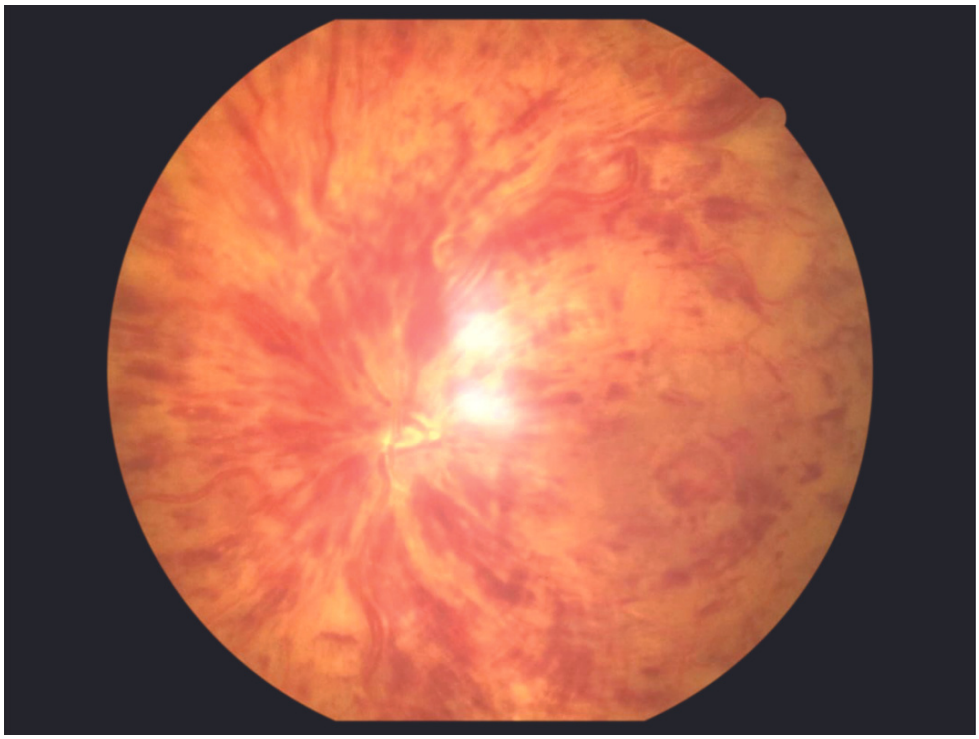
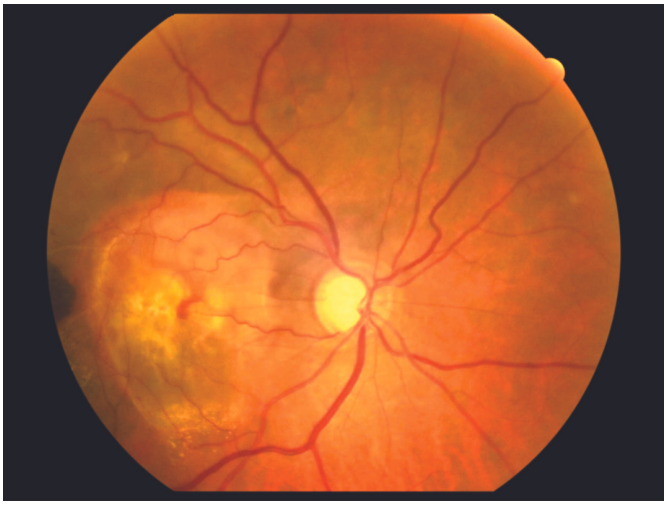
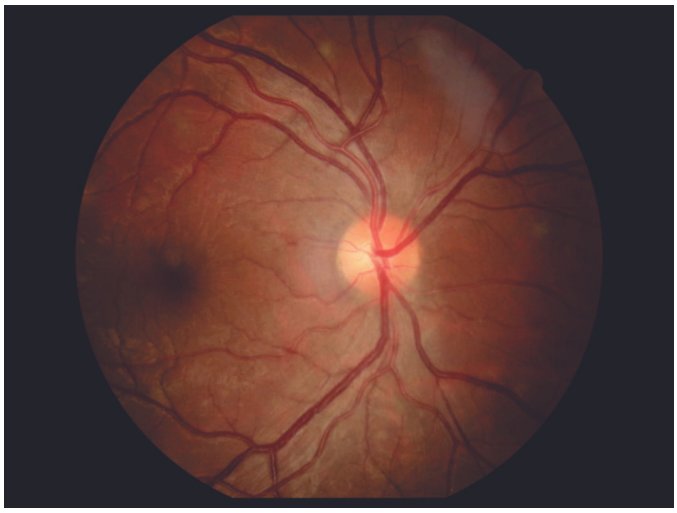
HJO

Himachal Journal
of Ophthalmology

Official Journal of Himachal Pradesh Ophthalmological Society







Volume 2, Issue 1

Mellow the eyes with
the freshness of Aqua

Aquaray® Plus

Sodium Hyaluronate 0.18% & CMC

Lubricant Eye Drop

Dry Eye Syndrome

Aquaray® Lubricant Eye Drop

Carboxymethylcellulose Sodium 0.5%
with Stabilized Oxychloro Complex

Aquaray® gel Eye Drop

Carboxymethylcellulose Sodium 1%
with Stabilized Oxychloro Complex

Aqua for eyes

Raymed

Raymed Pharmaceuticals Limited
Corporate Office: SCO-859, Manimajra, Chandigarh.
Tel.: +91 172 2731528 E-mail : admin@raymedindia.com

Himachal Pradesh Ophthalmological Society

Executive Members 2023-24

HPOS Office Bearers

Patron	Dr. S.K. Soni
President	Dr. Sandeep Mahajan
General Secretary	Dr. Anil Kumar Verma
Treasurer	Dr. Vinay Gupta
Chairman Scientific Committee	Dr. SudhirSalhotra
Editor Journal	Dr. Deepak Kumar Sharma

Executive Members

Dr. RL Sharma

Dr. Rakesh Gupta

Dr. AnchitWapa

Dr. NishantVardhan

Dr. Aditya Kashyap

Dr. Shalu Gupta

Dr. ShrutiAnand

Dr. PawanPrashar

Dr. JitenderRoodkee

Dr. RavinderShashni

Dr. Shahid Khan

Himachal journal of Ophthalmology instructions for authors.

The Himachal Journal of Ophthalmology (HJO) is the official scientific publication of the Himachal Pradesh Ophthalmological Society (HPOS) for circulation to the members of HPOS, advertisers, and subscribers. It covers clinical, experimental, basic science, and translational research studies related to medical, ethical and social issues in the field of Ophthalmology and vision sciences. Articles with clinical interest and implications are given preference.

Himachal Journal of Ophthalmology accepts the following articles:

1. Original articles
2. Review articles
3. Case reports
4. Case series
5. Brief communication and letter to the editor
6. Surgical Technique
7. Photo essay

The word count for original articles is 3000 words; for reviews, it is 5000 words; for case reports and series, it is 1000 words; for letters to the editor and letters in response, it is 500 words; for guest editorials, it is 1500 words; for photo essays, it is 500 words; and for surgical techniques, it is 1500 words.

- A manuscript will be reviewed for possible publication with the understanding that it is being submitted to the Himachal Journal of Ophthalmology alone and has not been published anywhere, has been simultaneously submitted, or already been accepted for publication elsewhere.
- The journal expects that authors would authorize one of them to correspond with the Journal for all matters related to the manuscript.
- All manuscripts received are duly acknowledged and given a Manuscript Number.

- On submission, editors initially review all the submitted manuscripts for suitability for a formal review. Manuscripts with insufficient originality, serious scientific or technical flaws, or lack of a significant message may be rejected before proceeding for a formal peer review. Manuscripts that are unlikely to be of interest to the Himachal Journal Of Ophthalmology readers are also liable to be rejected at this stage itself.
- Manuscripts that are found suitable for publication in the Himachal Journal of Ophthalmology are sent to two or more expert reviewers for Peer Review.
- During submission, the contributor is requested to provide names of two or three qualified reviewers who have experience in the subject of the submitted manuscript, but this is not mandatory. The

reviewers should not be affiliated with the same institutes as the contributor/s. However, the selection of these reviewers is at the sole discretion of the editor.

- The Journal follows a double-blind review process, where the reviewers and authors are unaware of each other's identity.
- Every manuscript is also assigned to a member of the editorial team, who, based on the comments from the reviewers, makes a final decision on the manuscript.
- The comments and suggestions (acceptance, rejection, or amendments in the manuscript) received from reviewers are conveyed to the corresponding author. If required, the author is requested to provide a point-by-point response to the reviewers' comments and submit a revised version of the manuscript. This process is repeated till reviewers and editors are satisfied with the manuscript.
- Manuscripts accepted for publication are copy edited for grammar, punctuation, print style, and format.
- Page proof is sent to the corresponding author. The corresponding author is expected to return the corrected proof within three days. It may not be possible to incorporate corrections received after that period.
- All the manuscripts are subject to final editing by the Editor and the Editorial Board.

Preparation of Manuscripts

Manuscripts must be prepared following the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" developed by the International Committee of Medical Journal Editors (October 2008).

Disclaimer

The information and opinions presented in the Himachal Journal of Ophthalmology (HJO) reflect the views of authors and not the journal or it's editorial board or the publishers. Neither the HJO nor anyone else involved in creating, producing or delivering the HJO or the materials contained therein assumes any liability or responsibility for the accuracy, completeness or usefulness for any information provided in the journal nor shall they be liable for any direct or indirect, incidental, special, consequential or punitive damages arising out of the use of HJO. The Himachal Journal of Ophthalmology nor it's publishers nor any other party involved in the preparation of material contained in the HJO represents or warrants that the information contained herein is in every respect accurate or complete and they are not responsible for any errors or omissions or for the results obtained from the use of such material. Readers are advised to confirm the information contained therein with other sources.

Himachal Journal of Ophthalmology

Contents

Volume 2, Issue 1

Editorial

Advancing Vision: A Journey of Knowledge and Innovations in Ophthalmology

In the ever-evolving field of Ophthalmology, continuous research and technological advancements pave the way for providing superior patient care. The beauty of our profession lies in the comprehensive management of patients, where learning, teaching, and research go hand in hand. Cataract, being the leading cause of ocular morbidity, remains a significant problem in society. However, over the past few decades, cataract surgery techniques have experienced substantial progress. The quest for knowledge has led to enhanced patient outcomes and improved quality of life. From the traditional intracapsular cataract extraction to conventional extracapsular cataract extraction and now phacoemulsification and femtosecond laser-assisted cataract surgery, the field has witnessed unprecedented advancements. Moreover, advancements in intraocular lenses offer precise and customized solutions, ensuring optimal visual rehabilitation.

The relentless efforts of scientists and Ophthalmologists have also helped to bridge the gap between research and practice in the field of retinal surgery and glaucoma management. Ophthalmologists now have effective options for tackling complex retinal disorders, including macular holes, retinal detachment, and diabetic retinopathy. The management of retinal pathology has been revolutionized by advancements in imaging technologies, therapeutic medications, surgical equipment, and instruments. The study of glaucoma has provided profound insights into its pathophysiology and management options. Ophthalmologists are engaged in a continuous pursuit of knowledge to better understand the disease and enhance outcomes for patients. Significant progress in the field is demonstrated by the development of newer antiglaucoma drugs like Rhokinase inhibitors and gene therapy. The commitment to knowledge acquisition and continuous education forms the foundation of advancement in ophthalmology. The Himachal Journal of Ophthalmology takes pride in providing a platform for the dissemination of research findings, clinical experiences, and innovative practices. The quest for knowledge is an ongoing process, and together, let us forge ahead to conquer new horizons in Ophthalmology, ultimately improving the lives of our patients.

Dr. Deepak Kumar Sharma
Editor Himachal Journal of Ophthalmology
Associate Professor Deptt of Ophthalmology
SLBSGMC Mandi at Ner Chowk H.P.
Mobile: +919816073935
E-Mail: editorhjo2023@gmail.com

Cultivated Limbal Epithelial Transplant Versus Conjunctival Limbal Auto Transplant in Uniocular Limbal Stem Cell Deficiency: Long Term Results

Dr. Rajan Sharma[1*], MS, Dr. Ashok Sharma[2], MS, Dr. Verinder S Nirankari[3], MD

[1]* Research Associate, Cornea Centre, SCO 2463 - 2464, Sector 22 C, Chandigarh, 160022, India.

[2] Director, Cornea Centre, SCO 2463 - 2464, Sector 22 C, 160022, Chandigarh, India

[3] Clinical Prof, Department of Ophthalmology, University of Maryland, USA

Abstract

Purpose: To evaluate and compare long-term efficacy of cultivated limbal epithelial cell transplant (CLET) and conjunctival limbal autograft (CLAU) in uniocular limbal stem cell deficiency (LSCD) in chemically injured eyes.

Methods: This was a retrospective, interventional, comparative study, and comprised of sixty- one patients with unilateral severe LSCD who underwent CLET (10) and CLAU (51 patients).

Surgical procedure

Surgical procedure in CLET included superficial keratectomy, excision of fibrovascular tissue, securing amniotic membrane supporting cultured limbal stem cells and placement of bandage contact lens. CLAU included superficial keratectomy, excision of fibrovascular tissue, securing limbal stem cells graft with / without AMT.

Results: Following CLET ocular surface improved in all 10 patients and visual acuity improved significantly in three cases. CLAU was performed in 33 eyes and combined CLAU + AMT in 18 eyes. Visual acuity improved significantly in 26 (51%) eyes. Ocular surface and symblepharon grades improved in all patients during a mean 58.7±21.9 months follow up.

Conclusion: CLET and CLAU is safe and effective in rehabilitating the ocular surface before PKP in uniocular severe LSCD. CLET has the advantage of avoiding iatrogenic limbal stem cell deficiency. CLAU enabled us to repair symblepharon simultaneously by taking extra conjunctiva.

Key Words: Corneo-scleral limbus; limbal stem cell niche; limbal epithelial stem cell deficiency; cultivated limbal epithelial transplant, conjunctival limbal auto transplant.

Introduction

A healthy corneal epithelium, conjunctival epithelium, limbus and normal tear film constitute a normal ocular surface. Healthy corneal epithelial cells are maintained by the normal corneal epithelial cell homeostasis. Limbal stem cells residing in the limbal niche play an important role in corneal homeostasis.[1,2] Thoft et al introduced the well - known concept of x, y, z hypothesis to explain the maturation of limbal stem cells from the limbus towards the central cornea. [3]

In this hypothesis, X represents the proliferative phase of the basal epithelium; Y represents stages of differentiation and maturation during centripetal migration; and Z equates to superficial desquamation. This upward maturation has been demonstrated in the limbal palisades where LESCs are located deeply and transient amplifying cells (TACs) are located more centrally and superficially.[4] This hypothesis explains the regular maintenance of the ocular surface. Limbal stem cells in addition to epithelial cell homeostasis provide a barrier to conjunctival epithelial cells at the limbus. Several clinical and experimental studies established that limbal stem cell damage results in changes in the ocular surface including conjunctivilization, corneal vascularization, recurrent erosions and decrease in vision. These clinical signs suggest the diagnosis of LSCD. [5]

Various surgical options for LESC transplantation can be broadly classified into two approaches: a) direct transplantation of healthy limbal tissue (autologous, allogeneic or cadaveric) or b) transplantation of bioengineered sheet of cultivated LESCs (autologous or allogeneic). [6]

Kruse et al. introduced the concept of conjunctival transdifferentiation. [7] According to this concept, the conjunctival cells present on the cornea, change into corneal epithelium like cells in the absence of corneal vessels over a period of time. On the basis of this concept, the surgical procedure, conjunctival autograft was introduced. However, later studies revealed that conjunctival transdifferentiation does not represent a true conversion to a differentiated corneal phenotype but rather an alteration of the conjunctival epithelium due to external factors.[8] The LSCD partial or total once occurs remains permanent. Later, surgical procedure called conjunctival limbal auto transplant (CLAU) was introduced to treat LSCD.[9] In this procedure, 2-3 mm of limbal conjunctiva from 12 o' clock and 6 o'clock used to be dissected, and after performing superficial keratectomy, 2 mm beyond the limbus was placed and secured at 12 and 6 o clock. The procedure has been reported to be successful in LSCD treatment and ocular surface rehabilitation. However, the procedure theoretically carried a risk of iatrogenic LSCD.

Advancements in cell culture techniques enable the clinicians and researchers to culture limbal stem cells and use this modality clinically in patients with LSCD with success. CLET involves procuring small biopsies of limbal tissue (1-2 mm sized) from healthy eye of same person (autologous) or

other person (allogeneic). [10, 11] The advantage of CLET is the considerably small donor tissue size for culturing the limbal epithelial cells. Therefore, whatever little risk of iatrogenic LSCD existed with limbal tissue transplant is eliminated. The LSC cultures provided a higher number of cells (yielded 90%) compared to cadaveric keratolimbal cell cultures (60%). Although both allogeneic and autologous limbal epithelial stem cells have been used in clinical trials, the autologous stem cells are preferred over the former because of higher success rate, fewer complications and nil immunoreactivity risk thus, no need for systemic immunosuppression.[12]

We herein report, technique and long - term outcome of CLET and CLAU in patients with limbal stem cell deficiency due to chemical injuries.

Methods

In this retrospective, non-randomized, and interventional case series, 61 patients (61 eyes) who had undergone limbal stem cell transplants (CLAU 51; CLET 10) between January 1, 2001, to December 31, 2018 were included. The study was conducted in strict adherence to the tenets of the Declaration of Helsinki. The study was approved by the institutional review board of the Cornea Centre, Chandigarh, India. A written informed consent was obtained from all the patients. The details of obtaining limbal biopsy for culture, conjunctiva, and limbal tissue for CLAU were explained. Details of CLET and CLAU were also explained to the patients and their relatives. The review of medical records of patients who underwent cultivated epithelial cell transplant (CLET) for over two decades was done and the data analyzed. The data on age, gender, type of chemical agent, type of limbal stem cell deficiency, grade of severity, type of LSCT, ocular surface grades, and visual acuity were analyzed.

Patients included in this study had undergone complete ophthalmological work-up. LSCD was clinically diagnosed if any one or more of the following findings were found positive: partial or complete conjunctivilization of the cornea; superficial vascularization; limbal ischemia; loss of palisades of Vogt; loss of corneal transparency, and epithelial defect. Patients who had LSCD due to causes other than chemical or thermal were excluded. Patients with keratinization, descemetoceles, and impending corneal perforation were excluded. Patients who were treated for bilateral chemical injury or had not completed at least 1 year of follow up after surgery were also not included in this study.

Before considering CLAU, slit lamp biomicroscopy of the normal eye was performed. In all normal eyes, no evidence of chemical injury and an intact perilimbal vascular arcade was observed. All patients were explained the complete procedure from the biopsy sample from the uninjured eye, the

culture of the epithelial sheet in the laboratory and the subsequent transplant of the sheet onto the affected injured cornea.

