VOL. 5, ISSUE 1, NOVEMBER 2021

JOSA

JOURNAL OF OPHTHALMOLOGICAL SOCEITY OF ASSAM

GUWAHATI, ASSAM, INDIA

OPHTHALMOLOGICAL SOCIETY OF ASSAM
FROM DARKNESS TO LIGHT

OFFICIAL PUBLICATION OF
OPHTHALMOLOGICAL SOCIETY OF ASSAM

WWW.OSA.IND.IN

OPHTHALMOLOGICAL SOCIETY OF ASSAM (Estd. 1967)

Regd. No: KAM (M)/240/A 23/273 of 2010-2011
(Valid upto 02.04.2022)
(Life affiliated to All India Ophthalmological Society)

Executive Body (2019-2022)[1]

President	Premeswar Nath
Vice President	Subhra Kinkor Goswami
General Secretary	Jayanta Kumar Das
Assistant General Secretary	Amarendra Deka
Treasurer	Kruto Kalita
Chairperson Scientific Committee (CSC)	Arundhati Borthakur
Chairperson Academic & Research Committee (ARC)	Biraj Jyoti Goswami
Editor Journal, Editor Proceedings, Webmaster	Madhurjya Gogoi
Members:	
Central Zone	Gopal Chandra Das
East Zone	Anup Jyoti Bora
North Zone	Sanjib Buragohain
South Zone	Haimanti Choudhury
West Zone	Dhrubajyoti Sarmah
Regional Institute of Ophthalmology, Guwahati	Pankaj Baruah
Silchar Medical College	Nilanjan Kaushik Thakur
Assam Medical College, Dibrugarh	Rajiv Kumar Das
Immediate Past President	Harsha Bhattacharjee
Immediate Past General Secretary	Rajendra Nath Gogoi
Immediate Past Treasurer	Arup Deuri

Website : www.osa.ind.in
Email : ophsocassam1967@gmail.com

[1] Tenure of Executive Body has been extended twice in view of Covid situation; , by 1 year upto end 2021 in view of Covid situation vide GBM 2020, and by 1 year upto end 2022 vide GBM 2021

Journal of Ophthalmological Society of Assam (JOSA)

Volume 5 Issue 1 December 2021

About the Journal

Journal of Ophthalmological Society of Assam (JOSA), is the official scientific publication of Ophthalmological Society of Assam (OSA). It is a peer-reviewed open access semiannual online journal. The journal's full text is available online at http://www.osa.ind.in/journal.htm. The journal allows free access (Open Access) to its contents and permits authors to self-archive the final accepted version of the articles on any OAI-compliant institutional/subject-based repository.

Scope : Journal of Ophthalmological Society of Assam covers all aspects of clinical, experimental, basic science, interdisciplinary, multidisciplinary and translational research studies related to ophthalmology and vision science, with a preference for articles of applied interest.

Editorial Office: Dr. Madhurjya Gogoi, 113, 1st Floor, Excelcare Hospitals, Paschim Boragaon, NH 37, Guwahati-781033, Assam, Ph.: 9954237312, email: journal.osa@gmail.com

Contents

Editorial	Madhurjya Gogoi	1
GUEST EDITORIAL		
Genius borrows nobly – avoid plagiarism	Rolika Bansal, Santosh G Honavar	2-4
REVIEW ARTICLES		
Low concentration atropine for the control of myopia progression: an overview	Batriti Shympliang Wallang	5-16
Current trends in the use and outcome of anterior chamber intraocular lens (IOL) implantation	Swapnali Sabhapandit	17-24
INVITED ARTICLES		
Intraocular lens exchange, Indications and Outcome	Arundhati Tamuli	25-26
Vision Care Centre's modified Guidelines during pandemic in 2021	Nilanjana Ghosh	27-29
Newer medications in Glaucoma management	Shahinur Tayab	30-32
CASE REPORTS		
Spontaneously reattached retinal detachment with macular hole – A case report	Debdulal Chakraborty	33-35
The therapeutic dilemma in a non-responsive case of chronic central serous chorioretinopathy with secondary choroidal neovascular membrane – a case report	Tania Basaiawmoit, Jennifer V Basaiawmoit	36-39
A tale of Stage 4B to Stage 5 ROP in 10 days: a case report	Ronel Soibam	40-42
JOSA Instruction for authors		43-49

Editorial

Madhurjya Gogoi

It is encouraging to note that in the midst of the pandemic, ophthalmic services have resumed in some measure; and with it interest in clinical research too. Submissions based on original research has not been forthcoming for the last two years, and as such, this issue largely features review articles, invited articles, and for the first time, a guest editorial on the issue of plagiarism.

A brief overview of JOSA since inception (2017) is tabulated below.

Year	Received/Invited	Accepted	Under Review	Withdrawn	Rejected
2017	8	7	1	0	0
2018	7	6	0	0	1
2019	15	9	2	2	2
2020	6	6	2	0	1
2021	8	8	0	0	0
Total	30	22	3	2	3

JOSA has been attempting to strengthen and expedite the peer review process, as well as the stated aims of a biannual publication, and metrics like indexing and abstracting. The following are under consideration:

- Online manuscript management and peer review system;
- Creating and managing journal website (with domain);
- Pre-press and print services (including copyediting, typesetting, printing, distribution services);
- Post-publication services (including indexing & marketing support, subscription services)

However, the core issue remains the quality of the submission, and in this regard, attention is invited to the Up-Dated ICMJE Recommendations of December 2021. The fundamental role of robust methodology and collaborative research are highlighted.

JOSA takes the opportunity to gratefully acknowledge all who have nursed it in its formative years. Inadvertent errors of omission and commission may have crept in; and for that the editor takes responsibility.

With prayers for the wellbeing of one and all,

----Editorial team

30 November 2021
Guwahati, Assam

- Suggestions / feedback regarding JOSA are most welcome at: journal.osa@gmail.com
  Website: www.osa.ind.in; Weblink to JOSA: https://www.osa.ind.in/journal.php
  Facebook group 'Ophthalmological Society of Assam'
- Presently, only the PDF is being emailed to all life members. The print issue shall be made available in due course.

Guest Editorial

GENIUS BORROWS NOBLY – AVOID PLAGIARISM

Rolika Bansal, MS, Santosh G Honavar, MD, FACS, FRCOphth
Centre for Sight, Hyderabad, India

"If you steal from one author it's plagiarism; if you steal from many it's research". – Wilson Mizner

The origin of the word *plagiarism* is derived from the Latin word *plagiarius* which literally means *kidnapper* or *thief. Marcus Valerius Martialis* a Roman poet described it as stealing someone else's creative work. Plagiarism or literary theft happens to be the commonest form of scientific misconduct that authors commit and is considered an ethical offense.[1]

Often as authors begin writing a manuscript, while looking for inspiration during review of literature, they fall into the trap of plagiarism pertaining to factors like peer pressure to publish, limited knowledge, lack of vocabulary to express thoughts, technology advancement, urgent need for career progression or even an accidental mention. Sure, plagiarism saves time, however it blocks unsculptured creativity and prevents authors from providing original information to the readers resulting in academic dishonesty.

As per Stanford University, plagiarism is defined as the "use, without giving reasonable and appropriate credit to or acknowledging the author or source, of another person's original work, whether such work is made up of code, formulas, ideas, language, research, strategies, writing or other form"[2] which basically refers to using previously published work by another author without valid consent, credit or acknowledgement and quoting it as one's own work. Fishman[3] described the five key elements of plagiarism as the "*use of words, ideas, or work products attributable to another identifiable person or source, without attributing the work to the source with legitimate expectation of original authorship too obtain some benefit, credit or gain which need not be monetary*". These elements establish the components of **actus reus** (using others ideas or words without duly attributing them) and **mens rea** (illegitimately earned credit).[3]

It has been quoted that academic plagiarism need not be necessarily deliberate. The possibility of unintentional failure of inserting a citation must be considered. Often collusion is considered as a part of academic plagiarism i.e. "the behaviour of authors, who write collaboratively, or copy from one another, although they are required to work independently."

Types of plagiarism

1. *Verbatim plagiarism* – word-by-word facsimile of a previously published manuscript. This includes substantial copying, paraphrasing and recycling the work previously published without citation of the prior work. Minor copying of short phrases can also occur without misattribution of data.[4]
2. *Mosaic or patchwork plagiarism* – Contents obtained from multiple sources without using quotation marks or maintaining the original layout.
3. *Loose plagiarism* - Copying with minimal changes in someone else's work
4. *Text recycling* – matter gets recirculated in the same article or in some other.
5. *Image recycling* – photographs minimally edited by either cropping or rotation.
6. *Segmented or "salami-slicing"* – Often the authors tend to submit all the work done as original article with few case reports to derive more publications out of a project.
7. *Self-plagiarism* – Recycling previously published own work by reframing the text in different journals. Duplication is also included in this wherein the same article is repeatedly published in several similar manuscripts.

Plagiarism can be successfully avoided by[5]:

1. Reframing the sentences based on our own understanding of the previously quoted information along with additional supportive data therefore adding to the already available pool of knowledge. Paraphrasing with no added intellectual contribution is of no advantage.[6]
2. By writing the text in quotation marks with a legitimate citation to the original article
3. Without text repetition, refer to the original publication
4. Properly cited relevant appendix should be included

"Originality is undetected plagiarism" –William Ralph Inge

As defined by "The Committee on Publication Ethics (COPE)", the protocol suggested to be followed by the editors as they come across plagiarism has been enlisted in figure 1.[1] It is recommended for the editors to follow this protocol to avoid scientific misconduct and to ensure a flow of creativity and standards of their journal especially in developing countries.[7]

Moylan and Kowalczuk reported that over 15 years articles from BioMed Central journals (who complied with COPE guidelines) 134 (0.07%) retraction notices were issued out of which plagiarism was noted in 22 (16%) articles.[8] Whereas Fang et al stated that out of the 2047 articles retracted articles by PubMed, 9.8% were due plagiarism and that the retractions have increased by 10 fold since 1975, mainly constituting authors from India, the United States, China and Italy (India being the highest).[9] Amos reported that out of the 53 countries with retracted literature from 2008-2012, India ranked second after China in terms of plagiarized articles.[10]

With the advent of technology, there has been a significant increase in plagiarism. However, instructional strategies and several innovative plagiarism detection software have been created due to technology advancement to forestall plagiarism.[11] Turnitin, eTBLAST, Plagiarism Checker X, iThenticate, Citeplag, Plagiarism detect, Plagium, Plagiarism detector, Plagiarisma are the most effective detection websites and softwares available. Universities and institutions are advised to be associated with one of these genuine software to check dissertations, thesis and assignments for assessment of plagiarism.[12] However, it has been noted that mass retractions of plagiarized articles indicates inability of software to detect manipulative paraphrasing.[13] Therefore, these require timely updates and an overall improvement in terms of strategy planning to eliminate plagiarism.

Plagiarism is considered as intellectual theft and is highly condemned as it questions the author's credibility and affects the standards of the journals without adding any information to the already available scientific information. An anti-plagiarism strategy formation includes utilization of semantic digital technologies and following COPE protocols at the editor level to prevent publication of falsified information and retraction of plagiarized articles to maintain the journal reputation by adhering to global editorial guidance.

References

1. Wager E. How Should Journal Editors Respond to Cases of Suspected Misconduct? J Microbiol Biol Educ. 2014 Dec 15;15(2):146–50.
2. What Is Plagiarism? | Office of Community Standards [Internet]. [cited 2021 Nov 21]. Available from: https://communitystandards.stanford.edu/policies-and-guidance/what-plagiarism
3. Fishman T. "We know it when we see it" is not good enough: toward a standard definition of plagiarism that transcends theft, fraud, and copyright. 4th Asia Pac Conf Educ Integr 4APCEI [Internet]. 2009 Sep 30; Available from: https://ro.uow.edu.au/apcei/09/papers/37
4. Sengupta S, Honavar SG. Publication ethics. Indian J Ophthalmol. 2017 Jun;65(6):429–32.
5. Horrom TA. The perils of copy and paste: plagiarism in scientific publishing. J Rehabil Res Dev. 2012;49(8):vii–xii.
6. Newman AB. Plagiarism: Policy and Practice. J Gerontol A Biol Sci Med Sci. 2019 Mar 14;74(4):499.
7. Joob B, Wiwanitkit V. Self-Plagiarism. Am J Roentgenol. 2013 Jul 1;201(1):W161–W161.
8. Moylan EC, Kowalczuk MK. Why articles are retracted: a retrospective cross-sectional study of retraction notices at BioMed Central. BMJ Open. 2016 Nov 23;6(11):e012047.
9. Fang FC, Steen RG, Casadevall A. Misconduct accounts for the majority of retracted scientific publications. Proc Natl Acad Sci U S A. 2012 Oct 16;109(42):17028–33.
10. Amos KA. The ethics of scholarly publishing: exploring differences in plagiarism and duplicate publication across nations. J Med Libr Assoc JMLA. 2014 Apr;102(2):87–91.
11. Anderson MS, Steneck NH. The problem of plagiarism. Urol Oncol. 2011 Feb;29(1):90–4.
12. Lemke AJ, Kazi I, Felix R. Magnetic resonance imaging of orbital tumors. Eur Radiol. 2006 Oct;16(10):2207–19.
13. Gasparyan AY, Nurmashev B, Seksenbayev B, Trukhachev VI, Kostyukova EI, Kitas GD. Plagiarism in the Context of Education and Evolving Detection Strategies. J Korean Med Sci. 2017 Aug;32(8):122

Review article

Low concentration atropine for the control of myopia progression: an overview

Batriti Shympliang Wallang

Abstract:
The increasing trend in the prevalence of myopia around the world and the associated ocular complications of high myopia has made it an important public health issue. Various strategies for the slowing of myopia progression in childhood have been researched, of which low concentration atropine has shown the best efficacy to date. This review discusses the rationale and mechanism of action of atropine. It also provides an overview of the emerging data regarding the best low dose concentration which balances efficacy with adverse effects, as well as a summary of the proposed treatment protocols in regular practice.
Key words: Low concetration atropine, myopia

Introduction:

Axial myopia is a refractive condition of the eye characterized by a mismatch between the focal length of the lens and axial length of the eye resulting in images focusing in front of the retina. Any refractive error of -0.5D or more is defined as myopia[1]. While myopia was previously considered to be an inconvenient refractive state of the eye, determined by various genetic and environmental factors[2-6], it has now become a growing health concern. Various epidemiological studies have demonstrated a growing prevalence of myopia that is expected to affect 50% of the global population, or 4.8 billion people, by the year 2050[7]. Of these, 9.8% are expected to have high myopia. Prevalence rates around the world show regional variations. The highest rates are reported from the east Asian region where up to 80-90% of young adults at high school are myopic[3,8]. Prevalence of high myopia (< -5.00D) varies from 2-5% in Caucasian populations and 5-10% in Asian populations[9].

A recent systematic review on myopia prevalence in Indian urban children between 5 to 15 years of age showed an increase in myopia prevalence from 4.44% in 1999 to 21.5% in 2019 and predicted an increase to 48.1% by 2050[10]. A hospital-based study in 2020 estimated an overall prevalence of 2.5% of high myopia in Indians[11]. These figures are particularly alarming because high axial myopia is associated with a higher risk of other vision-threatening ocular morbidities like retinal detachments, choroidal neovascularization[12], myopic macular degeneration, glaucoma, and cataract[13,14]. The risk of developing high myopia has been shown to significantly increase with younger age of onset[15]. This carries with it both a social impact, in terms of lower quality of life indicators and negative psychosocial effect, as well as a large economic burden[16,17]. Taking these facts into consideration, there has been a growing interest in developing means of delaying either myopia onset or progression in school-aged children to limit high and pathological myopia in later life.

Various treatments have been studied for controlling the progression of myopia in children and include optical therapies (under-corrected eyeglasses, multifocal eyeglasses, bifocal and multifocal contact lenses), orthokeratology contact lenses, topical anti-muscarinic agents, and topical timolol maleate 0.5%[18,19]. Modification of environmental factors such as increased outdoor activities and reduced near work have also been shown to reduce myopia progression[2-6]. As of 2011, a Cochrane database review concluded that anti-muscarinic agents are the "the most likely effective treatment' for myopia progression[18]. More recent studies have shown promising results with orthokeratology or combined treatment as well[20].

Corresponence to: Batriti Shympliang Wallang[1], DO, [1]Consultant Ophthalmologist, Bansara Eye Care Centre, Shillong, Meghalaya.
Email: drbatriti@gmail.com
Date Received: 30.10.2021
Date accepted: 09.01.2022

Mechanism of action of atropine:

Atropine is a non-selective competitive muscarinic acetylcholine receptor antagonist. It has a high affinity for all 5 types of muscarinic receptors. Muscarinic receptors are found in the cornea, iris, ciliary body, and muscles, epithelium of crystalline lens, amacrine cells of the retina, retinal pigment epithelium, choroid and scleral fibroblasts[21].

Atropine was initially thought to exert its effects by inhibiting accommodation. The hypothesis was that excessive accommodation resulted in myopia. However, a study on the use of atropine in chicks showed inhibition of myopia despite the absence of muscarinic receptors in their striated ciliary muscles refuting this[22]. Further animal studies showed that eyes unable to accommodate, by the destruction of the Edinger Westphal nucleus or sectioning of the optic nerve, also developed myopia in response to imposed hyperopic defocus[23]. This has shifted the research to non-accommodative mechanisms.

The exact mechanisms of emmetropisation and myopization are still not fully understood. It is hypothesized that emmetropisation occurs by a feedback mechanism consisting of an afferent arm, perhaps located in the retro-equatorial, mid-peripheral fundus, and an efferent arm. It has been shown in animal studies that peripheral defocus results in axial elongation of the eye, pointing to this area as the afferent sensory part of emmetropisation [24]. The messengers transmitting signals between the afferent and efferent arms and the exact target tissues causing axial elongation are not clear. Possible messengers have been thought to be dopamine, levodopa, or dopamine-like agonists [25], and muscarinic antagonists. The potential target tissues may be the sclera, choroid, Bruch's membrane, or retinal pigment epithelium (RPE) [22].

Dopamine agonists have been shown to inhibit myopia progression in various animal models. Atropine causes increased dopamine release in chick retinas. GABAergic transmission is known to have an important role in the control of eye growth and refractive development in animals and dopamine reduced levels of GABA transporter 1 and 3[22]. However, muscarinic receptors in the retina are specifically found in amacrine cells, but studies on chick eyes with ablated amacrine cells found atropine to still inhibit form-deprivation myopia [26]. This suggested the involvement of muscarinic receptors in other ocular tissues or the action of atropine through non-muscarinic receptors.

At the level of the RPE, atropine is thought to act by altering the growth factors and neurotransmitters regulating scleral growth and choroidal changes. The RPE may be a relay station for transmitting a signaling cascade to the sclera or choroid[22]. Atropine increased dopamine release but reduced b and d waves on electroretinogram (ERG), with dampening of RPE oscillations. It is suggested that dampening of retinal function boosts dopamine release.

The role of the choroid in axial elongation is suggested by changes in its thickness in response to optical defocus to adjust the retinal plane of focus (choroidal accommodation)[22]. Atropine has been found to transiently increase the choroidal thickness in animal and human eyes[27].

The sclera as an effector tissue is suggested due to scleral thinning and scleral tissue remodeling with axial elongation. Studies on chick and mouse eyes have shown a reduction in synthesis of glycosaminoglycans in the scleral extracellular matrix by atropine, increasing the thickness of the scleral fibrous layer and possibly retarding axial elongation[22].

While various studies have pointed to these potential sites, the exact mechanism of atropine in myopia progression control is still not clear.

Which concentration is the best?

A summary of landmark studies:

Atropine 1%:

Atropine use in the control of myopia progression has been described since the 1920s. Earlier studies had confirmed that myopia progression varied with age, with maximum progression occurring before 12 years of age as compared to the later teens. Accordingly, this has been the target age group for initiation of atropine therapy to have the greatest impact in delaying myopia progression. There was also an indication that cessation of atropine resulted in a recurrence of myopia progression[28] and there was uncertainty over whether this rebound may

perhaps negate the overall effect of atropine administration in the first place.

The first randomized placebo-controlled trial providing robust data on the efficacy of atropine 1% was carried out in 1989 by Yen et al. There was no data on the effect of atropine on the axial length (AL)[29]. Complications associated with high axial myopia and pathological myopia may have a direct relation with AL and changes in Bruch's membrane. Therefore, when looking at the rationale for atropine in myopia progression control, this becomes an important outcome measure[30,31].

A greater clinical acceptance of atropine for myopia in regular practice came with the Atropine for the Treatment of Childhood Myopia (ATOM) studies.

ATOM 1 was a randomized placebo-controlled (RCT) trial of 1% atropine on 400 Asian children was published by Chua et al in 2006[31].

- It showed that 1% atropine brought about a 77% reduction in myopia progression compared to placebo over a 2-year study period.
- There was also no AL change in this period.
- This was followed by a 1-year washout period of observation published separately[32]. As expected, there was a rebound increased myopia progression and change in AL in the atropine treatment group but the overall myopia progression remained lower in the atropine group as compared to placebo over the total 3 years.
- There was also no long-term or permanent effect of atropine on pupil size and amplitude of accommodation which reverted to the pretreatment levels.

Although these studies had proven the efficacy of 1% atropine, there was still some concern in adopting it in regular clinical practice due to the theoretical side effects of the medication. These included possible increased exposure of the lens and retina to UV rays from a mydriatic pupil and possible cataract or retinal damage, direct toxicity of long-term atropine itself to the retinal tissues, and possible systemic side effects of long-term topical atropine administration. ATOM 1 reported no significant adverse effects with the use of photochromatic glasses as well as only one eye being used for medication, preserving the second eye for near vision, in the study protocol.

There has been a large body of literature since for the use of atropine in myopia[33-39]. In broad summary, successively lower concentrations of atropine have been studied in an attempt to balance the efficacy in myopia progression control with the side effects of its mydriatic and cycloplegic action. Summarized details of RCTs can be found in Tables 1 and 2.

Atropine 0.01%:

At present, practice patterns for the use of low concentration atropine are largely based on the Atropine for the Treatment of Childhood Myopia 2 (ATOM 2) study. The ATOM 2 study looked at lower concentrations of atropine of 0.5%, 0.1%, and 0.01%. The study had been designed in 3 phases. Phase 1 studied the effect of atropine 0.5%, 0.1%, and 0.01% on myopia progression and AL elongation over 2 years[40]. Phase 2 looked into the difference in rebound phenomenon between these concentrations after 1 year of wash out[41], and phase 3 followed up myopia progressors from phase 2 that were re-started on 0.01% atropine over another 2 years[42]. Salient information that emerged from ATOM 2 is as follows:

- Concentration as low as 0.01% atropine had a significant effect in reducing myopia progression (in terms of change in spherical equivalent (SE)) over the first 2 years.
- The efficacy may be dose-dependent with 0.5% showing the maximum retardation in myopia progression and AL elongation and least with 0.01%. However, the difference between them became insignificant over 2 years of follow-up. The efficacy of 0.01% atropine improved in the second year, (not seen with 0.5% or 0.1%), which suggests a plateau in myopia progression with time and possibly a concentration threshold beyond which there is no further improvement in efficacy as seen with the higher concentrations.
- 0.01% showed the minimum, clinically negligible, side effects on pupil diameter and accommodative amplitude compared to 0.5% or 0.1%.

- 0.01% showed the least rebound in myopia progression, after 1 year of washout, as well as the minimum number of progressors (24% vs 59% and 68% for 0.1% and 0.5% respectively). Progressors were those children who increased by more than 0.5D of SE over 1 year of washout.
- Younger children and those with greater myopia progression in the 1st year of the study were more likely to be progressors in the washout period.
- The overall 5-year myopia progression was least for 0.01% atropine concentration. 0.01% showed a 50% reduction in myopia progression when compared historically to the placebo group of ATOM 1.

