence extending centripetally from the borders toward the center.

Auto fluorescence in other retinal pathologies

ABCA4-related disease and cone-rod dystrophies of other origins can present with autofluorescent rings that surround decreased or absent foveal autofluorescence. They progressively expand with time. These rings co-localize with areas of reduced visual sensitivities.¹¹

Best's macular dystrophy is an early-onset macular dystrophy resulting in central vision loss. This is due to autosomal dominant mutations in the BEST1 gene, encoding bestrophin-1. Shed photoreceptor debris and lipofuscin accumulate in the subretinal space resulting in bilateral yolk-like lesions in the macula.^{9,11}

The vitelliform stage of disease has well-circumscribed, homogenous hyper-autofluorescence in the macula. The pseudohypopyon stage shows a gravitational layer of hyper-autofluorescence settling under iso-autofluorescent fluid. The vitelliruptive stage showed a dark lesion bordered by condensations of hyper-autofluorescent material. The atrophic stage is characterized by diffuse decrease in signal due to chorioretinal atrophy.

Pattern dystrophies refer to a collection of late-onset, symmetric macular dystrophies with a clinically stable, benign course. They are commonly associated with autosomal dominant mutations in the PRPH2 gene on chromosome 6. This gene codes for a membrane glycoprotein on rod and cone photoreceptor outer segments. As a result, yellow, orange, or gray material accumulates subretinally or at the level of RPE leading to hyper-autofluorescent lesions.¹³

Retinitis pigmentosa (RP) refers to a genetically

heterogeneous group of retinal dystrophies characterized by the degeneration of rod photoreceptors. FAF is a viable supplemental imaging modality to monitor RP and correlate phenotype with genotype. The hyper-autofluorescent ring, known as the Robson-Holder ring, corresponds to the border of inner/outer segment junction disruption. This ring corresponds to outer segment dysgenesis and lipofuscin production.¹⁴ The normal retina lies within the ring. Spatial preservation of retinal sensitivity as measured by multifocal ERG correlates with the radius of the autofluorescent ring, indicating intact retinal sensitivity.

Similar hyper-autofluorescent rings are also seen in several other retinal dystrophies, including Leber's congenital amaurosis (LCA), bull's eye maculopathy, X-linked retinoschisis, Best macular dystrophy, cone dystrophy and cone-rod dystrophy. This shared phenotype on FAF suggests an underlying common mechanism for the pathogenesis of retinal dystrophies.

Choroideremia is an X-linked recessive defect in the CHM protein which encodes the rab escort protein (REP1). They begin in adolescence. Male carriers experience night blindness and visual field constrictions due to centripetal atrophy of the choroid, RPE, and photoreceptor layer but the macula is spared. FAF shows bilateral, symmetric, midperipheral zones of hypo-autofluorescence due to RPE atrophy, which have scalloped edges with a preserved area of central stellate autofluorescence. The atrophic zones extend with age and eventually involve the fovea.¹³

Fundus albipunctatus results from an autosomal recessive defect in RDH5, which encodes a retinol dehydrogenase in the RPE. Patients are unable to oxidize 11-cis-retinol to 11-cis-retinal.³ This impairment of rhodopsin recycling, delays the regeneration of photoreceptor pigments which manifests as delayed dark adaptation and stationary night blindness. Due to decreased lipofuscin production there is severely attenuated background autofluorescence. In SD-OCT these lesions reveal dome shaped hyper-reflective material extending from the RPE.

Multiple evanescent white dot syndrome (MEWDS) is a disease affecting young, healthy women 20–50 years old and manifests as a self-limited, unilateral presentation with multifocal 100–200 µm white spots scattered in the paramacular and mid-peripheral fundus.¹⁵ On FAF, the multifocal lesions have

increased signal strength due to photoreceptor loss and unmasking of natural RPE autofluorescence. Hypo-autofluorescent foci at the fovea correspond with foveal granularity on fundus and accumulation of hyper-reflective material interdigitating between the RPE and photoreceptor layer on OCT.

Discussion

It is possible to expand the comprehension of retinal disease pathogenesis and to monitor their course. Fluorescence reference systems compare FAF images taken in different subjects or at different times. For precise measurement, AF can also be averaged between different retinal zones or acquired at specific desired points. Optical aberrations may be reduced by incorporating adaptive optical systems in the FAF devices. They allow to image the retinal cells with a cellular-level of resolution. Ultra-widefield non-contact imaging system enable the clinician to visualize the retina with a 200° field of view.

Retinal metabolism is now investigated with a novel technique named fluorescent lifetime imaging ophthalmoscopy. It employs a modified SLO device that detects the alterations in the lifetime AF signal with a single-photon counter. The AF lifetime is longer with age and shorter in the central retina than in the periphery in healthy eyes.

At present, there are no reference databases to classify the normal and pathological FAF phenotypes. The inter-individual and intra-individual variability of media opacities, refractive error and cellular LF content and genetic expression during the ageing process, make the possibility to develop such database likely challenging.

Conclusion

Fundus autofluorescence provides information regarding the metabolic state and overall health of the RPE and photoreceptor layer. FAF is now a non-invasive tool for the evaluation of the prognosis and progression of several diseases. It is now extensively used in geographic atrophy in AMD and phenotypic characterization of retinal dystrophies. FAF is also critical in the diagnosis of white dot syndromes and drug toxicities. The applications of this simple, in-vivo imaging modality will continue to evolve and may replace more invasive procedures such as fluorescein angiography in future.

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Conservative Management of Large Cyclodialysis Cleft And Effect On Corneal Astigmatism

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Abstract

We report the changes in corneal topography due to hypotony following traumatic cyclodialysis cleft. A 12 year old boy presented with cyclodialysis cleft of 6 clock hours along with induced hypotony and corneal astigmatism, following trauma with fire cracker. He was managed conservatively, intraocular pressure measurements and corneal topography was done to monitor changes over a period of 6 months. Corneal topography showed reversal of 3D with the rule astigmatism induced to 0.5D after closure of post traumatic cyclodialysis cleft on medical management. Cyclodialysis cleft can cause alteration in corneal astigmatism which can revert with its closure.

Keywords: Cyclodialysis cleft, hypotony, astigmatism.

Introduction

Cyclodialysis cleft (CDC) occurs when there is separation of meridional fibres of ciliary muscle from its attachment to scleral spur and ciliary body band¹. It may result following blunt ocular trauma or inadvertently during anterior segment surgery. This creates direct communication, resulting in drainage of aqueous humour from anterior chamber to suprachoroidal space. The resultant excessive filtration of aqueous results in ocular hypotony.² Ocular hypotony may go unnoticed or it may cause complications like hypotony maculopathy, corneal edema, choroidal effusion or hemorrhage, disc edema, exudative retinal detachment or cataract.