Limbal biopsy: Limbal biopsies approximately 2 x 2 mm (less than 1 clock hour), 100 microns deep, were obtained from the limbus of uninjured eye. The excision of the biopsy tissue was performed in the operation theatre with the use of a surgical microscope. The area of biopsy was marked with the help of calipers. At limbus, 0.5 mm of the cornea lip in front of the conjunctival insertion and 1.5 mm of limbal conjunctiva behind the insertion was included. In four cases, the corneal lip was not included. A corneal incision (2 mm) 0.5 mm infront of the conjunctiva insertion100 microns deep was given. Limbus biopsy tissue 2 mm x 2 mm was

excised.

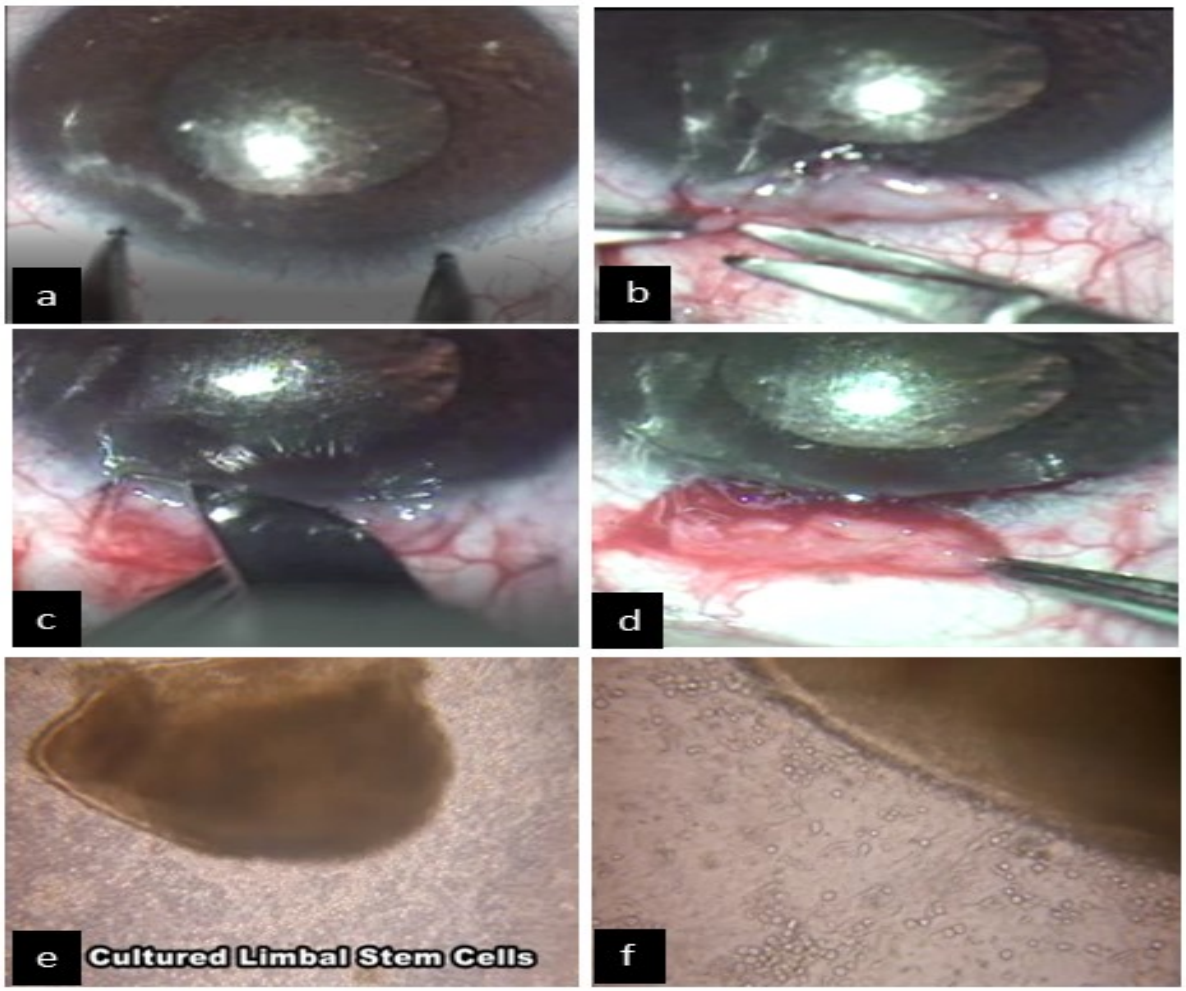


Figure 1 Procuring limbal biopsy and culture of limbal epithelial cells (a) 2.0 x 2.0 mm area marked at limbus (b) conjunctiva dissected up to the insertion (c) 100 micron deep corneal incision ahead of conjunctival insertion (d) Excision of conjunctiva limbal biopsy tissue (e) Cultured limbal epithelial cells on HAM (f) Cultured limbal epithelial cell under high magnification.

Limbal stem cell culture: The limbal stem epithelial cells were cultivated and prepared by Reliance Life Sciences Pvt. Ltd.; (ReliNethra), Worli, Mumbai-400018, India, using an explant
culture technique. The limbal tissues were shredded into many small pieces. Human amniotic membrane was tested for transfusion transmissible diseases including HIV, HBV, HCV, CMV, syphilis, and Mycoplasma. The de-epithelialized human amniotic membrane is seeded with these numerous small pieces. These seedlings were overlaid with 1.7 ml of epithelium medium (DMEM and F-12 into 1:1 ratio) with 20% autologous serum and 1% PS. Human amniotic membrane supporting explants were examined daily and epithelium medium was put on alternate days. Epithelial outgrowth was observed after 4 to 5 days. The epithelial outgrowth expanded and reached full between 14 to 21 days. The cultures were released for limbal stem epithelial cell transplant surgery after 80 to 85% coverage occurred.[13]

During the cultivation process, testing was done for the sterility of the human amniotic membrane. The microbial limit test, endotoxin test and sterility test of limbal culture media, and spent limbal culture media (day

10) were performed. The pH of transport the media at 25+/- 3 degrees celcius was around 7.2 pH, and the release of cultured graft was done when 70-85% of the human amniotic membrane was covered.

Surgical Procedure

CLET:

The surgery involved the dissection of the conjunctiva and sub-conjunctival fibrous tissue dissection (2 mm behind the limbus) with conjunctival scissors and the crescent knife. Dissection from the periphery to the central cornea was done with both blunt and sharp techniques. Symblephra and conjunctival adhesions were released carefully, avoiding any injury to the extraocular muscles and tissues. The excised tissues were then sent for histopathological examination. The cultivated limbal epithelial cells over the amniotic membrane scaffold were then gently placed over the cornea, limbal region and then unfolded with the epithelial side upward. The amniotic membrane was then sutured to the host ocular surface with 10-0 monofilament nylon sutures, and finally, a bandage contact lens was applied, and graft was secured.

Postoperative management included 1% prednisolone acetate eye drops 8 times/ day tapered weekly to once a day in 4-8 weeks and moxifloxacin eye drops 4 times a day for 2-4 weeks, dependin upon epithelial healing.

Preparation of preserved human amniotic membrane: Human amniotic membrane used in this study was prepared and preserved under aseptic measures using the following method.[14]The human placenta was obtained shortly after elective Caesarean section delivery. The donor had been screened serologically for human immunodeficiency virus, hepatitis type B and C viruses, and syphilis. The human placenta was cleaned and cleared off blood clots under lamellar flow hood using sterile Earle's Balanced Salt Solution (Life Technologies Inc., Gaithersburg, MD) containing 50 µg/ penicillin, 50 µg/ml streptomycin, l00 µg/mL neomycin, and 2.5 µg/ml amphotericin B (Life Technologies Inc.).[15] The amnion was separated from the rest of the chorion by blunt dissection through the potential spaces situated between these two layers. The amnion was flattened onto a nitrocellulose paper with a pore size of 0.45 micron (Bio-Rad, Gainesville, Fla), with the epithelium/basement membrane surface up. The paper with the adherent amniotic membrane is then cut into 3 × 4 cm disks and stored before transplantation at -80° C in a sterile vial containing Dulbecco's Modified Eagle Medium (Life Technologies Inc) and glycerol (Baxter Healthcare Corporation, Stone Mountain, Ga) at the ratio of 1:1 (V/V).[16]

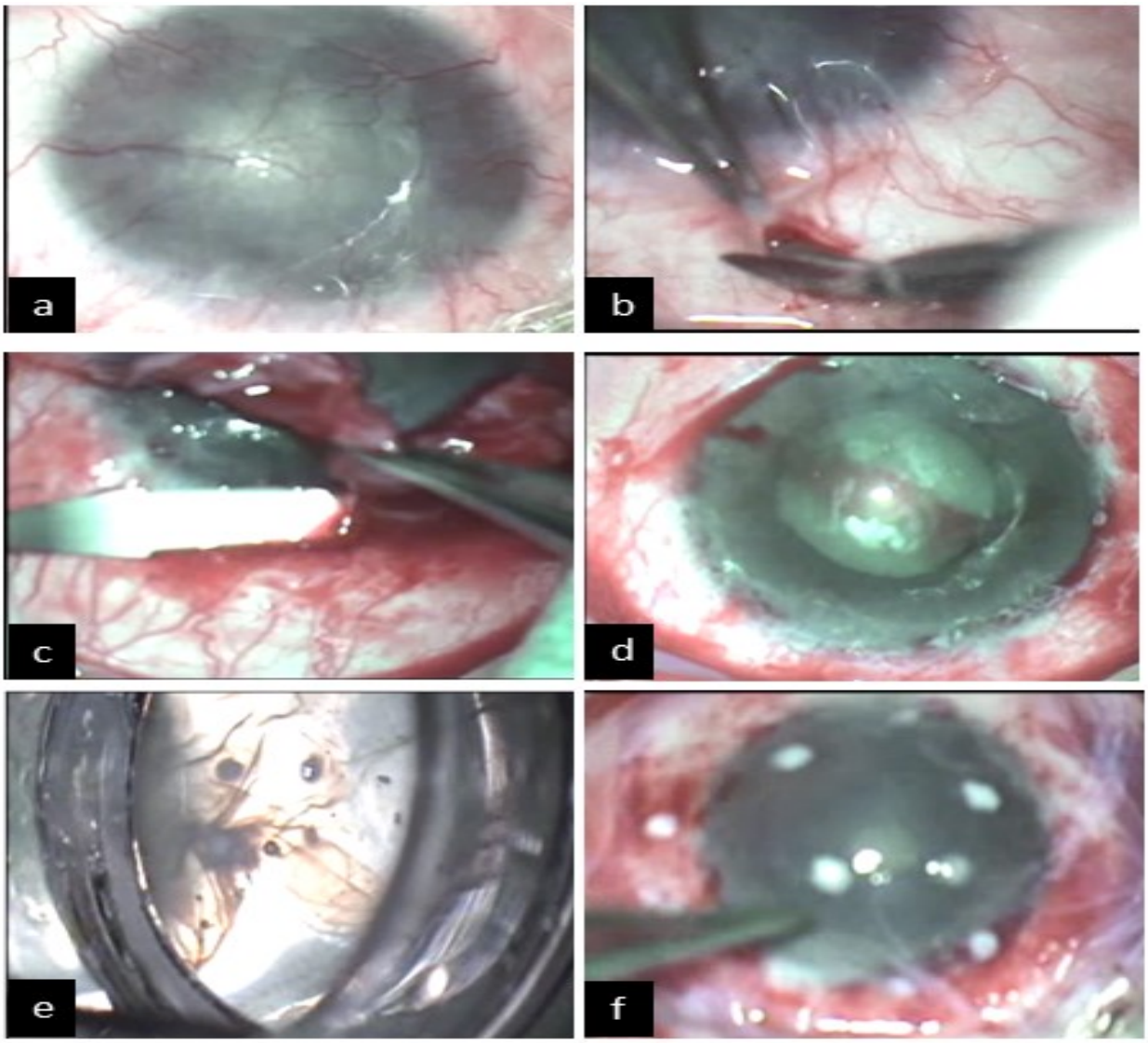


Figure 2 Surgical procedure of CLET (a) Pre-operative picture showing total LSCD (b) conjunctiva peritomy (c) lamellar dissection of fibrovascular tissue (d) Sclera, limbus and cornea cleared off fibrous tissue (e) HAM supporting cultivated limbal epithelial cells (f) Cultivated limbal epithelial cells supported by HAM transplanted

CLAU: Surgical Procedure

A limbal stem cell graft was harvested from the normal eye. Four mm-sized two grafts were procured from 12 O'clock and 6 o'clock. For patients having LSCD less than 180^0 only one limbal graft was used. Peritectomy was performed 2 mm away from the limbus. Dissection was done up to the insertion of the conjunctiva at the limbus. A100-micron deep incision was given 0.5 mm in front of the insertion of the conjunctiva. Limbal stem cell grafts were excised using Vannas scissors.

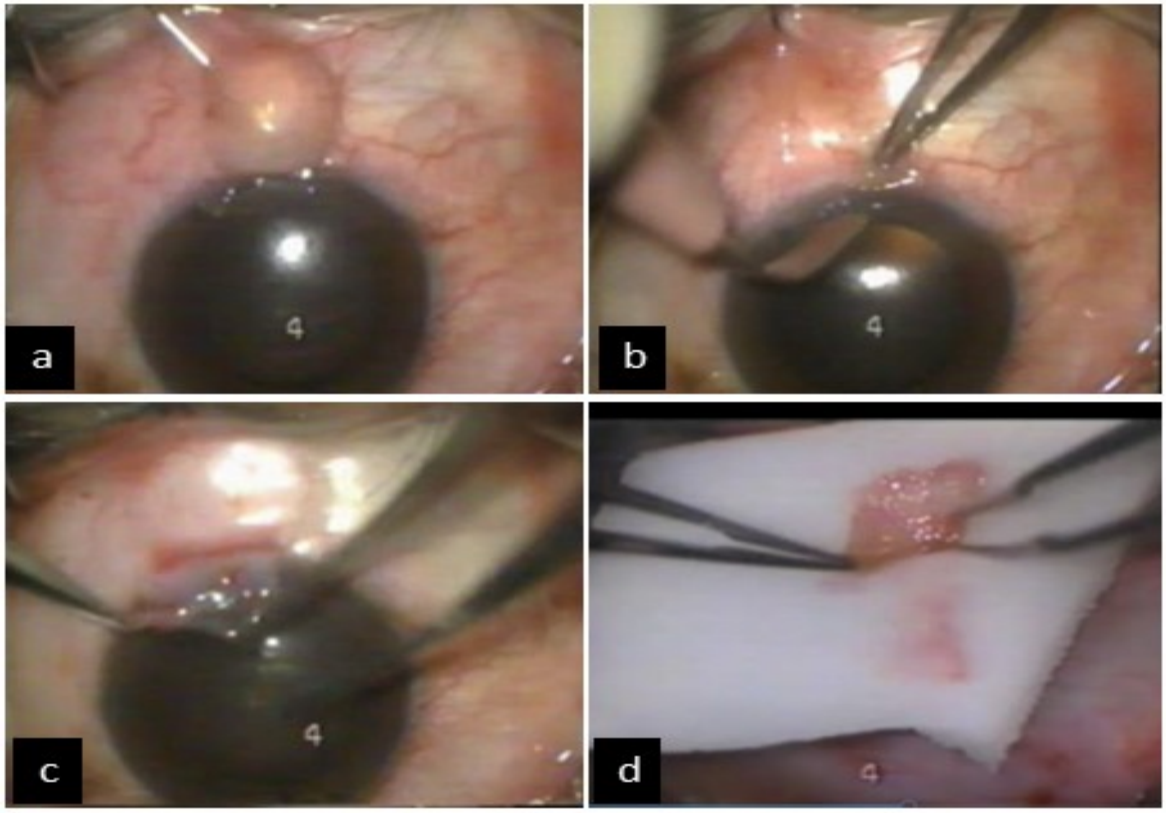


Figure 3 Acquisition of conjunctival limbal graft (a) Subconjunctival inj. of lignocaine with adrenaline (b) 100 micron deep corneal incision in front of conjunctiva insertion (c) Conjunctival limbal graft (d) Excised conjunctival limbal graft

Preparation of the recipient eye: - Peritomy 2 mm from the limbus was performed. Dissection was done up to the limbus. The conjunctival and subconjunctival fibrous tissues were dissected on to the cornea. On the cornea, exact plane of dissection was identified. Dissection was performed carefully as the cornea may be of irregular thickness. Once the dissection is over, the corneal surface was smoothened. Bleeding vessels were cauterised lightly. Limbal stem cell grafts were sutured at 12 o'clock and 6 o'clock position. Corneal portion was sutured with 10 '0' nylon suture and conjunctiva was sutured with 8 '0' vicryl sutures. Limbal grafts were secured using fibrin glue in some of the cases. A bandage contact lens was applied.[17]

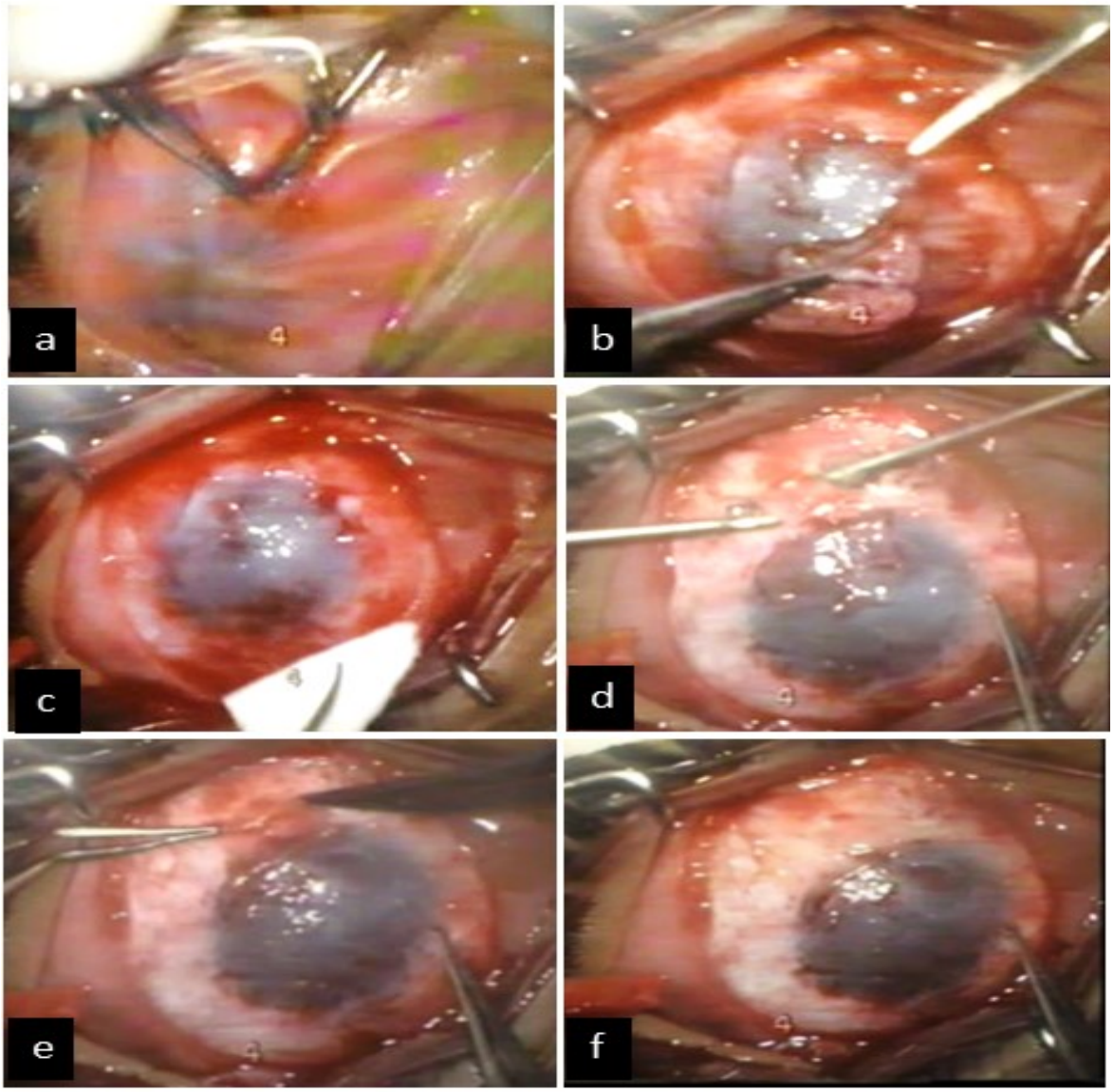


Figure 4 Surgical procedure of CLAU (a) Initiating peritomy and excision of conjunctiva and subconjunctival fibrous tissue in a total LSCD (b) Partially completed lamellar dissection (c) Smoothening of conjunctiva, limbus and cornea surface (d) Simultaneous instillation of 2 components of fibrin glue (e) Fibrin glue assisted adherence of conjunctiva limbal graft (f) Secured conjunctiva limbal autograft .