A subset of patients from ATOM and ATOM 2 were also studied for changes in ERG and there was no significant effect of atropine found suggesting no or minimal retinal toxicity over the study period[43]. There was also no significant effect found on intraocular pressure or astigmatism[44]. These findings have been corroborated by other studies[45].

The ATOM studies concluded by recommending 0.01% atropine as the best dose showing sustained efficacy with minimal adverse effects. The data from ATOM has led to the wide adoption of 0.01% atropine in the control of myopia progression in regular clinical practice. Other studies and meta-analyses for 0.01% atropine have found similar results[46-56]. There were, however, several drawbacks of the ATOM studies and several unanswered questions:

- The absence of a placebo group was the greatest limitation of the ATOM 2 study. There was no comparison of natural myopia progression and AL elongation of a placebo group against the effect of low concentration atropine to determine its true significance. It was considered medically unethical to have a placebo group when there was a clear efficacy of atropine therapy established.
- A meta-analysis of low dose atropine in one study showed no actual dose-dependency of atropine on myopia progression as there was clinically a small difference between the 0.01% and 0.1% group[57].
- When comparing axial elongation of the 0.01% group of ATOM 2 against the placebo group of ATOM, there was no real effect of 0.01% in slowing AL (0.41mm/ 2 years vs 0.38mm/ 2 years in placebo).
- There is also still uncertainty over how atropine affects eye growth in the longer term. Will slowing or control in the rate of myopia progression and AL be sustained once achieved? When exactly should it be stopped? The design of the study with washout of all concentration groups meant that there is no data on the effect of atropine over a longer period of sustained administration. The authors mention that the fact that the 5-year follow-up of ATOM2 found slower progression across all groups in older children is suggestive that the natural history of axial elongation slows with age and that this should allow the medication to be tapered off or stopped safely.
- Despite the efficacy in myopia control of all concentrations, there were still poor responders with the continued high progression of myopia despite the administration of atropine. The exact factors associated with poor response were still not clear. It had been postulated by other authors that these children may benefit from higher concentrations of atropine[58,59].

0.05% Atropine:

In an attempt to address some of these questions, a more recent study, the Low-Concentration Atropine for Myopia Progression (LAMP) Study was carried out and published in 2018. It aimed at studying the efficacy and safety of 0.05%, 0.025%, and 0.01% concentration atropine in 4 phases.

The first phase compared these 3 concentrations to placebo over 1 year[60]. The second phase followed up the same group of patients for another year[61]. The placebo group, however, was switched to 0.05% atropine ("switchover group") for ethical reasons considering the superior efficacy of atropine 0.05% demonstrated in phase 1. Phase 3 involved randomizing the children of each concentration group into continued treatment or washout over another year[62].

- All concentrations were found effective in slowing myopia progression in comparison to placebo. The efficacy of 0.05% atropine remained the best over 3 years, in both the continued treatment and washout subgroups.
- Continuing therapy with 0.05% atropine into the 3rd year showed better efficacy than stopping treatment at 2 years.
- The rebound effect was concentration-dependent as was seen with ATOM 2. The difference between the treatment groups however was small. Factors found to be associated with greater rebound were the use of higher concentration of atropine and younger age at cessation of therapy. Older ages showed lesser rebound progression in all concentrations with less difference between the concentrations, probably due to the natural slowing down in progression with age.
- There was a definite concentration-dependent response for both myopia progression and AL elongation that was in question from ATOM 2. This dose-dependency persisted in the second year of follow-up.
- There was no significant difference between AL elongation of 0.01% and placebo group, as with ATOM 2.
- The safety profile of all concentration groups was found to be good. There was no clinically significant increase in pupil size or reduction in accommodative amplitude over 3 years and it went back to pretreatment levels within 4 months of washout for all groups. The best-corrected distance and near vision were unaffected.
- A validated vision and quality of life questionnaire administered over the different phases also showed no significant difference across all groups.
- The effect of age on treatment response was published separately and showed that younger age was associated with a poorer response to all concentrations of atropine[63]. It was found that younger children on 0.05% atropine achieved a similar reduction in myopia progression as older children on the lowest concentration of 0.01% atropine.
- As with ATOM 2, this study also found a better efficacy of 0.01% atropine in the 2nd year compared to the 1st. The authors postulate that this may be due to a lower concentration taking more time to reach its concentration threshold for maximal effect compared to higher concentrations.

The study found 0.05% atropine to be the best concentration when balancing efficacy with adverse effects. With the recent publication of phase 3, it appears that sustained administration of atropine will be more efficacious than 2-year administration followed by washout. Sustained administration of 0.05% also appeared to be well tolerated. This is in contrast to an earlier study on the safety profile of low concentration atropine had concluded that 0.02% was the maximum concentration at which there was no clinically significant change in pupil size and accommodative amplitude[64]. It also showed 0.01% to have no significant effect on axial elongation. As with ATOM 2, a drawback of the study is the absence of a placebo group to directly analyze the data against the natural progression of myopia.

A 4th phase wherein all continued treatment groups will be switched to 0.05% atropine, based on the superior efficacy findings of phases 1 to 3, and followed up to 5 years for data on sustained, long-term administration of low dose atropine. Patients from the washout groups will be followed up as such unless found to progress by ≥0.5D wherein they would be re-started on 0.05% atropine.

Low concentration atropine in Indian children:

Most of the data on which use of low concentration atropine has been based on has been on East Asian ethnicity. It is known that there is a racial difference in type and distribution of muscarinic receptors which affects the bioavailability of atropine at target receptors and likely affects its ultimate efficacy[65]. Various studies have demonstrated differences in efficacy between Caucasian and Asian eyes[38,66-70].

A study published by Kothari and Rathod in 2017 on atropine 1% in 60 eyes of myopic Indian children, between the ages of 5-16 years, showed a 67% reduction in myopia progression over 1 year[71]. The concentration was well tolerated with the use of progressive photo grey spectacles. Up to 57% of children continued to progress by

≥0.5D of sphere in their study as compared to 14 % in ATOM. The studies, however, cannot be directly compared due to differences in mean age, baseline myopia, and sample size. The authors felt that 1% atropine for myopia progression was still relevant as an option for progressors using low concentration atropine.

Saxena et al published with I-ATOM study, a multicentric randomized trial on 0.01% atropine in 100 children of 6-14 years over 1 year [72]. There was a 54% reduction in myopia progression in the atropine group with no side effects. There was a greater reduction in axial length as compared to the placebo group but was not found to be clinically significant. A progression of >0.5D of SE was found in 13% for the atropine group as compared to 38% for placebo. It was found that younger age and greater myopia at baseline were associated with more progression.

Another study by Sivaraman et al on 0.01% atropine in 60 Indian children in southern India showed approximately 55% reduction in myopia progression over 1 year[73].

These published studies were limited by short-term follow-up and cannot be directly compared to other large sample RCTs.

Study (Author, Year)	Intervention	Country, Mean age /age range(y), Total no. of patients	Baseline refraction (D)	Follow up, (m)	Mean increase in myopia, D/y	Mean change in axial length, mm	Reported adverse effects	Conclusion
Yen et a, 1989[29]	A1% vs C1% vs. placebo	Taiwan, 6-14, 247	-0.50 to -4.00	12	*A1%*: 0.22±0.54 *C1%*: 0.58±0.49 *Placebo*: 0.91±0.58 *p*<0.01	-	Photophobia, loss of near vision	A!% is efficacious. Large drop out (final no.96)
Shih et al, 1999[33]	A0.1% with full eye glass correction vs. A0.25% with partially undercorrected eye glasses vs. A0.5% with bifocals vs. T0.5% with full correction	Taiwan, 6-13, 200	-0.50 to -6.75	24	*A0.5%*: 0.04±0.63 *A0.25%*: 0.45±0.55 *A0.1%*: 0.47±0.91 *T0.5%*: 1.06±0.61 *p*<0.01	-	0.5%: Photophobia, recurrent allergic blepharitis 0.25%, 0.1%: no ocular side effects No systemic side effects	All concentrations efficacious. Best effect with 0.5%. Maximum drop out with 0.5% No masking.
Shih et al, 2001[34]	0.5% with MF lenses vs. MF lenses vs. SV lenses	Taiwan, 6-13, 227	-3.3±0.1D	18	*A0.5%*: 0.42±0.07/18m *MF lenses*: 1.19±0.07/18m *SV lenses*: 1.4±0.09/18m *p*<0.0001	*A0.5%*: 0.22 *MF lenses*: 0.49 *SV lenses*: 0.59 p<0.0001	Not reported	A0.5% and MF lenses significantly slowed MP. MF and SV lenses did not significantly slow MP so effect may be largely due to Atropine. 17.2% drop out.
Chua et al, 2006[31] (ATOM 1)	A1% (in one eye) vs. placebo (in one eye)	Singapore, 6-12, 400	-1 to -6,	24	*A1%*: -0.28±0.92 *Placebo*: -1.2±0.69 *P*<0.001	*A1%*: -0.14±0.28 *Placebo*: 0.20±0.30 *p*<0.001	No serious adverse effects. Hypersensitivity reactions, blurred near vision reported	A1% efficacious for MP in low to moderate myopia Further studies needed to evaluate safety and efficacy in bilateral administration.
Tong et al, 2009[32] (ATOM 1)	A1% with 1 year washout	Singapore, 6-12, 400	-1 to -6	12	*A1%*: -1.14±0.8 *Control*: -0.38±0.39 *p*<0.0001	*A1%*: 0.29±0.37 *Placebo*: 0.52±0.45 *p*<0.0001	Amplitude of accommodation and near vision reverted to pre treatment levels by 6 months	Greater rebound with A1% compared to control. Overall better progression control with A1% (over 3 years)
Chia et al, 2009[78] (ATOM 1)	A1% on astigmatism	Singapore, 6-12, 400	-1 to -6, Astig ≤-2.00	24	*A1%*: 0.3±0.19 *Control eye*: 0.24±0.17 *Placebo*:0.33±0.18 *Control eye*: 0.33±1.16 *p*<0.05	-	-	No effect on astigmatism
Kumaran et al, 2015[44]	A1% vs placebo on biometric measures	Singapore, 6-12, 400	-3.36	36	Minimal change in biometric measures	-	-	Reduction in vitreous chamber depth seemed to cause reduction in AL
Yi et al, 2015[35]	A1% vs. placebo	China, 7-12	-1.23 (0.32)	12	*A1%*: 0.32±0.22 *Placebo*: -0.85±0.31 *p*<0.0001	*A1%*: -0.03±0.07 *Placebo*: 0.32±0.15 *p*<0.0001	No ocular side effects	Myopia reduction and no change in AL in treatment group

Table 1. Table of Randomised Controlled trials for Atropine 1% and 0.5% concentration
*Abbreviations: y – years, m – months, D – Dioptres, A – Atropine, C – Cyclopentolate, T – Tropicamide, MF – multifocal, SV – Single Vision, MP – Myopia Progression, AL – Axial Length

Study (Author, Year)	Intervention	Country, Mean age/ age range(y), Total no. of patients, Follow up (m)	Baseline refraction (D)	Mean increase in myopia, D/y	Mean change in axial length, mm	Reported adverse effects	Conclusion
Chia et al, 2012 [40] (ATOM 2)	A0.01% vs. A0.1% vs. A0.5%	Singapore, 6-12, 400, 24	≥-2	*A0.5%*: -0.30±0.6/2y *A0.1%*: -0.38±0.6/2y *A0.01%*: -0.49±0.63/2y *p*=0.02	*A0.5%*: 0.27±0.25 *A0.1%*: 0.28±0.28 *A0.01%*: 0.41±0.32 *p*<0.01	Allergic conjunctivitis. Decreased visual acuity, light sensitivity, impaired accommodative amplitude more for A0.05%	Discussed in text
Chia et al, 2014[41] (ATOM 2)	A0.01% vs A0.1% vs. A0.5% after 1 year wash out	Singapore, 6-12, 400, 12	≥-2	*A0.5%*: -0.87±0.52 *A0.1%*: -0.68±0.45 *A0.01%*: -0.28±0.33 *p*<0.001	*A0.5%*: 0.35±0.20 *A0.1%*: 0.33±0.18 *A0.01%*: 0.19±0.13 *p*<0.001	Pupil size and near visual acuity returned to normal. Reduced amplitude of accommodation for A0.5% group	Discussed in text
Chia et al, 2016[42] (ATOM 2)	A0.01% vs. A0,1% vs. A0.5% over 5 years followup	Singapore, 6-12, 192, 24	Baseline ≥2 Included those who progressed ≥0.5 in washout phase	*A0.5%*: -1.98±1.1/ 5y *A0.1%*: -1.83±1.16/ 5y *A0.01%*: -1.38±0.98/ 5y *A0.01% vs. A0.1%*: *p*<0.003 *A0.01% vs. A0.5%*: *p*<0.001	*A0.5%*: 0.87±0.49/ 5y *A0.1%*: 0.85±0.53/ 5y *A0.01%*: 0.75±0.48/5y *p*<0.185	No significant ocular side effects mentioned.	Discussed in text. (There may be some bias in comparison of groups at 5 years since only some patients from each group were re-treated at 3 years)
Yam et al, 2018[60] (LAMP phase 1)	A0.01% vs A0.025% vs. A0.05% vs. placebo	Hong Kong, 4-12, 438, 12	>-1 (-1.9 to -5.8)	*A0.05%*: -0.27±0.61 *A0.025%*: -0.46±0.45 *A0.01%*: -0.59±0.61 *p*<0.001	*A0.05%*: 0.20±0.25 *A0.025%*: 0.29±0.20 *A0.01%*: 0.36±0.29 *p*<0.001	Photophobia (became comparable to placebo at 1 year) Allergic conjunctivitis	Discussed in text
Yam et al, 2020[61] (LAMP phase 2)	A0.01% vs. A0.025%vs A0.05%	Hong Kong, 4-12, 383, 12 (extension of phase 1)	>-1 Patients from phase 1 (-2.0 to -5.9)	*A0.05%*: -0.55±0.86/ 2y *A0.025%*: -0.85±0.73/ 2y *A0.01%*: -1.12±0.85/ 2y *A0.05% vs. A0.025%*: p<0.015 *A0.05% vs. A0.01%*: *p*<0.001 *A0.025 vs. A0.01%*: *p*<0.02	*A0.05%*: 0.39±0.35/2y *A0.025%*: 0.50±0.33/2y *A0.01%*: 0.59±0.38/2y *A0.05% vs. A0.01%*: *p*<0.04 *A0.05% vs. A0.025%*: *p*<0.001 *A0.025% vs. A0.01%*: *p*<0.10	Photophobia, allergic conjunctivitis	Discussed in text
Fu et al, 2020[47]	A0.01% vs A0.02% vs. control	China, 6-14, 400, 12	-1.25 to -6.00	*A0.02%*: -0.38±0.35 *A0.01%*: -0.47±0.45 *Control*: -0.70±0.60 *p*<0.001	*A0.02%*: 0.30±0.21 *A0.01%*: 0.37±0.22 *Control*: 0.46±0.35 *p*<0.001	Photophobia, mild near vision blur (disappeared on follow up), allergic conjunctivitis and blepharitis (n=1).	A0.02% had better efficacy than 0.01%. Similar changes in biometric parameters between groups
Wei et al, 2020[50]	A0.01% vs placebo (crossover of groups at 12m)	China, 6-12, 220, 24	-1 to -6.00	*A0.01%*: -0.49±0.42 *Placebo*: -0.76±0.50 *p*<0.001	*A0.01%*: 0.32±0.19 *Placebo*: 0.41±0.19 *p*<0.004	Photophobia, allergic conjunctivitis	A0.01% effective in reducing myopia progression and AL elongation with good tolerance
Heida et al, 2021[51]	A0.01% vs. placebo	Japan, 6-12, 168, 24	-1.00 to -6.00	*A0.01%:* -1.26 (95%CI, -1.35, -1.17)/2y *Placebo:* -1.48 (95%CI, -1.57, -1.39)/ 2y *P*<0.001	*A1%:* 0.63 (95%CI, 0.59, 0.67)/ 2y *Placebo:* 0.77 (95%CI, 0.73,0.81)/ 2y *P*<0.001	Photophobia with suspected hemiplegic alteration migraine due to light sensitivity (n=1)	A0.01% efficacious over a longer period of time in Japanese school children with no significant adverse effects
Saxena et al, 2021[72]	A0.01% vs placebo	India, 100, 6-14, 12	-0.5 to -6	*A0.01%:* -0.16±0.4 (*p*=0.005) *Placebo:* -0.35±0.4 (*p*<0.01) *Difference between groups:* 0.19 (*p*=0.02)	*A0.01%:* 0.22±0.2 (*p*<0.001) *Placebo:* 0.28±0.28 (*p*<0.001) *Difference between groups*: 0.06 (*p*<0.001)	No clinically significant ocular side effects	Discussed in text
Yam et al, 2021 (LAMP phase 3)[62]	A0.01%, A0.025%, A0.05% each in continued treatment (CT) vs. washout (WO) over 1 year	Hong Kong, 350, 4-12, 12 (extension of phase 2)	>-1 Patients from phase 2: (-2.0 to -8.7)	*A0.05%*: WO: -0.68±0.49 CT: -0.28±0.42 P<0.001 *A0.025%*: WO: -0.57±0.38 CT: -0.35±0.37 p<0.004 *A0.01%*: WO: -0.56±0.40 CT: -0.38±0.49 p<0.04 *WO group over 3 y*: A0.05%: -1.15±1.13 A0.025%: -1.47±0.77 A0.01%: -1.81±1.10 P<0.03 *CT group over 3 y*: A0.05%: -0.73±1.04 A0.025%: -1.31±0.92 A0.01%: -1.60±1.32 P<0.001	*A0.05%*: WO: 0.33±0.17 CT: 0.17±0.14 p<0.001 *A0.025%*: WO: 0.29±0.14 CT: 0.20±0.15 p<0.04 *A0.01%*: WO:0.29±0.15 CT: 0.24±0.18 p<0.13 *WO group over 3 y*: A0.05%: 0.70±0.47 A0.025%: 0.82±0.37 A0.01%: 0.98±0.48 P<0.04 *CT group over 3 y*: A0.05%: 0.50±0.40 A0.025%: 0.74±0.41 A0.01%: 0.89±0.53 P<0.001	No clinically significant side effects. Photophobia not significantly different between WO and CT groups. Allergic conjunctivitis similar across groups	Discussed in text

Table 2: Table of Randomised Controlled Trials for Atropine concentrations of <0.05%
*Abbreviations: y- years, D – Dioptres, m- months, A – atropine, AL – axial length

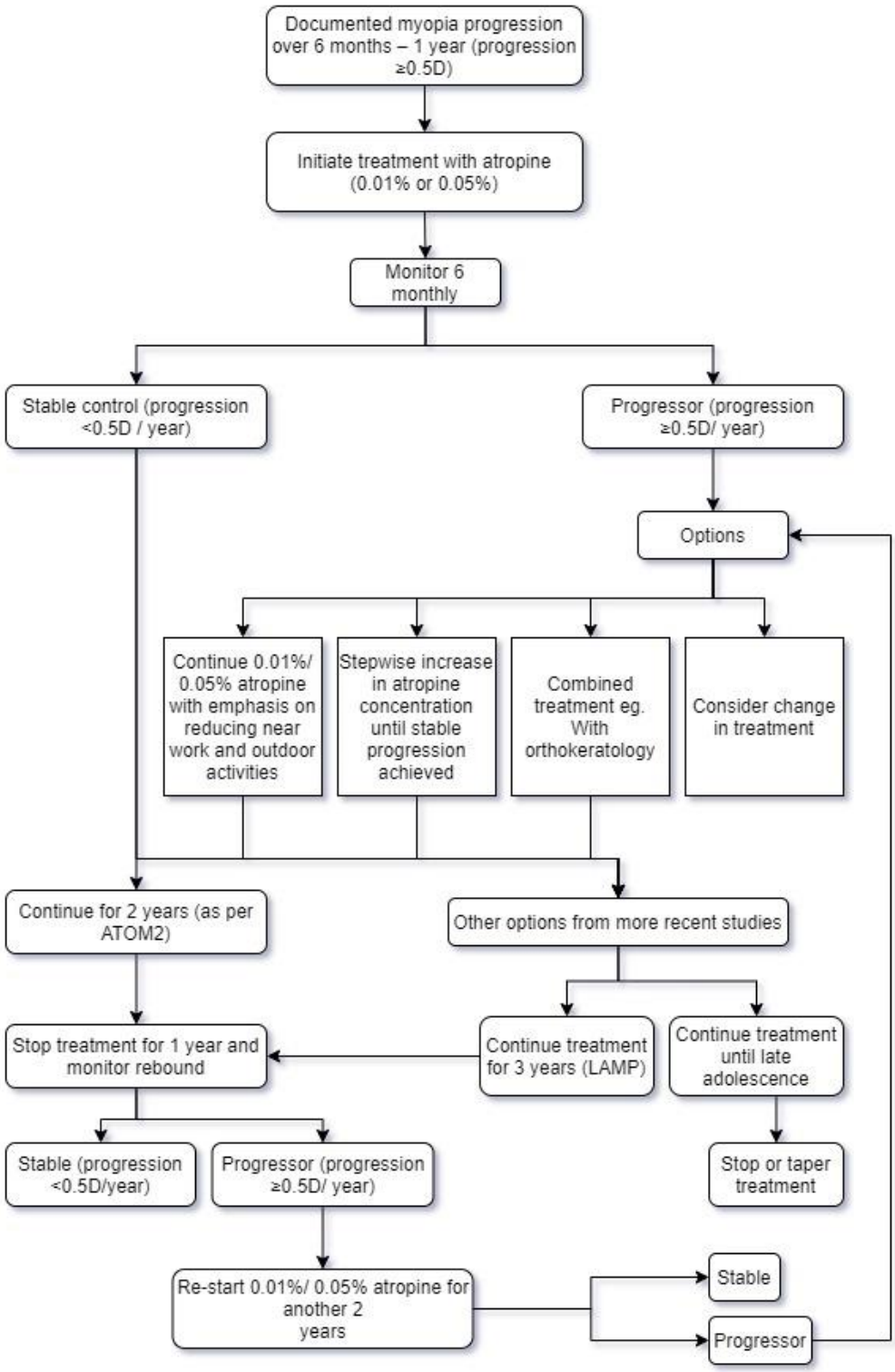


Figure 1. Proposed treatment protocols for low concentration atropine

How to initiate low concentration atropine in clinical practice:

It has been recommended that children be watched for progression over the preceding 6 months to one year before deciding on initiating them on measures for myopia control[42,62,74,75]. A progression of ≥0.5D is an indication to start treatment. However, there is still no consensus on the age to start treatment. Published studies have administered low concentration atropine at a minimum of 4 years of age and a maximum of 14 years. However, some clinicians feel that it may be left at the discretion of the ophthalmologist to start earlier or later in case of risk factors for progression like strong family history, or moderate to high myopia, or continued progression into the late teens[76]. The safety profile on long-term low-dose atropine in younger ages is still not established. The efficacy of atropine treatment in genetically predisposed individuals is also not known. Figure 1 shows a summary of the treatment protocols that have been advocated.

Parents and guardians should optimally be counseled on the risks and benefits of atropine therapy. Specific baseline parameters to be checked on initiation of therapy, other than the routine clinical examination, are cycloplegic refraction and axial length for follow-up. A 6 monthly follow-up is advised to check for the response. At the initiation of therapy, it may be prudent to re-assess the patient over a shorter period to ensure compliance and the absence of any adverse effects.

With the recent publication of the 3rd phase of the LAMP study, there is evidence for a longer period of sustained atropine administration of at least 3 years rather than a washout period after 2 years. The 4th phase will provide stronger evidence for sustained administration. However, the absence of commercially available 0.05% atropine, at present, may make it more difficult to initiate this treatment in many practices.

In the case of non-responders (who continue to progress by ≥0.5D) despite atropine treatment, various suggestions include progressively increasing the concentration of atropine[58,59], or else combining treatment such as emphasis on outdoor activities, reducing near work, and combined treatment with orthokeratology[20] or switching treatment.