Case Report

A 12-year-old child presented with blunt injury due to fire cracker in right eye. Visual acuity at presentation was Finger counting close to face in right eye and 6/6 on Snellen chart in left eye. Manifest refraction in right eye was + 5.00 D @ 100° with no improvement with glasses, 0.5DS/ +0.25 DC@100° in left eye. Corneal topography showed with-the-rule astigmatism with 42D @15° and 46D @105 (Figure 1A). There was no corneal edema, scarring or anterior segment changes as the possible causes of astigmatism. Intra-ocular pressure (IOP) was 4 mm Hg in right eye and 18 mm Hg in left eye. Anterior segment examination revealed traumatic mydriasis, inferior iridodialysis and posterior rosette cataract in the right eye and was normal in left eye. Gonioscopy showed cyclodialysis cleft from 11- 5 clock hours (Figure 1B), with peripheral anterior synechiae in all

the quadrants. Left eye showed wide open angle. Fundus examination of right eye revealed media haziness due to dispersed vitreous haemorrhage. Left eye fundus was within normal limits. The central corneal thickness was 530 microns and 535 microns in right and left eye, respectively.

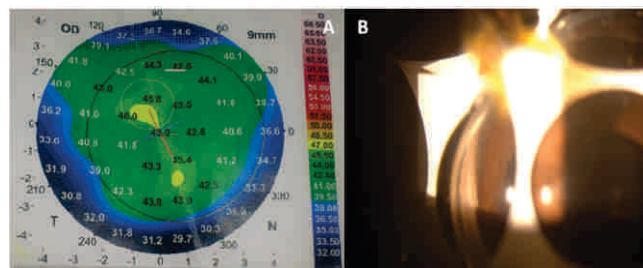


Fig.1A:Corneal topography showing with-the-rule astigmatism.1B:Gonioscopy showing cyclodialysis cleft.

Patient was conservatively managed on ointment atropine sulphate 1% thrice a day, topical prednisolone 1% and oral prednisolone (1mg/kg body wt.), and weekly followed for IOP, gonioscopy and fundus examination. Oral steroids were tapered over 4 weeks. There was gradual increase in IOP and decrease in astigmatism in right eye on subsequent visits.

At the end of eight weeks, corneal astigmatism reduced to 0.5D @90 with corneal topography of 44D @ 180° and 44.5 D @90° (Fig 2A). The IOP was 14mm Hg. Gonioscopy showed scarring in all the quadrants with closed CDC (Fig 2B). Right eye fundus revealed healed choroidal rupture with macular scarring. Patient underwent cataract surgery

with in bag single piece hydrophobic intra-ocular lens (IOL) implantation via clear corneal incision at 90°. Postoperatively, visual acuity improved to 6/60, the IOP is being closely monitored to look for late onset glaucoma.

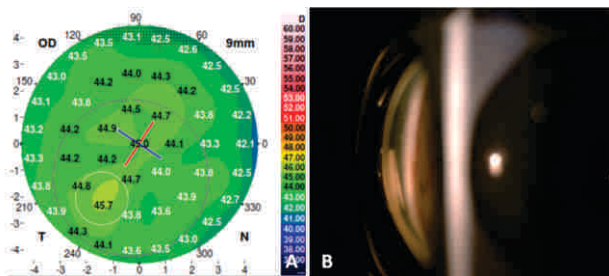


Fig.2A: Corneal topography at the end of eight weeks. 2B: Gonioscopy showing scarring at cyclodialysis site.

Discussion

Cyclodialysis cleft can cause profound and persistent hypotony by creating a direct passage for the aqueous humour to suprachoroidal space. Hypotony (pressure at or below 5 mm Hg) can cause visual disturbances and problems through various mechanisms like cystoid macular edema, optic nerve edema, choroidal effusion, exudative retinal detachment, corneal edema³. Changes in the macular region are primarily responsible for decreased vision in hypotonous globe, prolonged and persistent hypotony may cause irreversible maculopathy and fibrosis.⁴ The magnitude of hypotony due to cleft may not be proportional to the size of cleft.

Another cause of visual blurring is the instability of hypotonous globe during blinking, which can cause corneal distortion and astigmatism. Causes of corneal astigmatism remains unclear, eyelid pressure plays an important role. Eye lid retraction and narrowing has been shown to alter corneal astigmatism along 90° and 180° meridian.⁵ Moon et al. reported short term reduction in with-the-rule astigmatism and increase in against-the-rule astigmatism with botulinum toxin A in patients of blepharospasm.⁶ Besides eyelid pressure there are various factors like tear film distribution, diurnal variation, systemic factors like age, gender effect the corneal topography, but the effects are temporary.^{7,8,9}

Atkinci et al. reported traumatic CDC induced corneal astigmatism in 75% cases in series of 12 patients but size of cleft and degree of astigmatism was not correlated.¹⁰ Razejinejhad et al. noticed the effect of closure of superiorly located traumatic CDC by laser

photocoagulation on corneal astigmatism.²

In our case, we followed CDC of 6 clock hour to close on medical management. Spontaneous closure occurs less frequently and often only in clefts of smaller size. Non-surgical management is the first line therapy in all the CDC sized up to 4 clock hours¹¹. Mydriatics relax the ciliary muscles allowing apposition of detached meridional muscles to the sclera. We continued topical therapy for more than 8 weeks. Closure either by laser coagulation or surgery is advisable if cleft fails to close following conservative management for 6-8 weeks.¹¹

At 8 weeks we undertook cataract surgery for posterior rosette cataract. Visual acuity remained subnormal due to macular scarring.

Conclusion

Changes in corneal topography due to hypotony following traumatic CDC may results in large astigmatism. Large CDC of 6 clock hours can be managed conservatively with reversal of astigmatism.

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Post SICS Tunnel Melt in Rheumatoid Eye in a Steroid Responder- A Unique Case Report

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Abstract

This case report aims to present a unique case of post SICS scleral tunnel melting secondary to uncontrolled rheumatoid arthritis (RA) which progressed to corneal melt even after scleral patch grafting of scleral melt.

Keywords : Rheumatoid arthritis, scleral melting, steroid responder, corneal melting.

Introduction

Rheumatoid arthritis (RA) is a systemic disease that can affect more than just the joints.¹ It is a disorder of autoimmune origin causing chronic inflammation.¹ The etiopathogenesis of this autoimmune disorder is still unknown. Ocular manifestations involved with RA are keratoconjunctivitis sicca, episcleritis, scleritis, corneal changes, and retinal vasculitis.²⁻⁴ We report a case of 60 years old female who presented with scleral tunnel melting with uncontrolled rheumatoid arthritis. This emphasizes the importance of timely diagnosis and early intervention of this grave sight threatening complication in rheumatoid patients.

Case report

Sixty years old female presented to our institute with chief complaints of blurring of vision in left eye (L/E) for 2 months which was associated with pain and watering. There was history of joint pain involving finger joints and wrist associated with morning stiffness. She had undergone cataract surgery in right eye (R/E) 2 years back and in L/E 9 months back. On examination, visual acuity in R/E was 6/9 and in L/E was 6/18. R/E examination revealed no remarkable findings. L/E showed a sectoral area of scleral thinning superior to cornea in upper quadrant with Seidel's test positive. (Figure 1 and 2)



Fig. 1: Showing scleral melting with uveal show in upper quadrant



Fig.2: Positive Seidel's test.