In patients with combined CLAU and AMG, after suturing of stem cell graft, AMG is placed on the corneal surface. AMG is sutured with 8 ‘0’ vicryl suture to the conjunctiva. A bandage contact lens is applied. Topical Moxifloxacin 0.5% (4 times), Fluoromethalone (Thrice a day) carboxymethyl cellulose eye drops (6 times) is prescribed. Patients were monitored for corneal.

Results: CLET

Ten patients (10 eyes) underwent CLET procedure for uniocular total LSCD following chemical injuries. All 10 patients had improvement in the ocular surface and stabilization of corneal epithelium. Details of clinical presentation, severity grades of LSCD, additional procedures and outcome of CLET procedure are shown in table 3.

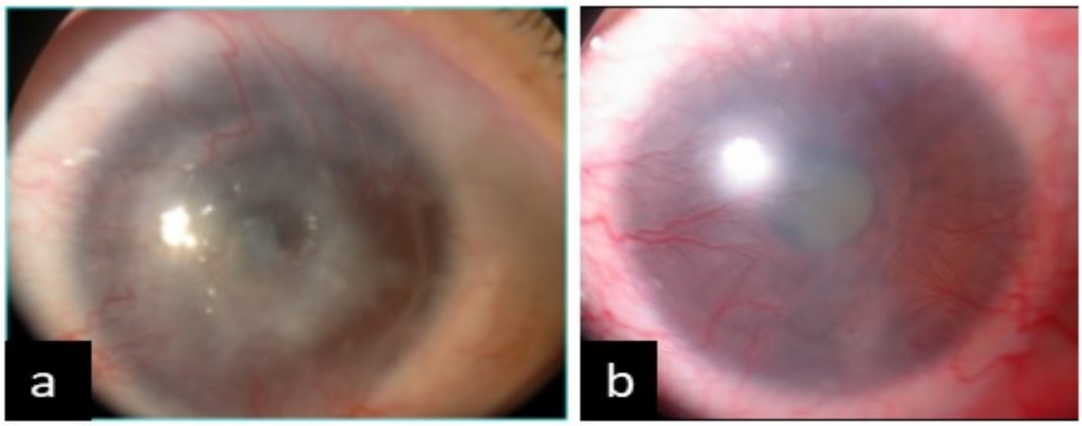


Figure 5 (a) Pre-operative image showing total LSCD (b) Post-CLET clear cornea, stable epithelium and few superficial corneal vessels appearing at 6 months

Results: CLAU

Thirty-two patients had chemical injuries due to acids and 19 patients had due to alkalies. Thirty-three eyes underwent ALSCT and 18 eyes underwent combined ALSCT and AMG. Visual acuity improved in 26(51%) eyes. Eighteen (57%) following ALSCT and 10 (77%) following combined ALSCT and AMG had improvement in visual acuity. Ocular surface improved in all 51(100%) of eyes. (Table 4) Ocular surface grades were better in eyes with ALSCT and AMG.(Figure 6). Thirty-three eyes healed within 6 weeks. Eighteen (37%) eyes took longer time and developed non-healing corneal epithelial defects. Patients with non-healing epithelial defects were treated with autologous serum drops and reapplication of bandage contact lenses. Four patients developed suture granulomas and three regressed after suture removal and use of topical steroid drops. Donor site healed within 2 weeks in all patients. Ocular surface and symblepharon grades improved in all patients during 58.7±21.9 months follow up.

Nine patients had associated symblepharon release. Recurrence of symblepharon was observed in six patients. Resurgery to treat symblepharon was done in 4 patients. None of the patients developed any problem at the site from where limbal stem cell graft was harvested.

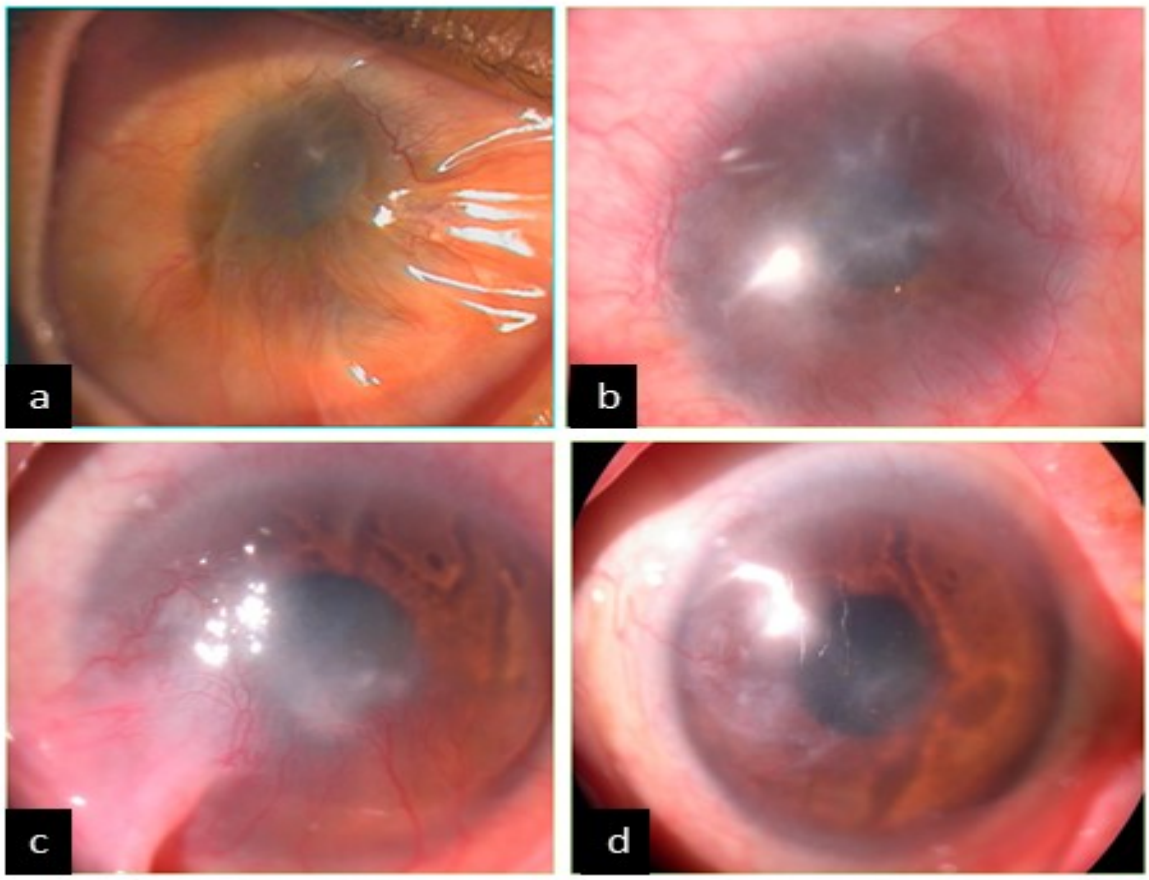


Figure 6 (a) Pre-operative image showing total LSCD (b) Post- CLAUT clear cornea, stable epithelium and minimum corneal vascularization (c) Pre-operative image showing a partial LSCD (d) Post-CLAUT and AMT clear cornea, stable corneal epithelium and minimum vascularisation.

Discussion

Transplantation of LESC is considered an ideal therapeutic option to treat LSCD of varied etiology. However, there is no consensus on the type of limbal stem cell transplant procedure and method of limbal stem cell culture. In this retrospective study, we compared the surgical procedures and outcomes of CLET and CLAU in patients with LSCD following chemical eye injury.

Limbal stem cell damage (LSCD) is characterised by corneal opacification, conjunctivilization, corneal vascularization, and keratinization.[5] Before considering penetrating keratoplasty or deep anterior lamellar keratoplasty in these patients, limbal stem cell transplant is necessary for ocular surface rehabilitation. In this study, CLAU alone or combined with AMG was found effective in improving the ocular surface in unilateral chemical injuries. CLAU alone is effective but to provide a better micro-environment and avoid persistent epithelial defects, we combined it with AMG. There has been a concern of theoretical risk of inducing iatrogenic LSCD in donor eyes. However,

long-term studies have shown no signs of LSCD in the donor eyes after CLAU.[18] We also did not observe any signs of LSCD in any of the donor eyes.

Both CLAU and CLET were equally effective in improving ocular surface in LSCD following uniocular chemical injuries. Theoretically, CLET provides a greater number of cells on the recipient ocular surface. Although, CLAU provided fewer numbers of cells, it provided a 'niche' which enables the mother cells to provide daughter cells continuously. Combined CLAU and AMT improve the micro-environment for the survival of limbal cells. CLET needs a minute piece of limbal tissue for culture and eliminates the risk of any probable iatrogenic limbal stem cell deficiency.

For assessment of success in the CLET procedure, the primary measure is achieving a stable ocular surface. A stable ocular surface is defined as the cornea with no superficial vessels, conjunctivilization, or epithelial defects. Improvement in visual acuity is considered a secondary measure.[19] CLET has been reported to have about a 70% success rate in unilateral LSCD due to burn injury.[19] Transplanted CLET tissue survival rates have been reported to be around 71% at 5 years.[11,20,21]Table 3 shows results of various CLET studies done using HAM or denuded HAM as substrate. [25-30] Sangwan et al. reported 71% surgical success in 200 patients with unilateral LSCD. [30] Vazirani et al. also reported similar surgical success in 70 patients with unilateral LSCD. Authors did not find significant difference in outcomes between different sources of limbal biopsies (same or fellow eye).[33] In a recent systemic review, CLET studies reported similar surgical outcome between them but better outcome when compared to direct limbal tissue transplant techniques.[34]CLAU can provide long-term ocular surface stability and successful visual outcomes in patients with unilateral LSCD. Table 4. shows results of important CLAU studies. [35-41] In all studies surgical outcome was significantly better in autologous conjunctival limbal grafts as compared to live-related allogeneic grafts.

Various methods have been used to cultivate limbal epithelial stem cells. However, similar results have been reported with different methodologies. [22] The explant culture system and the suspension culture system are the two main ex vivo culture methods adopted for the culture of LESCs. The most commonly described explant culture technique uses HAM as a substrate for the cultured cells. In this study, we used the HAM evolving technique of ex vivo–cultured LSCT.A study has shown that HAM provided the niche function for cultured LSCs and maintained the limbal-like environment for the transplanted area of the cornea following penetrating keratoplasty.

The survival of cases depends on the severity of the disease entity, culture technique, and maintenance of the niche environment for LSCs in the culture and after clinical transplantation.[23] Autologous cultivated limbal epithelial transplantation using a xeno-free explant culture technique was effective in long-term restoration of corneal epithelial stability and improvement of vision in eyes with ocular surface burns.[21]Haagdorens et al. in their detailed review have listed & discussed CLET studies on various substrates.[24]

Ocular surface inflammation is detrimental to the limbal niche and the survival of limbal epithelial cells.[42] All cases of LSCD consistently exhibit various degrees of inflammatory response that need treatment. Following the initial injury, sufficient time should elapse before considering LSCT to allow inflammation to subside. Studies have shown better results of LSCT if performed later as compared to early procedure following chemical injury.[40] Even we waited for 12 months after chemical injury to perform LSCT (CLET or CLAU). In early cases, subconjunctival injection of bevacizumab has been advocated along with CLAU to reduce the corneal neovascularization, reducing conjunctival inflammation and supporting restoration of a stable ocular surface. Concomitant use of subconjunctival injection of bevacizumab prevents graft failure and has been reported to cause no toxicity for the transplanted LSCs. [43]

Type of chemical involved and efficiency of initial treatment determines the severity of LSCD. In addition, homicidal injuries are known to cause severe limbal stem cell damage as the assailant has specific motive, and uses stronger chemicals. [44, 45] Thermal burns occur less frequently than chemical injuries to the eyes. Thermal burns in children usually occur following cracker injuries.

The crackers burn at a high temperature (as hot as 1000°C to 1600°C, or 1800°F to 3000°F), depending on the fuel and oxidizer used. This much higher temperature is more than sufficient to cause severe skin burns or ignite clothing.[46] Flame injuries are equally damaging and cause severe eyelid edema, ulceration, and necrosis of the eyelid skin. Because of reflex closure of the eyelids, and Bell's phenomenon, corneal, limbal and conjunctival involvement is less. Contact thermal eye burns because of molten iron or burning cracker powder can cause corneal injury, and melt.

These may contain chemical and cause thermo-chemical injury. However, severe chemical and thermal injuries often lead to corneal ulceration recalcitrant to medical therapy. The reasons for such ulceration are partial or total necrosis of corneal limbus, which is the source of stem cells of corneal

epithelium.[47] In cases where the patient is suffering from non-healing epithelial defect, impending perforation, or active perforation, definitive treatment should be done before LSCT.

Patients suffering from lid deformities, including entropion, ectropion, or lid coloboma, have a poor prognosis to LSCT. These deformities should be corrected before considering an LSC transplant. Pseudopterygium and symblepharon are frequently associated with LSCD.

Both these deformities should be corrected before LSCT. In case, we chose to correct simultaneous the risk of recurrence of disease is higher. We observed recurrence of pseudopterygium in 1/1 (100%) cases of CLET and 6/9 (66%) in case of limbal tissue transplantation. Symblepharon can be operated simultaneously with either CLET or CLST. With CLST, we use conjunctival tissue to correct symblepharon and risk of recurrence is less. We did not use intra-operative mitomycin to prevent recurrence. However, with CLST, correction of symblepharon is easier as we can have large area of conjunctiva to correct symblepharon. Results of symblepharon correction is better with conjunctival tissue compared to AMG.

Repeat CLET at a mean follow-up of 2.3±1.4 (median: 1.96, range: 1 to 7.5) years, 33 of the 50 recipient eyes (66%) maintained a completely epithelialized, avascular, and clinically stable corneal surface. A 2-line improvement in visual acuity was seen in 38 of the 50 recipient eyes (76%). None of the donor eyes developed any clinical features of ocular surface disease, conjunctival overgrowth of the donor site, or decreased vision throughout the follow-up period. Repeat autologous cultivated limbal epithelial transplantation successfully restores corneal epithelial stability and improves vision in eyes with a recurrence of limbal stem cell deficiency, following failed primary surgery for ocular burns, without adversely affecting donor eyes.[26]

To provide early visual rehabilitation, a combination of CLET and penetrating keratoplasty has been performed. However, combined procedures (CLET + PKP) has been seen to have worst impact on the outcome (survival at 1 year).[19]Also, children <15 years of age and poor visual acuity (<20/200) pre-operatively have been reported to have poor surgical outcomes.[19] Better visual results have been reported in patients in whom penetrating keratoplasty is performed after stabilising the ocular surface by performing CLET. The 2-stage approach of autologous cultivated limbal epithelial transplantation followed by PK successfully restores ocular surface stability and vision in eyes with chronic ocular burns. The single-stage approach is associated with poorer clinical outcomes and should be avoided.

The 2-stage approach of autologous cultivated limbal epithelial transplantation followed by PK successfully restores ocular surface stability and vision in eyes with chronic ocular burns. The single-stage approach is associated with poorer clinical outcomes and should be avoided. [48] We did not perform combined CLET and penetrating keratoplasty in any of our patients. We performed DALK in 2 patients and penetrating keratoplasty in 1 patient after CLET and DALK in 4 patients and penetrating keratoplasty in 3 patients after CLAU.

As also seen in Table 4, allograft LSCT techniques (CLET auto, CLAU) have higher success and lower complication rate than allogeneic LSCT.[12] Corneal edema with epithelial rejection lines, peripheral epithelial defects, hyperemic circum-limbal vessels up to the corneal stroma and aggravation of corneal neovascularization indicate immune rejection. Delayed recognition can result in worsening corneal opacification and neovascularization. Reasonable use of topical immunosuppressives and a close follow-up within 6 months after allogeneic CLET are critical in improving the prognosis. [49]Conjunctival limbal allograft can be living related (lr-CLAL) or cadaveric (KLAL).

HLA compatibility testing can be performed in the lr-CLAL. Ozer et al also performed HLA compatibility and sampling done in the lr-CLAL series of 21 patients. The survival rate in the 1st, 2nd and 3rd year were 65%, 54% and 37% respectively. [41] Titiyal et al. prospectively compared CLAL versus KLAL in unilateral chemical/thermal burn cases (20 cases) and found that the former was much better in terms of visual gain (80% v/s 50%) and ocular surface stability (70% v/s 20%) at 6 months. The mean age of the patients was around 17.5 years. [50] Javadi et al in their patients compared lr-CLAL and KLAL and found a lower success rate (39.1% versus 80.7%). The lower success rate in the KLAL group was associated with no HLA matching before the procedure and systemic immunosuppression for a shorter period of duration (1 year).[39]

Limitation of study

This is a non-randomized, retrospective comparative study. Grading of LSCD using a new grading system may provide a better comparison with other studies. The higher cost of culture of limbal stem cells and the need to have an elaborative laboratory set up are additional limitations of using CLET in developing countries.
Limbal stem cells play a crucial role in corneal epithelial cell homeostasis. However, a case of clear graft in a patient with LSCD has been repeated without LSCT. The fate of cultivated limba
epithelial cells is not certain. Following CLST, for how much time limbal tissue containing limbal niche remain functional is also not known. In a study, the evidence for the persistence of donor epithelial cells up to 3.5 years after limbal allograft transplantation has been documented. The study supported the use of systemic immunosuppressive therapy.[51]

Future considerations

Current therapeutic approaches for ex vivo expansion of limbal stem cells only take advantage of surrogate limbal niches. However, new insights into the molecular composition of the limbal niche and innovative biosynthetic scaffolds have added novel niche-based stem cell culture strategies. Promising experimental

approaches include Collagen-based organotypic coculture systems of limbal epithelial stem cells with their niche cells and biomimetic hydrogel platforms pre-functionalized with appropriate biomolecular and biophysical signals are newer promising experimental approaches. In future, clinical application of these novel regenerative strategies is expected to improve long-term outcomes of limbal stem cell transplantation for ocular surface reconstruction. [52]

Conclusion: Limbal stem cell transplant is an important advancement to rehabilitate the ocular surface following chemical injury. Both CLET and CLST are effective in improving the ocular surface and increasing visual acuity in selective cases. Sufficient time should be allowed to elapse after chemical insult before considering LSCT procedure. Sequential surgery PKP/DALK should follow LSCT procedures CLET or CLAU, rather than a combined approach. CLET requires elaborative laboratory set up and involves high cost. CLAU is cost effective and is better in patients requiring concomitant symblepharon and LSCT.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity can not be guaranteed.