There is still some controversy regarding whether it will be more effective to initiate therapy in pre-myopic children (refractive error of <+0.75) or to wait for progression[77].

Conclusion:

Low concentration atropine is certainly efficacious in the control of myopia progression and limitation of axial length elongation in simple myopia and can be adopted in routine clinical practice. There is still some debate as to the best concentration of atropine, but recently emerging data points towards 0.05% atropine and a longer, sustained administration to be the best approach. Treatment protocols would likely need to be tailored to the patient according to their response. Despite the positive evidence for use of low concentration atropine, it is not foolproof. There is still a sizeable percentage of non-responders to treatment. Since multiple variables affect AL elongation, it is difficult to accurately determine the factors involved. It is also not known whether atropine would be effective for other types of myopia such as pathological myopia. Better knowledge of the exact mechanisms of refractive control of the eye would allow for the development of even better-targeted approaches for myopia progression control.

Acknowledgement: Dr Wakaru Shullai[2], MS.[2]Consultant Ophthalmologist, Bansara Eye Care Centre, Shillong, Meghalaya

References:

1. Flitcroft DI, He M, Jonas JB, et al. IMI - defining and classifying myopia: a proposed set of standards for clinical and epidemiological studies. *Invest Ophthalmol. Vis. Sci.* 2019; 60: M20-M30
2. Rose KA, Morgan IG, Ip J, et al. Outdoor activity reduces the prevalence of myopia in children. *Ophthalmology* 2008; 115: 1279-1285
3. Saw SM, Zhang MZ, Hong RZ, et al. Near work related activity, night lights, and myopia in the Singapore-China study. *Evidence based Eye Care* 2002; 3: 198-199
4. Dirani M, Shekar SN, Baird PN. The role of educational attainment in refraction. The genes in myopia (GEM) twin study. *Invest. Ophthalmol. Vis. Sci.* 2008; 49: 534-538

5. Saw SM, Chua WH, Hong CY, et al. Near work in early-onset myopia. *Invest. Ophthalmol. Vis. Sci.* 2002; 43: 332-334
6. Lim HT, Yoon JS, Hwang SS, Lee SY. Prevalence and association of sociodemographic factors of myopia in Korean children: The 2005 third Korean National Health and Nutrition Survey (KHANES III). *Jpn. J. Ophthalmol.* 2012; 56: 76-81
7. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology* 2016; 123: 1036-1042
8. Lin LKL, Shih YFF, Hsaio CK, et al. Epidemiologic study of the prevalence and severity of myopia among schoolchildren in Taiwan. *J. Formos. Med. Assoc.* 2001; 100: 684-691
9. Pan CW, Klein BE, Cotch MF, et al. Racial variations in the prevalence of refractive errors in the United States: the multi-ethnic study of atherosclerosis. *Am. J. Ophthalmol.* 2013; 155: 1129-38.e1
10. Priscilla JJ and Verkicharla PK. Time trends on the prevalence of myopia in India - A prediction model for 2050. *Ophthalmic Physiol. Opt.* 2021; 41: 466-474
11. Verkicharla PK, Kammari P and Das AV. Myopia progression varies with age and severity of myopia. *PLoS ONE* 2020; 15: e0241759
12. Wong TY, Ferreira A, Hughes R, et al. Epidemiology and disease burden of pathologic myopia and myopic choroidal neovascularisation: an evidence based systematic review. *Am. J Ophthalmol.* 2014; 157: 9-25
13. .Praveen VR, Vasavada AR, Jani UD, et al. Prevalence of cataract type in relation to axial length in subjects with high myopia and emmetropia in an Indian population. *Am. J. Ophthalmol.* 2008; 145: 176-181
14. Saw SM, Gazzard G, Shih-Yen EC, et al. Myopia and associated pathological complications. *Ophthalmic Physiol. Opt.* 2005; 25: 381-391
15. Gwiazda J, Hyman L, Dong LM, et al. Factors associated with high myopia after 7 years of follow up in the Correction of Myopia Evaluation Trial (COMET) Cohort. *Ophthalmic Epidemiol.* 2007; 14: 230-7
16. Smith TST, Frick KD, Holden BA, et al. Potential lost productivity resulting from the global burden of uncorrected refractive error. *Bull. World Health Organ.* 2009; 87: 431-437
17. Vital S, Cotch MF, Sperduto R, et al. Costs of refractive correction of distance vision impairment in the United States, 1999-2002. *Ophthalmology* 2006; 113: 2163-2170
18. Walline JJ, Lindsley K, Vedula SS, et al. Interventions to slow progression of myopia in children. *Cochrane Database Syst. Rev.* 2011; 12: CD004916
19. Ang M, Flanagan JL, Wong CW, et al. Review: Myopia control strategies recommendations from the 2018 WHO/IAPB/BHVI Meeting on Myopia. *Br. J. Ophthalmol.* 2019; 0: 1-6
20. Suzhen Wang, Jie Wang and Ningli Wang. Combined Orthokeratology with Atropine for Children with Myopia: A Meta-Analysis. *Ophthalmic Res.* 2021; 164(5): 723-731
21. Upadhyay A and Beuerman RW. Biological mechanisms of atropine control of myopia. *Eye & Contact Lens* 2020; 46(3): 129-135
22. McBrien NA, Moghaddam HO, Reeder AP. Atropine reduces experimental myopia and eye enlargement via a nonaccommodative mechanism. Invest. *Ophthalmol. Vis. Sci.* 1993; 34: 205-215
23. Wildsoet CF. Neural pathways subserving lesions of the optic nerve and ciliary nerve. *Curr. Eye Res.* 2003; 27: 371-385
24. Smith EL 3rd, Hung LF, Huang J, et al. Effects of optical defocus on refractive development in monkeys: evidence for local, regionally selective mechanisms. *Invest. Ophthalmol. Vis. Sci.* 2010; 7: e43172
25. Feldkaemper M, Schaeffel F. An updated view on the role of dopamine in myopia. *Exp. Res. Eye* 2013; 114; 106-119
26. Fischer AJ, Miethke P, Morgan IG, et al. Cholinergic amacrine cells are not required for the progression and atropine-mediated suppression of form-deprivation myopia. *Brain Research* 1998;794(1): 48-60
27. Nickla DL, Zhu X, Wallman J. Effects of muscarinic agents on chick choroids in intact eyes and eyecups: Evidence for a muscarinic mechanism in choroidal thinning. *Ophthalmic Physio. Opt.* 2013; 33:245-256
28. Brodstein RS, Brodstein DE, Olson RJ, et al. The treatment of myopia with atropine and bifocals. A long-term prospective study. *Ophthalmology* 1984; 91: 1373-1379
29. Yen MY, Liu JH, Kao SC, Shiao CH. Comparison of the effect of atropine and cyclopentolate on myopia. *Ann. Ophthalmol.* 1989 May;21(5):180-2, 187
30. Jonas JB, Ohno-Matsui K, Jiang WJ, et al. Bruch membrane and the mechanism of myopization: a new theory. *Retina* 2017; 37: 1428-40
31. Chua WH, Balakrishnan V, Chan YH, et al. Atropine for the Treatment of Childhood Myopia. *Ophthalmology* 2006; 113: 2285-2291
32. Tong L, Huang XL, Koh ALT, et al. Atropine for the Treatment of Childhood Myopia: Effect on Myopia Progression after Cessation of Atropine. *Ophthalmology* 2009; 116: 572-579
33. Shih YF, Chen CH, Chou AC, et al. Effects of different concentrations of atropine on controlling

myopia in myopic children. *J. Ocul. Pharmacol. Ther.* 1999 Feb;15(1):85-90
34. Shih YF, Hsiao CK, Chen CJ, et al. An intervention trial on efficacy of atropine and multi-focal glasses in controlling myopic progression. *Acta. Ophthalmol. Scand.* 2001; 79: 233-236
35. Yi S, Huang Y, Yu SZ, et al. Therapeutic effect of atropine 1% in children with low myopia. *J AAPOS* 2015 Oct;19(5):426-9
36. Synuita LA, Isenberg SJ. Atropine and bifocals can slow the progression of childhood myopia in children. *Binocul Vis Strabismus Q.*2001;16:203-208
37. Chiang MF, Kouzis A, Pointer RW, et al. Treatment of childhood myopia with atropine eyedrops and bifocal spectacles. *Binocul. Vis. Strabismus Q.* 2001; 16: 209-215
38. Polling JR, Kok RG, Tideman JW, et al. Effectiveness study of atropine for progressive myopia in Europeans. *Eye (Lond)* 2016; 30: 998-1004
39. Wang YR, Bian HL, Wang Q. Atropine 0.5% eye drops for the treatment of children with low myopia: A randomized controlled trial. *Medicine (Baltimore)* 2017; 96: e7371
40. Chia A, Chua WH, Cheung YB, et al. Atropine for the Treatment of Childhood Myopia: Safety and Efficacy of 0.5%, 0.1% and 0.01% Doses (Atropine for the Treatment of Myopia 2). *Ophthalmology* 2012; 119: 347-354
41. Chia A, Chua WH, Wen L, et al. Atropine for the Treatment of Childhood Myopia: Changes after Stopping Atropine 0.01%, 0.1% and 0.5%. *Ophthalmology* 2014; 157: 451-457
42. Chia A, Lu QS, Tan D. Five-Year Clinical Trial on Atropine for the Treatment of Myopia 2. Myopia Control with Atropine 0.01% Eye drops. *Ophthalmology* 2016; 123: 391-399
43. Chia A, Li W, Tan D, et al. Full-field electroretinogram findings in children in the atropine treatment for myopia (ATOM 2) study. *Doc. Ophthalmol.* 2013; 126: 177-186
44. Kumaran A, Htoon HM, Tan D, et al. Analysis of changes in refraction and biometry of atropine and placebo treated eyes. *Invest. Ophthalmol. Vis. Sci.* 2015; 56: 5650-5655
45. Khanal S, Rathod SN, Phillips JR. The acute effect of atropine eye drops on the human full-field electroretinogram. *Doc. Ophthalmol.* 2020; 2021 Jun;142(3):315-328
46. Clark TY, Clark RA. Atropine 0.01% Eyedrops Significantly Reduce the Progression of Childhood Myopia. *J. Ocul. Pharmacol. Ther.* 2015 Nov;31(9):541-5. doi: 10.1089/jop.2015.0043. Epub 2015 Jul 28. PMID: 26218150.
47. Fu A, Stapleton F, Wei L, Wang W, Zhao B, Watt K, Ji N, Lyu Y. Effect of low-dose atropine on myopia progression, pupil diameter and accommodative amplitude: low-dose atropine and myopia progression. *Br. J. Ophthalmol.* 2020 Nov;104(11):1535-1541
48. Li FF, Kam KW, Zhang Y, et al. Differential Effects on Ocular Biometrics by 0.05%. 0.025%, and 0.01% Atropine: Low-Concentration Atropine for Myopia Progression Study. *Ophthalmology* 2020; 127: 1603-1611
49. Zhao Y, Feng K, Liu RB, et al. Atropine 0.01% eye drops slow myopia progression: A systematic review and Meta-analysis. *Int. J. Ophthalmol.* 2019; 12: 1337-1343
50. Wei S, Li SM, An W, et al. Safety and Efficacy of Low-Dose Atropine Eyedrops for the Treatment of Myopia Progression in Chinese Children: A Randomised Clinical Trial. *JAMA Ophthalmol.* 2020; 138: 1178-1184
51. Hieda A, Hiraoka T, Fujikado T, et al. Efficacy and Safety of 0.01% atropine for prevention of childhood myopia in a 2-year randomized placebo-controlled study. *Jpn. J. Ophthalmol.* 2021; 63: 315-325
52. Pineles SL, Kraker RT, VanderVeen DK, et al. Atropine for the Prevention of Myopia Progression in Children. A report by the American Academy of Ophthalmology. *Ophthalmology* 2017; 124: 1857-1866
53. Tran HDM, Tran YH, Tran TD, et al. A Review of Myopia Control with Atropine. *J. of Ocular Pharmacol. and Therapeut.* 2018; 34(5): 374-379
54. Li FF, Yam JC. Low-Concentration Atropine Eye Drops for Myopia Progression. *Asia Pac. J. Ophthalmol.* 2019; 8: 360-365
55. Zhao Y, Feng K, Liu JH, et al. Atropine 0.01% eye drops slow myopia progression: a systematic review and Meta-analysis. *Int. J. Ophthalmol.* 2019; 12(8): 1337-1343
56. Tsai HR, Chen TL, Wang JH, et al. Is 0.01% Atropine an Effective and Safe Treatment for Myopic Children? A systematic Review and Meta-analysis. *J. Clin. Med.* 2021; 10: 3766
57. Gong Q, Janowski M, Luo M, et al. Efficacy and adverse effects of atropine in childhood myopia: a meta-analysis. *JAMA Ophthalmol.*2017;135:624-630
58. Wu PC, Yang YH, Fang PC, et al. The long-term results of using low-concentration atropine eye drops for controlling myopia progression in school children. *J. Ocul. Pharmacol. Ther.* 2011;27:461-466
59. Chuang MN, Fang PC, Wu PC. Stepwise low concentration atropine for myopic control: a 10-year cohort study. *Sci. Rep.* 2021; 11: 17344
60. Yam JC, Jiang Y, Tang SM, et al. Low-concentration Atropine for Myopia Progression (LAMP) Study. A Randomised, Double-Blinded, Placebo-Controlled Trial of 0.05%, 0.025%, and 0.01% Atropine Eye Drops in Myopia Control. *Ophthalmology* 2018;1-12

61. Yam JC, Li FF, Tang AM, et al. Two-Year Clinical Trial of the Low-Concentration Atropine for Myopia Progression (LAMP) Study. Phase 2 Report. *Ophthalmology* 2019; : 1-10
62. Yam JC, Zhang XJ, Zhang Y, et al. Three-Year Clinical Trial of Low-Concentration Atropine for Myopia Progression (LAMP) Study: Continued Versus Washout. Phase 3 Report. *Ophthalmology* (2021), doi:https://doi.org/10.1016/j.ophtha.2021.10.002
63. Cooper J, Eisenberg N, Schulman E, et al. Maximum atropine dose without clinical signs or symptoms. *Optom. Vis. Sci.* 2013; 90: 1467-1472
64. Salazar M, Shimada K, Patil PN. Iris pigmentation and atropine mydriasis. *J. Pharmacol. Exp. Ther.* 1976; 197: 79-88
65. Larkin GL, Tahir A, Epley KD, et al. Atropine 0.01% Eye Drops for Myopia Control in American Children. A multi-ethnic Sample across Three US States. *Ophthalmol. Ther.* 2019; 8: 589-598
66. Sachhi M, Serafino M, Villani E, et al. Efficacy of atropine 0.01% for the treatment of childhood myopia in European patients. *Acta Ophthalmol.* 2019; 97: e1136-e1140
67. Myles W, Dunlop C, McFadden SA. The effect of Long-Term Low-Dose Atropine on Refractive Progression in Myopic Australian School Children. *J. Clin. Med.* 2021; 10: 1444
68. Loughman J, Flitcroft DI. The acceptability and visual impact of 0.01% atropine in a Caucasian population. *Br. J. Ophthalmol.* 2016; 100: 1525-1529
69. Li SM, Wu SS, Kang MT, et al. Atropine slows myopia progression more in Asian than white children by meta-analysis. *Optom. Vis. Sci.* 2014; 91: 342-350
70. Kothari M, Rathod V. Efficacy of 1% atropine eye drops in retarding progressive axial myopia in Indian eyes. *Indian J. Ophthalmol.* 2017; 65(11): 1178
71. Saxena R, Dhiman R, Gupta V, et al. Atropine for the Treatment of Childhood Myopia in India. *Ophthalmology* 2021; 128(9): 1367-1369
72. Sivaraman V, Gopalakrishnan A, Hussaindeen JR, et al. Efficacy of low-dose atropine to reduce myopia progression among Indian children. *Indian J. Ophthalmol.* 2021; 69: 1358-9
73. Ang M, Flanagan J, Wong CW, et al. Review: Myopia Control Strategies recommendations from the 2018 WHO/ IAPB/ BHVI Meeting on Myopia. *Br. J. Ophthalmol.* 2020; 104: 1482-1487
74. Wu PC, Chuang MN, Choi J, et al. Update in myopia and treatment strategy of atropine use in myopia control. *Eye* 2019; 33: 3-13
75. Kesarwani SS, Mumbai Group of Paediatric Ophthalmologists and Strabismologists. Consensus statement and guidelines for use of dilute atropine sulphate in myopia control. *Indian J. Ophthalmol.* 2019; 67: 461-3
76. Wong CW, Foo LL, Morjaria P, et al. Highlights from the 2019 International Myopia Summit on 'controversies in myopia'. *BrJ Ophthalmol.* 2020;0:1-7
77. Chia A, Chua WH, Tan D. Effect of topical atropine on astigmatism. *BrJ.Ophthalmol.* 2009; 93(6):799-80

Review article

Current trends in the use and outcome of anterior chamber intraocular lens (IOL) implantation

Swapnali Sabhapandit [1]

Abstract:
Anterior chamber placement of intraocular lenses is a necessity for eyes with aphakia and poor capsule or zonular support. There are mainly two types of anterior chamber intraocular lens (ACIOL), angle supported and iris claw lenses. The review was based on extensive Pubmed and Medline database regarding the design, history, surgical techniques, outcomes and complications in these ACIOLs. The visual acuity improved in majority patients for both types of ACIOL. The commonest complications noted were glaucoma, corneal decompensation, uveitis, pupillary distortion, cystoid macular edema and retinal detachment. However, with improvement in technique and ACIOL designs, these complications were low in incidence. As these lenses are placed in compromised eyes, the benefits outweigh the risk of surgery considerably. This review attempts to understand the position of ACIOL in today's ophthalmology practice and the current concepts in their usage.

Key words: Anterior chamber, intraocular lens, angle supported, iris claw, corneal decompensation, glaucoma, vitrectomy.

1. Introduction

The need of secondary intraocular lens (IOL) implantation after a cataract surgery arises due to multiple reasons, such as trauma, complicated cataract extraction, lens coloboma, Marfans syndrome, pseudoexfoliation syndrome and other congenital or metabolic syndromes where the capsule and/ or zonules are either absent or unable to support a conventional posterior chamber IOL. [1] The three major methods for secondary IOL implantation are anterior chamber IOL (ACIOL), iris fixated IOL and scleral fixated IOL. There is no clear consensus on the best option for secondary IOL in the absence of large prospective, randomised trials. Hence, it is imperative for the surgeon to decide the IOL choice based on the ocular status, surgical skills, patient's requirements and resources available. ACIOLs are also used in refractive error correction in phakic condition. [2] However, this review will attempt to understand the history, indications, outcome and complications of ACIOL (angle supported and iris supported in anterior chamber) use in aphakia.

1.1 History of ACIOLs

The use of ACIOL in aphakic cases started in 1950s with the Baron ACIOL.[3] However, due to the rigid nature of the IOL inherent to the polymethyl methacrylate (PMMA) material used and the closed loop design leading to high incidence of pigment dispersion, glaucoma, cystoid macular edema and corneal decompensation, these early ACIOLs rapidly fell into disfavour.[4, 5] The advent of open loop, flexible haptics in ACIOL since the 1980's changed the scenario and ACIOL became more acceptable.[5, 6] Charles D Kelman pioneered the design and usage of this IOL. [5, 7, 8] Gradually, iris claw ACIOL, in use since the 1970s, also found favour for aphakia correction. [5,8,9] As of today, US FDA approves use of only angle supported open loop ACIOL for use in aphakic correction. [10] However, off label use of iris claw ACIOL is popular around the world.

2. Types of ACIOL

2.1 Closed loop ACIOL: As early as 1953, Strampelli and Danheim designed a triangular ACIOL, followed by multiple other designs such

---

Conflict of Interest: None.
Funding source: None
Received : 29 October 2021
Accepted : 16 December 2021

Correspondence to :
Swapnali Sabhapandit, MS, Head, Department of Ophthalmology, Asian Institute of Gastroenterology Hospitals, Mindspace road, Gachibowli, Hyderabad India 500032. Email: drswapnali@gmail.com

as Choyce, Barraquer, Leiske, Surgidev, Cisco Optiflex etc. [5,11-13] The rigid design, closed non-flexible haptics of these ACIOLs led to increased chaffing of iris and anterior chamber angle tissue, causing synechiae formation, pigment dispersion, uveitis-glaucoma-hyphema syndrome and cystoid macular edema. Due to endothelial cell loss, corneal decompensation was also higher. [5,12,13] With advent of open loop ACIOL, these lenses were discontinued worldwide.

2.2 Open loop ACIOL: After intense research on the design, material quality and manufacturing techniques of ACIOL, changes were made in the newer lenses. These included open loop flexible haptics, flexible material, better IOL vaulting, tumble-polishing to avoid sharp and brittle optic edge or haptics and four point touch at the anterior chamber angle for better rotational stability. [5] The Kelman Multiflex III (Alcon Inc, USA) is the prototype of these newer ACIOLs, and is popular worldwide (Figure 1). This IOL is made of PMMA and comes in a range of 12 to 14.5mm diameter. The vault is 0.5mm anteriorly, preventing pupillary block. The two haptics are flexible and provides fixation at four points in the angle. The sizing is calculated as roughly 1mm bigger than the horizontal corneal white-to-white diameter.[14]

A randomised control trial conducted in Nepal comparing aphakia versus Kelman Multiflex III after intracapsular cataract extraction showed only 5% patients having poor visual outcome less than 6/60 at 1 year. The commonest cause was uveitis with secondary glaucoma, followed by correctable refractive error.[7]

The L122UV (Bausch and Lomb Inc, USA) is another angle supported ACIOL. The design is similar to the Kelman Multiflex III, except that it is biconvex as opposed to the plano-convex design of the latter.. The MTA3UO ACIOL (Alcon Inc, USA) is another plano-convex ACIOL made of PMMA. A study comparing these two ACIOLs in aphakic patients with and without uveitis showed good outcome till 5 years follow up, with uveitic eyes showing greater risk of epiretinal membrane formation.[15]

Newer ACIOLs made of acrylic material are also being evaluated. These include foldable Acri.Lyc 15A (Acritec) and Acrysof ACIOL (Cachet, Alcon Surgical, USA), a foldable hydrophobic acrylate IOL.[16,17] Both lenses are delivered using an IOL injecting system.

A case series on Acri.Lyc usage showed minor complications following implantation, including corneal edema, increased IOP, hyphema, distorted pupil shape, iris bombe, vitreous hemorrhage, displaced ACIOL and cystoid macular edema. However, statistically significant visual improvement occurred postoperatively and was not influenced by the complications. [17] Similar results were demonstrated in a retrospective case series on Acrysof ACIOL.[16]

2.3 Iris claw ACIOL: Although the US FDA has approved only angle supported ACIOL use in aphakia correction, trials on iris claw ACIOLs on pediatric and adult cases of aphakia are ongoing in US. In other countries, iris claw IOLs are popularly used, placed either in anterior chamber or retro-pupillary fixated. The Medallion IOL which is a precursor of the modern iris claw IOL was introduced in the 1970s by Binkhorst and Worst. [18] Further modification was made by Worst and Singh and other surgeons, finally leading to the Artisan IOL (Ophtec BV) that has been used since then. [8,19] It is made of PMMA with a rigid 5mm optic and two haptics with flexible claws for iris enclavement. Standard diameter is 8.5mm with availability of 6.5mm and 7.5mm. As the corneal white-to-white measurement is not needed, hence sizing issues are not seen, even in eyes with abnormal angle or anterior segment dimensions. The Artisan IOL is available from +2.0 diopter (D) to +30.0 D power. Fixation to mid-peripheral iris is done with enclavation forceps, needle or sutures. Proper centration over pupil is needed to maintain mydriasis and protect iris vessels (Figure 2).