Anterior chamber was formed with pupillary peaking superiorly. Intra ocular lens was present in the bag. Intraocular pressure was 6mmHg. Fundus revealed no evidence of hypotonous maculopathy. Investigations showed RA Factor positive with ESR 30 mm in 1st hour, CRP and ANA negative. L/E scleral patch grafting was done. Post-operatively, vision in L/E was 6/18 with healthy scleral graft covered by conjunctiva. (Figure 3)

Oral steroids along with topical antibiotic steroid drops and lubricants were started. On 7th day followup, vision in L/E dropped to 6/24 and microcystic epithelial edema developed with IOP 42 mmHg. Oral steroids were tapered and topical antiglaucoma drops along with oral acetazolamide was started. The IOP returned to 16mmHg after treatment with healthy graft. However, post 4 months, the patient started developing corneal melt in upper quadrant. (Figure 4)

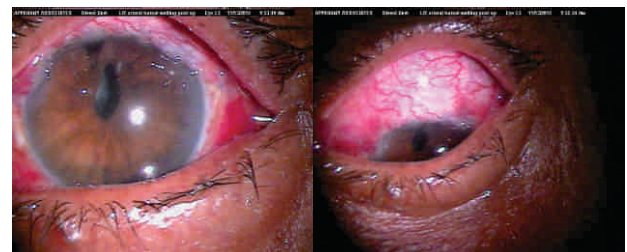


Fig. 3: post operative day 1

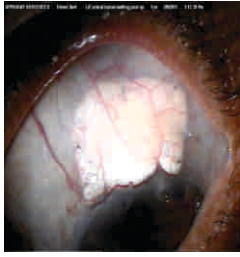


Fig.4: Showing 4 month post operative normal scleral graft with corneal melt area in upper quadrant.

Patient was sent to rheumatologist and was put on Methotrexate 7.5mg once daily for a week. The melt resolved and we are still following up the patient.

Discussion

Rheumatoid arthritis (RA) is a systemic disease of autoimmune origin causing inflammation that can affect more than just the joints.¹The ophthalmic manifestations of RA include keratoconjunctivitis sicca, episcleritis, scleritis, peripheral ulcerative keratitis, and retinal vasculitis which are described in the literature.⁵Scleritis is a chronic, painful, and potentially blinding inflammatory disease that is characterized by edema and cellular infiltration of the scleral and episcleral tissues. It may be classified into anterior and posterior. Anterior scleritis can be diffuse, nodular, necrotizing with inflammation (necrotizing), and necrotizing without inflammation (scleromalacia perforans).⁶ Perez et al has also reported case similar to ours with scleritis post cataract surgery.⁷Sudipta Das also reported 4 cases of postoperative scleritis.⁸

However, on contrary none described steroid responsiveness as in our case. All reports suggested reinforcement of the sclera as treatment particularly when the uveal tract is exposed, to prevent prolapse of ocular contents and secondary infection. The current recommendation for this situation is the concomitant use of systemic immunosuppressive drugs, which reduces the severity of vasculitis and increases the chance of survival of the patch graft in such patients.^{9,10}In this case, the high level of ESR and CRP and the melting graft postoperatively indicated the presence of active scleritis. Following consultation with a rheumatologist, more aggressive immunosuppressive therapy should be adopted the way we did to prevent the graft melting.

Conclusion

We conclude that ocular manifestations, however rare should be foreseen, investigated, and treated in

patients with suspected arthritis as the complication is grave and sight threatening.

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Corneoscleral Melting in A Case of Congenital Erythropoietic Porphyria.

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Abstract

Congenital erythropoietic porphyria (CEP), also known as Gunther's disease, is a rare autosomal recessive disorder characterized by defective bone marrow heme synthesis. As a consequence of defective heme-porphyrin complex, hemolysis occurs and excessive porphyrins of type I isomer are deposited in tissues like bones, skin, teeth and eyes. These porphyrins undergo oxidation in sunlight and cause phototoxic damage to the underlying tissues. The total number of reported cases of this disorder worldwide is less than 200 and very few case reports are available in literature describing the ocular spectrum of disease. We are reporting a rare case of congenital erythropoietic porphyria with corneoscleral melting and uveitis.

Keywords: Congenital erythropoietic porphyria, corneoscleral melting, phototoxicity.

Case report

A 12 year old male child born after consanguineous marriage presented to us with the symptoms of blurred vision, pain, watering and photophobia in left eye for the past 10 days. On examination, bilateral hyperkeratotic plaques were seen over sclera in the interpalpebral aperture with an overlying 2x3mm area of corneoscleral melting with surrounding infiltration on the nasal aspect of left eye (Figure 1; a,b). Anterior uveitis along with reactionary hypopyon of 0.5mm was present in left eye. Bilateral fundus examination was normal. Complete lid closure was there with mild conjunctival scarring. Systemic examination revealed hyperpigmented parchment like skin with multiple atrophic scars more prominent over ears and nose (Figure 2a). Brownish discolouration of upper incisors was observed. Fingertips and toes appeared mutilated (Figure 2b). He belonged to a nomadic family and as told by the parents, there was history of blistering of skin and reddish coloured urine since early childhood. His mental development was normal. Investigations revealed mild anaemia with increased urine uroporphyrin I and coproporphyrin levels. Red fluorescence of urine was observed under Wood's lamp. X-rays of hands and feet revealed acral osteolysis. Skin biopsy did not reveal any dysplastic change. He was started on oral steroids along with topical antibiotics, lubricants and cycloplegics. Resolution of hypopyon and disappearance of corneal infiltrates along with halt in progression of

corneoscleral melting was observed within a week of starting treatment.

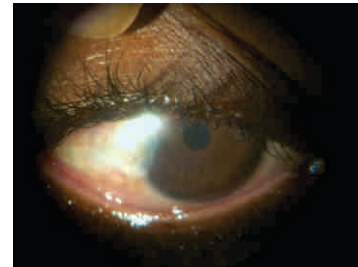


Fig. 1a: Right eye showing thickened hyperkeratotic plaque over temporal aspect of sclera



Fig. 1b: Left eye showing corneoscleral melting over superonasal aspect of sclera with surrounding corneal infiltration and reactionary hypopyon.



Fig.2a: Showing hyperpigmented, parchment-like skin with multiple atrophic scars



Fig. 2b: Showing mutilated fingertips with scarring

Conclusion

Congenital erythropoietic porphyria (CEP) is a rare autosomal recessive disorder with deficient activity of enzyme uroporphyrinogen III synthase in erythrocyte precursor cells¹. There is overproduction of isomer I porphyrinogens that cannot be used to form heme and induces hemolysis and accumulation of porphyrinogens in tissues like skin, bone, teeth and eyes. Spontaneous oxidation of these porphyrinogens to their corresponding porphyrins in sunlight causes damage to the underlying tissue and scarring. Phototoxicity in skin leads to recurrent blistering of the sun exposed skin followed by scarring and tissue distortion. Deposition in teeth causes reddish-brown discoloration, excretion of excess uroporphyrins and coproporphyrins in urine causes port wine discoloration of urine, deposition in bones along with expansion of marrow cavity in response to ongoing hemolysis makes them fragile and prone to fractures. Acral osteolysis and onycholysis may occur. Ocular manifestations comprise of blepharitis, loss of eyelashes, conjunctival scarring, symblepharon, lid shortening due to scarring, lagophthalmos, corneal scarring and corneal vascularisation. Few cases of scleral melting have also been reported^{3, 4}; Siddique et al, 2011). Alterations of eyelids, conjunctiva and sclera are directly related to the phototoxicity due to sunlight. Corneal scarring and vascularisation occurs secondary to lagophthalmos and dry eye. Ocular complications are dealt in a conventional manner. However, surgical correction of lid scarring and lagophthalmos is not advocated as it will further aggravate the scarring and tissue distortion. Till date no permanent cure to congenital erythropoietic porphyria has been discovered. Strict avoidance of sunlight is advocated. Repeated blood transfusions are given to suppress in-vivo erythropoiesis.