Financial support and sponsorship

Nil

Conflict of interest

There are no conflicts of interest

Presented at Annual meeting American Academy of Ophthalmology.

Correspondence to: Dr. Rajan Sharma
Cornea Centre, SCO 2463-2464, Sector 22-C,
Chandigarh, India, PIN 160022
Mob. No.: + 91 9814809495
E mail: rajansharma122@gmail.com

References

1. Ramírez BE, Victoria DA, Murillo GM, Herreras JM, Calonge M. In vivo confocal microscopy assessment of the corneoscleral limbal stem cell niche before and after biopsy for cultivated limbal epithelial transplantation to restore corneal epithelium. Histol Histopathol. 2015;30(2):183-192.
2. Massie I, Dziasko M, Kureshi A, et al. Advanced imaging and tissue engineering of the human limbal epithelial stem cell niche. Methods Mol Biol. 2015;1235:179-202.
3. Thoft RA, Friend J. The X, Y, Z hypothesis of corneal epithelial maintenance. Invest Ophthalmol Vis Sci. 1983;24(10):1442-1443.
4. Bath C, Muttuvelu D, Emmersen J, Vorum H, Hjortdal J, Zachar V. Transcriptional dissection of human limbal niche compartments by massive parallel sequencing [published correction appears in PLoS One. 2013;8(11).

5. Chen JJ, Tseng SC. Abnormal corneal epithelial wound healing in partial-thickness removal of limbal epithelium. Invest Ophthalmol Vis Sci. 1991;32(8):2219-2233.
6. Daya SM, Chan CC, Holland EJ; Members of The Cornea Society Ocular Surface Procedures Nomenclature Committee. Cornea Society nomenclature for ocular surface rehabilitative procedures. Cornea. 2011;30(10):1115-1119.
7. Kruse FE, Chen JJ, Tsai RJ, Tseng SC. Conjunctival transdifferentiation is due to the incomplete removal of limbal basal epithelium. Invest Ophthalmol Vis Sci. 1990;31(9):1903-1913.
8. Sangwan VS. Limbal stem cells in health and disease. Biosci Rep. 2001;21(4):385-405.
9. Kenyon KR, Tseng SC. Limbal autograft transplantation for ocular surface disorders. Ophthalmology. 1989;96(5):709-723.
10. Pellegrini G, Traverso CE, Franzi AT, Zingirian M, Cancedda R, De Luca M. Long-term restoration of damaged corneal surfaces with autologous cultivated corneal epithelium. Lancet. 1997;349(9057):990-993.
11. Schwab IR. Cultured corneal epithelia for ocular surface disease. Trans Am Ophthalmol Soc. 1999;97:891-986.
12. Le Q, Chauhan T, Yung M, Tseng CH, Deng SX. Outcomes of Limbal Stem Cell Transplant: A Meta-analysis. JAMA Ophthalmol. 2020;138(6):660-670.
13. Pellegrini G, Dellambra E, Golisano O, et al. p63 identifies keratinocyte stem cells. Proc Natl Acad Sci U S A. 2001;98(6):3156-3161.
14. Kim JC, Tseng SC. Transplantation of preserved human amniotic membrane for surface reconstruction in severely damaged rabbit corneas. Cornea. 1995;14(5):473-484.
15. Sharma A, Pandey S, Sharma R, Mohan K, Gupta A. Cyanoacrylate tissue adhesive augmented tenoplasty: a new surgical procedure for bilateral severe chemical eye burns. Cornea. 1999;18(3):366-369.
16. Anderson DF, Ellies P, Pires RT, Tseng SC. Amniotic membrane transplantation for partial limbal stem cell deficiency. Br J Ophthalmol. 2001;85(5):567-575.
17. Sharma A, Sharma R. Limbal stem cell transplants and amniotic membrane grafts in ocular surface disease: current perspectives. J Clin Ophthalmol. 2018;2:70-79.
18. Cheung AY, Sarnicola E, Holland EJ. Long-Term Ocular Surface Stability in Conjunctival Limbal Autograft Donor Eyes. Cornea. 2017;36(9):1031-1035.
19. Ramachandran C, Basu S, Sangwan VS, Balasubramanian D. Concise review: the coming of age of stem cell treatment for corneal surface damage. Stem Cells Transl Med. 2014;3(10):1160-1168.
20. Borderie VM, Ghoubay D, Georgeon C, et al. Long-Term Results of Cultured Limbal Stem Cell Versus Limbal Tissue Transplantation in Stage III Limbal Deficiency. Stem Cells Transl Med. 2019;8(12):1230-1241.
21. Sangwan VS, Basu S, Vemuganti GK, et al. Clinical outcomes of xeno-free autologous cultivated limbal epithelial transplantation: a 10-year study. Br J Ophthalmol. 2011;95(11):1525-1529.
22. Shortt AJ, Secker GA, Notara MD, et al. Transplantation of ex vivo cultured limbal epithelial stem cells: a review of techniques and clinical results. Surv Ophthalmol. 2007;52(5):483-502.

23. Tsai RJ, Tsai RY. Ex vivo expansion of corneal stem cells on amniotic membrane and their outcome. Eye Contact Lens. 2010;36(5):305-309.
24. Haagdorens M, Van Acker SI, Van Gerwen V, et al. Limbal Stem Cell Deficiency: Current Treatment Options and Emerging Therapies. Stem Cells Int. 2016;2016:9798374.
25. Baradaran-Rafii A, Ebrahimi M, Kanavi MR, et al. Midterm outcomes of autologous cultivated limbal stem cell transplantation with or without penetrating keratoplasty. Cornea. 2010;29(5):502-509.
26. Basu S, Ali H, Sangwan VS. Clinical outcomes of repeat autologous cultivated limbal epithelial transplantation for ocular surface burns. Am J Ophthalmol. 2012;153(4):643-650.e6502.
27. Kolli S, Ahmad S, Lako M, Figueiredo F. Successful clinical implementation of corneal epithelial stem cell therapy for treatment of unilateral limbal stem cell deficiency. Stem Cells. 2010;28(3):597-610.
28. Pathak M, Cholidis S, Haug K, et al. Clinical transplantation of ex vivo expanded autologous limbal epithelial cells using a culture medium with human serum as single supplement: a retrospective case series. Acta Ophthalmol. 2013;91(8):769-775.
29. Sangwan VS, Matalia HP, Vemuganti GK, et al. Clinical outcome of autologous cultivated limbal epithelium transplantation. Indian J Ophthalmol. 2006;54(1):29-34.
30. Sangwan VS, Basu S, Vemuganti GK, et al. Clinical outcomes of xeno-free autologous cultivated limbal epithelial transplantation: a 10-year study. Br J Ophthalmol. 2011;95(11):1525-1529.
31. Sejpal K, Ali MH, Maddileti S, et al. Cultivated limbal epithelial transplantation in children with ocular surface burns. JAMA Ophthalmol. 2013;131(6):731-736.
32. Subramaniam SV, Sejpal K, Fatima A, Gaddipati S, Vemuganti GK, Sangwan VS. Coculture of autologous limbal and conjunctival epithelial cells to treat severe ocular surface disorders: long-term survival analysis. Indian J Ophthalmol. 2013;61(5):202-207.
33. Vazirani J, Basu S, Kenia H, et al. Unilateral partial limbal stem cell deficiency: contralateral versus ipsilateral autologous cultivated limbal epithelial transplantation. Am J Ophthalmol. 2014;157(3):584-90.e902.
34. Ganger A, Singh A, Kalaivani M, et al. Outcomes of surgical interventions for the treatment of limbal stem cell deficiency. Indian J Med Res. 2021;154(1):51-61.
35. Gomes JA, dos Santos MS, Cunha MC, Mascaro VL, Barros Jde N, de Sousa LB. Amniotic membrane transplantation for partial and total limbal stem cell deficiency secondary to chemical burn. Ophthalmology. 2003;110(3):466-473.
36. Santos MS, Gomes JA, Hofling-Lima AL, Rizzo LV, Romano AC, Belfort R Jr. Survival analysis of conjunctival limbal grafts and amniotic membrane transplantation in eyes with total limbal stem cell deficiency. Am J Ophthalmol. 2005;140(2):223-230.
37. Wylegala E, Dobrowolski D, Tarnawska D, et al. Limbal stem cells transplantation in the reconstruction of the ocular surface: 6 years experience. Eur J Ophthalmol. 2008;18(6):886-890.
38. Miri A, Al-Deiri B, Dua HS. Long-term outcomes of autolimbal and allolimbal transplants. Ophthalmology. 2010;117(6):1207-1213.
39. Javadi MA, Jafarinasab MR, Feizi S, Karimian F, Negahban K. Management of mustard gas-induced limbal stem cell deficiency and keratitis. Ophthalmology. 2011;118(7):1272-1281.

40. Eslani M, Cheung AY, Kurji K, Pierson K, Sarnicola E, Holland EJ. Long-term outcomes of conjunctival limbal autograft in patients with unilateral total limbal stem cell deficiency. Ocul Surf. 2019;17(4):670-674.
41. Ozer MD, Altınkurt E, Yilmaz YC, Gedik AC, Alparslan N. The Surgical Outcomes of Limbal Allograft Transplantation in Eyes Having Limbal Stem Cell Deficiency. J Curr Ophthalmol. 2020;32(2):132-141.
42. Nubile M, Curcio C, Dua HS, et al. Pathological changes of the anatomical structure and markers of the limbal stem cell niche due to inflammation. Mol Vis. 2013;19:516-525.
43. Cavallini GM, Pellegrini G, Volante V, et al. Chemical injury treated with autologous limbal epithelial stem cell transplantation and subconjunctival bevacizumab. Clin Ophthalmol. 2014;8:1671-1673. Published 2014 Aug 30.
44. El-Hofi AH, Helaly HA. Evaluation of limbal transplantation in eyes with bilateral severe ocular surface damage secondary to chemical injury. Clin Ophthalmol. 2019;13:383-390. Published 2019 Feb 18.
45. Saini JS, Sharma A. Ocular chemical burns--clinical and demographic profile. Burns. 1993;19(1):67-69.
46. "Sparklers Can Burn at 2,000 Degrees Fahrenheit" (PDF). United States Consumer Product Safety Commission. Retrieved 11 August 2014.
47. Tseng SC. Concept and application of limbal stem cells. Eye (Lond). 1989;3 (Pt 2):141-157.
48. Basu S, Mohamed A, Chaurasia S, Sejpal K, Vemuganti GK, Sangwan VS. Clinical outcomes of penetrating keratoplasty after autologous cultivated limbal epithelial transplantation for ocular surface burns. Am J Ophthalmol. 2011;152(6):917-924.e1.
49. Qi X, Xie L, Cheng J, Zhai H, Zhou Q. Characteristics of immune rejection after allogeneic cultivated limbal epithelial transplantation. Ophthalmology. 2013;120(5):931-936.
50. Titiyal JS, Sharma N, Agarwal AK, Prakash G, Tandon R, Vajpayee R. Live Related versus Cadaveric Limbal Allograft in Limbal Stem Cell Deficiency. Ocul Immunol Inflamm. 2015; 23(3):232-239.
51. Djalilian AR, Mahesh SP, Koch CA, et al. Survival of donor epithelial cells after limbal stem cell transplantation. Invest Ophthalmol Vis Sci. 2005;46(3):803-807.
52. Schlötzer-Schrehardt U, Freudenberg U, Kruse FE. Zukunftstechnologie Tissue-Engineering : Fokus auf die Stammzellnische [The emerging technology of tissue engineering : Focus on stem cell niche]. Ophthalmologe. 2017; 114 (4):327-340.

Drug Holiday in Glaucoma - The selective Laser Trabeculoplasty way

Dr. Anuj Sharma[1] DNB, MNAMS

[1] Consultant Deptt of Ophthalmology Sri Sathya Sai Institute of Higher Medical Sciences Prasanthi Gram Puttaparthi Sri Satya Sai District AP 515134

Glaucoma refers to a group of disorders characterized by progressive optic nerve atrophy and optic nerve head cupping producing typical visual field defects and may be associated with raised intra-ocular pressure (IOP). The target of glaucoma management is the stabilization of nerve fibre damage and prevention of visual field loss by achieving target IOP. Different modalities for achieving target IOP are medical treatment, filtration surgery and laser treatment. Laser trabeculoplasty is a treatment option in glaucoma, in which laser energy is targeted at trabecular meshwork to improve aqueous outflow. It can be performed with various types of laser energy, including Argon laser, diode laser and frequency-doubled NdYAG laser. Laser trabeculoplasty can be considered as first-line therapy in selected patients or as an alternative where medical therapy is contraindicated or will not be used reliably by the patient. It may reduce the number of long-term medications required. Invasive surgery, with the risk of associated complications, can be reduced or avoided if laser trabeculoplasty is effective.

Keywords: Glaucoma, Selective laser trabeculoplasty, Argon laser trabeculoplasty

Introduction

Glaucoma refers to a group of disorders in which there is cupping and atrophy of the optic nerve, producing characteristic visual field loss, and is usually, but not always, associated with increased IOP. [1] Patients with glaucoma may present as a continuum, ranging from the initial asymptomatic stages with accelerated retinal ganglion cell death and axonal loss of optic nerve, to the symptomatic stages with functional impairment from visual field loss and eventually blindness. [2]

Glaucoma can be further classified into pen-angle glaucoma (OAG) and angle-closure glaucoma (ACG) [1]

In OAG, despite an open angle, dysfunction occurs with the trabecular outflow pathway. [3]

According to the American Academy of Ophthalmology, primary open-angle glaucoma (POAG) is a chronic, progressive optic neuropathy in which IOP and other currently unknown factors contribute to damage, and in which, in the absence of other identifiable causes, there is a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons. This condition is associated with an anterior chamber angle that is open by gonioscopic appearance. [4]

Normal tension glaucoma (NTG) is a subgroup in which the IOP is not raised above the normal range. [1] In ACG, outflow obstruction is caused by mechanical occlusion of angle structures by the peripheral iris. [5]

Goals of glaucoma management: -

- Controlling IOP within the target range remains one of the most important targets in the process of glaucoma control.
- A further targeted outcome would be stabilization of optic nerve or retinal nerve fibre status and stabilization of visual field. [4]
- Substantial visual field loss is associated with reduced quality of life (QOL) [3], making visual field loss a relevant outcome measure. As POAG is chronic and asymptomatic in its early stages, and various treatment methods are associated with respective advantages and disadvantages, therapeutic decisions should consider the life expectancy of the patient as well as treatment efficacy and the patient's QOL.

Overview

Therapeutic choices for open-angle glaucoma: -

Therapeutic choices for lowering IOP can be grouped into medical treatment, filtration surgery and laser treatment. All three methods can reduce IOP in glaucomatous patients.

Medical treatment: -

Medication in terms of topical eye drops is commonly considered the first-line treatment in OAG. The mechanisms of the eye drops include reducing aqueous production and increasing uveoscleral and/or trabecular outflow. [4] Prostaglandin analogues and beta-blockers are commonly used as first-line treatment, where the IOP lowering effect is reported to be 25-33% and 20-25% respectively. [4] Other agents e.g. alpha-adrenergic agonists, and carbonic anhydrase inhibitors act as alternatives or adjuncts when the first-line regimen fails to lower the IOP to within the target range. There are newer antiglaucoma medications also available now e.g. rhokinase inhibitors, (ripasudil, netarsudil). While this method is the most non-invasive approach to IOP control, the risks and benefits of treatment initiation have to be balanced carefully, especially when each group of medication has its side effect profile both locally and systemically.

Disadvantages of medications: -

- Examples of ocular side effects included burning, stinging, conjunctival hyperemia, itching, ocular secretion, ocular pain, tearing, brow ache, dryness, foreign body sensation, eyelid redness, eyelid oedema, blurred vision, visual acuity loss, accommodation difficulties, and night vision problems.
- Systemic side effects of certain commonly used ocular medication e.g. beta blockers are well known [6] and it is contraindicated in certain groups of patients e.g. asthmatic patients and heart block. [8]
- The drawback of this therapeutic choice is effectiveness, which depends also on the adherence to treatment and technique of application of eye drops by the patients or their caretakers. [4]

- It has been shown that even with good support and a free supply of medication, nearly 45% of the patients may take less than 75% of the required medication. [5]
- Instilling eye drops may also be difficult for patients with visual impairment and fine motor problems. Once initiated, the eye drops are expected to be used for a long period, usually life-long, to keep the IOP within the target range.
- The cost of medication has formed the main component of glaucoma treatment cost, representing 42 to 56% of the cost in all stages, and 34% of lifetime cost. [7], [8]

Cost issues of medications: -

- Disease burden of glaucoma to society can be in the form of direct healthcare cost, which includes the cost for treatment of glaucoma and its associated comorbidities, indirect loss due to loss of productivity and efficacy, need for the caretaker, and loss of well-being which can be expressed in terms of disability-adjusted life-year (DALY). [9] Treatment of glaucoma may impose a significant burden on healthcare systems.

Filtration surgery for Glaucoma

Filtration surgery involves creating of a new drainage passage of aqueous humour in the eye, thereby reducing the IOP. A wide range of filtration surgery has evolved, with the first line being trabeculectomy. [4] Except in selected cases, it is usually performed when medical or laser therapy fails. [4] In a meta-analysis, it has been shown that filtration surgery as initial treatment may preserve the visual field marginally better than initial medical treatment at 5 years of follow-up in more severe glaucoma cases. However, it was associated with more local eye discomfort, higher incidence of cataracts and lower visual acuity up to 5 years of follow-up. Currently, there is a trend towards micro-invasive glaucoma surgery (MIGS). It has shown promising results in lowering IOP in cases of mild or moderate glaucoma. [10]

Laser

Laser trabeculoplasty is a treatment option in glaucoma, in which laser energy is targeted at trabecular meshwork to improve aqueous outflow. It can be performed with various types of laser energy, including argon laser, diode laser and frequency doubled NDYAG laser.

Laser trabeculoplasty can be considered as first-line therapy in selected patients [11], [12] or as an alternative where medical therapy is contraindicated or will not be used reliably by the patient. [5] It may reduce the number of long-term medications required. Invasive surgery, with the risk of associated complications, can be reduced or avoided if laser trabeculoplasty is effective.