The Artisan IOL has consistently shown excellent results in visual outcome in aphakia. Chen et al. assessed the efficacy and safety of this IOL to correct aphakia. The visual acuity was improved in all 72 recruited patients till 3 years follow up, except 2 patients with postoperative ischaemic optic neuropathy and retinal detachment. [20] The mean endothelial loss was

9.78%, iris pigment deposits was 5.6%, while postoperative intraocular pressure (IOP) was not significantly increased throughout the follow-up. 16.7% patients noted glare and halos during night driving. A case report by Kheirkhah et al.. about the Artisan IOL use in aphakic correction in Fuchs' heterochromic iridocyclitis mentioned best corrected visual acuity (BCVA) of 20/20 one month postoperatively with no subsequent iris atrophy, glaucoma, IOL displacement, pupil ovalization, vitreous inflammation or clinical cystoid macular oedema.[21]

Artisan ACIOL when compared to scleral-sutured posterior chamber IOL (PCIOL) after vitrectomy and lens extraction showed shorter surgical time and faster BCVA recovery, with comparable long-term BCVA and IOP. Iris depigmentation, iritis, pupil distortion and single case of IOL dislocation was noted. [22] A study on 5 year follow up of this IOL in 128 patients showed improved BCVA at 1 year which remained stable up to 5 years. The mean endothelial cells density decreased slightly during follow up. [23] Koss et al. reported non-significant loss of corneal endothelial cells in 18 aphakic eyes with these lenses. The rate of loss was inversely proportional to the axial length, being minimal for eyes with axial length of 24 mm or more. [24] Most studies report endothelial cell loss in the first year. [25] Cagini *et al.* reported that simultaneous keratoplasty (Descemet's stripping automated endothelial keratoplasty, DSAEK) and aphakic iris claw ACIOL implantation in patients with aphakia and bullous keratopathy was safe, without major postoperative complications. [26]

3. Surgical technique :

3.1 Angle supported ACIOL- The primary aim is to place the ACIOL gently in the iridocorneal angle touching the scleral spur with no iris tissue entrapment.

The steps involved are-

a. The implantation of angle supported ACIOL in aphakic cases should be preceded by complete bimanual anterior vitrectomy.

b. The scleral tunnel should be made either superiorly or temporally. Any clear corneal incision made earlier need to be closed with single 10-0 nylon suture. Some surgeons prefer to extend the incision to 6mm positioning the extensions more posteriorly.

c. The ACIOL needs to be around 3 diopter less in power than the calculated posterior chamber IOL. A common formula used is: Power of PCIOL Calculated- (PCIOL A constant- ACIOL A constant).

d. The white-to-white diameter (WTW) along the determined axis of ACIOL placement is measured, and 1mm needs to be added to WTW for sizing of the ACIOL.

e. The pupil must be constricted with acetylcholine 1% intracamerally.

f. An iridotomy is created away from the haptics to prevent pupil block and also ensure haptic does not rotate into the iridotomy. Anterior vitrectomy cutter is used with a low cut rate of around 100. The cutter is turned posteriorly and foot pedal is activated to vacuum and cut active (level 3). As soon as iris is sucked in, the pedal is released and the opening examined for patency. In case an intraoperative iridotomy is not done, Nd: YAG laser peripheral iridotomy can be done next day.

g. The ACIOL is inserted via the scleral tunnel under ophthalmic viscosurgical device (OVD) cover into the anterior chamber with plain angulated forceps. A sheet glide can be used to ensure smooth entry over iris plane till the opposite angle.

h. Since this ACIOL has a 0.5mm anterior vaulting, the orientation of the IOL needs to be checked before insertion.

i. The trailing haptic is then tucked into the angle with forceps.

j. Once the scleral tunnel is secure, the haptics are checked for any iris tissue entrapment. This is done by lifting one haptic centrally and anteriorly with Sinsky hook and releasing it, followed by same manouvere in other haptic. If the pupil is peaked or oval shaped, it signifies that iris or vitreous may be trapped between haptic and angle. The angle supported ACIOLs should not be rotated as it may tear the angle tissue or lead to hyphema.

3.2 Iris claw ACIOL- This IOL can be used in the anterior chamber in eyes with pupil size less than 5 mm, central pupil position and adequate iris tissue. If pupil is irregular or torn, suture

pupilloplasty can be done prior to IOL placement. Small iris defects, corectopia where optic can be placed over pupil are included for this IOL. This IOL is avoided in cases with uveitis and large corectopia or iris tissue loss. An A constant of 115 (ultrasound biometry) or 115.7 (optical biometry) is recommended. The steps include-

a. Two paracentesis are done at 2 and 10 o'clock and pupil constricted with intracameral acetylcholine 1%.
b. A limbal incision of 5.5mm is made in the desired axis, followed by a superior iridotomy by anterior vitrector or iridotomy scissors.
c. Under OVD cover, the Artisan iris claw IOL is inserted through the limbal tunnel and centered over the pupil. The IOL is gently rotated till 3 and 9 o'clock position so that haptic slots are positioned over mid peripheral iris. If any localized iris thinning is present, the haptics can be adjusted accordingly.
d. The IOL is slightly tilted down towards the nondominant hand and enclavation forceps or needle or Vacufix is inserted via paracentesis using the nondominant hand. The instrument is then used to pick up the midperipheral iris tissue and pulled up towards inferior part of the claw. Once the iris tissue is properly entrapped into the claw, the procedure is repeated for the other haptic.
e. Pupil shape should not be distorted on completion of these steps. The OVD is removed and the incision wound is closed.

4. Complications in use of ACIOL:

4.1 Iris fixated ACIOL:

a. *Visual outcome:* Multiple studies have shown good results in the best corrected visual acuity (BCVA) after iris claw ACIOL use.[8] A meta-analysis of 6 studies comparing anterior chamber versus retropupillary placed iris claw ACIOL (RPCIOL) demonstrated substantial improvement in vision in both groups. [27] Teng et al compared visual outcome in iris claw and posterior chamber IOL till 1 year. The BCVA was better in iris claw IOL group (mean= 0.40) as compared to the other IOL (mean= 0.30). [28] Guell et al. noted similar improvement in BCVA up to 5 years in cases without capsule support. [23] Chen et al. also reported improvement in 70 of 72 eyes undergoing this IOL implantatation. [20] De Silva et al. studied visual outcome in iris claw IOL use during primary surgery or as a secondary procedure, and found around 70% eyes had BCVA of 6/12 or better at 22.4 months.[29]

b. *IOP increase:* The American Academy of Ophthalmology reported a 0 to 3.3% rate of glaucoma in iris claw IOL use. [22] Helvaci et al. noted a high but transient IOP elevation in eyes post iris claw IOL insertion. [30] Teng et al. and Guell et all. also observed rise in IOP on first post-operative day, which normalized by 1 month. [23,28] De Silva et al. noted 9.5% eyes showed transient IOP increase in their study.[29] Cagini et al. studied IOP post DSAEK with iris claw IOL and found it to be stable. [26] Use of peripheral iridotomies significantly reduced the risk of glaucoma in iris claw IOL usage.[27]

c. *Corneal endothelial cell loss:* The proximity of the ACIOLs to the corneal endothelium is a major concern, and phakic ACIOLs have shown endothelial cell loss in a progressive manner. [31] Iris claw lens have shown equal cell loss at 1 year compared to PCIOL in Teng et al. study. [23] Guell et al. also noted slight decrease in cell count until 5 years follow up. [28] Comparative meta-analysis between AC and RPCIOL showed no significant difference in cell loss till 33 +/- 21.8 years.[27] Koss and Kohnen noted that cell loss was more in eyeballs having axial length more than 24mm.[24]

d. *Pupillary irregularities:* Helvaci et al. studied changes in pupil in AC versus RPCIOL for iris claw IOL, and found similar changes (3% in AC and 5% in RPCIOL respectively). [30] In a study by Chen et al., no pupillary irregularities were detected except loss of iris pigments. [20] Improvement in the surgical technique and IOL material has probably resulted in negligible cases of pupil distortion post usage of this IOL recently.

e. Chronic uveitis: De Silva et al. reported an incidence of anterior uveitis in 7.7% patients implanted with iris claw ACIOL. [29] Similar findings were noted by Teng et al. when comparing with PCIOL usage. [23] Figure 3 shows a case of chronic iritis with pupil ovalisation following use of Artisan ACIOL in complicated cataract surgery.

f. Cystoid macular edema (CME): The primary cause of CME in iris claw ACIOL use is the constant chaffing of iris tissue resulting in a low grade, chronic uveal insult, along with the aphakic status of the eye. [22,31] If insufficient iris tissue is entrapped, then long standing movement of the IOL on the iris can also cause CME. Guell et al. noted CME at 1 year after surgery, as also in a study by De Silva et al. (7.7%).[28,29]

g. Other complications: Retinal detachment, spontaneous IOL dislocation, intraocular haemorrhage, glare and haloes at night, wound leak were some of the rare complications mentioned in different studies of eyes with iris claw ACIOL implantation. [8]

4.2 Angle supported ACIOL:

a. Visual outcome: Since the time closed loop rigid ACIOL have been replaced by open loop flexible ACIOL, the visual outcome have improved drastically after surgery. Auffurth et al and Drolsum noted a significant drop in complications with BCVA approaching 6/6 in their studies of open loop ACIOLs.[5,32] The Kelman Multiflex III ACIOL has consistently shown good visual outcome in most studies, comparable to scleral fixated PCIOL. [14] Newer acrylic angle supported ACIOL have also reported good visual outcome, including a study by Omulecki et al. where the use of a foldable Acri.Lyc 15A ACIOL showed increase in BCVA till 6 months post-surgery. [17] Similar results were reported by Giles et al.[33]

b. IOP increase: Older ACIOLs had higher rate of glaucoma (32.1%) due to rigid nature and fixation of haptics to the iris as reported by Dai et al. [34] A comparative study between open loop flexible ACIOL and scleral-fixated PCIOL by Everekliogl u et al. showed increased IOP in the former group, although visual acuity was better in the same patients. [35] Newer ACIOLs such as Kelman Multiflex III, Acri.Lyc 15A, MTA3UO, L122UV have shown lower incidence of glaucoma.[14,16,17,33]

c. Corneal endothelial cell loss: Older ACIOL had a higher incidence of corneal decompensation, as high as 42.9%.[34] With newer designs, the incidence has reduced presently (Figure 4). The use of these IOLs along with penetrating keratoplasty in aphakic bullous keratopathy showed good visual outcome, with raised IOP, graft rejection and CME being the main complications. [36] Inadvertent upside down insertion of Kelman Multiflex ACIOL led to corneal decompensation in a case series, along with iritis, raised IOP, pupil capture and CME. [37] The loss of endothelial cells is reported to be more in secondary ACIOL surgery rather than in primary implantation. [38] Esquenazi et al. showed a 24% and 28% reduction in endothelial cell count in first and second year respectively after DSAEK with ACIOL implantation. [39] Agarwal et al. had studied endothelial cell loss at 6 months in air assisted ACIOL implantation and noted statistically significant reduction.[40] Omulecki et al. also noted minor changes of corneal edema in their study of foldable acrylic ACIOL usage in aphakia.[17]

d. IOL stability: Few earlier studies found IOL dislocation at 7.1%.[34] However, recent AAO safety update showed no such complication with the newer models of angle supported ACIOLs.[25]

e. Cystoid macular edema: In the study by Everekliogl u et al., CME was reported in the ACIOL group. [35] Other studies showed varying incidence of CME from 0.1% to 5% in acrylic ACIOL. [16,17,33] Moreover, the AAO safety update also noted higher incidence of CME in scleral fixated PCIOL compared to these ACIOL.[25]

f. Other complications: Some studies have reported sporadic incidence of retinal detachment, hyphema, pupil distortion with angle supported ACIOL.[33,41,42]

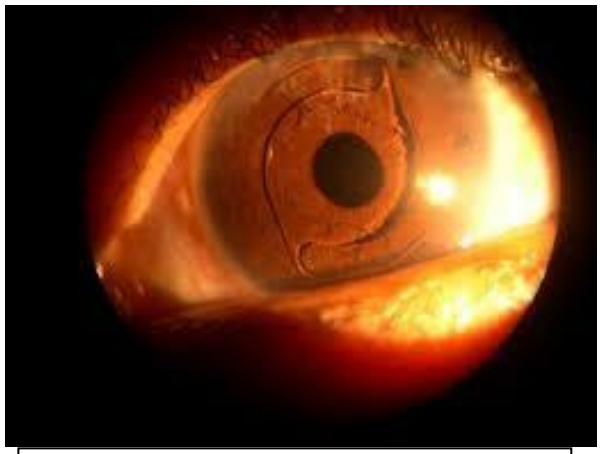


Figure 1: Kelman Multiflex III angle supported intraocular lens (ACIOL)

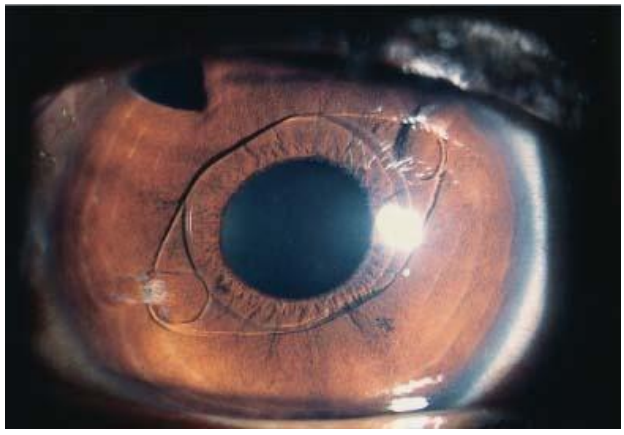


Fig 2: Artisan iris claw ACIOL with peripheral iridotomy

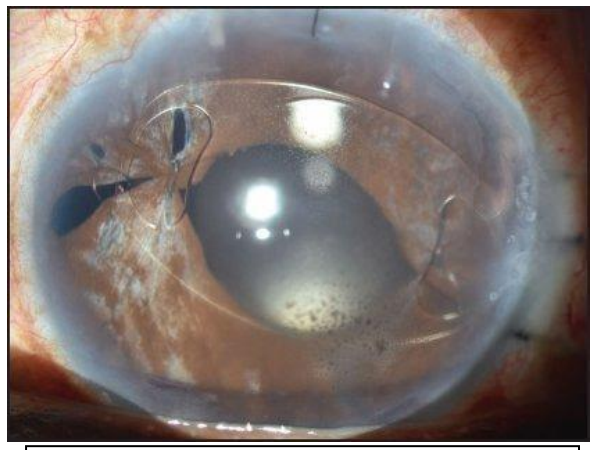


Fig 3: Chronic iritis with pupil ovalisation in Artisan iris claw ACIOL implantation (post-operative 1 year)

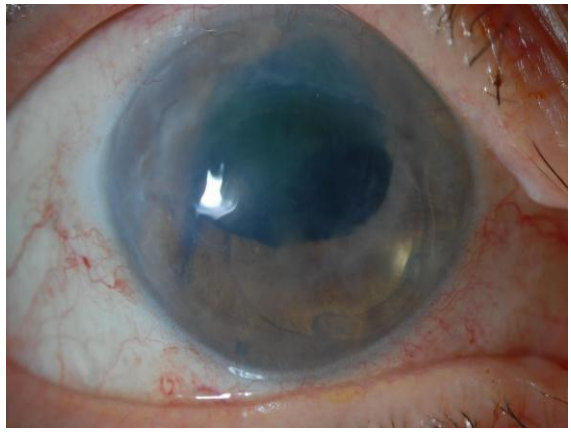


Fig 4: Corneal decompensation with irregular pupil after ACIOL implantation

5. Conclusion:

The armamentarium of IOLs available in cases of capsule or zonular support loss has increased in recent years. Both angle supported and iris claw ACIOLs have shown consistently good results in terms of visual outcome and longevity. The improvement in IOL material, manufacturing process and design of optic and haptic has greatly reduced the previous major complications of cystoid macular edema, glaucoma and corneal decompensation.

6. Literature search

PubMed and MEDLINE search was done with combinations of following search terms: Aphakia; anterior chamber intraocular lens; iris claw; angle supported; surgical procedures; complications;diagnosis; treatment and management.

Relevant articles from literature search and their references when applicable were included. Articles published after 1950 and articles published in non-English languages were included if there was an English comprehensive summary of the article. Clinical studies, randomized control trial, review articles, case series, and case reports were included in the review.

Disclosures:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Liang,I.-C., Chang,Y.-H, Hernández Martínez A. et al.. Iris-Claw Intraocular Lens: Anterior Chamber or Retropupillary Implantation? A Systematic Review and Meta-Analysis. Medicina, 57, 785, 2021.
2. Alio JL, de la Hoz F, Perez-Santonja JJ, et al. Phakic anterior-chamber lenses for the correction of myopia: a 7-year cumulative analysis of complications in 263 cases. Ophthalmology, 106: 458-466, 1999.
3. Emmrich K: Correction of the aphakic eye with anterior chamber lenses. Dtsch Gesundheitsw 13: 353-355, 1958.
4. Cotlier E, Herman S: Aphakic flat anterior chamber. Treatment by anterior vitriotomy. Arch Ophthalmol 86: 507-516, 1971
5. Auffarth GU, Wesendahl TA, Brown SJ, Apple DJ: Are there acceptable anterior chamber intraocular lenses for clinical use in the 1990s? An analysis of 4104 explanted anterior chamber intraocular lenses. Ophthalmology 101: 1913-1922, 1994.
6. Apple DJ, Kincaid M, Mamalis N. Intraocular Lenses: Evolution, Designs, Complications, and Pathology. Balti- more: Williams & Wilkins, 1989.
7. Hennig A, Pradhan 0, Gregson RMC, et al. Intra-ocular lens implantation during cataract surgery in Nepal [letter]. Lancet; 341:375, 1993.
8. Moschos MM, Nitoda E. The correction of aphakia using anterior chamber intraocular lens. In Vivo. 11-12;30(6):733-738, 2016.
9. Kohnen T and Hengerer FH: Anterior chamber intraocular lenses for aphakia correction. Ophthalmologe *111*: 310-314, 2014
10. Maloney RK, Nguyen LH, John ME: Artisan phakic intraocular lens for myopia: short-term results of a prospective, multicenter study. Ophthalmology 109: 1631-1641, 2002
11. Strampelli B: Tolerance of acrylic lenses in the anterior chamber in aphakia and refraction disorders. Ann Ottomol Clin Ocul 80: 75-82, 1954
12. Apple DJ, Brems RN, Park RB, et al. Anterior chamber lenses. Part I: Complications and pathology and a review of designs. J Cataract Refract Surg. 13:157-74. 1987.
13. Apple DJ, Hansen SO, Richards SC, et al. Anterior chamber lenses. Part II: A laboratory study. J Cataract Refract Surg. 13:175-89, 1987.
14. Wagoner MD, Cox TA, Ariyasu RG, et al. Intraocular lens implantation in the absence of capsular support: a report by the American Academy of Ophthalmology. Ophthalmology. 110(4):840–859, 2003.
15. Suelves AM, Siddique SS, Schurko B et al: Anterior chamber intraocular lens implantation in patients with a history of chronic uveitis: five-year follow-up. J Cataract Refract Surg 40: 77-81, 2014.
16. EM, Wiedemann P. Aphakia correction by injection of foldable intra ocular lens in the anterior chamber. Ophthalmol Eye Dis 5: 17-22, 2013.
17. Omulecki W, Bartela J, Synder A, et al. Results of implantation a new type of foldable anterior chamber intraocular lens. Klin Oczna 113: 216-222, 2011.
18. Worst JG. Iris claw lens. J Am Intraocul Implant Soc. 6:166–167, 1980.
19. Singh D. Iris claw lens – Six years' experience. Indian J Ophthalmol. 34:181–2, 1986.
20. Chen Y, Liu Q, Xue C, et al: Three-year follow- up of secondary anterior iris fixation of an aphakic intraocular lens to correct aphakia. J Cataract Refract Surg 38: 1595-1601, 2012
21. Kheirkhah A, Nikdel M, Ghadimi H: Implantation of iris-claw Artisan intraocular lens for aphakia in Fuchs' heterochromic iridocyclitis. Indian J Ophthalmol 62: 373-374, 2014.
22. Joanne F. Shen, Sophie Deng, MD, Kristin M. Hammersmith, et al. Intraocular Lens Implantation in the Absence of Zonular Support: An Outcomes and Safety Update. A Report by the American Academy of Ophthalmology. Ophthalmology; 127:1234-1258, 2020.
23. Güell JL, Verdaguer P, Elies D, et al. Secondary iris-claw anterior chamber lens implantation in patients with aphakia without capsular support. Br J Ophthalmol 98: 658-663, 2014.
24. Koss MJ, Kohnen T: Intraocular architecture of secondary implanted anterior chamber iris-claw lenses in aphakic eyes evaluated with anterior segment optical coherence tomography. Br J Ophthalmol 93: 1301-1306, 2009.
25. S. MacRae, J. T. Holladay, G. Hilmantel et al. Special report: American Academy of Ophthalmology Task Force recommendations for specular microscopy for phakic intraocular lenses, Ophthalmology, 124(1), 141-142, 2017.
26. Cagini C, Fiore T, Leontiadis A, Biondi L, et al. Simultaneous Descemet stripping automated endothelial keratoplasty and aphakic iris-fixated intraocular lens implantation: a case series. Cornea 30: 1167-1169, 2011.
27. Liang,I.C, Chang,Y.H, Hernández Martínez, A et al. Iris-Claw Intraocular Lens: Anterior Chamber or Retropupillary Implantation? A Systematic Review and Meta-Analysis. Medicina 57: 785, 2021.
28. Teng H, Zhang H: Comparison of Artisan iris-claw intraocular lens implantation and posterior chamber intraocular lens sulcus fixation for aphakic eyes. Int J Ophthalmol *7*: 283- 287, 2014.
29. De Silva SR, Arun K, Anandan M et al. Iris-claw intraocular lenses to correct aphakia in the absence of capsule support. J Cataract Refract Surg 37: 1667-1672, 2011.
30. Helvaci S, Demirduzen S, Oksuz H: Iris-claw intraocular lens implantation: Anterior chamber versus retropupillary implantation. Indian J Ophthalmol 64: 45-49, 2016.

31. S. M. R. Jonker, T. T. J. M. Berendschot, A. E. Ronden, et al. Long-term endothelial cell loss in patients with artisan myopia and artisan toric phakic intraocular lenses. Ophthalmology, vol. 125(4), 486–494, 2018.
32. Drolsum L, Haaskjold E: Secondary implantation of flexible open loop anterior chamber IOLs. Acta Ophthalmol (Copenh) 71: 482-486, 1993.
33. Giles K, Ernest M, Christelle D et al. Aphakia correction by injection of foldable intra ocular lens in the anterior chamber. Ophthalmol Eye Dis 5: 17-22, 2013.
34. Dai YH, Xie LX, Huang YS et al. Analysis of patients with extraction of open-loop anterior chamber intraocular lenses. Zhonghua Yan Ke Za Zhi 47: 546-549, 2011.
35. Evereklioglu C, Er H, Bekir NA et al. Comparison of secondary implantation of flexible open-loop anterior chamber and scleral-fixated posterior chamber intraocular lenses. J Cataract Refract Surg 29: 301-308, 2003.
36. Zaidman GW, Goldman S: A prospective study on the implantation of anterior chamber intraocular lenses during keratoplasty for pseudophakic and aphakic bullous keratopathy. Ophthalmology 97: 757-762, 1990.
37. Fintelmann RE, Kim SK, Hwang DG: Upside-down lens syndrome: ocular complications secondary to inverted implantation of the Kelman Multiflex anterior chamber intraocular lens. Am J Ophthalmol 152: 122-125, 2011.
38. Ravalico G, Botteri E, Baccara F: Long-term endothelial changes after implantation of anterior chamber intraocular lenses in cataract surgery. J Cataract Refract Surg 29: 1918-1923, 2003.
39. Esquenazi S, Schechter BA and Esquenazi K: Endothelial survival after Descemet-stripping automated endothelial keratoplasty in eyes with retained anterior chamber intraocular lenses: two-year follow-up. J Cataract Refract Surg 37: 714-719, 2011.
40. Agarwal T, Gupta S, Sharma N et al. Air- assisted implantation of anterior chamber intraocular lens. Eye Contact Lens 41: 164-166, 2015.
41. Artaria LG: Long-term results of secondary implantation of anterior chamber lenses. Klin Monbl Augenheilkd 200: 571-573, 1992.
42. Pojda SM, Herba E, Zatorska B et al. The long term clinical outcome of anterior chamber lenses after cataract surgery. Klin Oczna 104: 99-103, 2002.