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Cysticercosis with ocular and lingual manifestations- A rare case report and review of literature

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Abstract

A rare case of cysticercosis with ocular and lingual manifestation is being reported here in a 28 year old female who presented to Ophthalmology OPD with no ocular movement in left eye for last 7 days along with a unilateral painless swelling on anterior part of tongue for last 6 months. Ocular involvement of cysticercosis is known and often misdiagnosed clinically. Excisional biopsy of tongue swelling on histopathological examination revealed cysticercosis. Patient was kept on conservative management. The case is being reported because of its rare presentation.

Keywords: Cysticercosis, taenia solium, ocular cysticercosis, tongue.

Introduction

The word Cysticercus is derived from Greek words Kystis = cyst and Kertos = tail because of their appearance.¹The pork tapeworm (Taenia solium) is known to cause two different types of infections, with adult tapeworms in the intestine or with larval forms in the tissues (cysticercosis). Humans are the only definitive hosts for T. solium while pigs are the usual intermediate hosts. Humans acquire infections by ingesting undercooked pork containing cysticerci leading to intestine tapeworms. While the infections that cause human cysticercosis follow the ingestion of T. solium eggs, usually from fecally contaminated food. Cysticercosis mainly involves intermuscular and subcutaneous tissues and commonly affected organs in humans are central nervous system, eye and skeletal muscles.²Ocular involvement occurs in 10-30% of the infected patients in endemic areas and may be extra ocular or intraocular.³ Patient may present with pain, decreased vision, recurrent redness of eye and even blindness if cysticercus enlarges.⁴ Oral cavity is not a common site for cysticercus because of high muscular activity of oral tissues in humans, which prevent lodgement and development of cysticerci but if present, tongue, labial or buccal mucosa and floor of mouth are mainly the involved areas.⁵We are presenting here a rare case of cysticercosis with dual manifestation and its management is discussed.

Case Report

A 28 year old female presented to Ophthalmology OPD with history of painless loss of ocular movement in left eye from last 7 days and painless swelling on

dorsum of anterior part of tongue from last 6 months. There was no history of trauma, eye surgery, fever, dysphagia or excessive salivation. Patient did not give any history of seizures. The patient was a vegetarian by diet and there was no history of tobacco addiction. Ophthalmological examination revealed complete ophthalmoplegia in left eye. Slit lamp examination and indirect ophthalmoscopy were within normal limits except for complete ophthalmoplegia in left eye.

ENT consultation was sought and patient was found to have a single, submucosal, firm and nontender swelling on anterior two thirds of tongue. It was around 3cm × 2cm in size. The movement of the tongue was normal and there was no cervical lymphadenopathy. MRI brain along with neck was done which showed a calcified granuloma in left perisylvian frontal parenchyma at the gray-white matter junction without perilesional edema, suggestive of nodular calcified neurocysticercosis with normal orbital study (Figure 1). A well defined cystic lesion (19 × 17 × 14mm) was seen in the intrinsic muscles of right half of anterior tongue (Figure 2). On fine needle aspiration cytology (FNAC) from tongue swelling, colourless fluid with whitish flakes was aspirated which on cytological examination showed mixed inflammatory response with numerous eosinophils, macrophages, plasma cells and histiocytes (Figure 2). Excisional biopsy of tongue swelling followed by histopathological examination revealed cysticercosis. Patient was evaluated further including stool examination for ova or cyst to rule out cysticercosis elsewhere. Patient was prescribed Albendazole 400mg, twice a day and

Prednisolone 1mg/kg body weight on tapering dose for 15 days. Patient recovered with fu

ll ocular movement in all gazes and now the patient is on regular follow-up and is doing fine without any complaint.



Fig.1: MRI picture showing calcified granuloma in left perisylvian frontal parenchyma at the gray-white matter junction.



Fig.2: Showing nodular swelling on dorsum of tongue on (R) side with Microphotograph showing cysticercus larva with irregular membrane infolding and scolices (H & E X 4)

Discussion

Cysticercosis is a rare infestation in human beings. The manifestations of the disease are different and depend on the location of cysticercus in the body. The parasite may remain viable for a long period of time depending on the location, type and immunity of host. The death of parasite in tissues cause leak of parasitic antigens into surrounding tissues which can elicit inflammatory reaction in the body. Dead or degenerated parasite is slowly invaded by inflammatory cells, macrophages and finally replaced by fibrous tissue with subsequent calcification.⁶ Central nervous system, skeletal muscles and subcutaneous tissues are the commonly affected sites.

Ocular manifestations of cysticercosis vary from asymptomatic to painful blind eye and may be associated with neurological symptoms such as headache, fits, diplopia, and restriction of the ocular movements, nystagmus and papilloedema.⁷ Approximately 4% involve the eyelid or orbit, 20% involve the subconjunctival space, 8% involve the anterior segment, and 68% involve the posterior segment.⁶ In our case, patient presented with painless loss of ocular movement without any other obvious clinical finding on detailed ophthalmological examination. There is no specific sex and age predilection, although orbital cysticercosis is more commonly seen in younger age group. Either eye may be affected but bilateral involvement is rare. An excisional biopsy gives definitive diagnosis as done in the present case from tongue swelling. Once the infection is diagnosed, systemic involvement especially CNS involvement must be ruled out by laboratory tests and radiologic imaging studies including MRI scan as done in this case.⁸ Serological tests like ELISA (enzyme-linked immunosorbent assay) or EITB (enzyme-linked immunoelectro transfer blot) are useful to detect antibodies to *Taenia solium* in serum, cerebrospinal fluid and saliva. Among all the sites, oral cysticercosis is rarer and very few cases have been reported in literature. Within the oral cavity, tongue is most common site involved followed by the lips and floor of mouth. Oral form usually presents as a painless swelling and easily detected because of their superficial nature in contrast to cerebral cysticercosis which can present as intracranial space-occupying lesion with convulsions and more serious clinical entity.⁹ Clinical presentation of intestinal infestation by *Taenia solium* could be asymptomatic or may present with nausea, epigastric pain and loose motions. Surgical excision is the treatment of choice in patients presenting with obvious swelling and material should be submitted for histopathology to confirm the diagnosis. This infestation can be prevented by adequate cooking of pork, good personal hygiene, proper fecal disposal and effective treatment of human intestinal infections.

Conclusion

Cysticercosis with dual manifestation is a rare entity. This case emphasizes the importance of routine radiological and histological examination for proper diagnosis in such cases. Cysticercosis should be kept in mind in any patient presenting similar complaints and with painless tongue swelling. Routine blood

examination with eosinophils count, stool examination and radiographic investigation to rule out multiple organ involvement should be a part of clinical conundrum. Excision of swelling is the treatment of choice.

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Surgical treatment of lower lid retraction using hard palate mucosal graft in a young patient

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Abstract

The case report describes the surgical management of a 24 year old male patient who presented with lower lid retraction of right eye. Hard palate mucosal graft was used as spacer material to support the tarsal plate. The postoperative outcome was highly satisfactory, with complete eye closure and good cosmesis achieved. We conclude that hard palate mucosal graft can be effectively used for the management of lower lid retraction.