Argon Laser Trabeculoplasty

Histopathology and Mechanism: - Argon Laser Trabeculoplasty (ALT) was shown by Wise and Witter to be an effective treatment for lowering intraocular pressure (IOP) in open angle glaucoma (OAG) in 1979. [13]ALT employs the application of argon laser burns to the trabecular meshwork (TM) in the anterior chamber angle of the eye. These burns cause coagulative damage to uveoscleral meshwork, disruption of the trabecular beams and heat-induced damage to surrounding collagen fibres. [14]

The mechanical theory of ALT: - The precise mechanism of action is unknown but one theory, known as the mechanical theory, is that the thermal energy causes coagulation and, hence, contraction of the areas of application. This contraction causes shrinkage of the inner TM ring applying traction on the intervening meshwork and Schlemm's canal. The traction causes the separation of the trabecular sheets and prevents the collapse of Schlemm's canal, therefore facilitating the outflow of aqueous humour and lowering IOP. Similar histopathological changes in the ultrastructure of the TM as those produced by ALT have been documented after the application of 1064 nm neodymium: yttrium-aluminium-garnet (Nd: YAG) and diode lasers. [15, 16]

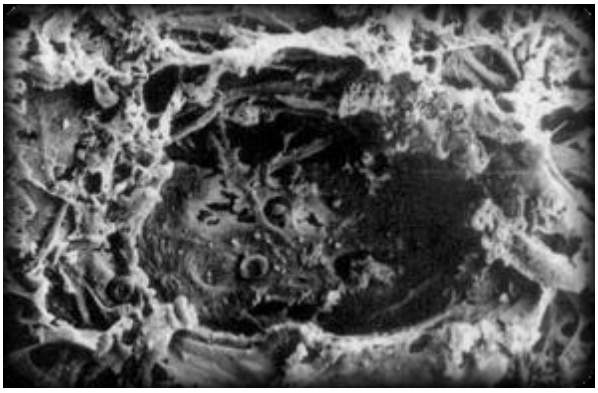


Figure 1: Scanning electron microscopy (SEM) after argon laser trabeculoplasty showing crater formation and disruption of the rope like components of the trabecular meshwork.

Cellular Theory of SLT: - Another theory, the cellular theory, postulates that ALT causes increases in both cell division [17] and phagocytic activity[18] in the trabecular endothelial cells. This is thought to cause the clearing of debris from the trabecular meshwork as well as stimulate the growth of healthy trabecular tissue, thus facilitating aqueous outflow. Furthermore, ALT has been shown to induce the expression and secretion of IL-1 and TNF alpha. [19] This in turn leads to increased expression of stromelysin in trabecular cells which plays an important role in remodeling of the trabecular extracellular matrix and increasing aqueous outflow. [11]

Clinical Efficacy: ALT was shown to produce lower IOP in the Glaucoma Laser Trial (GLT), better visual acuity and better optic disc status in treated eyes when compared to eyes treated medically when employed as the initial treatment of glaucoma. [20] In the seven-year follow-up of the GLT study initial treatment with ALT was again found to be as, if not more, efficacious than initial medical treatment of glaucoma with an average IOP reduction of 7-10 mmHg. [21] That IOP reduction was 1.2 mmHg greater than that demonstrated by the primary medical treatment group. Despite these findings, ALT is most commonly used after medical options have been explored without resulting in adequate IOP control in hopes of postponing or eliminating the need for

filtering or cyclodestructive surgery. While ALT has proved to be an effective treatment, long-term failure of IOP control is common. The side effects include post-op IOP spikes, iritis and peripheral anterior Synechiae. [22, 23] The amount of energy delivered during treatment correlated with the incidence of these side effects but did not affect the long-term reduction in IOP. [24, 25]

Seeking to reduce the frequency of these side effects led investigators to attempt to lower the total amount of energy delivered to the TM without losing the efficacy of the treatment.

Selective Laser Trabeculoplasty (SLT): - SLT is a technique that uses an Nd YAG laser to selectively target pigmented trabecular cells without causing widespread thermal damage to the trabecular meshwork. This technique was developed by Latina and Park in 1995 by applying lasers pulses of various frequencies, duration and power to a mixed cell culture of pigmented and non-pigmented TM cells. [26] They found that with lasers capable of pulses in the sub-microsecond range it was possible to define a range of energy pulses in which pigmented TM cells could be selectively damaged and killed while leaving adjacent non-pigmented TM cells unharmed. The theory upon which SLT is based and which makes this selective killing possible is called selective thermolysis. The brevity of the laser pulses is critical to produce selective thermolysis because to specifically target pigmented TM endothelial cells the pulse duration must be shorter than the thermal relaxation time of melanin.

Thermal relaxation is the time required for a chromophore to convert electromagnetic energy into thermal energy. At pulse durations less than the thermal relaxation time, energy is deposited in the melanin granules faster than it can diffuse. The thermal energy is therefore limited to the pigmented granules in the TM endothelial cells with very little dissipated to surrounding structures, limiting their damage. The thermal relaxation time of melanin is approximately 1 microsecond explaining why pulse durations below this threshold allow for selective targeting. When cultures irradiated using low energy, q-switched, frequency-doubled Nd: YAG laser emitting at 523 nm in 10 sec pulses were examined the damage was strictly limited to lysosomes containing pigment granules.

This was seen as fractured melanin granules and ruptured lysosomal membranes on transmission electron microscopy. At pulses that approached this threshold, such as the 1 microsecond pulses of the pulsed dye laser used in this study, damage was seen to subcellular organelles surrounding the pigment granules in addition to the granules themselves. This gave evidence of the importance of thermal diffusion in the production of collateral damage to surrounding structures. At the light microscopy level, the damage induced by these two lasers was so subtle that it was difficult for the investigators to distinguish irradiated areas by phase contrast microscopy. Using stains to identify compromised cells they found non-pigmented cells remained viable even when all of their adjacent pigmented cells had been killed. Cultures irradiated with longer pulse durations at energies above the threshold that caused cell damage showed complete vaporization of both pigmented and non-pigmented cells at the burn sites.

The q-switched, frequency-doubled Nd: YAG laser application delivers about 0.6 – 1.0mJ per pulse which is 1% of what traditional ALT delivers at 60-100 m J per pulse. SLT can be applied over a much larger area because spatial targeting is unnecessary. SLT is usually applied with a spot size of 400 μm versus the 50 μm

spot size in ALT. Coupling the lower amount of energy delivered in SLT with a larger spot size over which this energy is applied leads to a far lower fluence (energy/area) in SLT when compared with ALT. Due to the low fluency required together with the approximately 1mm tissue penetration and relative transparency of collagen in the trabecular beams to 523 nm light, it was hypothesized that the results found on the two-dimensional cell cultures could be applied to the three-dimensional trabecular meshwork with similar selectivity.

Histopathology: - Microscopic studies have subsequently shown the selectivity of SLT when applied to human eyes. Scanning electron microscopy (SEM) performed on the TM after the application of ALT showed crater formation with evidence of coagulative damage at the base and edges. [16] This was seen in the form of whitening and bleb formation. There was also disruption of the collagen scaffolding and trabecular beams with debris from these structures in the adjacent intratrabecular spaces. SEM on SLT-treated specimens, on the other hand, showed minimal mechanical disruption of the collagen scaffolding and trabecular beams with no evidence of crater formation or coagulative damage.

Transmission electron microscopy (TEM) on ALT specimens showed similar disruption of trabecular beams and collagen scaffolding immediately surrounding the laser lesions. Additionally, trabecular endothelial cells were found to be disrupted with many of them appearing to be detached from the trabecular beams. The pigment granules within these cells were rounded and intact. SLT specimens examined with TEM showed no disruption of the TM which was lined with a continuous layer of trabecular endothelial cells.

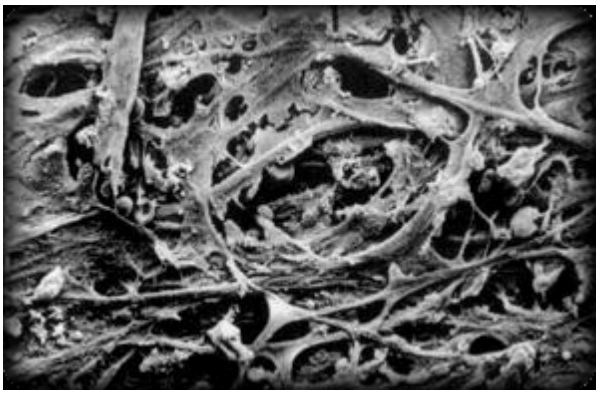


Figure 2: SEM after selective laser trabeculoplasty showing intact trabecular meshwork beams

In contrast to the ALT treated specimens many of the intracytoplasmic pigment granules in the SLT treated specimens were cracked and fragmented as Latina and Park [26] found in cell culture. This is precisely where SLT is designed to interact. Many of these endothelial cells were also vacuolated.

Mechanism of Action of SLT: - The lack of coagulative damage induced by ALT suggests that any IOP reduction caused by SLT is due to the selective killing of pigmented trabecular meshwork cells and the biologic response that ensues. Multiple biologic reactions have been documented and all of them can be at least partially attributed to the induced expression of various cytokines after SLT.

Figure 3: SLT Treated trabecular meshwork endothelial cells release cytokines, which bind with the Schlemm's canal endothelial cells (SCEs) and open the cellular barrier formed by these cells (on transmission electron microscopy)

As with ALT, SLT has been shown to increase expression of IL-1 and TNF-alpha with the addition of IL-8. [27] These cytokines are important in the recruitment of macrophages which may help to clear debris from the TM and facilitate aqueous outflow. A study by Alvarado et al [27] found that SLT applied to trabecular meshwork cells in culture produces increased levels of these cytokines in the culture medium. When endothelial cells from the TM and Schlemm's canal were incubated with this culture medium it was found that it significantly altered their genetic expression. The increase in cytokine activity and altered expression of genes occurs simultaneously with an increased rate of conductivity of aqueous humor across monolayers of these two cell types.
This increased conductivity is also reproducible by administering exogenous IL-1 alpha and 17- beta, TNF-alpha and IL-8 to these cellular monolayers. This is an important finding because the endothelial cells of Schlemm's canal form the last barrier of the outflow tract and exert important control over how much aqueous humor leaves the eye and enters the venous circulation. If SLT produces the same four-fold increase in conductivity in Schlemm's canal endothelial cells in vivo that it produces in vitro it could explain much of the IOP reduction seen clinically.

The TM extra-cellular matrix has been shown to be both increased and modified in primary open angle glaucoma (POAG). [11, 12] This is thought to be another pivotal factor in the outflow resistance and elevated IOP in this condition. The normal turnover of the TM extra-cellular matrix is partially governed by the activity of metalloproteinases (MMPs). [28, 29] The activity of MMPs, in turn, is increased by the cytokines IL-1 and TNF-alpha. [31, 32, 33] The ratio of MMP concentration to the concentration of their inhibitors' is also increased by these cytokines. These inhibitors are called tissue inhibitors of metalloproteinases, or TIMPs. MMP-2 is the predominant gelatinase in the aqueous humor and its inhibitor, TIMP-2, is upregulated in POAG. [23] This imbalanced ratio of MMP-2 to TIMP-2 is thought to be responsible for the decreased collagenase activity of aqueous humor from POAG eyes in vitro. [24] The increased expression of cytokines after SLT could influence the ratio between these two factors and induce remodeling of the extracellular matrix in the TM. This finding is similar to the finding of increased expression of stromelysin, another MMP, due to increasedIL-1 and TNF-alpha activity after ALT. [22]

Another one of the main factors that is thought to contribute to the etiology of POAG is the relative dearth of endothelial cells in the TM when compared to healthy controls. The endothelial cells in the TM and Schlemm's canal undergo mechanical deformation due to stretching when IOP is elevated. [25] This mechanical stretching has been shown to induce various changes in signal transduction, genetic expression and permeability in the

anterior segment of the human eye. [26, 32] Among the up regulated genes are PIP 5K1C, VIP, tropomodulin, and MMP2 which are known to influence outflow resistance. A similar increase in MMP-2 as well as a decrease in TIMP-2 in TM endothelial cells due to mechanical stretch have been found in other studies. [27] This increased expression of MMP-2 was shown to correlate with the ability of eyes challenged with increased flow rates to restore IOP to normal levels after a couple of days. [11] This effect was hypothesized to be a result of pruning of the TM extracellular matrix and subsequent reduction in outflow resistance.

The decreased cellularity of the TM in POAG when compared to age matched normal controls [33] may lead to increased IOP due to an inability of the present cell population to generate equivalent levels of these factors in response to a given IOP as would be produced by abnormally populated TM. This decreased cellularity of TM endothelial cells may also contribute to elevated IOP by not being able to produce sufficient concentrations of cytokines to adequately alter the permeability of the Schlemm's canal's endothelial cells. The importance of this is that laser treatments have been shown to increase cell division in the TM [17]. This is likely to be at least partially due to the ability of cytokines to act as growth factors for TM endothelial cells.

SLT, by inducing cytokine expression, may be triggering a repopulation of the TM endothelial cells and therefore restoring the ability of this cell population to adequately respond to increases in IOP. The new population of TM cells could then secrete factors important in the regulation of the permeability of Schlemm's canal endothelial cells and in the proper turnover in the TM extracellular matrix. There is one more piece of evidence that supports the importance of the biological response induced by SLT in lowering IOP. This evidence comes from a study that found that untreated eyes contra lateral to SLT treated eyes exhibit a statistically significant pressure reduction. [34] This study found a 9.7% IOP reduction in these untreated eyes at 6 months. A mechanical mode of action is ruled out in the contra lateral eye as the laser was not applied there. This suggests that the inflammatory cascade induced in the treated eye has some crossover effect in the untreated eye.

In summary, there is strong evidence that SLT is inducing biological responses in the TM that are responsible for IOP reduction. These mechanisms are the increased expression of cytokines, increased permeability of the endothelial cells in the TM and Schlemm's canal, remodeling of the extracellular matrix of the TM and repopulation of TM endothelial cells. All of these mechanisms influence each other, and the induction of cytokine expression plays a potential role in modulating all of them. Clinical trials thus far conducted have shown reasonable response rates, effective IOP reduction and minimal side effects. The first study to look at the clinical applicability of this procedure was published in 1998. [34] This study included a total of 53 eyes with uncontrolled open-angle glaucoma (OAG) treated with 180° degrees of SLT followed for 26weeks. They found that 70% of the treated subjects had a reduction of IOP of greater than 3mmHg with an average drop of 4.6 mmHg (18.7%) after 26 weeks (about 6 months).

The magnitude of this reduction was uninfluenced by previous treatment with ALT. This demonstrated that effective, clinically significant IOP reduction could be accomplished without inflicting coagulative damage to the trabecular meshwork.

Interestingly, this study also found that there was a statistically significant, albeit less extensive, 9% reduction in the IOP of the fellow untreated eyes in these subjects. Subsequently there have been many other studies published addressing the clinical efficacy of SLT.

SLT vs ALT:

Clinical trials that have compared ALT to SLT have also shown that the two treatments have similar efficacy. A study comparing 154 patients treated with ALT to 41patients treated with SLT, all on maximal medical therapy, found that there was no significant difference in success of treatment at an average follow-up time of 34.4 months. [13] This equivalence was found two separate criteria for success: one was and IOP reduction of greater than 20% of baseline IOP (P=0.12) and the second was an IOP reduction of greater than 3mmHg (p=0.20). There was no significant difference in the percentage reductions in IOP with27.1% and 23.5% decreases in the SLT and ALT groups respectively (P=0.75). Briefly, over an average follow-up period of 5.6 months 21 these three studies reported an average IOP reduction of 4.8 mmHg (2.85-6.9) for SLT and 5.0 mmHg (2.63-6.6) for ALT. This corresponded to percentage reductions of 20.9% (13.4-29.2) for SLT and 22.0% (13.0-29.2) for ALT. None of the IOP reductions differed significantly in any of the three studies. This establishes that SLT is a viable treatment alternative to ALT. In fact, it may offer some advantages such as a decreased incidence of complications and a potential for repeatability that make it a more attractive treatment option when compared to ALT.

SLT after ALT:

Due to the fact that SLT does not cause coagulative damage to the TM, it offers the possibility of benefiting patients who have failed previous ALT. SLT can be applied without causing further scarring and potential outflow obstruction as is thought to be a possible problem with repeat ALT treatments. Damji et al [33] found that patients with previously failed ALT had a greater reduction in IOP with SLT (6.8 mmHg, 29.8%) than with repeat ALT (3.6 mmHg, 16.0%) (P= 0.01) after 6months. Another study that compared pressure reduction and response rates of SLT either as the primary laser treatment or after previous ALT found that there was no difference in IOP reduction in these two groups. [35] They reported 5.8 mmHg (23.5%) and 6.0 mmHg (24.2%) reductions in IOP at 26 weeks in the primary SLT and previous ALT groups, respectively. Both groups had a 3 mmHg IOP reduction response rate of 70%.

Repeat SLT treatments:

SLT has been shown to be as effective as ALT with less histological damage to the trabecular meshwork. Additionally, the efficacy of SLT has been demonstrated in patients with previous ALT. These two facts have led to the promise of SLT being a repeatable treatment. Repeat ALT is not favored due to the permanent changes it causes on the first application and the mixed findings on its long term efficacy. One study found that response rates on repeat SLT always exceeded 50%, in some cases by a considerable amount. [36]

SLT as initial therapy:

The Glaucoma Laser Trial Follow-up Study established ALT as a viable first line treatment option for POAG. Despite this it continues to be employed after medical therapy has failed to control IOP in order to avoid the need for incisional pressure lowering surgery. Given the equivalent efficacy of SLT and ALT, it follows that SLT may be viable option for primary treatment of POAG as well. In fact, there have been studies that support this hypothesis. One study examined the response of 45 eyes with either POAG or ocular hypertension with a mean baseline IOP of 25.5 mmHg to primary treatment with SLT. [37] At 18 months follow-up the mean drop in IOP was 7.7 mmHg (30%) with 43 of the 45 eyes responding with a greater than 20% reduction. Forty of the eyes had an IOP reduction of greater than 5 mmHg.

Advantages of SLT:

The advantages of SLT are:

- It is an effective modality for long term IOP reduction which is cost effective, is as effective as single drug for IOP reduction, effect is independent of most parameters except initial IOP and is enhanceable and repeatable.
- It is not dependent on patient compliance, does not involve the ongoing expenses of medications, can be used as initial therapy in preference to drugs and have minimal follow up requirements.
- It causes no systemic side effects associated with medical therapy and avoids risks associated with filtration surgery, such as haemorrhage, infection or cataract.
- It is cost-effective, time-effective and produces real benefits for the patient. SLT is as effective as ALT in IOP reduction without causing structural damage.