Invited article

Intraocular lens exchange, Indications and Outcome

Arundhati Tamuli

When Harold Ridley introduced intra ocular lens to the world, very few could realise that intraocular lens (IOL) explantation will be another job over and above implantation. In fact, it happened that the very first IOL, Ridley did implant, eventually became the first ever IOL explanation as well as the first ever IOL exchange of the world as it was a huge refractive surprise of -14 dioptre.

As IOL explantation is rather a difficult procedure than implantation, IOL exchange has become a subject of much needed discussion. Earlier, complications of anterior chamber IOL were predominant causes of IOL exchange. Gradually, with introduction of posterior chamber (PC) IOL, the main indication of IOL exchange became IOL malposition, along with refractive surprises, wrong IOL implantations etc. With recent advances in IOL technology to provide visual acuity at all distances, despite achieving perfect visual acuity, the commonest cause for IOL exchange became patient dissatisfaction due to dysphotopsia, glare, halo or reduced contrast sensitivity. Over time, the rate of IOL exchange has declined as surgeons became more experienced and IOL technology improved to reduce subjective symptoms.

Indications of IOL exchange:

1. Refractive surprise[1-5]: Post-operative refraction that is way away from the desired goal, can be considered a refractive surprise. It can be due to a myriad of reasons. In most situations these can be corrected by Lasik or other means, taking patient satisfaction into consideration. However refractive surprise is one of the most common indication of IOL exchange.
2. IOL related complications: IOL malposition, torn or broken IOL, IOL haze/opacity, IOL induced inflammatory reactions are some notable complications related to IOL where IOL exchange procedure is executed. A recent study showed that procedures like Descemet stripping endothelial keratoplasty, Descemet stripping automated endothelial keratoplasty, Descemet membrane endothelial keratoplasty, and pars plana vitrectomy with intraocular gas or air injection predisposed lenses to opacification[6]. ACIOLs were notorious for many anterior segment complications and were frequently explanted some time ago. Dissatisfied patients with Multifocal IOLs who may experience dysphotopsia, glare, halo, contrast sensitivity issues are newer indications of IOL exchange.
3. Pseudophakic children with large myopic shift to reduce anisometropia & associated aniseikonia [7] where IOL exchange is considered best option.
4. Phakic IOLs: Refractive IOLs are needed to be explanted when we need to address a cataract where phakic IOLs are in situ.
5. Explantation of IOL along with vitreo-retinal procedure may be needed when required.

Procedure of IOL explant and exchange:

The approach to a case planned for IOL exchange depends on several factors, such as

- Corneal/ wound condition
- Severity of Anterior chamber inflammation
- Condition of Iris
- Condition of capsule (to consider rhexis continuity, capsular phimosis, posterior capsule integrity, cyclitic membrane etc)
- Whether Rigid or foldable IOL and the make.

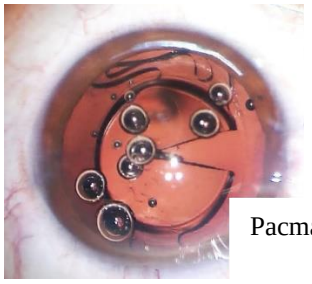
Upon considering the above parameters several combined approaches were described by different authors. We need to understand that explantation is a difficult procedure than implantation and should be handled by experienced surgeon only.

1. Explantation of rigid IOL requires an incision equivalent to IOL diameter. It can even be a self-sealing one. Implanted IOL may be positioned in the capsular bag, sulcus or even intra-scleral fixation as per the situation. In many cases even iris claw lenses are placed in absence of adequate capsular support.

Correspondence to:
Dr Arundhati Tamuli, Dibrugarh, Assam.
email: arundhati.tamuli@gmail.com
Date received: 20.10.2021
Date accepted: 31.12.2021

2. Explantation of foldable IOL may be considered with a smaller incision. Explantable IOL can be cut, folded or manipulated out with several techniques.
3. Additional procedures like vitrectomy, Descemet striping endothelial keratoplasty can be carried out along with IOL exchange procedures.
4. IOL power calculation still remains a challenge in such cases, as recalculation is frequently needed as previous biometry may be considered invalid or unavailable.

Harmoni modular IOL



Pacman

Surgical principle and techniques

- The IOL that requires explantation should be liberated from capsular adhesions, fibrous band or entangled iris, otherwise disasters may ensue in many situations.
- 'Pacman technique' is a widely practiced technique to explant a foldable IOL. In this technique a quarter of the IOL is cut and removed with specialized scissors (or by a vannus scissor). The remaining three quarter is manipulated out though a wound equivalent to the radius of the IOL optic. When the IOL is cut, it looks like the 'Pacman', which is a cartoon character of a popular computer game.
- Arup Bhaumik's technique of refolding the IOL for explantation into IOL cartridge while in the anterior chamber has gained much appreciation and acceptance. [8]

Outcome of IOL exchange

One study found that IOL decentration was the topmost indication of IOL exchange, and also that in the bag re-implantation shows best visual outcome and iris supported one the least[9] . The outcome of monofocal IOL exchange for multifocal IOL due to subjective symptoms are mostly satisfactory, as reported in many studies.

Conclusion

IOL explantation procedure is required to be learnt by every anterior segment surgeon. One may require to handle such a case when situation arises. Every single case requiring IOL explant and exchange is unique. Indication for exchange, IOL power calculation, surgical technique and experience matters much to the final outcome of the procedure.

The much talked about Light Adjustable Lens (LAL) and Harmoni Modular Lens (ClarVista Medical) were developed to reduce the need for IOL exchange when desired refractive goal is not achieved. We are still waiting for the perfections in the future.

Keywords: IOL exchange, IOL explantation

References:

1. Carlson A.N. Stewart W.C. Tso P.C. Intraocular lens complications requiring removal or exchange. *Surv Ophthalmol.* 1998; 42: 417-440
2. Salz J.J. Reader III, A.L. Lens implant exchanges for incorrect power: results of an informal survey. *J Cataract Refract Surg.* 1988; 14: 221-224
3. Olsen T. Sources of error in intraocular lens power calculation. *J Cataract Refract Surg.*1992;18:125-129
4. Smith L.F.F. Stevens J.D. Larkin F. Restori M. Errors leading to unexpected pseudophakic ametropia. *Eye.* 2001; 15: 728-732
5. Kora Y. Shimizu K. Yoshida M. et al.Intraocular lens power calculation for lens exchange. *J Cataract Refract Surg.* 2001; 27: 543-548
6. Grzybowski A, Markeviciute A, Zemaitiene R. A narrative review of intraocular lens opacifications: update 2020. *Ann Transl Med.* 2020;8(22):1547.
7. Kraus CL, Trivedi RH, Wilson ME. Intraocular lens exchange for high myopia in pseudophakic children. *Eye*. 2016;30:1199-1203.
8. Bhaumik, Arup; Mitra, Santanu1 A simple technique of intraocular lenses explantation for single-piece foldable lenses, Indian Journal of Ophthalmology: December 2017 - Volume 65 - Issue 12- p 1428-1430
9. Leysen I, Bartholomeeusen E, Coeckelbergh T, Tassignon MJ. Surgical outcomes of intraocular lens exchange: five-year study. J Cataract Refract Surg. 2009 Jun;35(6):1013-8. doi: 10.1016/j.jcrs.2009.01.024. PMID: 19465286.

Invited article

Vision Care Centre's modified Guidelines during pandemic in 2021

Nilanjana Ghosh

Background and the essence of these amends:

World underwent a change when they got locked down and did again come out with new rules and regulations to embrace the new normal. Life was never the same again. Ophthalmology requires close contact check up and hence new regulations were formulated to ensure safety of both patients and health care providers. Vision Care Centres (VCC) underwent few makeovers as well. Few changes suggested by various institutes have been incorporated. However, each set up has its own set of limitations and challenges. Hence the modifications need to be customized according to the local need so that the safety is ensured alongside providing services effectively. Eye care is a close contact care and hence infection transmission are high. Preventions need to be utmost to enhance service provision interrupted and assure effective service delivery and health service utilization ensuring a disease-free cure and care.

Modifications recommended by a private institute of repute after in-depth searching and review from all other private sectors –

Panellists, researchers, clinicians and all other stakeholders participated and suggested the recommendations under the following subheadings for effective treatment being met minimizing transmission. Some areas where the modifications are made are Vision Technicians procuring consumable in adequate quantities from the secondary centre ("COVID-19 VC Supplies pack") and aid in preparation of the vision centre before starting the services from the first day after the lockdown to start patient care. As dress code and Personal Protective Equipment (PPE) for Vision Technicians are in direct contact with the patients and come under Red Category the PPE may re-used after a break if the exposed portion of the mask is untouched. Cleaning protocol for equipment and the VC facility with a modified workflow flowchart for COVID 19 are another mandate with temperature guns to be made available in VCs if more than 15 patients per day report. Assistance from field assistants for these VCs and temperature monitoring should be done. Along with these the clinical examination protocol and guidelines for spherical equivalent prescriptions along with optical outlet protocols need to be maintained. Alongside the usual preventive precautionary general information COVID-19 Symptoms protocols needs to be reiterated for every visit[1].

GoI recommendations for the same amalgamates similar guidelines in realm of its scope of work:

MoHFW on Safe Ophthalmology Practices in Covid-19 also reinforced its own set of preventive guidelines for practicing care in ophthalmology and made a mandate that not practising these are liable to be taken as offence in eve of any complaint or disease caused. As the examination & procedures related to ophthalmology involves close interactions with the patient, the document outlines the preventive and response measures to be observed to minimize and avoid the spread of COVID-19 in eye care facilities among Ophthalmologist, Ophthalmic assistants/technicians, nurses, support staff, patients and their attendants.

Eye care facilities in containment zones shall remain closed and those operating outside will be allowed to open up within stipulated times. The basic preventive measures for elderly (above 65 years of age), persons with comorbidities, pregnant women and children below the age of 10 years should be encouraged to stay at home, unless they are patients themselves needs to be

---

Correspondence to: Dr. Nilanjana Ghosh, Assistant Professor, Department of Community and Family Medicine, AIIMS, Guwahati, Assam
Email: drnilanjanaghosh@rediffmail.com
Date received : 19.09.2021
Date accepted:: 02.01.2022

reiterated. Preventive measures of COVID 19 are to be followed along with self-monitoring of health and immediate reporting in event of any illness.

Eye-care facilities need to follow some universal dictums like encouraging tele-counselling and teleconsultation, practicing screening of cataract and other ocular morbidity patients in outreach areas only after duly following social distancing, hand hygiene and personal protective measures. Remote consultations by the NGOs in vision centres is also to be encouraged. Retrieval of eye balls/Corneas from home settings is allowed only if spread of infection is reduced and cornea may be utilized for therapeutic as well as optical purposes.

Queue discipline, ensuring social distancing in the premises, mandatory hand hygiene and thermal screening provisions and staff manning entry points equipped with appropriate personal protection as entailed in guidelines. Query regarding Covid-19 like symptoms and contact history, attendants & any hospital visitors with their mobile numbers and IDs should needs to be maintained for contact tracing. Preliminary screening of patients should be done as per flow chart of Annexure-I.

Guidelines of CPWD for air conditioners needs to be practiced with maintaining effective and frequent sanitation within premises with focus on lavatories and other water use areas. Proper disposal of face covers / masks / gloves in accordance with the Bio-Medical Waste

Management Rules is needed. App-based mobile phone check in & payment, digital prescription, artificial intelligence is the new normal needs to be appreciated and accepted like app-based registration system. However, ***triaging by an ophthalmologist/ trained ophthalmic personnel through telephonic conversation to determine the emergency/non-emergency needs to be.***

Modify process flow (like unidirectional flow of patients) in OPD is need of hour and it to minimize people's movements. (Fig.1)

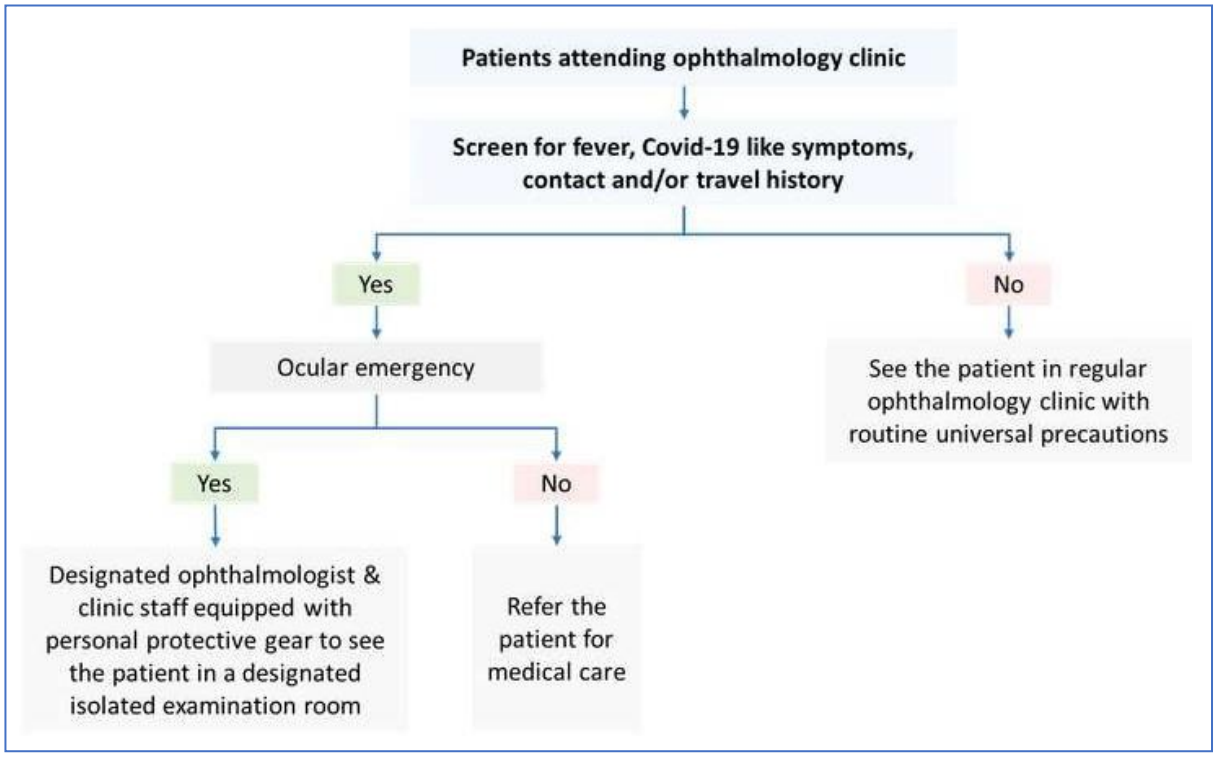
Rearranging seating arrangement and reinforcing cleaning with regular disinfection (using 1% sodium hypochlorite) of frequently touched equipment such as Trial Frame, Trial Lenses, etc. is needed. Contact procedure like Tonometry, Gonioscopy, Keratometry, A- Scan, B-Scan, UBM, OCT, FFA etc., the instruments should be cleaned with 70% alcohol swab, before and after every new case or iatrogenic injuries may result. A no touch patient care and screening of patients before entering the wards with minimal attendant is enforced. Cleanliness and hygiene of the ward is to be duly maintained as is instrument sterilization as per the manufacturer's protocol.

In event of a Covid-19 patient being admitted the COVID Care Protocols will come into forth like an isolation ward and protocols for OT services. Although a pre-surgical Covid-19 test may be evaded a thorough history taking & examination must be done to ensure wellbeing of both service provider and beneficiary.

Disinfecting equipment's as per protocol before next use is in place. Duty staggering with self-monitoring of symptoms with immediate reporting remains the mainstay. Alongside the usual protocols like ill person in isolated, providing a mask before each check-up, informing on premise nodal officer , a risk assessment by the designated public health authority and actions initiated in accordance and disinfection of the premises if the person is found positive remains in place per se.

Hence the covid cure and care guidelines have undergone brief modifications to accommodate the operationally feasible sustainable solutions in eye care. However, the usual protocols remain unchanged from 2020. May the world get free of the pandemic and people of the new normal. Till then prevention is the only cure.

Fig.1 – Patient flow modified



References:

1. Protocol for vision centres LVPREI.[Available at www. lvpei.org,last accessed on 11.09.2021]
2. 2. Lai THT, Tang EWH, Chau SKY, Fung KSC, Li KKW. Stepping up infection control measures in ophthalmology during the novel coronavirus outbreak: an experience from Hong Kong. Graefes Arch Clin Exp Ophthalmology. 2020 May;258(5):1049-1055. doi: 10.1007/s00417-020-04641-8. Epub 2020 Mar
3. GuidelinesonSafeOphthalmology. Available at https://www.mohfw.gov.in › pdf Available from 28th Dec.2020[last accessed on 12.09.2021]..
4. https://www.mohfw.gov.in/pdf/GuidelinesonpreventivemeasurestocontainspreadofCOVID1 9 inworkplacesettings.pdf

*****

Newer medications in Glaucoma management

Shahinur Tayab

The management of glaucoma is primarily focused on lowering of intraocular pressure (IOP) as it is the only modifiable risk factor. IOP lowering with topical medications is the most commonly offered treatment before surgical options are explored. In this article we will focus on 1) Newer medications 2) Newer methods of drug delivery

Newer medications

The IOP lowering in glaucoma was possible through 5 pharmacological classes (prostaglandin analogs, β-adrenoceptor antagonists, carbonic anhydrase inhibitors, α2- adrenoceptor agonists, cholinergic agents) of drugs until very recently. However, despite strict adherence some patients continue to progress. This was an indicator to develop novel IOP lowering agents with novel mechanisms of action. In POAG the site of aqueous resistance is believed to be the trabecular outflow pathway. But most of the medications acted either through the alternative pathway i.e. uveoscleral outflow pathway or by reducing the production of aqueous humor. Now we have 3 drugs which act through the conventional outflow pathway- netarsudil, ripasudil and latanoprostene bunod.

ROCK inhibitors

Rho is a small GTP binding protein belonging to the Rho family. It is responsible for regulating cell shape, motility, proliferation and apoptosis. [1,2] Rho kinases (ROCKs) are the downstream effectors of Rho which mediate RhoA- induced actin cytoskeletal changes through effects on myosin light chain phosphorylation.[3,4] ROCKS are protein serine/threonine kinases. Two ROCK isoforms have been identified in mammals- ROCK 1 and ROCK 2. Both RhoA GTPase and ROCK 1 and ROCK 2 isoforms are expressed in trabecular meshwork.[5] The inhibition of this pathway leads to relaxation of trabecular meshwork by decreasing actin stress fibers, focal adhesion and cell to cell interactions. Giant vacuoles increase in the inner wall of Schlemm's canal when trabecular meshwork relaxes. This causes widening of Schlemm's canal and washout of extracellular material.[6] This is how ROCK inhibitors cause IOP lowering.

Ripasudil, a Rho-associated kinase was initially approved for clinical use in Japan in 2014. It is available as 0.4% solution, to be applied twice daily. After topical application, Ripasudil is rapidly absorbed into the ocular tissue. The maximum IOP reduction is achieved at 2-3 hrs after topical application. The peak effect during the day was found to be 6.7 mm Hg and 7.3 at night.[7] When Ripasudil was added to Latanoprost it gave an additive IOP lowering of 3.2 mm Hg and when given along with Timolol it had an additive effect of 2.9 mm Hg.[8]

A second ROCK inhibitor Netarsudil was approved for use in the USA in 2017. It is available as a 0.02% solution to be applied once daily in the evening. Netarsudil has a dual action mechanism- as a ROCK inhibitor and an inhibitor of norepinephrine transporter.[9] Norepinehrine is believed to decrease IOP by increasing α adrenergic signaling which ultimately causes decreased aqueous humor production. So, by inhibiting norepinephrine transporter the action of norepinephrine can be prolonged, leading to a decrease in aqueous humor formation.[10] Netarsudil has also been found to increase the outflow facility from 0.27+/ -0.10 to 0.33+/- 0.22 µl/ min/mm Hg in treated eyes.[11] Another important use of ROCK inhibitors is in the healing of corneal endothelium. They can increase endothelial proliferation and decrease apoptosis.[12]

The main side effect of ROCK inhibitors is conjunctival hyperaemia which is due to its vasodilatory effect. It is usually transient. Subconjunctival haemorrhage and corneal verticillata were also noted with use of Netarsudil in the ROCKET trials. Rarely reported are cases of bullous epithelial keratopathy.[13]

Both ripasudil and netarsudil are available in the Indian market since 2020.

Nitric oxide Donors

As early as 1990s evidence was available regarding the IOP lowering potency of nitric oxide (NO).[14] NO binds to soluble guanylate cyclase (sGC) which converts guanosine-5'-triphosphate (GTP) into cyclic guanosine monophosphate (cGMP). cGMP is believed to effect changes in trabecular meshwork and Schlemm's canal cell volume thereby decreasing the resistance to aqueous humor outflow which leads to IOP reduction.[15] This knowledge led to the development of a NO-donating prostaglandin agent. Latanoprostene bunod 0.024% (Vyzulta) was approved by FDA for use in USA in 2017.

Correspondence to: Dr Shahinur Tayab,
Glasucoma Services, Sri Sankardeva Nethralaya,
Guwahati, Assam
Email: tayabshahinur@gmail.com
Date Received: 21.10.2021
Date accepted: 21.12.2021

Latanoprostene bunod is metabolized into latanoprost acid and butanediol mononitrate. Butanediol was further metabolized into 1, 4 butanediol and NO. IOP lowering starts 1-3 hours after topical application with the peak effect at 11 to 13 hours later. Latanoprostene bunod is applied once daily in the evening. Prostaglandin lowers IOP through uveoscleral pathway and NO moiety through trabecular pathway. A fixed dose combination of latanoprost and netarsudil has been approved and made available in the USA in 2019 (Rhopressa). Vyzulta and Rhopressa are currently not available in India.

Newer methods of drug delivery

All IOP lowering medications are applied as topical/ eye drops. Topical application of anti-glaucoma medications has a number of disadvantages. First disadvantage being related to adherence. Patients often forget to apply the medications regularly and on time. The next disadvantage of topical medication use is the inability to properly instill the eye drop. This leads to wastage and also disease progression as the medications fail to reach its target site. Another important disadvantage is the ocular surface related problems due to prolonged exposure to preservatives contained in eye drops. So, an ideal approach would be to have a drug delivery system which would ensure sustained and continuous release of medication without the patient requiring to apply the medication himself. There are mainly two routes for sustained drug delivery system- extraocular and intraocular. All the PG analogues namely, bimatoprost, travoprost and latanoprost are being developed for the sustained release delivery system.

Extraocular sustained release system

There are 3 sustained release drug delivery system which are under trial (phase 2 and phase 3).

1) OTX-TP Ocular Therapeutix's travoprost-containing intracanalicular plugs[16]
2) Mati Therapeutics latanoprost-eluting punctal plugs[17]
3) Allergan's bimatoprost-releasing periocular rings[18]

Intraocular sustained release system

There are eight different technologies being evaluated for sustained intraocular release of drug despite being invasive in nature. Most notable among all is Allergan's bio erodible intracameral implant of bimatoprost (Bimatoprost SR). It is in phase 3 and phase 3 extension studies and the results are encouraging. It employs the Novadur platform which is already validated for Ozurdex intravitreal injection(19).