Keywords: Lower lid retraction, hard palate grafts.

Introduction

The most frequent cause of lower eyelid retraction occurs is thyroid-associated orbitopathy (TAO) associated with fibrosis of the capsulopalpebral fascia. Other causes include surgeries involving extraocular muscles, lower eyelid blepharoplasty, weakening of the orbicularis oculi or trauma to the lower lid. The complications arising from lower lid retraction include dry eyes, exposure keratitis, and corneal ulcer. Surgery to correct lower lid retraction is needed only when the symptoms are severe. But nowadays cosmesis has become an emerging cause for surgical correction of lower lid retraction, especially in younger age-group.

Case report

A 24-year-old patient presented in our OPD with complaints of right eye appearing larger than the fellow eye since 5 months with apparent forward protrusion of right eye. There was no history of conjunctival congestion, pain, incomplete closure of eye, diminution of vision, deviation of eye or restriction in ocular motility. Patient gave history of head trauma a year back which was not associated with any ocular complaint back then. Patient had no history or current symptoms of thyroid disorder or any ocular surgery done in the past. The only concern with which patient presented in OPD was cosmesis.

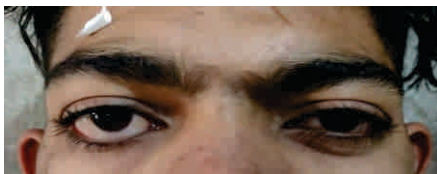


Fig1. Clinical picture of the patient with pseudoproptosis of right eye.

The exclusionary systemic investigations (complete blood count, ESR, thyroid profile and CT scan brain) as well as the ocular investigations (orthoptics and refraction testing) revealed no abnormality. Hertel's exophthalmometry revealed no proptosis (right eye 19mm, left eye 18mm). Right eye lower lid was measured to be 2.5mm retracted from the limbal margin.(Figure 1)

After getting pre-anaesthetic clearance, lower lid reconstruction with buccal mucosa graft placement was done under local anaesthesia. A 4cm x2.5cm mucosal graft was harvested by an ENT surgeon from right border of hard palate starting from the posterior margin of corrugations.(Figure 2)



Fig.2: Mucosal graft obtained from hard palate.

The lower lid was everted to expose conjunctival side. Lateral canthotomy was done and conjunctival incision was given 3mm below lower lid margin along the length of the lower lid, exposing the lower margin of tarsal plate. The graft was sutured subconjunctivally with mucosal side facing the conjunctiva, superiorly to the tarsal plate and inferiorly to the orbital septum using 6-0 vicryl. (Figure 3,4)

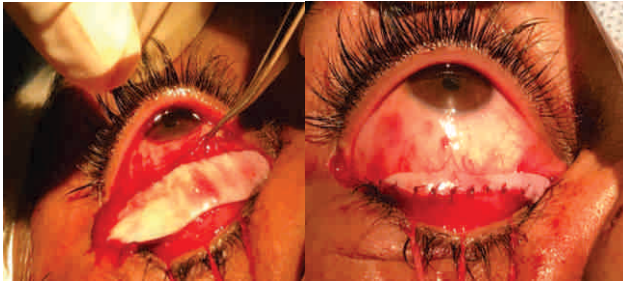


Fig. 3, 4: Intraoperative picture of patient showing application of graft.

Lateral canthotomy was closed with tarsal plate end sutured to lateral orbital periosteum with 4-0 prolene. (Figure 5)

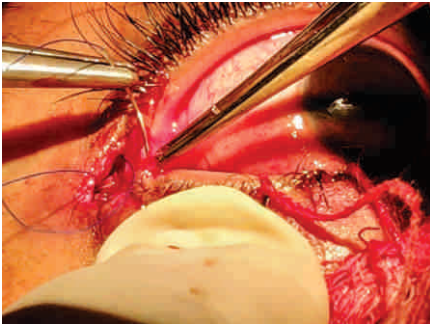


Fig.5: Intra-operative picture of patient showing closure of lateral canthotomy

Apposing forniceal sutures were applied with 6-0 silk passing from conjunctiva to skin via the graft.(Figure 6)



Fig.6: Intraoperative picture of patient showing application of forniceal sutures.

On follow-up visit of the patient after one week, the apposing sutures were removed. Good advancement of lower lid was achieved and patient was also satisfied on further follow up visits(Figure 7).



Fig.7: Clinical photograph of patient at one week follow-up.

Discussion

The various structures supporting the lower eyelid include the capsulopalpebral fascia, tarsus, orbicularis oculi muscle, medial canthal tendons and lateral canthal tendons. Contraction of posterior lamella and the lower eyelid retractor that is capsulopalpebral fascia and inferior tarsal muscle, causes lower eyelid retraction.² Thyroid-associated ophthalmopathy is reported to be a common cause of shortening of the lower eyelid posterior lamella.¹ Posterior lamella shortening can be caused due to post-traumatic scars and after lower eyelid blepharoplasty. Rarely, idiopathic congenital lower eyelid retraction has also been reported.³⁻⁶ The number of patients who want to undergo surgery for aesthetic reasons is increasing nowadays. Through management point of view, administration of lubricating drops, in mild to moderate cases, and surgical correction is required in cases of severe exposure keratitis. Surgical correction of lower eyelid retraction can be performed with or without a graft. The severity of retraction decides the surgical technique to be used.⁷ Grafts are not required if the lower eyelid retraction is mild. Vertical tension in lower lid is relieved by retractor recession while the horizontal laxity is corrected by lateral tarsal strip procedure.^{8,9} For more than 2 mm retraction, grafts are to be used to push the lower eyelid margin upwards. Besides autografts, such as hard palate mucosa and ear cartilage, allografts can also be used such as preserved sclera, and synthetic grafts, such as polytetrafluoroethylene and porous polyethylene.¹⁰⁻¹³ Spacer grafts create a recess in the lower lid retractors while supporting the tarsus and consequently pushing the lower eyelid vertically up to a normal anatomic height and position. Recently, cadaveric skin grafts have also been used, by processing the dermal matrix to remove cells containing antigenic targets for infection and thereby leaves the dermal matrix immunologically inert.^{11,14}

Conclusion

Lower lid retraction is a cosmetically unacceptable condition besides having dry eye symptoms. A hard palate mucosal graft can be effectively used for the management of lower lid retraction.

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Residents' Corner

Ophthalmology Training & Teaching in India: Leadership Mantras for Young Ophthalmologists

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Introduction

Ophthalmology offers the adrenalin rush associated with performing delicate sight restoring surgeries, yet the eye specialists do not deal with stressful life and death situations. Residency training is one of the crucial phases in a doctors' life which transforms a theoretical generalist to a practical specialist geared up to take on the responsibility of caring for the patients. Throughout the years, the surgical training process in ophthalmology has progressed from unstructured apprenticeship to limitless period in the past, and then in the 20th century, shifted to a Halstedian pyramidal structure and currently on consistent rectangular model with specified timeline.¹ However, the "See one, do one, teach one" concept of the Halstedian model is still ingrained in the residency.