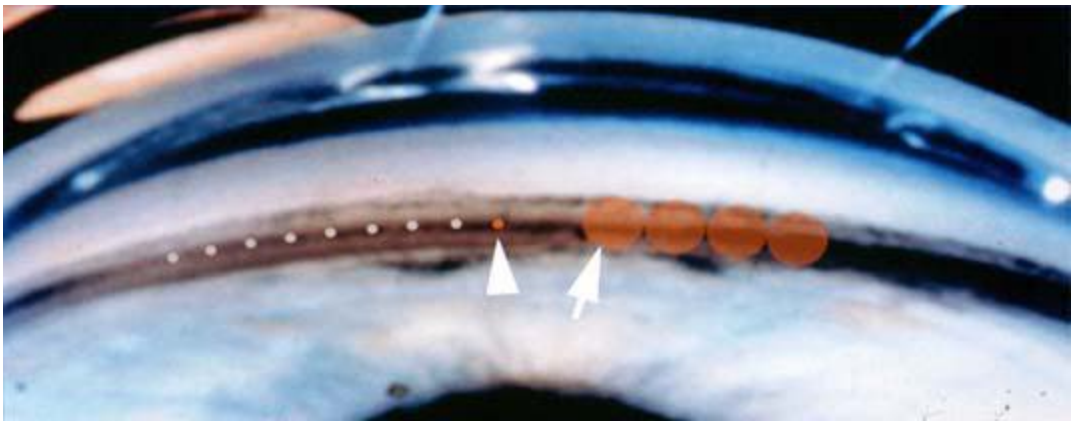


Figure 4: Argon laser trabeculoplasty (ALT) spot size (left arrow) versus selective laser trabeculoplasty (SLT) spot size (right arrow).

Adverse Effects

SLT administers 1/100th of the energy delivered by ALT. This most likely accounts for its relatively lower complication rate than ALT. The incidence of pain after SLT has been reported at 15% of patients. [35] The GLT group observed that 34% of patients receiving ALT had the formation of peripheral anterior synechiae (PAS). [20] These PAS did not have any effect on pressure control, the number of medications needed or the need for pressure-reducing surgery. In their original clinical study, Latina et al reported that there was no evidence of any PAS formation. [35] Other possible side effects are nonspecific conjunctivitis and corneal edema, but these are usually mild and transient occurrences.

Variables influencing the outcome of SLT: -

1. Higher baseline intraocular pressure: - Studies on SLT have thus far returned mixed results. One study found precisely the opposite with a greater success rate in patients with higher baseline IOP. [38]
2. Trabecular meshwork pigmentation: - An observational case study series found an increased degree of TM pigmentation has been found to result in a greater risk of complications, including post-op IOP spikes after SLT. [39] Despite this increased rate of adverse effects, another study found that TMs with greater degrees of pigment have significantly greater reductions in IOP at 7-month follow-up. [40] This study also found that patients with pseudo exfoliation have an increased response to SLT.

3. Number of medications: - The number of medications that a patient is on has also been shown to affect the outcome of SLT with the presence of fewer medications producing statistically significant better outcomes. [38] The type of medications an eye is treated with has also proved to be important in the outcome of SLT. Eyes treated with prostaglandins (PG) have been reported to have a diminished response to SLT. In one study there was a trend towards subjects on prostaglandins having a higher failure rate after SLT. [38] They found that 76% of responders (41/54) were taking prostaglandins, compared to 91% of nonresponses (49/54) (p=0.039). This decreased response rate may in part be since both prostaglandins and SLT are thought to act on the aqueous outflow tract. PGs have been shown to induce increased expression of MMP-1,2 and 3 both in vitro and in vivo.[41] In vivo, this induction corresponded with a decreased concentration of types I, III and IV collagen, which are some of the TM extracellular matrix substrates in which the MMPs degrade. As discussed above, SLT has been shown to act on this same pathway. The population of MMPs may be depleted by prostaglandin treatment precluding SLT from acting on this pathway. Another possibly redundant mechanism between these two treatments is that they both act by recruiting inflammatory cells. Prostaglandins may be precluding the ability of SLT to cause a cellular response. In an ongoing study at our center, we have found it to be more efficacious in virgin eyes. 48% of virgin eyes achieved target IOP reduction compared to 36% of eyes with a history of use of glaucoma medication (unpublished data).

Figure 5: clinical photograph demonstrating SLT procedure, observer viewing from side port

Degrees of TM treated with SLT:

SLT has a lot of evidence supporting its use as a treatment for open-angle glaucoma, possibly as a first-line treatment.

It remains a relatively new technique for which the optimal amount of power delivered and the extent of the trabecular meshwork that should be treated remains to be determined. One study by Chen et al found that 90 and 180 degrees of SLT had equivalent efficacy [40] . Both groups were composed of 32 eyes that were followed up for 7 months. The baseline IOPs were 25.44 and 26.06 for the 90 and 180-degree groups, respectively. The overall IOP reductions were 7.01 mmHg (27.6%) and 6.16 mmHg (23.6%), respectively (P=0.21). There was no significant difference between the IOPs at 1, 4 or 7 months. There was also a similar rate of treatment failure with 15 of the 32 patients in the 90-degree group requiring repeat SLT or trabeculectomy by the 7-month follow-up and 13 of the 32 in the 180-degree group.

Lanzetta et al [42] in 1999 reported that 3600 SLT could achieve clinically significant IOP reduction in eight eyes with high IOP that was uncontrolled with MTMT, even after previous ALT or trabeculectomy. The lower IOP that was observed after 24 hours had remained stable through 6 weeks. One eye had an immediate post-operative IOP rise of 10 mm Hg, which dissipated quickly.

In a study done by L Habib et al [43] in 2013, a retrospective review was performed for patients receiving primary SLT therapy, with the inclusion of subjects treated with 360° of SLT. Energy settings were collected upon treatment and IOP was collected at baseline up to 36 months. Pearson's correlation coefficient was used to determine whether there was a significant correlation between SLT energy and IOP reduction at all-time points. Kaplan-Meier analysis with log-rank test was performed to determine the differences in IOP reduction ≥20% from baseline among those treated with low (<85 mJ), medium (85-105 MJ), and high (>105 mJ) energy SLT. A total of 104 eyes (75 patients) were included. The mean total SLT energy was 93.73 mJ (standard deviation (SD) = 21.83 mJ, range: 34.4-122 MJ). A significant positive correlation ($P \leq 0.05$) between the amount of energy delivered and IOP reduction was found at all-time points. Log-rank test showed a significant difference in IOP reduction ≥20% from baseline between the three energy groups, with low-energy patients experiencing failure at an earlier time ($P = 0.05$). Within the range of total energy examined, there was a positive correlation between total energy used and the amount of pressure reduction achieved at up to 3 years of follow-up.

Six-year results of laser in glaucoma and ocular hypertension trial (LIGHT), found SLT as a viable option for OHT & mild to moderate eyes. (44)The national institute of Health and clinical excellence (NICE) guidelines recommend SLT as initial therapy for ocular hypertensives and moderate open angle glaucoma patients. [45] To summarize, we may conclude that SLT gives a drug holiday to the glaucoma patient.

Financial support and sponsorship

Nil

Conflict of interest

There are no conflicts of interest.

Correspondence to: Dr. Anuj Sharma, DNB, MNAMS
Consultant Deptt of Ophthalmology
Sri Sathya Sai Institute of Higher Medical Sciences
Prasanthi Gram Puttaparthi Sri Satya Sai District AP 515134
Mob. +919553158458
Email: anujsharma85@gmail.com

References

1. Thylefors B,Negrel AD.The Global Impact of Glaucoma. Bull World Health Organ. 1994;72(3):323-6.
2. Weinreb RN, Friedman DS, Fechtner RD, Cioffi GA, Coleman AL, Girkin CA, et al. Risk Assessment in the Management of Patients with Ocular Hypertension. Am J Ophthalmol. 2004 Sep;138(3):458-67
3. Stamer WD, Acott TS. Current Understanding of Conventional Outflow Dysfunction in Glaucoma. Curr Opin Ophthalmol. 2012 Mar;23(2):135-43.
4. American Academy of Ophthalmology. Preferred Practice Pattern: Primary Open-Angle Glaucoma [Online] 2010 [cited 2013 Aug 7].
5. Okeke CO, Quigley HA, Jampel HD, Ying GS, Plyler RJ, Jiang Y, et al. Adherence with Topical Glaucoma Medication Monitored Electronically the Travatan Dosing Aid Study. Ophthalmology. 2009 Feb;116(2):191-9.
6. Kanski JJ. Clinical Ophthalmology: A Systematic Approach. 6th ed. USA: Butterworth-Heinemann; 2007.
7. Rahman MQ, Beard SM, Discombe R, Sharma R, Montgomery DM. Direct Healthcare Costs of Glaucoma Treatment. Br J Ophthalmol. 2013 Jun;97(6):720-4.
8. Traverso CE, Walt JG, Kelly SP, Hommer AH, Bron AM, Denis P, et al. Direct Costs of Glaucoma and Severity of the Disease: A Multinational Long Term Study of Resource Utilisation in Europe. Br J Ophthalmol. 2005 Oct;89(10):1245-9.
9. Dirani M, Crowston JG, Taylor PS, Moore PT, Rogers S, Pezzullo ML, et al. Economic Impact of Primary Open-Angle Glaucoma in Australia. Clin Experiment Ophthalmol. 2011 Sep-Oct;39(7):623-32.

10. Saheb H and Ahmed I. Micro-invasive glaucoma surgery: current perspectives and future directions. Current Opinons Ophthalmol. 2012; 23(2) 96-104.
11. Knepper PA, Goossens W, Palmberg PF. Glycosaminoglycan stratification of the juxtacanalicular tissue in normal and primary open-angle glaucoma. Invest Ophthalmol Vis Sci.1996; 37:2414–2425.
12. Ueda J, Wentz-Hunter K, Yue BYJT. Distribution of myocilin and extracellular matrix components in the juxtacanalicular tissue of human eyes. Invest Ophthalmol Vis Sci.2002; 43:1068–1076.
13. Wise JD, Witter SL. Argon Laser Therapy for Open Angle. Glaucoma.Arch Ophthalmol 1979;97:319-322
14. Kramer TR and Noeker RJ.. Comparison of the Morphological Changes After Selective Laser Trabeculoplasty and Argon Laser Trabeculoplasty in Human Eye Bank Eyes. Ophthalmology.2001;108:773-779
15. Mchugh D, Marshall J, Ffytche TJ, Hamilton PA, Raven A. Ultrastructural changes of human trabecular meshwork after photocoagulation with a diode laser. Invest Ophthalmol Vis Sci. 1992Aug;33(9):2664-71.
16. Belgrado G, Brihaye-Van Geertruyden M, HerzeelR.. Comparison of argon and CW Nd:YAG laser trabeculoplasty. Clinical results. In: Laser technology in ophthalmology. Marshall J, editor. Berkeley, Amsterdam:KuglerandGhedini. 1998; 45-52.
17. Bylsma SS, Samples JR, Acott TS, Van Buskirk EM..Trabecular cell division after argon laser trabeculoplasty.Arch Ophthalmol. 1988;106(4):544-7.
18. Melamed S, Pei J, Epstein DL..Short-term effect of argon laser trabeculoplasty in monkeys. Arch Ophthalmol.1985; 103(10):1546-52.
19. Bradley JM, Anderssohn AM, Colvis CM, Parshley DE, Zhu XH, et al.Mediation of laser trabeculoplasty-induced matrix metalloproteinase expression by IL-1beta and TNFalpha. Invest Ophthalmol Vis Sci. 200041(2):422-30.
20. The Glaucoma Laser Trial Research Group. 1990. The Glaucoma Laser Trial (GLT).2. Results of argon laser trabeculoplasty versus topical medicines. Ophthalmology 97:1403-1413
21. The Glaucoma Laser Trial Research Group.. The Glaucoma Laser Trial (GLT) and glaucoma laser trial follow-up study: 7-year results. Am J Ophthalmol1995.120:718-731
22. Traverso CE, Greenidge KC, SpaethGL. Formation of peripheral anterior synechiae following argon laser trabeculoplasty. A prospective study to determine relationship to position of laser burns. Arch Ophthalmol 1984.;102(6):861-3.
23. Mermoud A, Pittet N, HerbortCP. Inflammation patterns after laser trabeculoplasty measured with the laser flare meter. Arch Ophthalmol.1992; 110(3):368-70.
24. Weinreb RN, Ruderman J, Juster R, Zweig K..Immediate intraocular pressure response to argon laser trabeculoplasty.Am J Ophthalmol.1983;95(3):279-86.
25. Weinreb RN, Ruderman J, Juster R, Wilensky JT. Influence of the number of laser burnSs administered on the early results of argon laser trabeculoplasty. Am J Ophthalmol.1983; 95(3):287-92.
26. Latina M, Park C. Selective targeting of trabecular meshwork cells: in vitro studies of pulse and continuous laser interactions. Exp Eye Res.1995; 60:359-72

27. Alvarado JA, Alvarado RG, Yeh RF, Franse-Carman L, Marcellino GR, et. al. A new insight into the cellular regulation of aqueous outflow: how trabecular meshwork endothelial cells drive a mechanism that regulates the permeability of Schlemm's canal endothelial cells. Br J Ophthalmol.2005; 89(11):1500-5.
28. Spaeth GL, Baez KA.. Argon laser trabeculoplasty controls one third of cases of progressive, uncontrolled, open angle glaucoma for 5 years. Arch Ophthalmol. 1992110(4):491-4.
29. Juzych MS, Chopra V, Banitt MR, Hughes BA, Kim C, et al..Comparison of long-term outcomes of selective laser trabeculoplasty versus argon laser trabeculoplasty in open-angle glaucoma.Ophthalmology 2004111(10),1853-1859
30. Alexander RA, Grierson I.. Morphological effects of argon laser trabeculoplasty upon the glaucomatous human meshwork. Eye.19893 (Pt 6):719-26.
31. Van der Zypen E, FankhauserF. Ultrastructural changes of the trabecular meshwork of the monkey (Macacaspeciosa) following irradiation with argon laser light. Graefes Arch Clin Exp Ophthalmol. 1984221(6):249-61.
32. Cvenkel B, Hvala A, Drnovsek-Olup B and Gale N. Acute ultrastructural changes of the trabecular meshwork after selective laser trabeculoplasty and low power argon laser trabeculoplasty. Lasers Surg Med .2003;33(3):204-8.
33. Damji KF, Shah KC, Rock WJ, Bains HS, Hodge WG.Selective laser trabeculoplasty vs. argon laser trabeculoplasty.Br J Ophthalmol.1999;83:718– 22
34. Huang SH, Adamis AP, Wiederschain DG, Shima DT, Shing Y, Moses MA. Matrixmetalloproteinases and their inhibitors in aqueous humor.Exp Eye Res.1996; 62(5):481-90
35. Latina MA, Sibayan SA, Shin DH, Noecker RJ, Marcellino G. 1998. Q-switched 532-nm Nd:YAG laser trabeculoplasty (selective laser trabeculoplasty): a multicenter, pilot, clinical study. Ophthalmology.1998; 105(11):2082-8.
36. De Leon JS, Dagianis JJ, Latina MA .Efficacy of Multiple Selective Laser Trabeculoplasty Treatments in Open Angle Glaucoma. ARVO 2005 (Abstract)
37. Melamed S, Ben Simon GJ, Levkovitch-Verbin H.. Selective laser trabeculoplasty as primary treatment for open-angle glaucoma: a prospective, nonrandomized pilot study. Arch Ophthalmol.2003;121:957–60.
38. Song J, Lee PP, Epstein DL,Stinnett SS, Herndon LW Jr, et al.High failure rate associated with 180 degrees selective laser trabeculoplasty.J Glaucoma.2005;14(5):400-8.
39. Harasymowycz PJ,Papamatheakis DG,Latina M, De Leon M,Lesk MR,et al. Selective laser trabeculoplasty (SLT) complicated by intraocular pressure elevation in eyes with heavily pigmented trabecular meshworks. Am J Ophthalmol.2005;139(6):1110-3.
40. Chen E, Golchin S, Blomdahl S. .A comparison between 90 degrees and 180 degrees selective laser trabeculoplasty. J Glaucoma.2004; 13(1):62-5.
41. Latina MA, Sibayan SA, Shin DH, et al: Q-switched 532nm Nd--YAG laser trabeculoplasty (selective trabeculoplasty),a multicenter, pilot, clinical study. Ophthalmology.1998; 105:2082—90.
42. Lanzetta P, Menchini U, Virgili G: Immediate intraocular pressure response to selective laser trabeculoplasty. Br J Ophthalmol .1999;83:29-32

43. Larissa Habib, James Lin, Tamara Berezina, Bart Holland, Robert D. Fechtner, Albert S. Khouri ,Oman J Ophthalmol. 2013 May-Aug; 6(2): 92–95.
44. Gazzard G, Konstantakopoulou E, Garway-Heath D, Adeleke M, Vickerstaff V, Ambler G, Hunter R, Bunce C, Nathwani N, Barton K; LiGHT Trial Study Group. Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial: Six-Year Results of Primary Selective Laser Trabeculoplasty versus Eye Drops for the Treatment of Glaucoma and Ocular Hypertension. Ophthalmology. 2023 Feb;130(2):139-151.
45. https://www.nice.org.uk/news/article/selective-laser-therapy-recommended-to-treat-glaucoma-and-ocularhypertension.

Corneal perforations: The Art of using Corneal Glue and our cumulative Experience

Dr. Ashok Sharma[1*], MS, **Dr. Rajan Sharma**[2], MS

*[1]Director & Senior Consultant, Cornea Centre, SCO 2463-2464, Sector 22 C, Chandigarh , India

[2]Research Associate, Cornea Centre, SCO 2463-2464Sector 22 C, Chandigarh, India

Corneal perforation constitutes a major cause of blindness in the developing countries and are either traumatic or nontraumatic in etiology, nontraumatic perforation being infectious or non-infectious. [1] Development of corneal perforation is an ocular emergency, not only impairs vision but also threaten the integrity of the eye. The corneal perforation is confirmed by performing Siedle's test (Fig 1).The occurrence of corneal perforation changes the line of management as it is an emergency and medical treatment alone is not sufficient, requiring additional treatment. [2] The defined treatment for corneal perforation before introduction of glue used to be tectonic penetrating keratoplasty. Tissue adhesives or Cornea Glue was then introduced and are of non biologic type (cyanoacrylate) and biologic type (fibrin glue). [3]

Our group for the first time in India introduced cyanoacrylate tissue adhesive (CTA) in corneal perforation and reported its use in corneal perforation in 1992. [4] Since then CTA became the gold standard treatment for corneal perforations sized lens than 3.0 mm. We were the first to prepare fibrin glue from human blood and use it clinical in India. [5] We compared the efficacy and complications of CTA with fibrin glue and found that although CTA provides better tectonic strength, the fibrin glue provides faster healing and causes lesser corneal vascularization. We published our results in "ophthalmology" a prestigious international ophthalmic journal ranked among top there journals. [5]

CTA is helpful in varied indications. We used CTA in healing limbal ulceration as an adjunct to tenonplasty. [6] We have also reported successful closure of scleral fistula using CTA in retinochoroidal coloboma successfully. [7] Our group had reported successful use of Fibrin glue for conjunctival closure in strabismus surgery. [8]Tissue adhesive can also be used in infective corneal perforation, provided bacterial and fungal corneal infection is responding to the treatment otherwise in a cases not responding to infection (bacterial or fungal) it can be temporarily used till tissue for tectonic keratoplasty becomes available (Fig 2).Post viral (both Herpes simplex or Herpes Zoster keratitis), glue can be successfully used.