References:

1. Riento K, Ridley AJ. Rocks; multifunctional kinases in cell behaviour. *Nat Rev Mol Cell Biol.*2003;4446-456.
2. Rikitake Y, Liao JK. Rho GTPases, statins, and nitric oxide. *Circ Res.*2005;97:1232-1235.
3. Leung T, Manser E, Tan L, et al. A novel serine/threonine kinase binding the Ras-related RhoA GTPase which translocates the kinase to peripheral membranes. *J Biol Chem.* 1995;270:29051-29054.
4. Leung T, Chen XQ, Manser E, et al. The p160 RhoA-binding kinase ROK alpha is a member of a kinase family and is involved in the reorganization of the cytoskeleton. *Mol cell Biol.* 1996;16:5313-5327.
5. Rao PV, Pattabiraman PP, Kopczynski C. Role of the Rho GTPase/Rho kinase signaling pathway in pathogenesis and treatment of glaucoma: bench to bedside research[review]. *Exp Eye Res*. 2017;158:23-32.
6. Gong H, Yang CY. Morphological and hydrodynamic correlations with increasing outflow facility by Rho-kinase inhibitor Y-27632. *J Ocul Pharmacol Ther.* 2014;30(2-3):143-153.
7. Tanihara H, Inoue T, Yamamoto T, et al; K-115 Clinical Study Group. Intra-ocular pressure-lowering effects of a Rho kinase inhibitor, ripasudil (K-115), over 24 hours in primary open-angle glaucoma and ocular hypertension: a randomized, open-label, crossover study. *Acta Ophthalmol.* 2015;93(4):e254-e260.
8. Tanihara H, Inoue T, Yamamoto T, et al. Additive intraocular pressure -lowering effects of the Rho kinase inhibitor ripasudil (K-115) combined with timolol or latanoprost: a report of 2 randomized clinical trials. *JAMA Ophthalmol.*2015;133(7);755-761.
9. Serle JB, Katz LJ, Mc Laurin E, et al; ROCKET-1 and ROCKET-2 Study Groups. Two Phase 3 clinical trials comparing the safety and efficacy of netarsudil to timolol inpatients with elevated intraocular pressure: Rho Kinase Elevated IOP Treatment Trial 1 and 2 (ROCKET-1 and ROCKET-2). *Am J Ophthalmol*.2018;186:116-127.
10. Langham ME, Diggs EM,(1972) Quantitative studies of the ocular response to norepinephrine. *Exp Eye Res* 13(2):161-171
11. Kazemi A, MC Laren JW, Kopczynski CC, Heah TG, Novack GD, Sit AJ. The effects of netarsudil ophthalmic solution on aqueous humor dynamics

in a randomized study in humans. *J Ocul Pharmacol Ther*. 2018;34(5):380-386.
12. Okumara N, Fujii K, Kagami T, Makiko N, Kitahara M, Kinoshita S, et al. Activation of the Rho/Rho Kinase Signaling Pathway Is Involved in Cell Death of Corneal Endothelium. *Invest Ophthalomol Vis Sci*. 2016;57(15):6843-51.
13. Ramakrishnan MS, AddisVM, Lehman AY, Sankar PS. Netrasudil-associated epithelial keratopathy. *Am J Ophthalmol Case Rep*. 2020;19:100800
14. Nathanson JA. Nitrovasodilators as a new class of ocular hypotensive agents. *J Pharmacol Exp Ther*. 1992;260(3):956-965
15. Ellis DZ. Guanylate cyclase activators, cell volume changes and IOP reduction. *Cell Physiol Biochem*. 2011;28(6):1145-1154.
16. Molla D, O'Connor M, Blizzard CD, Basett M, Desa A, Takach S, Cowe W, Wittbold J, Driscoll A, Sawhney A(2015) One-year stability of a sustained release travoprost biodegradable hydrogel punctum plug for the treatment of glaucoma. ARVO annual meeting abstract. *Invest Ophthalmol Vis Sci* 56 (7):5707
17. http;//www.matitherapeutics.com/about/pres/compare-latanoprost-to-timolol. Accessed 24 May 2019
18. Brandt JD, Sall K, duBiner H, Benza R, Alster Y, Walker G, Semba CP(2016) Six-month intraocular pressure reduction with a topical bimatoprost ocular insert: results of a phase II randomized controlled study. *Ophthalmology* 123(8):1685-1694
19. Boyer DS, Yoon YH, Belfort R Jr,Bandello F, Maturi RK, Augustin AJ, Li XY, Cui H, Hashad Y, Whitcup SM (2014) Three-year, randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with diabetic macula edema. Ophthalmology 121 (10):1904-1914

Case Report

Spontaneously reattached retinal detachment with macular hole – A case report

Debdulal Chakraborty, Dipankar Das, Sabiha Mashuda Khanam

Abstract: Spontaneous reattachment of rhegmatogenous retinal detachment (SRRRD) is a rare presentation. A macular hole coexisting in a patient with a SRRRD is rarer still. The authors describe a case of SRRRD with a macular hole presenting with decreased vision which has never been described before in scientific literature. The patient underwent vitrectomy with internal limiting membrane peeling and gas tamponade, leading to type I closure of the macular hole and subsequent visual improvement.

Keywords: Spontaneous reattachment of rhegmatogenous retinal detachment, Macular Hole

Introduction:

Spontaneous reattachment of rhegmatogenous retinal detachment(SRRRD) is a rare phenomenon. It was first described by Cantrill[1]. Many eyes with asymptomatic SRRRD may remain undetected[2]. While epiretinal membrane (ERM) has been known to develop in SRRRD[3] A macular hole(MH) in a patient of SRRRD has never been described before.

Case report

A 27 year old lady presented with decreased vision (20/80) in the left eye (OS) for 2 months. There was no history of prior trauma, retinal disease, surgery or consanguineous marriage of parents. Anterior segment was unremarkable and intraocular pressure was 12mmHg in OS. Dilated fundus examination in OS revealed a pigment-stippled retinal lesion with convex superior margin from 3-o'clock to 8-o'clock sparing the macula, consistent with diagnosis of SRRRD. Axial length was 23.8mm.

The other eye of the patient had 20/20 vision with normal anterior and posterior segment. Ultra-widefield Optos-image(Fig.1) documented SRRRD sparing the macula and a MH confirmed on spectral domain optical coherence tomography(SDOCT) (Fig.2a). In the temporal quadrant just beneath the demarcation line of the SRRRD, suspected breaks with a membrane sealing it were noted. MH surgery was advised which was refused initially by the patient. After two months, the patient returned with complaint of further decrease of vision in the affected eye (20/100). Persistence of the MH was confirmed again on clinical and SD OCT examination. At this visit, the patient agreed to our advice and underwent surgery comprising of triamcinolone assisted pars plana vitrectomy(PPV), staining of the internal limiting membrane(ILM) with Brilliant Blue G (BBG) (Ocublue, Auro labs Madurai, India), followed by ILM peeling and C3F8 gas tamponade(Fig. 3). Intra-operatively a small ERM inferior to the fovea was noted. Type 1 closure of the MH was observed 1month post-operatively (Fig.4), and confirmed on SDOCT(Fig.2b). VA at 1 month had improved to 20/60. At 12months follow-up, the MH was still closed with VA of 20/30.

Discussion:

Rhegmatogenous retinal detachment (RRD) is a progressive condition requiring surgical intervention. SRRRD is a rare event with only few reported cases [1-3]. SRRRD can be misdiagnosed as retinitis pigmentosa (RP), healed choroiditis or vasculitis [1-3]. While RP is usually bilateral with pale disc, attenuated retinal arteries, and history of night blindness, a healed vasculitis exhibits irregular pigmentary change and sclerosed vessels which were absent in the current patient. Macular holes have been described along with various retinal co-morbidities such as diabetic retinopathy, retinal vein occlusions, familial exudative vitreoretinopathy, heredo-macular disorders [2-4] and also following ocular trauma. Till date a macular hole developing in a patient of SRRRD has never been reported.

Correspondence to: Dr Debdulal Chakraborty, Senior Consultant, Incharge Vitreo-retina Services (SHP), Disha Eye Hospitals, Kolkata, West Bengal, India
Email: devdc@rediffmail.com, devdc.dr@gmail.com
Date received: 18.09.2021; Date accepted:: 27.12.2021

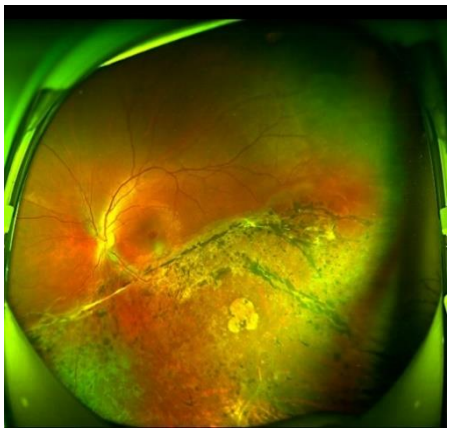


Fig1. Pre-operative widefield (Optos) image of left eye showing macular hole and inferior SRRRD

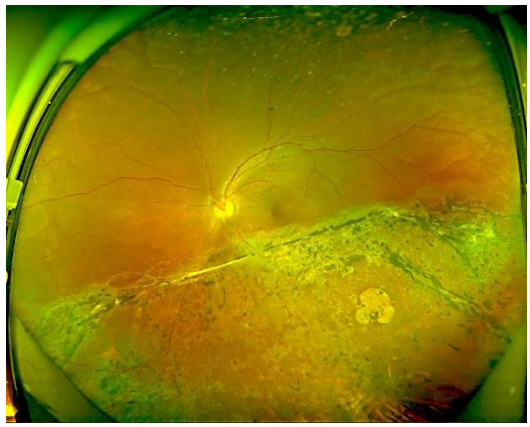


Fig2. (a) Pre-operative SDOCT image showing macular hole (b) SD OCT at one month following surgery showing type 1 closure of the macular hole.

Fig3. Intra-operative mage of macular area after ILM peeling and fluid air exchange.

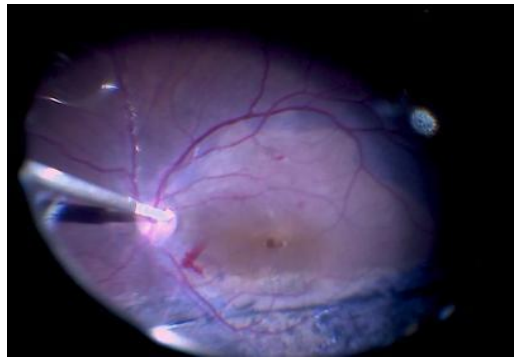


Fig4. Post- operative widefield (Optos) image of left eye showing sealed macular hole and inferior SRRRD

Supplementary video1: surgical procedure. This is not available in the PDF version-Ed

The exact mechanism of the retina re-attaching in SRRRD is not known. Thin membranes extending over the area of SRRRD running parallel to the retina developing as a wound healing response have been noted by Brüggemann et al[3]. Those membranes have been found to proliferate over retinal breaks leading to closure of the breaks and spontaneous reattachment of the retina[3]. Our patient had thin membranes covering suspected retinal breaks in the temporal periphery. Chung et al[3] have noted partial detachment of the vitreous in eyes with SRRRD. In our patient, there was no pre-existing posterior vitreous detachment(PVD) and triamcinolone assisted PVD induction was necessary. BBG was used to stain ILM. Inferior to the fovea a small epiretinal membrane was noted, which was removed along with the ILM. (supplemental video1). In heredo-macular degenerations, chronic degenerative changes in the macula and tangential traction by ERM and cystoid macular edema have been reported to be causative factors of MH[5-8].

Surgical intervention in MH has been noted to be less successful when surgery was performed beyond three months of presentation especially in idiopathic macular holes[7-9]. However in secondary macular holes, a period of observation has been recommended, especially in traumatic MH which may show spontaneous closure [6]. While the MH noted in our patient had OCT characteristics of an idiopathic macular

hole[10], whether the ERM noted in our patient had a role to play in the formation of the macular hole, thereby making it a secondary macular hole is a matter of conjecture. An untreated MH in an eye with a SRRRD may significantly decrease visual acuity in an already compromised eye and hence, early surgical closure of the MH may be best for the patient. Our patient with decreased vision for four months, however, did have type 1 closure of the MH and visual improvement following surgery. Shukla et-all[10] reported macular holes having oedematous edges in eyes with other retinal co-morbidities may behave like idiopathic holes and are better candidates for surgery. Our patient also had a macular hole with oedematous, edges noted on SD OCT and the surgical result was gratifying.

Conclusion:

We report a macular hole in SRRRD, which has never been described in literature and its treatment with PPV, ILM peeling and C3F8 gas tamponade leading to hole closure and improvement of vision in that eye.

Declarations:

i. Funding: No funding was received in any form by any of the authors

iii. Ethics approval : Ethics committee approval received from Institutional review board(Regn Number ECR/846/Inst/WB/2016/RR-19 : EC-CT-2020-138)

iv. Consent to participate: Written consent obtained from the patient for publication. The identity of the patient will not be disclosed in any way

v. Consent for publication: The authors hereby give you full permission, transfer, assign, or otherwise convey all copyright ownership, including any and all rights incidental there to, exclusively to the journal, in the event that such work is published by the journal

vi. Availability of data and material: Any supplementary data/ information will be available from the corresponding author on reasonable request

vii. Code availability : not applicable

viii. Authors' contributions

Dr Debdulal Chakraborty : Concept, Data collection, literature search, manuscript writing and review

Dr Dipankar Das: literature search, critical analysis of manuscript

Dr Sabiha Mashuda Khanam: literature search, Data collection

Competing interests: None. Source of Funding: Nil Receipt of grant: Nil. Previous publication/ presentation: Nil

References:

1. Cantrill HL. Spontaneous retinal reattachment. *Retina* 1981;1:216-9.
2. Song Ee Chung, Se Woong Kang, Chan-Hui Yi A Developmental Mechanism of Spontaneous Reattachment in Rhegmatogenous Retinal Detachment Korean J Ophthalmol 2012;Vol.26, No.2,
3. Brüggemann A, Hoerauf H. Atypical macular holes. Klin Monbl Augenheilkd 2008;225:281-5.
4. Bochicchio S[1], Pellegrini M, Cereda M, Oldani M, Staurenghi G.; Macular hole in a young patient affected by familial exudative vitreoretinopathy in young patient affected by familial exudative vitreoretinopathy. Retin Cases Brief Rep. 2020 Winter;14(1): 6-9. 10.1097/ICB. 00000000000 00613.
5. Jin ZB, Gan DK, Xu GZ, Nao-I N. Macular hole formation in patients with retinitis pigmentosa and prognosis of pars plana vitrectomy. Retina 2008 ;28, 610–614
6. Miller JB, Yonekawa Y, Eliott D, et al. Long-term follow-up and outcomes in traumatic macular holes. Am J Ophthalmol 2015;160:1255–1258.e1
7. Tolentino, F.I, Schepens, C. L., and Free- man, H. M.: Vitreoretinal Disorders. Diagnosis and Management. Philadelphia, W. B. Saunders, 1976, pp. 483-485. .
8. Gass JD. Idiopathic senile macular hole. Its early stages and pathogenesis. Arch Ophthalmol 1988;106:629–639.
9. Kuhn F, Morris R, Mester V,Witherspoon CD. Internal limiting membrane removal for traumatic macular holes. Ophthalmic Surg. Lasers 2001;32, 308–315
10. Shukla D. Evolution and management of macular hole secondary to type 2 idiopathic macular telangiectasia. Eye (Lond) 2011;25:532–533.

The therapeutic dilemma in a non-responsive case of chronic central serous chorioretinopathy with secondary choroidal neovascular membrane – a case report

Tania Basaiawmoit, Jennifer V Basaiawmoit

Keywords: Central serous chorioretinopathy, choroidal neovascular membrane, OCTA, Scleroderma

A 66-year-old female presented with gradual progressive diminution of vision in the right eye for 8 months. She also was a known case of hypertension, diabetes, hypercholesterolemia, hyperthyroidism and compromised renal parameters. Her left eye was diagnosed elsewhere with a scarred choroidal neovascular membrane (CNVM) in 2014 for which she had received many intravitreal injections and had been off treatment since 2016.

Her Visual Acuity in the right eye was 6/60 and in the left eye was finger counting at 3 meters. She was pseudophakic in both eyes. Fundus examination of the right eye revealed retinal pigment epithelial (RPE) changes at the macula with subretinal fluid (SRF) and the left eye showed features of scarred CNVM at the macula. There was no evidence of diabetic or hypertensive retinopathy in either eye. Optical coherence tomography (OCT) and OCT Angiography (OCTA) of both the eyes are shown in images 2, 3 and 4. OCTA showed normal superficial and deep plexus in both eyes.

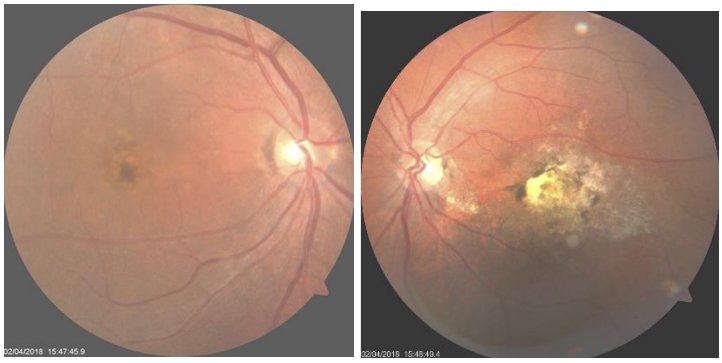


Fig 1: RE shows RPE changes at macula with SRF and LE showing scarred CNVM

The right eye was treated with three monthly consecutive doses of anti-vascular endothelial growth factor (anti-VEGF). The treatment showed no significant improvement in visual gain and suboptimal reduction of subretinal fluid after the 3 doses of anti-VEGF injection. OCTA however showed some reduction in the size of the tangled vessels at the final visit.

Due to unresponsiveness to anti-VEGF, the diagnosis was reconsidered as chronic central serous chorioretinopathy (CSCR) with secondary CNVM. The patient's detailed history at this visit revealed that the patient was on local triamcinolone injections in the scalp along with minoxidil application for 6 months for alopecia. The patient was thus advised to stop topical minoxidil and triamcinolone injections and was again given a trial of injection of anti-VEGF one month after stopping the steroids. However, the patient's vision remained at 6/60 with OCT features as shown in the figure below. A diagnosis of sick RPE syndrome was made and she was advised for a low vision device to aid in near vision.

The patient came back one year later for a follow-up visit, with vision in the right eye improved to 6/36 and near vision N 14 with additional light. RE fundus examination showed resolved SRF and OCT showed near-total resolution of sub-retinal fluid as seen in images 8 and 9. The patient informed that she was diagnosed by a dermatologist to have scleroderma and was started on oral Methotrexate (MTX) 7.5mg, 6 months before the patient came back for follow up.

Correspondence to: Tania Basaiawmoit, Vitreo Retina Surgeon, Bansara Eye Care Centre, Lady Veronica Path| Laitumkhrah, Shillong 793003 | Meghalaya
Email: taniavaid@gmail.com
Date received 24 Oct 2021; Date accepted: 30.12.2021

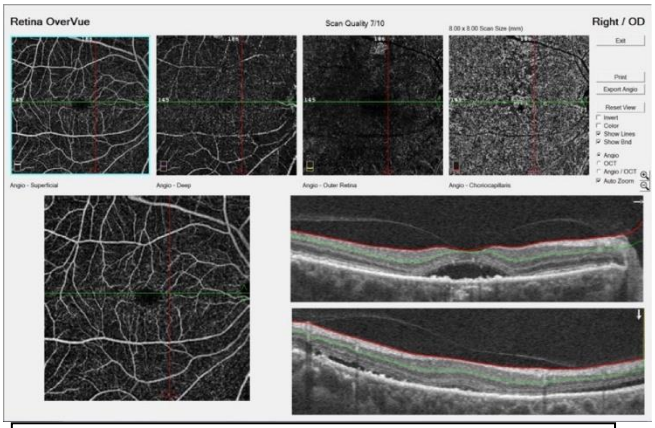


Fig 2: OCT and OCTA of RE showing irregular RPE with SRF and a central foveal thickness of 371 microns.

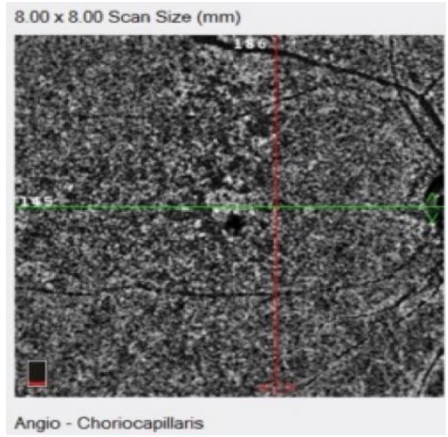


Fig 3: Segmentation of the choriocapillaris layer revealed a small suspicious area by the appearance of abnormal choroidal vessels with relatively high flow as compared to surrounding choriocapillaris

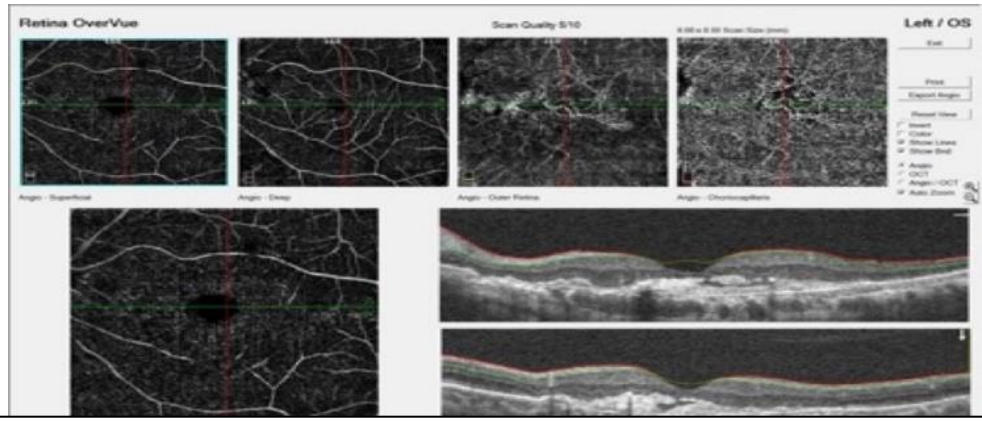


Fig 4: LE showing scarred CNVM complex with no s ubretinal or intraretinal fluid collection. OCTA shows the appearance of hyperreflective vessels in the outer retina and the choriocapillaris showed large choroidal vessels.

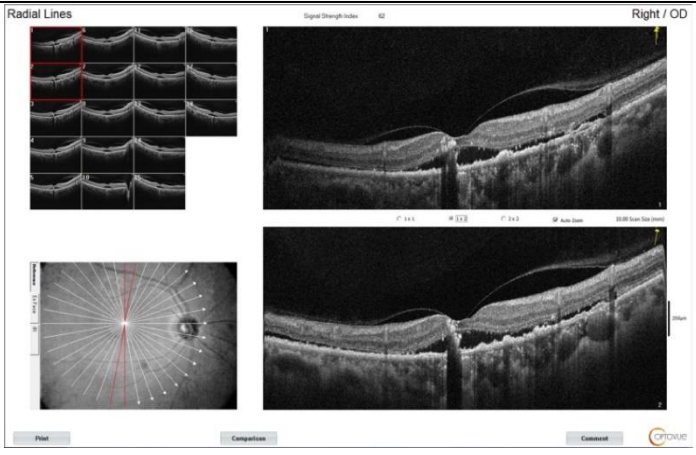


Fig 5: OCT image post 3rd dose of anti-VEGF showed vitreomacular adhesion, irregular RPE and persistent SRF with shaggy elongated photoreceptors.