Challenges of Residency Training

It is without a doubt that the residency training process in ophthalmology is intellectually, emotionally, and physically demanding. The crucial requirements of these residency programs are a working and atmosphere learning which promotes excellence in quality and safety of professionalism and care, faculty that has been trained to mentor, evaluate, train and teach, best exposure to clinical procedures and investigations, as well as patients, and the required equipment and facilities to offer standardized care.²

Vast Curriculum Versus Limited Hand-on Surgical Training

The residency curriculum is of course dynamic and ever changing as per the scientific and technological advancements in ophthalmology. While the universities and regulated bodies make it a point to update the curriculum regularly, in the residency programs, the predominant is the 'taught curriculum'.³ Even though similarities between taught and declared are ideal, there are discrepancies in adherence. Throughout the past decades, the practice of ophthalmology has tremendously changed worldwide. The treatment and management of

ophthalmic disorders and surgical techniques have undergone significant changes. However, with the exception of few teaching institutes in India, majority of residents are getting limited exposure to these latest advances. While cataract surgery training has shifted from ICCE and ECCE to SICS and phacoemulsification and foldable IOL, but other ophthalmic surgeries are still taught sparingly during the residency.⁴ There was an enormous variation across the country in residency training which needs immediate attention.

Necessity of Improving Residency Training

Several authors emphasized that the residency training in India still needs to be improved significantly. Without proper and updated residency training system in majority of medical colleges in India, how would young ophthalmologists become the leaders in their field? In India, 60% residency training for ophthalmology is under government run organizations while the rest are private institutions.⁵ The imparted training is typically done in various settings like medical colleges (including regional institutes), and private institutes. There isn't a coherent training system followed by all which leads to huge variations in quality of training. It is important to ensure that residents in India observe (and perform under supervision, if possible) a good variety of ophthalmic surgeries – not just cataract-lens implant surgery, but also in medical retina, basic vitreo-retinal procedures, refractive procedures, oculoplastic surgery, glaucoma surgery, squint surgery, routine ocular trauma and so on, that will help them to develop interest while selecting their field of interest during the fellowship.

Willingness to change, commitment, culture, goals, agility to introduce change and accept the change widely varies.⁶ Can all of this change? Is it possible to implement such a training system that not just produces conscientious and safe specialists with the best attitude, knowledge and skills, but those who practice optimal proficiency and exhibits leadership qualities? Can such a system be implemented without

being affected by the negative practices prevailing in the system?

The shortage of standardization shows the need for a stronger regulatory authority in order to make these changes and implement them efficiently.⁷ It is important to have such a training system which focuses on the actuality of the learning process, human resources, and the infrastructure. Additionally, the training system must be need based. Standards must be established and followed. There is a dire need to emphasize the residents' role as researchers and teachers throughout their residency to encourage them to become leaders.⁸ This is one of the major parts of competency based curriculum for residency training of young ophthalmologists around the globe.⁹

Role of Leaders and Ophthalmic Societies

There is a strong need for the authorities to do major rethinking and correction in the curriculum and training system.¹⁰ Numerous ophthalmologists have stressed the need of establishing a fresh training system for the residency students in ophthalmology.¹¹ Moreover, it has been stressed that potential of young ophthalmologists of India must be encouraged to take the leadership role. This can be done if the residency students have a great foundation of teaching and training. Two examples deserve special mention here - I-Focus, National Postgraduate Education Programme in Ophthalmology and Academic and Research Committee (ARC) wing of All India Ophthalmological Society, both have done commendable work to update residents in basic and cutting-edge ophthalmology and helped them to prepare for leadership role.

Role of Residents/Young Ophthalmologists

Residents in training would play a major role in shaping up the future of ophthalmology in the right direction if they have all the essential elements – skill based practice, practice based improvement and learning, professionalism, communication and interpersonal skills, patient care, leadership skills and medical knowledge.¹² The training system must provide them a chance for open minded learning of comprehensive ophthalmology and a broad based approach. It is up to the coordinators of residency training, as well as ophthalmology heads of various institutions to come up with the will to make these changes and also to lead this change throughout ophthalmology in India. There are numerous ways these changes can happen – a teaching schedule, one-

on-one mentorship for residents, encourage young ophthalmologist to teach, management of their time, as well as reorganization in the departments.

Pearls for Women Residents in Ophthalmology

Ophthalmology is becoming a preferred branch for female doctors as career as an eye specialist is considered rewarding for women wanting to maintain a work life and work family balance. It is extremely important for all resident doctors to get the best possible training during their residency. This is even more pertinent for women residents, as it becomes very difficult to devote time to full time rigorous training programmes at a later stage in life, particularly after marriage and kids. At an early age, it is possible to travel far and wide for the best training opportunities, especially in surgical disciplines like ophthalmology. Current ophthalmology practice is becoming difficult because of heightened patient expectations and an aggressive consumer culture that is spreading fast. In such a scenario, it is absolutely essential to get the best possible clinical training, so that their competence can become their big strength when these residents start doing clinical practice.

Role of Mentors

For mentors and teachers, teaching can indeed be challenging in a changing era of mentor protégé relationship. The residents of ophthalmology now are more focused and competitive than ever before. Some of them may suffer from work related stress due to excessive work load while others may have attitude problem, may not be doing their duties properly and lacking the basic discipline and a mindset that lacks respect for their seniors and mentors. Also, their learning style, as well as exposure to innovative learning modes has increased their expectations from their mentors and teachers. On the other hand, the mentors and teachers feel these young ophthalmologists just want to learn things way too quickly and on their own. There is a dire need to find a middle ground and for that there is a major need to create mutual goals that must be implemented. It is important to utilize the innovative teaching styles and techniques to help these technically driven residents to learn more efficiently. It is essential to keep in mind that these young ophthalmologists are the future of ophthalmology. Steps need to be taken to make immediate changes in the training and teaching in ophthalmology residency to ensure a bright and prosperous future of ophthalmology in India.

Conclusion

Leadership Mantras for Young Ophthalmologists

There are numerous ways through which these young ophthalmologists can become leaders of tomorrow. Firstly, it is essential for them to find the right mentor, someone who is genuinely interested in helping them adapt leadership qualities instead of someone who hardly offers any useful advice. Most importantly, they have to actually listen to their mentors, even if it is a hard feedback. Moreover, young ophthalmologists need to become more proactive if they truly want to become future leaders.¹³ There is no point in waiting for someone to hand them the responsibilities, they need to show their mentors and leaders that they have what it takes to be in a leadership role. These future leaders should also be engaged in member organizations right from the initial stage.¹⁴ Another important thing these young ophthalmologists must consider is stepping out of their comfort zone. They must trust their education and training, and must not be afraid to learn new technique and skill that can open more opportunities for them to move on to leadership roles.¹⁵