In patients with active infection, we tend to avoid bandage contact lens (BCL). In patients whom we do not want to use BCL, glue can be placed over a small sterile piece of drape. Our technique that uses a patch of sterile drape to apply CTA provides a smooth surface and eliminates the need for BCL application. [9] The key to success is to de-epithelise the cornea surrounding the perforation, dry the site and then apply minimal quantity of CTA by making a very small droplet.

CTA application in larger corneal perforations (3.5 mm to 4.5 mm) is a real challenge. This may occur in patients with underlying collagen vascular disease or Mooren's ulcer. There is always a risk of inadvertent entry of glue into the anterior chamber and cause severe intra-ocular inflammation. We used a barrier tissue in the perforation and then applied the CTA. We first used corneal tissue in the perforation, but we faced problem of grafted tissue swelling and subsequent lifting of the glue. Then we used partial thickness scleral patch and

customized the size and the shape of the corneal perforation. We fitted this tissue into the perforation and 10 'o'nylon sutures were placed when needed. Then we applied the glue over the edges and the surface. This technique was extremely helpful in the treatment of Mooren's ulcer cases (Fig 3).This procedure not only healed the perforation, also avoided major surgery and improved visual acuity as it caused least corneal astigmatism. [10] Immunosuppressive treatment for the control of underlying autoimmune diseases should be continued.

For those patients having underlying collagen vascular disease (Rheumatoid arthritis) and corneal perforation, but good corneal thickness around the corneal perforation, we made lamellar intra-stromal pocket at more than 50 % depth. Then placed a partial thickness scleral patch inside the lamellar pocket. After the placement of the patch graft, we applied a minimal quantity of glue over the margin of the central perforation. This procedure was extremely useful for the patients who were not on immunosuppression. These patients were in addition given immunosuppressive therapy. [11]

CTA application with retro corneal scleral patch support helped us to treat a patient with large corneal perforation, with surrounding corneal, limbal, scleral melt following an uneventful pterygium surgery. None of the other techniques could be applied in this patient. This innovative technique was published recently by us andgives us new and effective option for corneal perforation with corneo-scleral melt.[12]Tissue adhesives are also helpful in arresting stromal tissue melt (scleral, corneal, limbal). We have treated a patient with bilateral severe chemical eye injury with this technique. One eye was lost due to endophthalmitis.
In the left eye, continued corneal, limbal, scleral ulceration was treated with glue or RGP application of glue or RGP application of glue on ulcerative limbal and scleral area and tenoplasty. The eye could be saved and with repeated superficial keratectomy, the patient achieved 6/36 visual acuity. We published this case in "Cornea" journal. [6]

We feel that despite advancements, CTA remains the "Gold Standard" for the treatment of corneal perforation. We have also published our cumulative experience in recently in a detailed review. [13] The newer biological options including fibrin glue, mesenchymal cells and platelet rich plasma are effective options in stromal wound healing and are less toxic. Corneal perforation and glue is an interesting field and demands further research on newer options for thebetterment of the patients.

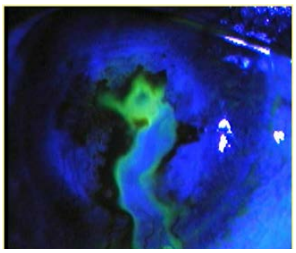


Figure 1: Positive Siedel's test

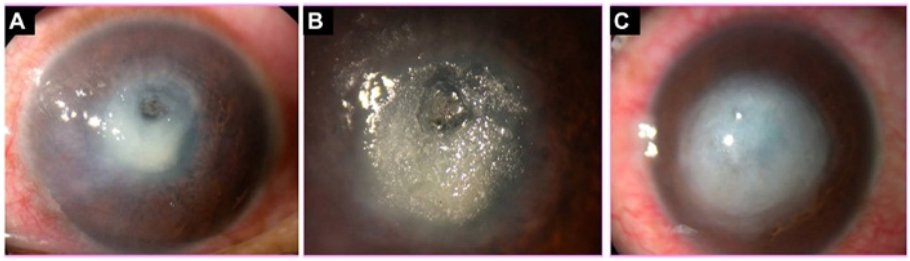


Figure 2: Shows cyanoacrylate tissue adhesive in post fungal keratitis perforation. (A) Corneal perforation before glue application. (B) After cyanoacrylate tissue adhesive application at 5 days. (C) Healed corneal perforation with resultant corneal leucoma at 14 weeks.

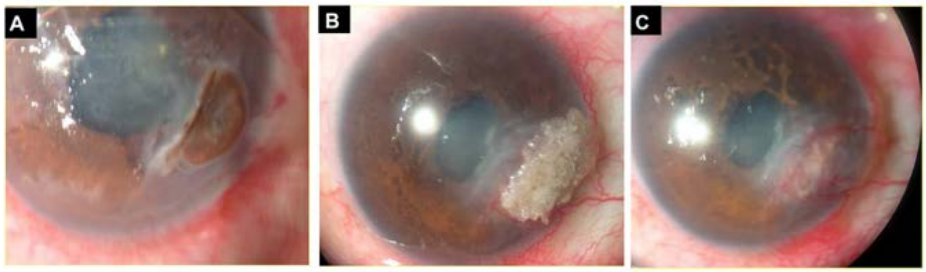


Figure 3: Scleral patch augmented CTA application in moderate corneal perforation using: (A) Perforation due to Mooren's Ulcer. (B) Customised partial thickness scleral patch + glue application at 1 week. (C) At 10 weeks, glue removed, and perforation healed.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity can not be guaranteed.

Financial support and sponsorship

Nil

Conflict of interest

There are no conflicts of interest.

Correspondence to: Dr. Ashok Sharma, Director & Senior Consultant
Cornea Centre, SCO 2463-2464, Sector 22 C, Chandigarh, India
Mobile +91-9814528495
Email: ashok.cornea@gmail.com

References

1. Jhanji V, Young AL, Mehta JS, Sharma N, Agarwal T, Vajpayee RB. Management of corneal perforation. SurvOphthalmol. 2011;56:522–38.
2. Deshmukh R, Stevenson LJ, Vajpayee R. Management of corneal perforations: An update. Indian J Ophthalmol. 2020 Jan;68(1):7-14.

3. Grinstaff MW. Designing hydrogel adhesives for corneal wound repair. Biomaterials. 2007;28:5205–14.
4. Saini JS, Sharma A, Grewal SP. Chronic corneal perforations. Ophthalmic Surg. 1992;23(6):399–402.
5. Sharma A, Kaur R, Kumar S, et al. Fibrin glue versus N-butyl-2-cyanoacrylate in corneal perforations. Ophthalmology. 2003;110:291–298.
6. Sharma A, Pandey S, Sharma R, Mohan K, Gupta A. Cyanoacrylate tissue adhesive augmented tenoplasty: a new surgical procedure for bilateral severe chemical eye burns. Cornea. 1999;18(3):366–369.
7. Gupta A, Narang S, Gupta V, Sharma A, Pandav SS, Singh P. Successful closure of spontaneous scleral fistula in retinochoroidal coloboma. Arch Ophthalmol. 2001;**119**(8):1220–1221.
8. Mohan K, Malhi RK, Sharma A, Kumar S. Fibrin glue for conjunctival closure in strabismus surgery. J PediatrOphthalmol Strabismus. 2003;40(3):158–160.
9. Sharma A, Mohan K, Nirankari VS. Management of nontraumatic corneal perforation with tectonic drape patch and cyanoacrylate glue. Cornea. 2012;31(4):465–6;author reply 466. PMID: 21857507.
10. Sharma A, Mohan K, Sharma R, Nirankari VS. Scleral patch graft augmented cyanoacrylate tissue adhesive for treatment of moderate-sized non-infectious corneal perforations (3.5–4.5 mm). Cornea. 2013;32:1326–1330.
11. Sharma A, Sharma R, Nirankari VS. Intracorneal scleral patch supported cyanoacrylate application for corneal perforations secondary to rheumatoid arthritis. Indian J Ophthalmol. 2021;69(1):69–73.
12. Sharma A, Sharma R, Nirankari VS. Retrocorneal Scleral Patch Supported Glue: A Technique for Management of Corneal Perforation and Corneoscleral Melt following Pterygium Surgery . J Ophthalmic Vis Res 2023;18:123–129.
13. Sharma A, Sharma N, Basu S, Sharma R, Aggarwal S, Gupta PC, Ram J, Nirankari VS. Tissue Adhesives for the Management of Corneal Perforations and Challenging Corneal Conditions. Clin Ophthalmol. 2023;17:209-223

Choroidal Tuberculoma Masquerading as Central Serous Retinopathy

Dr. Kanwaljeet Harjot Madan[1], MS,**Dr. S Mittal** S.[1], MS,**Dr. J.S. Thind** [1] MS

[1]Thind Eye Hospital, Jalandhar City. Punjab

Introduction

The ocular involvement of tuberculosis(TB) is not uncommon . Ocular TB may not be associated with the clinical evidence of pulmonary TB.The ophthalmic involvement could be due to direct infection or indirect immune-mediated hypersensitivity. The rich vascularity of uveal tissues permits easy hematogenous spread of infections from a caseous primary focus elsewhere in the body by eroding blood vessels or lymphatics. Choroidal tuberculomas are large single lesions and can arise in the early stages of progression of TB and indicate hematogenous dissemination before the development of symptomatic ocular TB[1] They commonly occur in young patients with a prolonged course of disease. We hereby report a case of choroidal tuberculoma which masqueraded as central serous retinopathy (CSR).

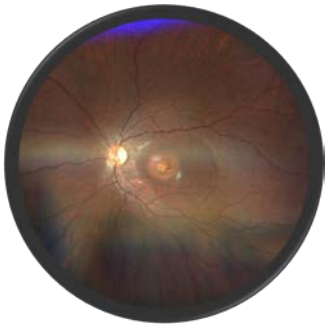
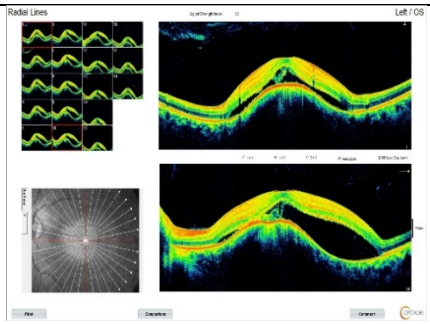
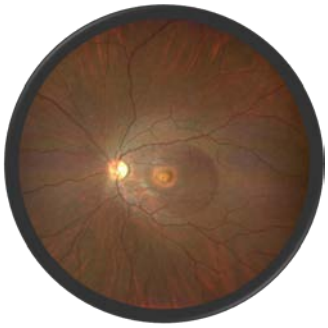
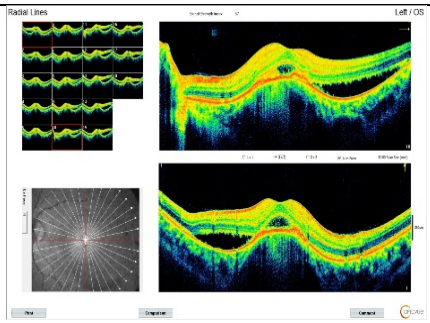
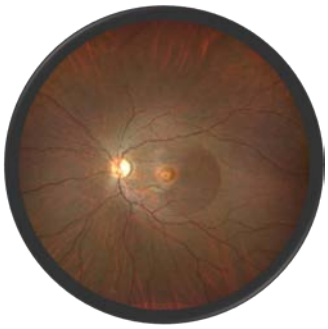
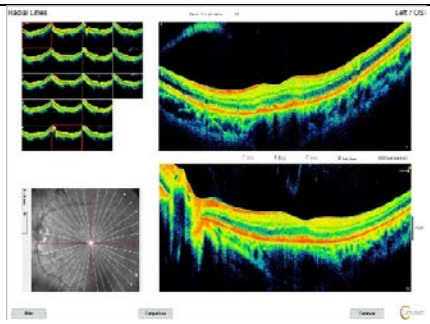
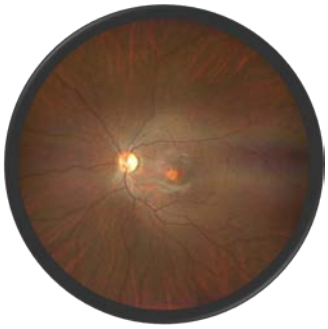
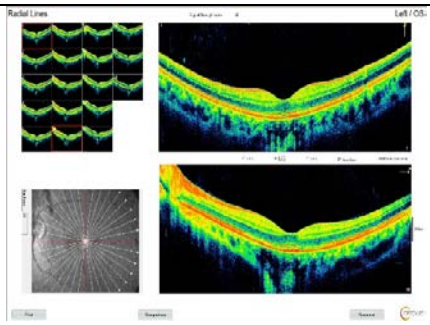
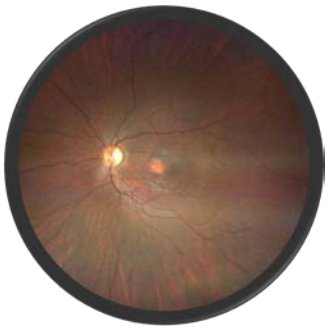
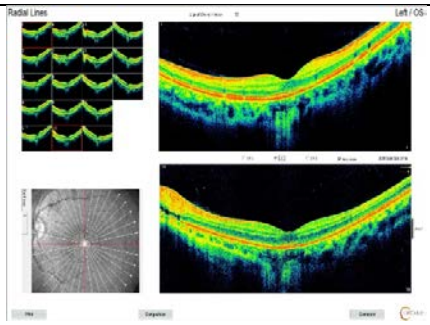
Key words: Choroidal tuberculoma, Optical coherence tomography, bevacizumab.

Method

A 20 year female patient presented with diminution of vision in left eye for 3 weeks.She was treated as a case of CSR elsewhere but her vision deteriorated.On examination,her best corrected visual acuity in right eye was 6/6 and in left eye was 6/60.Intraocular pressure was normal in both eyes.Her anterior segment examination was normal. Right eye fundus exam was normal.Left eye fundus exam revealed an elevated yellowish solitary subretinal mass associated with serous retinal detachment involving macula. The patient underwent further investigations.Indocyanine green angiography (ICG),Fundus fluorescein angiography (FFA) and Optical coherence tomography (OCT) were done.Systemic investigations were carried out to rule out secondaries.

Results

On OCT, there was a distinctive contact zone between the neursensory retina and the retinal pigment epithelium-choriocapillary suggestive of choroidal mass. FFA showed hyperfluorescnce in early phases with pooling of dye in late phases.ICG showed hypocyanescence of the lesion in early
phase which persisted in late phases. MRI Scan brain and ultrasonography abdomen were normal.The patient had positive QuantiFERON TB gold and tuberculin test (20x20 mm).Rest all blood investigations were normal.She was referred to chest physician to start anti tubercular therapy (ATT).She was started on ATT with oral steroids (1 mg/kg body weight).The patient was given 3 monthly injections of Bevacizumab.Her visual acuity improved to 6/6 with shrinkage of the tuberculoma.

Fundus Photo	OCT	BCVA
		**At the time of Presentation;BCVA 6/60**
		**1 week post 1st dose of Bevacizumab; BCVA 6/36**
		**1 week post 2nd dose of Bevacizumab; BCVA 6/18**
		**1 week post 3rddose of Bevacizumab; BCVA 6/9**
		**1 month post 3rd dose of Bevacizumab;BCVA 6/6**

Discussion

TB is an infection caused by Mycobacterium tuberculosis, commonly described as a systemic disease that involves not only the lungs but also many other organs, including the eye. [2] Although ocular TB is a rare event (1% of all cases of TB),it can occur with or without evidence of systemic TB and can involve any part of the eye. [3] The most common clinical presentation appears to be posterior uveitis, particularly choroidal TB. Multiple choroidal tubercles are reported to be the most common intraocular manifestation of tubercular posterior uveitis. Less commonly, intraocular TB may present as a large tuberculoma: a solitary yellowish or grayish white large lesion, generally located in the posterior pole.[4] Rapid multiplication of the bacilli within a tuberculoma can cause tissue destruction through liquefactive necrosis, thus forming a surrounding exudative retinal detachment.

Imaging techniques, such as fluorescein angiography and B-scan, can assist in excluding other diagnoses, especially intraocular tumors (e.g., melanoma) or infective abscesses. [3] OCT scans through areas of suspected granuloma can be very helpful in differentiating choroidal granulomas from other noninflammatory conditions. Salman et al were the first to describe a distinctive feature of attachment between the retinal pigment epithelial–choriocapillaris layer and the neurosensory retina over the granuloma (“contact” sign). [5] This was associated with surrounding subretinal fluid and inflammatory infiltrate in the deeper retinal layers.
Since there are no typical FFA findings for choroidal tuberculoma, and varying appearances may be noted, FFA can contribute to exclusion of other causes. Choroidal tuberculomas can exist in the presence or absence of active disease, and even underlying latent tuberculosis has to be treated with ATT.[6]

Conclusion

Choroidal tuberculoma can develop without evidence of systemic TB and is a rare ocular form of TB that raises both a diagnostic and a therapeutic challange,especially when occuring without other manifestations of the disease.It occurs probably due to high blood supply of the choroid.
Since delay in diagnosis and treatment results in poor prognosis and severe sequelae, effective therapy should be initiated as early as possible. Antitubercular therapy combined with systemic corticosteroids provide favourable results. Intravitreal injection of anti-vascular endothelial growth factor may be considered for highly vascularized choroidal tuberculoma.[7]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity can not be guaranteed.

Financial support and sponsorship

Nil

Conflict of interest

There are no conflicts of interest.

Correspondence to: Dr. Kanwaljeet Harjot Madan.

Thind Eye Hospital, Jalandhar City. Punjab

Mob.: +919814456777

Email : dr.khmadan@gmail.com

References

1. Sarvananthan N, Wiselka M, Bibby K. Intraocular tuberculosis without detectable systemic infection. Arch Ophthalmol.1998;116(10):1386–1388.
2. Yeh S, Sen HN, Colyer M, Zapor M, Wroblewski K. Update on ocular tuberculosis. Curr Opin Ophthalmol.2012;23(6):551–556.
3. Bodaghi B, LeHoang P. Ocular tuberculosis. Curr Opin Ophthalmol. 2000;11(6):443–448.
4. Mansour AM, Haymond R. Choroidal tuberculomas without evidence of extraocular tuberculosis. Graefes Arch Clin Exp Ophthalmol.1990;228(4):382–383.
5. Salman A, Parmar P, Rajamohan M, Vanila CG, Thomas PA, Jesudasan CAN. Optical coherence tomography in choroidal tuberculosis. Am J Ophthalmol. 2006;142(1):170–172.
6. Mansour AM, Haymond R. Choroidal tuberculomas without evidence of extraocular tuberculosis. Graefes Arch Clin Exp Ophthalmol. 1990;228(4):382–383. doi: 10.1007/BF00920066.
7. Babu K, Murthy P, Murthy K. Intravitreal bevacizumab as an adjunct in a patient with presumed vascularised choroidal tubercular granuloma Eye. 2010;24:397–9

Bilateral Ocular Ischemic Syndrome: Case report

Dr. Gitanjli Sood[1], MS, **Dr. Sandeep Mahajan**[1], MS
[1]SM Eye Institute Kangra Himachal Pradesh – 176001

Ocular ischemic syndrome (OIS) is an ocular manifestation of reduced perfusion of ophthalmic artery subsequent to stenosis of carotid artery. Ophthalmic artery is the first branch of intradural portion of internal carotid artery(ICA) thus it is directly affected by the perfusion abnormalities of the carotid vessel.[1]The first case was reported in 1963 by Hedges in a case of complete occlusion of ICA where the patient had retinal haemorrhages along with dilated retinal veins.[2] Patient usually present with gradual vision loss associated with dull aching pain; often called as ocular angina. [3] The intraocular pressure may be low despite neovascularisation due to ciliary body hypoperfusion. Thus, these constellations of unique signs and symptoms lead us to the diagnosis of this entity of OIS.