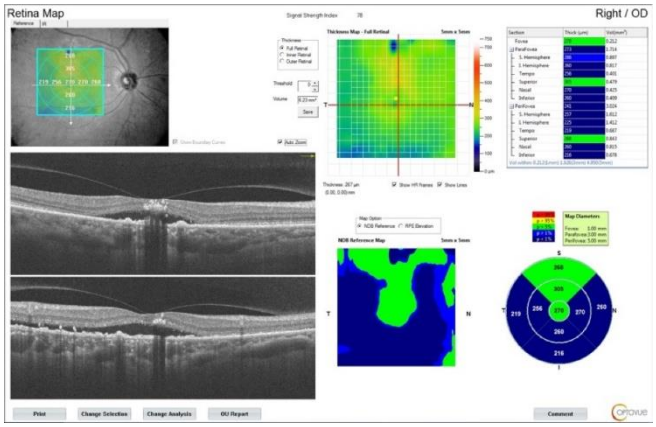


Fig 6: Persistent SRF with CFT was 270 microns is seen with altered RPE and multiple hyperreflectivity spots in inner retinal layers

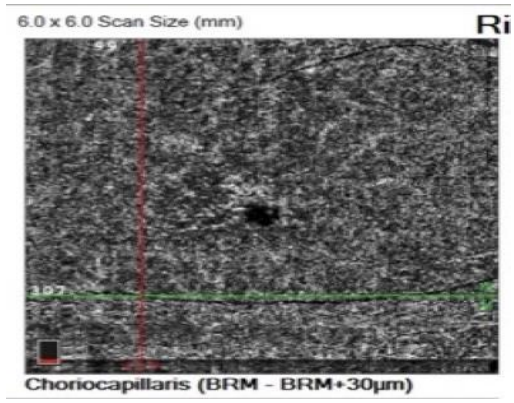


Fig 7: CNVM complex seems to have regressed in size as compared to the first visit OCTA

.

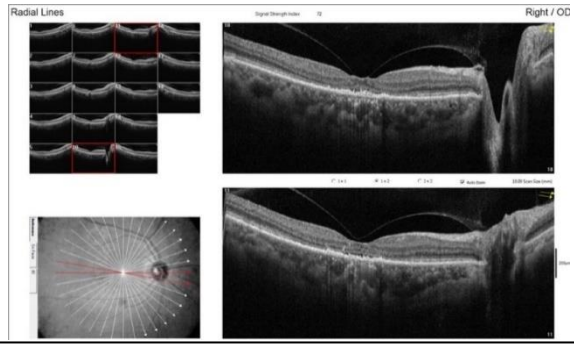


Fig 8: Near-total resolution of SRF seen with irregularity in photoreceptor layer.

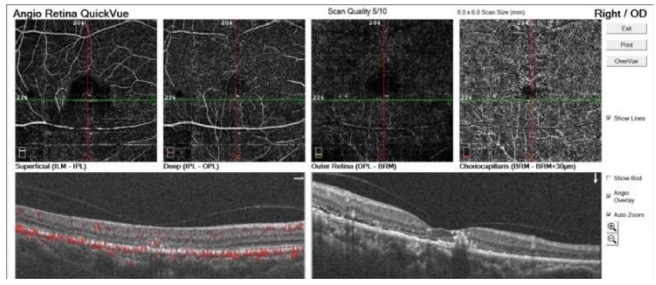


Image 9: OCTA shows no active CNVM complex.

Discussion:

Choroidal neovascularization (CNV) is an important complication of chronic central serouschorioretinopathy (CSC). The development of CNV is one of the major causes of reduced vision seen during long-term follow-up of patients with CSC. The prevalence of CNV secondary to CSC ranges from 2–15.6 per cent [1,2]

The detection of CNV in patients with CSC can be more challenging than the diagnosis of idiopathic CNV, because of the diffuse decompensation and abnormalities of the retinal pigment epithelium (RPE) layer seen in CSC[3,4,5] OCT angiography allows quick, non-invasive detection of CNVM and is claimed to be as sensitive as FA in detecting CNVM in CCSC eyes[6]. Several studies have demonstrated the superiority of OCTA over other imaging techniques in detecting CNVM in CCSC eyes[7,8,9,10,11].

Several treatments for CNVM secondary to CSCR have been reported such as PDT, intravitreal injections or a combination of both. Intravitreal injections alone can cause a significant reduction in foveal thickness with regression of CNVM[12,13].

In our case, we did not find a significant reduction of the SRF despite intravitreal injections. The patient's systemic diagnosis of Scleroderma could be the reason for the development of sick RPE syndrome or chronic CSCR and non-resolution of the subretinal fluid to intravitreal injections alone. Ocular findings in patients with scleroderma have been described by Gomes et al[14]. The retinal findings described in the article are retinal microvascular abnormalities,

drusen, central retinal vein occlusion, chorio-retinal scar and congenital hypertrophy of the RPE. CSCR was not mentioned as a retinal finding in their study.

One case report of a patient with scleroderma developing CSCR was published by Masako Taga et al where they concluded that damage to the retinal pigment epithelium secondary to the vascular lesion at the choroidal level plays a causative role in CSR. The findings in their case suggested that the deposition of immune complex in choroidal tissues as well as the gastrointestinal tract caused hyperpermeability of choroidal vessels and led to the development of CSC and the treatment of the systemic condition helped improve the CSCR despite a continuation of the systemic corticosteroids, which are a known causative factor in the non-resolution of CSCR[15]

In our case report, we found that the patient had significant improvement in vision and resolution of SRF aftershe was diagnosed and managed for scleroderma. There could be two possible explanations for the resolution of macular oedema; the first is the total cessation of triamcinolone injections to the scalp for the alopecia and the second contribution could be the initiation of MTX to treat the scleroderma. There have been studies that have shown the efficacy of MTX in chronic CSCR however a randomized control trial is warranted to better understand the effects of MTX in such patients.[16,17]

The purpose of this case report is to highlight the importance of a comprehensive evaluation in patients with chronic non-resolving CSCR and, if necessary, referral of such patients to physicians for systemic evaluation to rule out any other systemic disease that could be contributing to the ocular pathology. Scleroderma, though rare, should be considered in the differential diagnosis of systemic diseases causing chronic CSCR to help early management of such patients and prevent the development of sight-threatening complications such as CNVM.

References:

1. Loo, R. H. et al. Factors associated with reduced visual acuity during long-term follow-up of patients with idiopathic central serous chorioretinopathy. Retina **22**, 19–24 (2002).
2. Shiragami, C. et al. Clinical Features of Central Serous Chorioretinopathy With Type 1 Choroidal Neovascularization. Am J Ophthalmol **193**, 80–86 (2018)
3. Spaide, R. F. et al. Indocyanine green videoangiography of older patients with central serous chorioretinopathy. Retina 1996.**16**, 203–213
4. Piccolino, F. C., De La Longrais, R. R., Manea, M. & Cicinelli, S. Posterior cystoid retinal degeneration in central serous chorioretinopathy. Retina **28**, 1008–1012 (2008).
5. Chhablani, J. et al. Outcomes of Treatment of Choroidal Neovascularization Associated with Central Serous Chorioretinopathy with Intravitreal Antiangiogenic Agents. Retina **35**, 2489–2497 (2015).
6. Bonini Filho MA, de Carlo DE, Ferrara D, Adhi M, Baumal CR, Witkin AJ, et al. Association of choroidal neovascularization and central serous chorioretinopathy with optical coherence tomography angiography. JAMA Ophthalmol. 2015;133:899–906.
7. de Carlo TE, Bonini Filho MA, Chin AT, Adhi M, Ferrara D, Baumal CR, et al. Spectral domain optical coherence tomography angiography of choroidal neovascularization. Ophthalmology. 2015;122:1228–38. [PubMed] [Google Scholar]
8. Maftouhi MQ, Maftouhi AE, Eandi CM. Chronic central serous chorioretinopathy imaged by optical coherence tomographic angiography. Am J Ophthalmol. 2015;160:581–7. [PubMed] [Google Scholar]
9. Hage R, Mrejen S, Krivosic V, Quentel G, Tadayoni R, Gaudric A. Flat irregular retinal pigment epithelium detachments in chronic central serous chorioretinopathy and choroidal neovascularization. Am J Ophthalmol. 2015;159:890–903. [PubMed] [Google Scholar]
10. Cakir B, Reich M, Lang SJ, Buhler A, Stahl A, Bohringer D, et al. Possibilities and limitations of OCT-Angiography in patients with central serous chorioretinopathy. Klin Monbl Augenheilkd. 2017;234:1161–8. [PubMed] [Google Scholar]
11. Morara M, Veronese C, Melucci M, Tassi F, Balducci N, Ciardella A. Optical coherence tomography angiography of chronic central serous chorioretinopathy in elderly patients. Invest Ophthalmol Vis Sci. 2015;56:3349. [Google Scholar]
12. Ergun, E., Tittl, M. & Stur, M. Photodynamic therapy with verteporfin in subfoveal choroidal neovascularization secondary to central serous chorioretinopathy. Arch Ophthalmol **122**, 37–41 (2004). Return to ref 11 in article
13. Chan, W. M. et al. Treatment of choroidal neovascularization in central serous chorioretinopathy by photodynamic therapy with verteporfin. Am J Ophthalmol **136**, 836–845 (2003).
14. B. D. A. F. Gomes, M. R. Santhiago, P. Magalhães, N. Kara Jr., M. N. L. de Azevedo, and H. V. Moraes Jr., "Ocular findings in patients with systemic sclerosis," Clinics, vol. 66, no. 3, pp. 379–385, 2011.
15. Masako Taga, Hiroshi Takahashi,Hiroshi Yasui, Hiroyuki Tsukuda , Case or protein losing gastroenteropathy associated with scleroderma in which central serous chorioretinopathy developed Japanese Journal of Clinical Immunology 24(3):125-32 DOI:10.2177/jsci.24.125 (2001)
16. Kurup SK, Oliver A, Emanuelli A, Hau V, Callanan D. Low-dose methotrexate for the treatment of chronic central serous chorioretinopathy: a retrospective analysis. Retina.2012 Nov-Dec;32(10):2096-101. doi:10.1097/IAE.0b013e31825dd281. PMID: 22718154
17. Abrishami M, Mousavi M, Hosseini SM, Norouzpour A. Treatment of Chronic Central Serous Chorioretinopathy with Oral Methotrexate. J Ocul Pharmacol Ther. 2015 Oct;31(8):468-75. doi: 10.1089/jop.2014.0173. Epub 2015 Jul 14. PMID: 26172430.

A tale of Stage 4B to Stage 5 ROP in 10 days: a case report

Ronel Soibam

Introduction

Retinopathy of prematurity (ROP) is one of the most common causes of preventable blindness in children worldwide. It is a severe vasoproliferative vitreoretinal disorder seen in premature infants and is characterized by anomalous vascularization at the confluence of the vascular and avascular retina. Most of these cases resolve spontaneously but some cases show rapid progression of the disease. Patients with severe progressive partial tractional retinal detachment (Stage 4 ROP) and total tractional retinal detachment (Stage 5 ROP) require urgent surgery to prevent poor visual outcome. (1–3) Preferred surgical approach in these babies is simultaneous bilateral vitrectomy as both eyes can be treated in a single sitting under general anesthesia. (4, 5) We report here a case which showed an acute progression from Stage 4 ROP to stage 5 ROP in a short span of 10 days.

Case report

A female baby with gestational age of 27 weeks and birth weight of 720 g presented to us at postmenstrual age (PMA) of 39 weeks and at a weight of 2010 g. The baby had respiratory distress and hyperbilirubinemia after birth. She was treated with oxygen therapy for 20 days and was admitted in neonatal intensive care unit for 90 days after birth. At presentation the baby had stage 4B ROP in both the eyes. After extensive discussion with the parents about the risks and benefits of surgical treatment, they consented to the treatment of OD first. So, lens sparing vitrectomy and one-third dose intravitreal ranibizumab under general anesthesia was planned for OD (Fig.1a). On the post-operative day 1 and day 7, OD retina appeared to be settling (Fig1b). For OS vitrectomy with one-third dose intravitreal ranibizumab under general anesthesia was planned (Fig.2a). The baby developed upper respiratory tract infection and OS surgery was deferred. The baby reported after 10 days, OD retina appeared to be settling but in OS the ROP progressed from stage 4B to stage 5 (Fig.2b). The baby then underwent vitrectomy with lensectomy and one-third dose intravitreal ranibizumab under general anesthesia for OS (Fig.2c). At day 1, week 1, month 1 and month 2 the retina appeared to be settling in both eyes (Fig.2d).

Discussion

ROP is a blinding disease of preterm low birth weight babies. It can rapidly progresses from stage of partial retinal detachment to total retinal detachment in a span of few weeks. If one eye is operated at a time, the other eye is at risk of progression and poor visual outcome. (3) Also, If both the eyes are operated separately the baby will require administration of general anesthesia twice. Since these preterm infants suffer from multiple systemic comorbidities, administration of general anesthesia twice will increase mortality. (6) van der Griend el al have reported that the risk of general anesthesia related mortality in children and preterm infants is as high as 1 in 10,000.

To overcome this obstacle a new approach, immediate sequential bilateral vitreoretinal surgery has been suggested. (5,7) In this approach vitreoretinal surgeries are performed in both eyes under the same general anesthesia session. (4) The advantages of this approach are that only one time administration of general anesthesia is required and the second eye is operated without delay. This surgical approach was based on the concept of sequential bilateral cataract surgery which has been performed in pediatric cataract babies for the past many years. (8) The only disadvantage of this approach is development of endophthalmitis in both eyes.

Ronel Soibam, "The Eyecare Centre",
Guwahati Club, Hedayetpur road, Guwahati,
Assam.
Email: ronelsoibam@yahoo.co.in
Date received: 10.12.2021
Date accepted: 07.01.2022

Patients undergoing pars plana vitrectomy have 0.03%–0.08% risk of developing endophthalmitis but endophthalmitis after vitrectomy for ROP has not been reported in the literature. Also Yonekawa et al have documented that the risk of post vitrectomy bilateral endophthalmitis is 0.0009%– 0.0064%. (4) The risk of endophthalmitis can be reduced and the safety margin can be increased if second eye of the baby is operated using fresh set of instruments and rescrubbing by the entire surgical team. Literature review also shows that the risk of endophthalmitis after bilateral intravitreal injection and bilateral cataract surgery is comparable to one eye surgery. (8,9) The advantages of performing bilateral vitreoretinal simultaneous bilateral vitreoretinal surgery in ROP babies far outweigh the disadvantages.

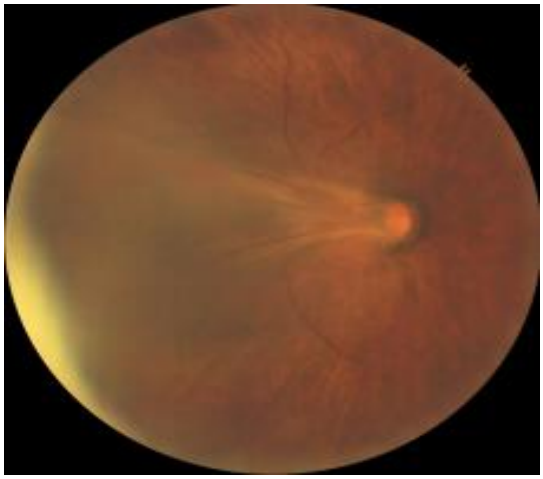


Fig.1a. Pre-Operative fundus photograph of right eye showing Stage 4B ROP

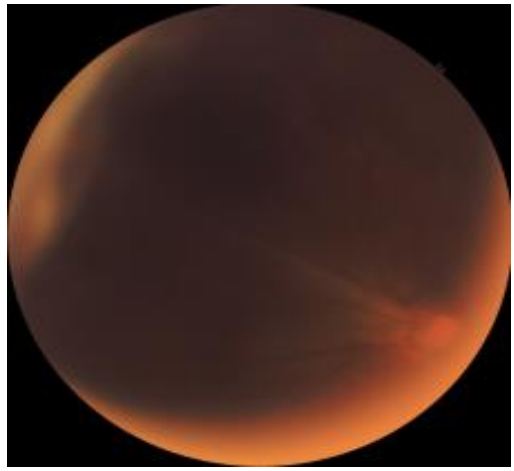


Fig.1b. Post Operative fundus photograph

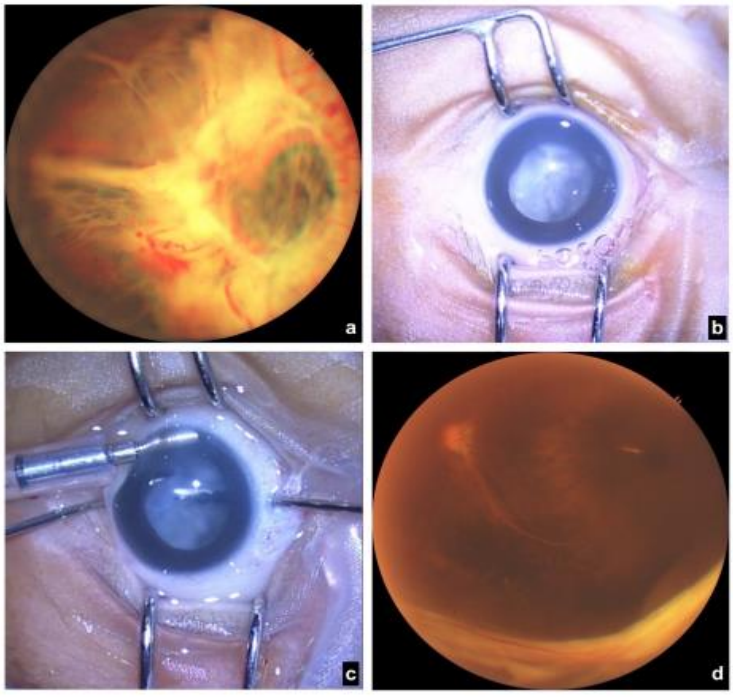


Fig. 2 (left)

(a) Fundus photograph of the left eye at presentation showing stage 4B ROP.

(b) Operation room photograph of the left eye showing stage 5 ROP.

(c) Intraoperative photograph showing membrane dissection using vitreous forceps and scissors.

(d) 1 month postoperative fundus photograph showing well settled retina.

References

1. Chen J, Smith LEH. Retinopathy of prematurity. Angiogenesis. 2007;10(2):133–40.
2. Fielder AR, Shaw DE, Robinson J, Ng YK. Natural history of retinopathy of prematurity: a prospective study. Eye (Lond). 1992; 6 (Pt 3):233–42.
3. Roohipoor R, Karkhaneh R, Riazi-Esfahani M, Ghasemi F, Nili-Ahmadabadi M. Surgical Management in Advanced Stages of Retinopathy of Prematurity; Our Experience. J Ophthalmic Vis Res. 2009 Jul;4(3):185–90.
4. Yonekawa Y, Wu W-C, Kusaka S, Robinson J, Tsujioka D, Kang KB, et al. Immediate Sequential Bilateral Pediatric Vitreoretinal Surgery: An International Multicenter Study. Ophthalmology. 2016; 123(8):1802–8.
5. Shah PK, Narendran V, Kalpana N. Safety and efficacy of simultaneous bilateral 25-gauge lens-sparing vitrectomy for vascularly active stage 4 retinopathy of prematurity. Eye (Lond). 2015 Aug;29(8):1046–50.
6. van der Griend BF, Lister NA, McKenzie IM, Martin N, Ragg PG, Sheppard SJ, et al. Postoperative mortality in children after 101,885 anesthetics at a tertiary pediatric hospital. Anesth Analg. 2011 Jun;112(6):1440–7.
7. Chandra P, Kumawat D, Tewari R, Sinha R. Surgical outcomes of immediate sequential bilateral vitreoretinal surgery for advancing retinopathy of prematurity. Indian Journal of Ophthalmology. 2019 Jun 1;67(6):903.
8. Malvankar-Mehta MS, Chen YN, Patel S, Leung AP-K, Merchea MM, Hodge WG. Immediate versus Delayed Sequential Bilateral Cataract Surgery: A Systematic Review and Meta-Analysis. PLoS One [Internet]. 2015 Jun 29 [cited 2020 Nov 27];10(6). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4485471
9. Filet JB, Scott IU, Flynn HW. Meta-analysis of I nfectious endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents. Ophthalmic Surg Lasers Imaging Retina. 2014 Apr;45(2):143–9.

Instruction for authors

Articles may be submitted at any time. It is mandatory to submit the following

1. ICMJE Form for Disclosure of Potential Conflicts of Interest
2. Authors' Declaration and Copyright Transfer form

Instructions for authors, Forms 1 and 2, above, are available at www.osa.ind.in/journal.htm.
Presently, all submissions may be made by email only at journal.osa@gmail.com.

Preparation of Manuscripts

Editorial and Ethics Policies of Journal of Ophthalmological Society of Assam conform to recommendation of the International Committee of Medical Journal Editors (http://www.icmje.org). Manuscripts must be prepared in accordance with "Uniform requirements for Manuscripts submitted to Biomedical Journals" developed by the ICMJE (December 2021). The uniform requirements and specific requirement of Journal of Ophthalmological Society of Assam are summarized below. Authors are requested to check for the latest instructions at the website of the journal (http://www.osa.ind.in/journal.htm).

Journal of Ophthalmological Society of Assam accepts manuscripts written in American English.

The Editorial Process

- A manuscript will be reviewed for publication subject to the Author's declaration
- The journal requires a corresponding author who will be responsible for all communication with the Journal related to the manuscript.
- All manuscripts received are duly acknowledged and given a Manuscript Number.
- On submission, all submitted manuscripts undergo a screening prior to a formal review. Manuscripts with insufficient originality, serious shortcomings, or outside the scope of JOSA may be rejected at this stage itself.
- Peer Review is undertaken by two or more subject expert reviewers. The contributor may suggest two or three qualified reviewers; such reviewers should not be affiliated with the same institutes as the author/co-authors. The selection of reviewers is at the sole discretion of the editorial board.
- The Journal follows a double-blind review process, wherein the identity of reviewers and authors are concealed from each other.
- The reviewers' comments (acceptance/ rejection/ amendments in manuscript) are conveyed to the corresponding author. The author is requested to submit a revised version of the manuscript incorporating a point by point response to reviewers' comments. This process may be repeated till reviewers and editors are satisfied with the manuscript.
- Manuscripts accepted for publication are copy edited.
- Page proofs are sent to the corresponding author. The corresponding author is advised to return the corrected proofs within 7 calendar days. It may not be possible to incorporate corrections received thereafter.
- *All* communication shall be by *email only* until further notice.
- The journal publishes articles online as 'Ahead of Print' on acceptance

Clinical Trial Registry

- Registration of clinical trials should conform to norms as updated by regulatory authorities in India from time to time. Kindly visit http://www.cdsco.nic.in
- For studies conducted in India, registration is required at http://www.ctri.in/
- Guidelines on registration for PG thesis conducted in India is available at http://ctri.nic.in/Clinicaltrials
- Other acceptable trial registers are http://www.actr.org.au/; http://www.clinicaltrials.gov/; http://isrctn.org/; http://www.trialregister.nl/trialreg/index.asp, http://www.umin.ac.jp/ctr. Kindly consult editorial board, JOSA for any clarification
- For clinical trials that have begun enrollment of subjects before June 2008, retrospective registration with clinical trial registry is admissible.

Authorship Criteria

JOSA strongly recommends prospective authors to adhere to guidelines of the International Committee of Medical Journal Editors (http://www.icmje.org)

Authorship credit should be based only on substantial contributions to each of the three components mentioned below:

1. Concept and design of study or acquisition of data or analysis and interpretation of data;
2. Drafting the article or revising it critically for important intellectual content; and
3. Final approval of the version to be published.

The order of naming the Authors should be based on relative contributions towards the study and writing of the manuscript. Once submitted, the order cannot be changed without written consent of all the contributors. JOSA prescribes a maximum number of 6 (six) authors for manuscripts. If the number of authors exceeds six, a justification signed by all authors should be submitted.

Acknowledgement is permissible for members responsible for acquisition of funding, collection of data, technical support, and general supervision.