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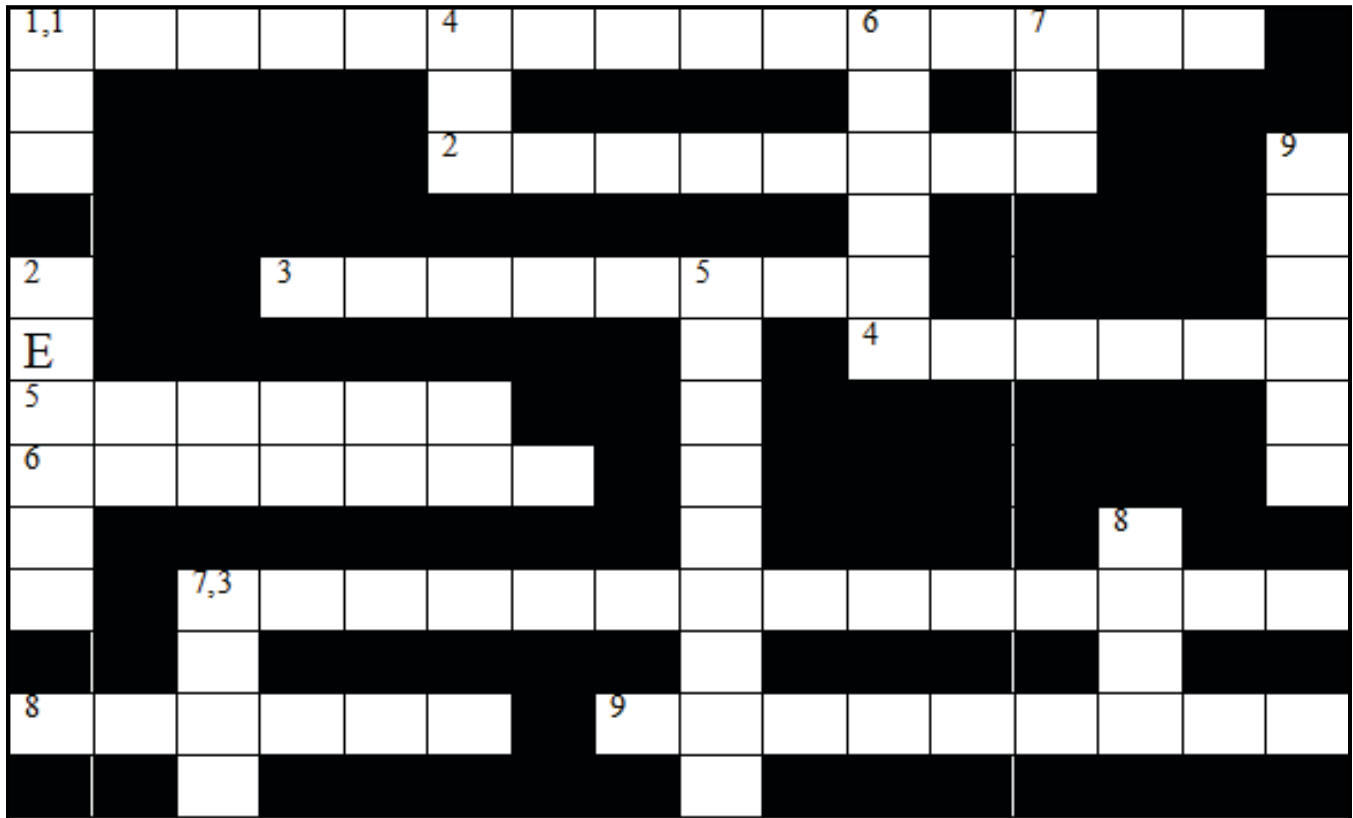
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HOS QUIZ- Ophthalmic crossword



HORIZONTAL ROWS:

1. The process by which a normal eye has coordinated growth of its refractive components during early childhood to reach refraction near plano is called
2. Fundus picture in CMV retinitis.
3. Father of vitrectomy.
4. Test done to measure stereopsis.
5. Uveitic condition with cold hypopyon
6. Phenomenon in which there is worsening of neurologic symptoms of multiple sclerosis when body gets overheated.
7. Angiod streaks is associated withelasticum.
8. A multisystem syndrome associated with subluxation of crystalline lens.
9. Oculo-auriculo-vertebral syndrome.

VERTICAL COLUMNS:

1. A test to detect function of photoreceptors.
2. Syndrome with euryblepharon, short stature, mental retardation, and skeletal abnormalities.
3. A three step test to detect vertical muscle palsy was described by.....
4. Preterm neonates who are kept under hyperbaric oxygen therapy are at risk of developing.....
5. An instrument used for measuring heterophorias and cyclodeviations.
6. A syndrome in which lenticonus occurs due to defective collagen type IV production.
7. A syndrome comprising of iris naevus, Chandler's syndrome, essential iris atrophy.
8. Spots seen on fundus in anemic retinopathy, endocarditis, leukemia.
9. A disease of defective copper metabolism where KF rings are seen on cornea of patients.

INSTRUCTIONS:

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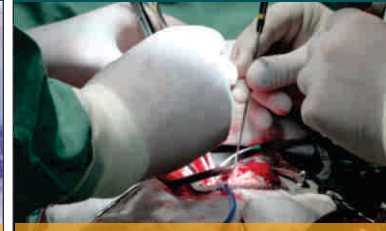
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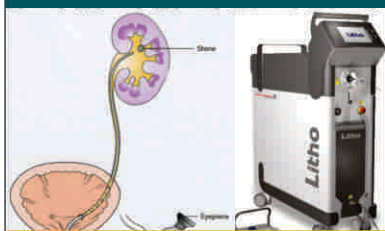
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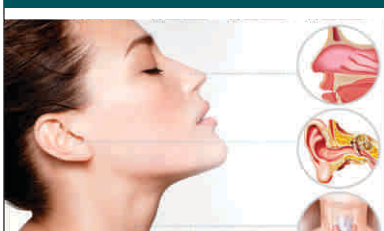
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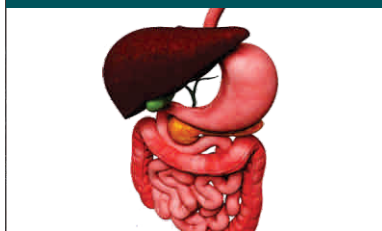
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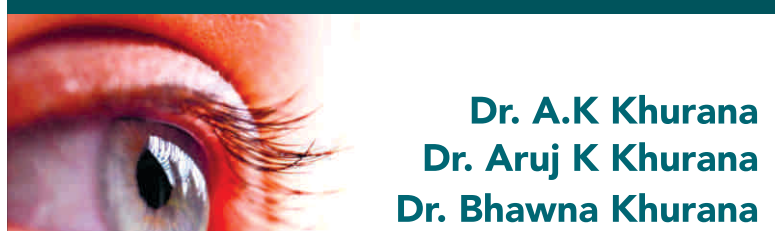
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Clip Sheet

Ocular Trauma Associated Retinal Pathologies

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DISEASE	PATHOGENESIS	CLINICAL PRESENTATION	TREATMENT
BERLINS EDEMA	Shock waves from blunt ocular trauma results in injury to photoreceptor and RPE junction due to inelastic nature of retina.	Temporary gray-white opacification of the neurosensory retina with RPE mottling and cherry red macular spot.	Not recommended. For some cases that do not improve high dose i.v. steroid trial can be given.
RETINAL CONCUSSION	Traumatic retinal opacification with reversible clinical features.	Transient blurry vision after trauma.	Obsevation Complete recovery is expected in a few days.
TRAUMATIC MACULAR HOLE	Multiple theories have been proposed like antero-posterior traction, degeneration theory, vascular theory. Most accepted one is focal antero-posterior traction mechanism.	Varied presentation in terms of shape and size and thickness of macular hole is observed.	Upto 44% MH close spontaneously more so in children and young adults upto 3 months. No consensus for time of surgical intervention. Induction of PVD, SF6 tamponade are some surgical interventions
TRAUMATIC RETINAL TEAR AND DETACHMENTS	Most of traumatic retinal tear end up in retinal detachment.	Retinal tear can be directly visualised on fundus examination. Tear can be a operculated one or of horse shoe shape.	Surgical intervention for retinal detachment is required.
TRAUMATIC RPE TEARS	Blunt traumatic injury causing only RPE tear and not damaging choroid.	FFA shows transmission or window defect. OCT is diagnostic. Fundus shows hypo-pigmented area corresponding to RPE tear.	Spontaneous recovery is expected with good visual prognosis. Poor prognosis if fovea is involved.