Contribution Details

Each contributor should have participated sufficiently in the work to take public responsibility for appropriate portions of the content of the manuscript. Contributors should mention the contributions made by each of them towards the manuscript. The nature of contribution could be: concept, design, definition of intellectual content, literature search, clinical studies, experimental studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review. At least one author should take responsibility for the whole work and he/she shall be designated as 'guarantor'.

Conflicts of Interest/ Competing Interests

All authors of must mandatorily submit the **conflict of interest form along with the main manuscript submission,** disclosing any and all possible conflicts of interest they may have with regard to the manuscript. The conflict of interest form is separate from the copyright transfer form

Submission of Manuscripts

All manuscripts must be submitted by email. Authors do not have to pay for submission, processing or publication of articles.

The manuscript should be submitted in the form of two separate files:

[1] **Covering Letter/Title Page/First Page File**

This file should provide

- The type of manuscript (Original Article, Review Article, Case Report/Short Case Series, Letter the Editor/Letter in Response, Guest Editorial, Research methodology, OSA Meeting Papers) title of the manuscript, running title, names of all authors/ contributors (with their highest academic degrees, designation and affiliations) and name(s) of department(s) and/ or institution(s) to which the work should be credited. All information which can reveal your identity should be here. Use files, preferably Microsoft Word files saved as .doc or .docx. Do not zip the files.
- The total number of pages, total number of photographs and word counts separately for abstract and for the text (excluding the references, tables and abstract), word counts for introduction + discussion in case of an original article.
- Source(s) of support in the form of grants, equipment, drugs, or all of these.
- Acknowledgement, if any. Acknowledgement should not be in the main article file.
- If the manuscript was presented previously, a full statement to that effect should be included with Subject title, place and date of presentation
- Registration number in case of a clinical trial
- Conflicts of Interest form
- Authors' declaration and copyright transfer form
- The name, address, e-mail, and telephone number of the corresponding author and Guarantor

[2] **Article File**:

- The file must not contain identity of the author(s), institution, or acknowledgements (Blinded)
- The main text of the article, beginning from Abstract, Key Words, Body of the Manuscript, References, Tables, Legend to Figures should be in this file in the specified sequence
- The pages should be numbered consecutively, beginning with the first page of the article file.
- Page headers/running title may include the title but not the authors' / institution identity.

- Use Microsoft Word .doc or .docx files.
- Do not zip the files.
- Limit the file size to 1 MB.

[3] **The Authors' Declaration and Copyright Transfer Form** has to be submitted in original with the signatures of all the contributors within two weeks of submission via email as a scanned image. It will not be possible to process the submission otherwise.

Copies of any Permission(s) of Copyright material

It is the responsibility of authors to obtain permissions for reproducing any copyrighted material. A copy of the permission obtained must accompany the manuscript. Kindly note that ***Plagiarism is unethical and liable for punitive action.***

Types of Manuscripts

- Editable checklists for reporting guidelines can be found at www.equator-network.org
- The following table lists the type of articles accepted by JOSA

TYPE of ARTICLE	Abstract	Word Limit	Combined Maximum of Tables & Figures	Maximum References	Type of study	Indicative websites
Original articles	Structured: Aim Methods, Results, Conclusion Maximum 250 words	3000 words	5	40	Randomized Controlled Trial (RCT), Prospective, Retrospective Observational / Interventional Study, Non-randomised Trial, Descriptive Data, Cost Analysis, Animal Studies	CONSORT,STROBE, RECORD, TREND, COREQ, SRQR, CHEERIES, STARD, REMARK, TRIPOD, CHEERS, ARRIVE, REFLECT
Review articles	Unstructured maximum 250 words	5000 words	10	100	Review of Observational studies, Systematic review, Meta-analysis, Qualitative Data By editorial invitation only. All review articles are subject to peer review	MOOSE, ENTREQ, PRISMA
CASE REPORT and CASE SERIES	Unstructured maximum 100 words	900 words	Maximum 4 tables or figures	10	Structure: Introduction, Case report and discussion. Must add to existing knowledge. Proper documentation required. Case series must contain 3-10 cases.	CARE
Letters to the editor and letters in response	No abstract required	300 words	Maximum 2 tables or figures	5	Should be either a response to a specific article published within the last 6 months, or introduction of a new issue. Letters in response are invited by Editorial board	Not applicable
Guest editorial	No abstract required	1000 words	Maximum 4 tables or figures	20	By invitation from Editorial board only	Not applicable
Research methodology	Unstructured maximum 250 words	3000 words	Maximum 5 tables and 5 figures	40	Scientific writing, statistics, legal, ethical aspects	Not applicable
OSA meeting papers	All papers that receive an award at an OSA meeting are required to be submitted to JOSA w.e.f. Golden Jubilee Conference 2017					As above

* Maximum word limit. Excluding title, abstract, tables and figures, legends and references.

Ethics

When human subjects are involved in India, authors are required to declare compliance with ICMR 'Ethical guidelines for biomedical research on human subjects (http://www.icmr.nic.in/ethical_guidelines.pdf) /Clearance from Ethics Committee/Institutional Review Board in accordance with the Helsinki Declaration of 1975, as revised in 2000. Patient's identity should not be revealed, especially in illustrative material. When reporting experiments on animals, indicate compliance with applicable regulatory requirements on use of laboratory animals.

References

JOSA recommends formats used by the National Library of Medicine (NLM) *in Index Medi*cus (https://www.nlm.nih.gov/bsd/uniform_requirements.html). References should b*e numbered c*onsecutively in the order in which they are first mentioned in the text (not in alphabetic order). Iden*tify references in text,* tables, and legends by Arabic numerals in superscript with square bracket after the punctuat*ion marks. References cited onl*y in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure. Names of non-indexed journals should be mentioned in full. Avoid using abstracts,"personal communication", and "unpublished observations" as references.

Tables

- Tables should be self-explanatory and should not duplicate textual material.
- **Each table should be limited to maximum of 5 columns and 20 rows**.
- Number tables, in Arabic numerals, consecutively in the order of their first citation in the text and supply a brief title for each.
- Explanatory notes, credit lines to be placed in footnotes.
- Explain in footnotes all non-standard abbreviations that are used in each table.
- For footnotes, symbols and their order should be: *, †, ‡, §, ‖,¶ , **, ††, ‡‡
- Tables with their legends should be provided at the end of the text after the references in the manuscript file, not as separate file
- The table number should be cited at the relevant place in the text.

Illustrations/Figures/Images

- Upload images **as separate files in JPEG** only format. *Do not* inserted images in the body of the manuscript. Each file size should be within 2MB with minimum resolution of 300 dpi or 1800 x 1600 pixels. Rename file with - MANUSCRIPT NUMBER_FIGURE NUMBER, e.g., JOSA_2017_17_Fig 1
- Submit good quality color images as JPEG files less than 2 MB in size, 1600x1200 pixels, 5-6 inches.
- Graphs can be submitted as images separately without incorporating them in the article file.

1) Files should not be zipped.
2) Figures should be numbered consecutively according to the order in which they have been first cited in the text.
3) Labels, numbers, arrows, letters and symbols should be clear and of uniform size and good contrast. The lettering for figures should be large enough to be legible after reduction to fit the width of a printed column.
4) When graphs, scatter-grams or histograms are submitted the numerical data on which they are based should also be provided.
5) Legends for illustrations: word limit 50, excluding the credit line, using double spacing, and tagged with Arabic numerals. Place legends **after** the References Section / Tables in the article file.
6) The Journal reserves the right to edit illustrations.

Videos: Video facility is not available presently. This section shall be updated in due course.

Protection of Patients' Rights to Privacy

Identifying information should not be included in written descriptions, photographs, scan reports, etc., and pedigrees. If the information is essential for scientific purposes, a written informed consent for publication must be obtained from the patient, or parent/ legal guardian of a minor, and copy of the consent should be submitted with the covering letter.

Sending a Revised Manuscript : The revised manuscript should be submitted by email quoting the manuscript number, incorporating point to point clarification to the reviewer's remarks, highlighting the

changes in the article. The "First Page" or "Covering Letter" file may be omitted while submitting a revised version.

Reprints and Proofs

A complimentary copy is offered to all Authors and Co-Authors whose articles are published in JOSA. The Journal provides no free printed reprints. To purchase reprints, kindly contact the editorial office.

Publication Schedule : Presently annual. JOSA is in the process of bringing out bi-annual issues.

Manuscript Submission, Processing and Publication Charges

The journal does not charge for submission and processing of the manuscripts. Black and white images are reproduced free of cost. However, color processing charges apply to images reproduced in color (Rs 4000 for 1-2 figures, Rs 6000 for 2-4 figures, Rs 8000 for 5-6 figures and so on). Charges may vary with reproduction size of the images and composites. The final decision is made by the Editorial Team. The Editor will inform the Author know about the exact charge / payment modalities at the time of provisional acceptance of the manuscript.

Copyrights

The entire contents of the Journal of Ophthalmological Society of Assam are protected under Indian and international copyrights. JOSA, however, grants to all users a free, irrevocable, worldwide, perpetual right of access to, and a license to copy, use, distribute, perform and display the work publicly and to make and distribute derivative works in any digital medium for any reasonable non-commercial purpose, subject to proper attribution of authorship and ownership of the rights. The journal also grants the right to make small numbers of printed copies for their personal non-commercial use under Creative Commons Attribution-Noncommercial-Share Alike 3.0 Unported License.

Checklist

2) Covering Letter/Title file
3) Author's Declaration and Copyright transfer form
4) Conflicts of interest disclosed
5) Article File
6) Images
7) Permissions: copyright material, borrowed figures/tables, patient's written consent

Presentation and Format

- Double spacing
- Margins 2.5 cm from all four sides
- Page numbers included at bottom
- Running title provided (not more than 50 characters)
- Abstract page contains the full title of the manuscript
- Key words provided (3-5)
- Manuscript title should be in Sentence case
- Remove 'Track Changes'

Language and Grammar

- Uniformly American English
- Write the full term for each abbreviation at its first use in the title, abstract, keywords and text separately unless it is a standard unit of measure.
- Numerals from 1 to 10 spelt out
- Numerals at the beginning of the sentence spelt out
- Check the manuscript for spelling, grammar and punctuation errors
- If a brand name is cited, also cite the manufacturer's name and city/state/country.
- Species names should be in italics

For ready to use templates authors may refer to www.ijo.in

For 'print-on-demand' kindly contact the editorial office.

Authors' Declaration and Copyright Transfer form

(One signed copy to be submitted with the manuscript)

Manuscript Title: _____

Manuscript Number: _____

I/we certify that the manuscript represents valid work. I/we submit that I/we meet the criteria for authorship as established by the ICMJE, in terms of my/our sufficient participation in the intellectual content, conception and design of this work, or, the analysis and interpretation of the data, as well as the writing of the manuscript, to take public responsibility for it and have agreed to have my/our name listed as an Author/Co-author.

I/we declare that this manuscript under my/our authorship is being submitted to Journal of Ophthalmological Society of Assam alone at that point in time, and has not been published/already accepted for publication, nor is being considered for publication elsewhere

I/we certify that all the data collected during the study is presented in this manuscript and no data from the study has been or will be published separately.

I/we undertake that, if requested by JOSA, I/we will provide the primary data on which the manuscript is based, for examination by the editorial board or their assignees.

All financial interests, direct or indirect, for individual authors in connection with this paper have been disclosed in the cover letter. Sources of outside support of the project are declared in the cover letter.

I/We hereby transfer, assign, *all copyright ownership*, including any and all rights incidental thereto, exclusively to the JOSA, in the event that our work is published by the Journal. The Journal shall own the work, including 1) copyright; 2) the right to grant permission to republish the article in whole or in part, with or without fee; 3) the right to produce preprints or reprints and translate into languages other than English for sale or free distribution; and 4) the right to republish the work in a collection of articles in any other mechanical or electronic format.

I/we hereby authorise the corresponding author to communicate with JOSA, including incorporating due changes, and he/she will act as the guarantor for the manuscript on our behalf.

I/we understand that the article will be published under the terms of the latest Creative Commons Attribution-NonCommercial-ShareAlike License, unless the journal notifies the author otherwise in writing.

All individuals who have made substantial contributions to the manuscript, but who are not auhors/co-authors, are duly acknowledged and have given me/us their written permission to be named. No contributor has been otherwise omitted.

Name	Signature with date	Nature of Contribution [1]
1.		
2.		
3.		
……		
Guarantor[2]:		

[1] Concept, design, intellectual content, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review

[2] One or more author takes public responsibility for the whole work and is designated as 'Guarantor'

Journal of Ophthalmological Society of Assam (JOSA)

Peer Review

All submissions shall be peer reviewed. The peer review process is designed to assure that JOSA publishes only original, accurate, and timely articles that contribute to knowledge in the Vision Sciences.

The Editor shall make a preliminary assessment on whether the manuscript meets the requirements of the journal and is worth sending out for thorough review.

If so, it is then assigned to three reviewers, presently by email only, that may include any member of the Editorial Board and/or other experts in relevant fields, as selected by the Editor-for review, preferably in a double blind process.

Reviewers are asked to assess submissions based on depth of original research, accuracy, appropriate documentation, readability, and suitability of content.

Reviewers shall make One of Four Recommendations:

1. Acceptance
2. Provisional Acceptance With Revision
3. Provisional Non-Acceptance
4. Rejection

For points 2, 3 and 4, reviewers are required to include comments explaining the recommendation.

Authors may expect to know the results of the manuscript peer review within four weeks from the date of submission.

Authors shall receive the reviewers' comments and be advised to revise their manuscripts in line with the reviewers' and/or editor's suggestions.

If the revised article is accepted for publication, the editor then determines the journal issue in which it will appear. All efforts are made publish an accepted article in the next issue of the journal.

Call for reviewers:

Interested reviewers may contact the editorial office by email at journal.oa@gmail.com

Mandatory: at least two publications in peer reviewed indexed journals in the preceding 10 years

1. Mashat BH. Polyhexamethylene biguanide hydrochloride: features and applications. British Journal of Environmental Sciences. 2016;4(1):49-55.
2. Available from cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/common_download.jsp?num_id_pk=MTIxNg== as accessed on 22.01.2021.
3. Vidhya C, Murali K, Sowmya R. Safety and efficacy of reconstituted atropine 0.01% eye drops for Indian children with myopic progression. Asian Journal of Ophthalmology. 2020 Apr 30;17(2):209-15.
4. Chia A, Chua WH, Wen L, Fong A, Goon YY, Tan D. Atropine for the treatment of childhood myopia: changes after stopping atropine 0.01%, 0.1% and 0.5%. American journal of ophthalmology. 2014 Feb 1;157(2):451-7.

In Pain and Inflammation associated with Cataract Surgery

Allergan

Rx

Amplinak™

Nepafenac Ophthalmic Suspension 1mg/ml

Truly Quiet Eye

WITH THE ADVANTAGE OF

- Disappearing Preservative*
- Micronized Suspension[1,2]
- Insertion Isolation Technology Pack[3]

References:

* Purite is a brand of Stabilised Oxychloro Complex, a disappearing oxidative preservative that breaks down into sodium chloride and water when exposed to light

1. Aldrich DS, Bach CM, Brown W, Chambers W, Fleitman J, Hunt D, et al, Ophthalmic Preparations, Vol. 39(5) [Sept.–Oct. 2013]
2. Allergan: Data on File (Quality control report) 3. Allergan: Data on File (Manufacturers packaging report)

Abridged Prescribing Information

Amplinak™ contains Nepafenac 0.1% w/v. **Indication:** Amplinak™ ophthalmic suspension is indicated for the treatment of pain and inflammation associated with cataract surgery. **Dosage and administration:** One drop of Amplinak™ ophthalmic suspension should be applied to the affected eye three-times-daily beginning 1 day prior to cataract surgery, continue the day of surgery and through the first 2 weeks of the postoperative period. **Contraindication:** Amplinak™ is contraindicated in patients with previously demonstrated hypersensitivity to any of the ingredients in the formula or to other NSID. **Adverse Event:** Ocular **Adverse Reactions**: The most frequently reported ocular adverse reactions following cataract surgery were capsular opacity, decreased visual acuity, foreign body sensation, increased intraocular pressure, and sticky sensation. These reaction occurred in approximately 5 to 10% of patients. Other ocular adverse reactions occuring at an incidence of approximately 1 to 5% including conjuctival edema, corneal edema, dry eye, lid margin crusting, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, photophobia, tearing and vitreous detachment. **Warnings and precautions:** For topical ophthalmic use only, not for injection. **Pregnancy:** Pregnancy category C. There are no adequate and well-controlled studies in pregnant women. Amplinak™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Storage:** Store Amplinak™ Opthalmic Suspension below 300 C. Protect from sunlight Show supplied: Amplinak™ Opthalmic suspension is supplied in 5 mL dropped bottles

Frequent **Ocular Discomfort** can be a sign of **Ocular Dryness**

For patients with **Ocular Dryness**

opt for

Rx **optive®**

...Science In Every Drop

Right From The Start

Works from inside the epithelial cells & improves Ocular Surface damage[1,2]

For any Allergan product or disease related query, please write to medinfo.india@allergan.com

Abridged Prescribing Information:
Optive® is a lubricant eye drop consisting of Sodium Carboxymethylcellulose (CMC) 0.5%, mild preservative PURITE along with Glycerin, Erythritol, Levocarnitine, Boric acid and some essential Calcium and Magnesium salts. **Indications:** For temporary relief of burning, irritation and discomfort due to dryness of the eye or exposure to wind or sun. Also, may be used as a protectant against further irritation. **CONTRAINDICATIONS:** Optive® is contraindicated in patients with hypersensitivity to any ingredients in this product. **WARNINGS AND PRECAUTIONS:** To avoid contamination or possible eye injury, do not touch tip of the bottle or vial to any surface and avoid contact with the eye. Recap after use. Do not use if OPTIVE® packaging shows evidence of tampering. Do not use if solution changes color or becomes cloudy. Discontinue use of OPTIVE® and consult a doctor if you experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens. Use before the expiration date marked on the container. **Side effects:** Eye stinging, burning, irritation or itching, excessive tearing, eye redness, sensitivity to lights and dry eyes (lack of effect). **Dosage:** 1 or 2 drops in the affected eye(s) as needed. **Packing:** Supplied in 5ml (Physician's sample) and 10ml (Sales pack) plastic dropper bottles.

References:
1. Comparison of Artificial Tears of Optive® and Systane® in Corneal Epithilial Cell Plumping Mark Mcdermott, Keping Xu, Presented at L80th Annual Meeting of the Association of Research in Vision and Opthalmology (ARVO); April 27 May 1, 2008, Fort Lauderdale, FL.
2. M Guillion, C. Maissa, Evaluation of the effects on conjunctival tissues of Optive eye drops over one month usage, Contact lens & Anterior Eye 33(2010) 93-99.

Allergan an AbbVie company | **ALLERGAN INDIA PVT LTD.** Level 7, Prestige Obelisk, No.3 Kasturba Road, Bangalore-560 001.
Phone No. :+91-80-4070 7070 | Fax : +91-80-4070 7007 | E-mail: IN-Allergan@Allergan.com

Allergan

In the treatment of **Bacterial Conjuctivitis**

ZYMAXID™

Gatifloxacin 0.5%

a class Z Ocular Surface Security*

- **Lower Resistance[1,2]**
- **Faster speed of kill of bacteria[4]**
- **Ocular surface Security*[3]**
- **Flexible BD dosing[5]**

**Allergan coined terminology*

1. Hedlin P et al. Poster Presented at Annual Meeting of the Association for Research in Vision and Ophthalmology (ARVO): April 25-29,2004

2. AK Reddy, P Garg, MR Alam, U Gopinathan, S Sharma and S Krishnaiah, Comparison of in vitro susceptibilities of Gram-positive cocci isolated from ocular infections against the second and fourth generation quinolones at a tertiary eye care centre in South India, Eye (2010) 24, 170–174

3. Allergan: Data on file

4. Callegan MC, Novosad BD, Ramadan RT, Wiskur B and Moyer AL, Rate of Bacterial Eradication by Ophthalmic Solutions of Fourth-Generation Fluoroquinolones, Adv Ther (2009) 26(4):447-454

5. Heller et al, Gatifloxacin 0.5% Administered Twice Daily for the Treatment of Acute Bacterial Conjunctivitis in Patients One Year of Age or Older, Journal Of Ocular Pharmacology and Therapeutics Volume 00, Number 00, 2014

Abridged Prescribing Information:

INDICATION: ZYMAXIDTM (gatifloxacin ophthalmic solution) 0.5% is a topical fluoroquinolone anti-infective indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms: Haemophilus influenzae, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus mitis group Streptococcus oralis, and Streptococcus pneumoniae. *Efficacy for this organism was studied in fewer than 10 infections. DOSAGE AND ADMINISTRATION: Patients 1 year of age or older: Instill 1 drop every 2 hours in the affected eye(s) while awake, up to 8 times on day 1. Instill 1 drop 2 to 4 times daily in the affected eye(s) while awake on days 2 through 7. IMPORTANT SAFETY INFORMATION: WARNINGS AND PRECAUTIONS: ZYMAXID™: solution should not be introduced directly into the anterior chamber of the eye. As with other anti-infectives, prolonged use of ZYMAXID™ may result in overgrowth of non-susceptible organisms, including fungi. If super infection occurs, discontinue use and institute alternative therapy. Patients should be advised not to wear contact lenses if they have signs and symptoms of bacterial conjunctivitis or during the course of therapy with ZYMAXID™. PREGNANCY: Because there are no adequate and well-controlled studies in pregnant women, ZYMAXIDTM solution should be used during pregnancy only if the potential benefit justifies the risk to the fetus. NURSING MOTHERS: It is not known whether this drug is excreted in human milk, Because many drugs are excreted in human milk, caution should be exercised when ZYMAXIDTM is administered to a nursing woman. PEDIATRIC USE: The safety and effectiveness of ZYMAXIDTM in infants below one year of age have not been established. ZYMAXIDTM has been demonstrated in clinical trials to be safe and effective for the treatment of bacterial conjunctivitis in pediatric patients one year or older GERIATRIC USE: No overall differences in safety or effectiveness have been observed between elderly and younger patients. ADVERSE REACTIONS: ZYMAXIDTM The most frequently reported adverse reactions occurring in ≥ 1% of patients in the gatifloxacin study population (N=717) were: worsening of the conjunctivitis, eye irritation, dysgeusia, and eye pain. Additional adverse events reported with other formulations of gatifloxacin ophthalmic solution include chemosis, conjunctival hemorrhage, dry eye, eye discharge, eyelid edema, headache, increased lacrimation, keratitis, papillary conjunctivitis, and reduced visual acuity. Note- to representative: Please provide full prescribing information when presenting this material.Clinical Pharmacology: Mechanism Of Action: Gatifoxacin is an 8-methoxy fluoroquinolone with a 3-methylpiperazinyl substituent at C7. The antibacterial action of gatifloxacin results from inhibition of DNA gyrase and topoisomerase IV. DNA gyraseia an essential enzyme that is involved in the replication, transcription and repair of bacterial DNA. Topoisomerase IV is an enzyme known to play a key role in the partitioning of the chromosomal DNA during bacterial cell division. The mechanism of action of uoroquinolones including gatifloxacin is different from that of aminoglycoside, macrolide and tetracycline antibiotics. Therefore, gatifloxacin may be active against pathogens that are resistant to these antibiotics and these antibiotics may be active against pathogens that are resistant gatifloxacin. There is no cross-resistance between gatifoxacin and the aforementioned classes of antibiotics. Cross resistance has been observed between systemic gatifloxacin and some other uoroquinolones. How Supplied: ZymaxidTM is supplied sterile in a 5 ml LDPE bottle ADVERSE REACTINS: ZYMAXIDTM The most frequently reported adverse reactions occurring in ≥ 1% of patients in the gatifloxacin study population (N=717) were; worsening of the conjunctivitis, eye irritation, dysgeusia, and eye pain. Additional adverse events reported with other formulations of gatifloxacin ophthalmic solution include chemosis, conjunctival haemorrhage, dry eye, eye discharge, eyelid edema,*