TRAUMATIC RETINO CHOROIDAL RUPTURE	Blunt traumatic injury causing compression and extension of globe. Sclera resists but Bruch's membrane and retina breaks.	Confirmed on FFA or ICGA. FFA shows hypofluorescence in early phases. Fundus shows chorioretinal defect, bare sclera.	Conservative. Surgery for retinal detachment may be required.
TRAUMATIC OPTIC NERVE AVULSION	Intraorbital injury displacing globe causing complete or incomplete avulsion of optic nerve.	Sudden loss of vision following ocular trauma.	No effective surgical management is available.
RETINAL DIALYSIS	Disinsertion of retina at the ora serrata following ocular trauma.	Most common quadrant involved is infero temporal while most pathognomic is superonasal.	Surgical intervention similar to as for retinal detachment is required.
Retinal pathologies following indirect ocular trauma			
TERSONS SYNDROME	Intraocular hemorrhage associated with SAH, intracerebral haemorrhage, or traumatic brain injury.	Hemorrhage may be present in the vitreous, sub-hyaloid, or intraretina/sub-internal limiting membrane.	6 months of observation period followed by vitrectomy if required.
PURSTCHER'S RETINOPATHY	Microembolization of retinal vasculature, resulting in arteriolar precapillary occlusion and microvascular infarct of retinal nerve fiber layer.	Loss of visual acuity after head trauma. Cotton wool spots, retinal hemorrhages, disc edema and purstcher flecken on fundus examination.	In most cases recovery is complete without treatment within 1 month.
VALSALVA RETINOPATHY	Intra ocular hemorrhages following raised intra thoracic pressure.	Fundus shows hemorrhages which can be pre retinal or sub ILM.	Conservative management.
SHAKEN BABY SYNDROME	Forcefully shaking of infant causing intracranial and intra ocular bleeds.	Fundus findings include retinal haemorrhage, choroidal rupture, retinoschisis.	Most retinal hemorrhages clear upto 4 weeks.
FAT EMBOLISM SYNDROME	Fracture of long bone and formation of fat emboli affecting various organ systems.	Fundus findings include cotton wool spots and flame shape hemorrhages.	Retinal findings disappear in weeks.
WHIPLASH RETINOPATHY	Subtle disturbance of macula after head and neck trauma.	Immediate mild reduction of central visual acuity in one or both eyes. Grayish swelling of the foveal zone accompanied by a small (50 to 100- μ) pit or depression in the fovea.	The retinal opacification and the visual disturbance are transient. The tiny depression in the retina with its whitish border is permanent

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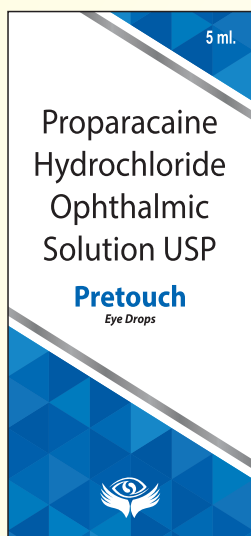
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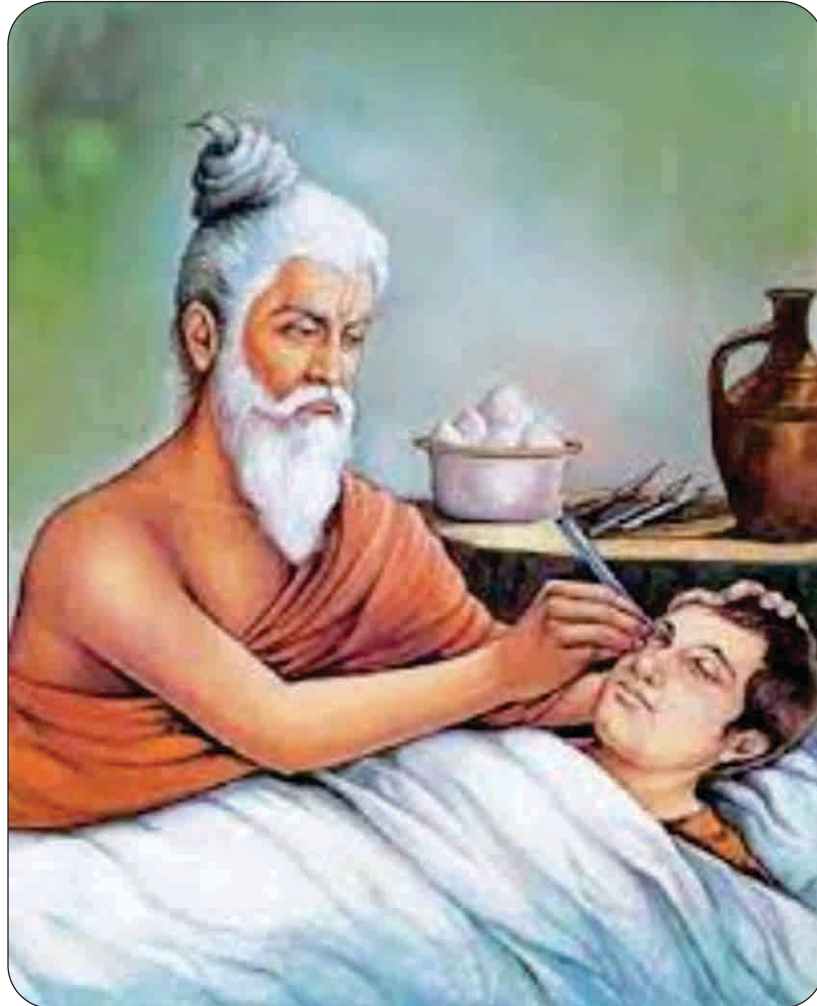


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Sir Nicholas Harold Lloyd Ridley

During World War II, Ridley saw Royal Air Force casualties with eye injuries, including Squadron Leader Gordon "Mouse" Cleaver of 601 Squadron. Ridley observed that when splinters of acrylic plastic (PMMA) from aircraft cockpit canopies became lodged in their eyes, this did not trigger inflammatory rejection as did glass splinters. This led him to propose the use of artificial lenses made of PMMA. Harold Ridley implanted the first intraocular lens on November 29, 1949. Knighthood was bestowed upon him in 2000.



Sushruta (600BC) was the First Surgeon who introduced Cataract Surgery to the world.

Sushruta, or Suśruta (Sanskrit: सुश्रुत, "well heard) was an ancient Indian physician known as the main author of the treatise The Compendium of Suśruta (Sanskrit: Suśruta-saṃhitā). The Mahabharata, represents him as a son of Vishvamitra, He described a classification of eye diseases and was first to perform surgery for cataract.



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