We report a case of bilateral OIS due to bilateral carotid artery stenosis that had typical clinical picture and patient was managed by doing timely pan retinal photocoagulation and started on systemic anticoagulants.

Keyword: Neovascularisation, Ocular ischemia

Case Report

A 60-year-old male presented with bilateral blurring of vision and dull pain since 2 months. His best corrected visual acuity was 6/18 in both eyes and intraocular pressure was 11 mm Hg in right eye (RE) and 12mm Hg in left eye (LE). On examination he had bilateral neovascularisation of iris (NVI) in RE it was all along the pupillary border and in LE it was at 12 o'clock (White arrow in Figure 1 A& B). RE was pseudophakic and LE had immature senile cataract. There was no neovascularisation of angle on gonioscopy. Dilated fundus examination revealed bilateral dilated veins with arterial narrowing and multiple dot and blot haemorrhages more in mid periphery. There was no obvious neovascularisation in retina (Figure 2 A& B). He was not hypertensive or diabetic and not on any systemic medication. Patient gave prior history of transient ischemic attacks. He was investigated and Carotid Doppler scan revealed atherosclerotic changes in bilateral carotid artery with 70-80% stenosis of bilateral internal carotid artery. Other blood investigations were within normal limits.

Thus a diagnosis of bilateral ocular ischemic syndrome (OIS) was made and patient underwent bilateral pan retinal photocoagulation. On two months follow up his NVI regressed (Figure. 1 C& D) and visual acuity was maintained. Patient was advised anticoagulants by the cardiologist and remains under follow up.

Discussion

OIS is a disorder of ocular function that occurs after the stenosis of the carotid artery.[1] The acute manifestations of the disease are transient ischemic attacks and retinal artery occlusion. In contrast, the chronic manifestations are retinopathy and neovascularization and its sequel. Usually a unilateral disease when there is

stenosis of common carotid or internal carotid artery of more than 70%. In around 10% of the cases, the obstruction is bilateral, thus bilateral disease is not very common.[2]

The anterior segment features are rubeosis iridis(67%) leading to neovascular glaucoma, low-grade inflammation in the anterior chamber, anterior and posterior synechiae, atrophy of sphincter pupillae (semi-dilated pupil) with sluggish reaction to light, spontaneous hyphema, asymmetric cataract, conjunctival and episcleral injection, and corneal edema with descemet`s folds (sometimes with bullous keratopathy), rarely scleral melting has been reported.[3]

Posterior segment manifestations are narrowed retinal arteries (90%), dilated and not tortuous retinal veins (90%), retinal haemorrhages (80%), microaneurysms (80%), retinal telangiectasia, cherry-red spot (12%), cholesterol emboli, glaucoma (neovascular glaucoma, normal-tension glaucoma), neovascularization (optic disc 35%, retina 8%), cotton-wool spots (6%), vitreous haemorrhage (4%), spontaneous retinal arteries pulsations (4%), anterior and posterior ischemic optic neuropathy (2%), choroidal neovascular membrane, areas of chorioretinal atrophy.[4]

Diagnosis is based on typical clinical picture and supported by fluorescein angiography which has a delay in arm to retina time, delayed choroidal filling and prolonged arterio-venous transit and late staining of vessels. ERG shows a reduction in amplitude of both a and b wave. Carotid Doppler Imaging and MR angiography will document the amount of occlusion of carotid vessels.[3]
The ocular manifestations require panretinal photocoagulation with or without anti VEGF injections and management of glaucoma. The systemic disease can be managed by aspirin if stenosis is less than 70%.

Carotid artery endarterectomy and stenting is required in cases of severe stenosis.[5]
A patient with diagnosed OIS should always remain under the care of ophthalmologists and physicians throughout life. So as to identify and treat the potential life and sight-threatening complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity can not be guaranteed.

Discussion

OIS is a disorder of ocular function that occurs subsequent to the stenosis of the carotid artery.[1] The acute manifestations of the disease are transient ischemic attacks and retinal artery occlusion. In contrast, the chronic manifestations are retinopathy and neovascularization and its sequel. Usually a unilateral disease when there is stenosis of common carotid or internal carotid artery of more than 70%. In around 10% of the cases, the obstruction is bilateral, thus bilateral disease is not very common.[2]

The anterior segment features are rubeosis iridis(67%) leading to neovascular glaucoma, low-grade inflammation in the anterior chamber, anterior and posterior synechiae, atrophy of sphincter pupillae (semi-dilated pupil) with sluggish reaction to light, spontaneous hyphema, asymmetric cataract, conjunctival and episcleral injection, and corneal edema with descemet`s folds (sometimes with bullous keratopathy), rarely scleral melting has been reported.[3]

Posterior segment manifestations are narrowed retinal arteries (90%), dilated and not tortuous retinal veins (90%), retinal haemorrhages (80%), microaneurysms (80%), retinal telangiectasia, cherry-red spot (12%), cholesterol emboli, glaucoma (neovascular glaucoma, normal-tension glaucoma), neovascularization (optic disc 35%, retina 8%), cotton-wool spots (6%), vitreous haemorrhage (4%), spontaneous retinal arteries pulsations (4%), anterior and posterior ischemic optic neuropathy (2%), choroidal neovascular membrane, areas of chorioretinal atrophy.[4]

Diagnosis is based on typical clinical picture and supported by fluorescein angiography which has a delay in arm to retina time, delayed choroidal filling and prolonged arterio-venous transit and late staining of vessels. ERG shows a reduction in amplitude of both a and b wave. Carotid Doppler Imaging and MR angiography will document the amount of occlusion of carotid vessels.[3]

The ocular manifestations require panretinal photocoagulation with or without anti VEGF injections and management of glaucoma. The systemic disease can be managed by aspirin if stenosis is less than 70%. Carotid artery endarterectomy and stenting is required in cases of severe stenosis.[5]

A patient with diagnosed OIS should always remain under the care of ophthalmologists and physicians throughout life. So as to identify and treat the potential life and sight-threatening complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity can not be guaranteed.

Financial support and sponsorship

Nil

Conflict of interest

There are no conflicts of interest.

Correspondence to: Dr. Gitanjli Sood, MS ; Consultant Vitreo Retina

S M Eye Institute Zamanabad Road Kangra HP-176001

Mobile: +919805873673, E-mail – gitz.sood@gmail.com

References

1. Mendrinos E, Machinis TG, Pournaras CJ. Ocular ischemic syndrome. Surv Ophthalmol. 2010 Jan-Feb;55(1):2-34.
2. Kobayashi S, Hollenhorst RW, Sundt TM Jr. Retinal arterial pressure before and after surgery for carotid artery stenosis. Stroke. 1971 Nov-Dec;2(6):569-75.
3. Sood G, Siddik AB. Ocular Ischemic Syndrome. 2022 Oct 31. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
4. Terelak-Borys B, Skonieczna K, Grabska-Liberek I. Ocular ischemic syndrome - a systematic review. Med Sci Monit. 2012 Aug;18(8):RA138-144.
5. Neale ML, Chambers JL, Kelly AT, Connard S, Lawton MA, Roche J, Appleberg M. Reappraisal of duplex criteria to assess significant carotid stenosis with special reference to reports from the North American Symptomatic Carotid Endarterectomy Trial and the European Carotid Surgery Trial. J Vasc Surg. 1994 Oct;20(4):642-9.

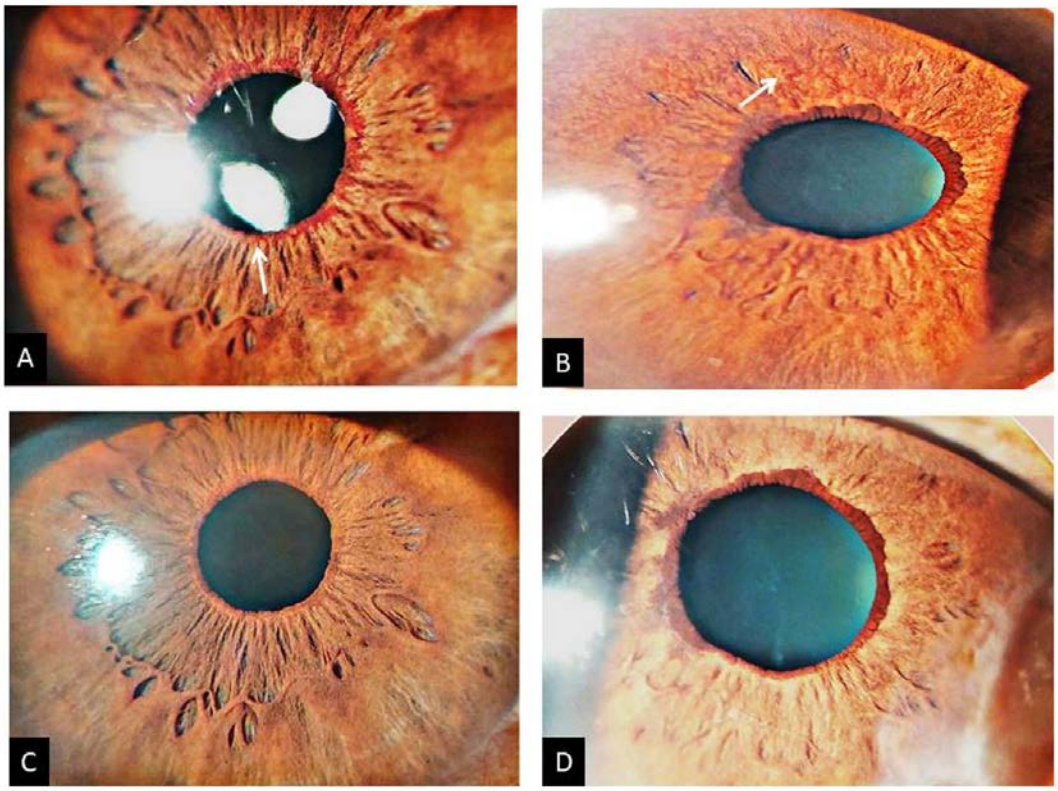


Figure 1. Anterior segment colour photograph A) Right eye is pseudophakic with 360 degree NVI. B) Left eye has immature senile cataract with NVI superiorly as shown by white arrow. Post pan retinal photocoagulation there is complete regression of neovascularisation (C&D).

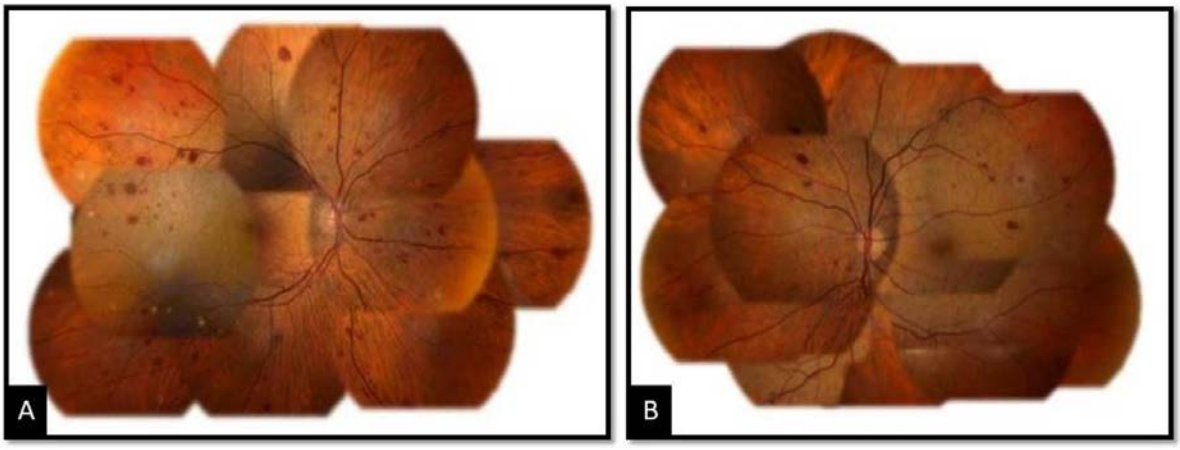


Figure 2. Colour fundus photograph of right eye (A) and left eye (B) showing clear media with dilated veins and arterial narrowing. Multiple dot and blot haemorrhages in mid periphery till equator.

Berlin's Edema Following Trauma with Flow Adjustment Knob of an Oxygen Cylinder in a Nursing Student: A Case Report

Dr. Neha Chauhan MS,FICO,FAICO(Glaucoma)[1*], **Dr. Deepak Kumar Sharma**,MS[2],**Dr. Gian Chand Rajput**,MS[3], **Dr. Anubhav Chauhan**,MS[4], **Dr. Pankaj Thakur**,MS[4].
[1*] Medical Officer (Specialist), Deptt. of Ophthalmology, SLBSGMC Mandi at Ner Chowk HP
[2] Associate Professor, Deptt. of Ophthalmology, SLBSGMC Mandi at Ner Chowk HP
[3] Professor, Deptt. of Ophthalmology, SLBSGMC Mandi at Ner Chowk HP
[4] Assistant Professor, Deptt. of Ophthalmology, SLBSGMC Mandi at Ner Chowk HP

Abstract

We report a case of a young nursing student who sustained ocular injury with the flow adjustment knob of an oxygen cylinder leading to a myriad of ocular complications including Berlin's edema. We also highlight the importance of Spectral domain OCT as a tool for diagnosis and follow up in such cases. The uniqueness of the case lies in the uncommon mode of injury and the progression of the condition into a full thickness macular hole well documented on OCT.

Keywords :Berlin's edema, commotio retinae, optical coherence tomography, oxygen cylinder, trauma.

Introduction

Commotio retinae is characterised by a transient, well defined greyish-white opacification of the retina occurring after blunt ocular trauma. The opacification may involve large areas of the peripheral retina or may be confined to the macula. When it involves the macula, it is referred to as Berlin's edema .[1]This whitening is indicative of cell damage,which occurs in the retinal pigment epithelium and outer segment layer of photoreceptors.[2] It usually has a good prognosis with resolution over a period of few weeks unless associated with other pathologies like choroidal rupture, haemorrhage or pigment epithelial damage.

Case Report

A 22 year old female nursing student presented to us in the emergency with history of trauma to the right eye with an oxygen cylinder flow adjustment knob (Fig1A;arrow)

The incident occurred while she was trying to regulate the oxygen flow by opening the knob; when the glass flowmeter burst and the knob flew and struck her right eye suddenly. On examination, there was periorbital swelling in the right eye (Fig.2). A 1cm partial thickness lid laceration was noted just below the right eyebrow. Her best corrected visual acuity was 6/60 in the right eye and 6/6 in the left eye on the snellen's chart. Pupillary reactions were sluggish in the right eye and brisk and reacted normally to light in the left eye. Slit lamp examination showed subconjunctival haemorrhage with 4+ cells in the anterior chamber in the right eye. The intraocular pressure (IOP) was 14 and 16 mm of Hg in the right and left eye respectively done with the Goldmann applanation tonometry and gonioscopy showed open angles in both eyes.

Posterior segment examination showed opacifcation of the central retina with a characteristic cherry red spot suggestive of commotio retinae (Fig 1C).There was pre retinal haemorrhage in the inferotemporal quadrant around 3 disc diameter in the linear dimension. OCT (Optical coherence tomography) done with the Topcon Spectral Domain OCT showed focal elevation of the retinal layers along with thickening and subretinal fluid (Fig1D). The patient was started on topical steroids, cycloplegics and oral steroids and the lid laceration was sutured (Fig 1B, arrow). On follow up after 1 week, her best corrected visual acuity was 6/36 in the right eye. Anterior chamber reaction was 2+ and IOP was 14 mm of Hg.

There was a dramatic decrease in the retinal opacification (Fig2E) however OCT still showed thickening of the retinal layers with focal elevation at the level of photoreceptor/outer segments at the level of fovea. At 2 weeks follow up, the opacification resolved completely however the vision was still the same. Her OCT showed a full thickness defect in the retinal layers suggestive of macular hole (Fig2F).

Discussion

Blunt trauma to the eye can cause a large number of ocular complications involving the anterior as well as the posterior segment. The mode of injury in our case is unique and to our knowledge has not been reported before.

The trauma was so extensive that it led to the involvement of the lid, uveal tissue as well as the posterior segment. Thus a detailed and complete ocular examination in these cases is mandatory. Commotio retinae commonly results from a counter coup mechanism[3] in such cases. It was originally postulated that commotio retinae was caused due to extracellular edema. [3]
In a study by Hui and associates[4]on a rabbit model, it was concluded that the severe retinal contusion was mainly due to disruption of the photoreceptor and RPE cells and partly due o breakdown of the blood-retinal barrier. It is now further proven from histopathological studies that disruption or fragmentation of the photoreceptor outer segment of the retina is the most common finding in patients with commotio retinae [5] which was also noted in our case. Thus we emphasise the role of Spectral domain OCT as an important tool in the diagnosis and follow up of eyes with Berlin's edema, as in our case the OCT was a very good tool in explaining the decrease in vision despite clinical improvement in signs and showed the progression of a partial disruption of the retinal layers into a full thickness retinal hole. The peculiar mode of injury also advocates the need for necessary precautions among the hospital staff while opening or dealing with oxygen cylinders.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity can not be guaranteed.

Financial support and sponsorship

Nil

Conflict of interest

There are no conflicts of interest.

Correspondence to: Dr. Neha Chauhan , MS, FGPGI, FICO, FAICO(Glaucoma))

Medical Officer (Specialist), Deptt of Ophthalmology

SLBS Govt. Medical College, Ner Chowk Distt. Mandi (H.P)

Email: drchauhan.chauhan95@gmail.com

Mobile:+919418185100

References

1. Berlin R. Zursogenannten commotio retinae. Klin Monatsbl Augenheilk. 1873; 1:42-78.
2. Recchia, Franco M.; Aaberg Jr., Thomas; Sternberg Jr., Paul (2006-01-01). Hinton, David R.; Schachat, Andrew P.; Wilkinson, C. P. (eds.). Chapter 140 - Trauma: Principles and Techniques of Treatment A2 - Ryan, Stephen J. Edinburgh: Mosby. pp. 2379–2401.
3. Wolter J R. Coup-countercoup mechanism of ocular injuries. Am J Ophthalmol.1963;56:785-796.
4. Hui YN, Wu YQ, Xiao QS et al. Repair of outer blood-retinal barrier after severe ocular trauma in rabbits. Graefes Arch Clin Exp Ophthalmol. 1993;231:365-369.
5. Pham, T.Q., Chua, B., Gorbatov, M., Mitchell,P.(2007). Optical coherence tomography findings of acute traumatic maculopathy following motor vehicle accident. Am J Ophthalmol, 143:348-50.

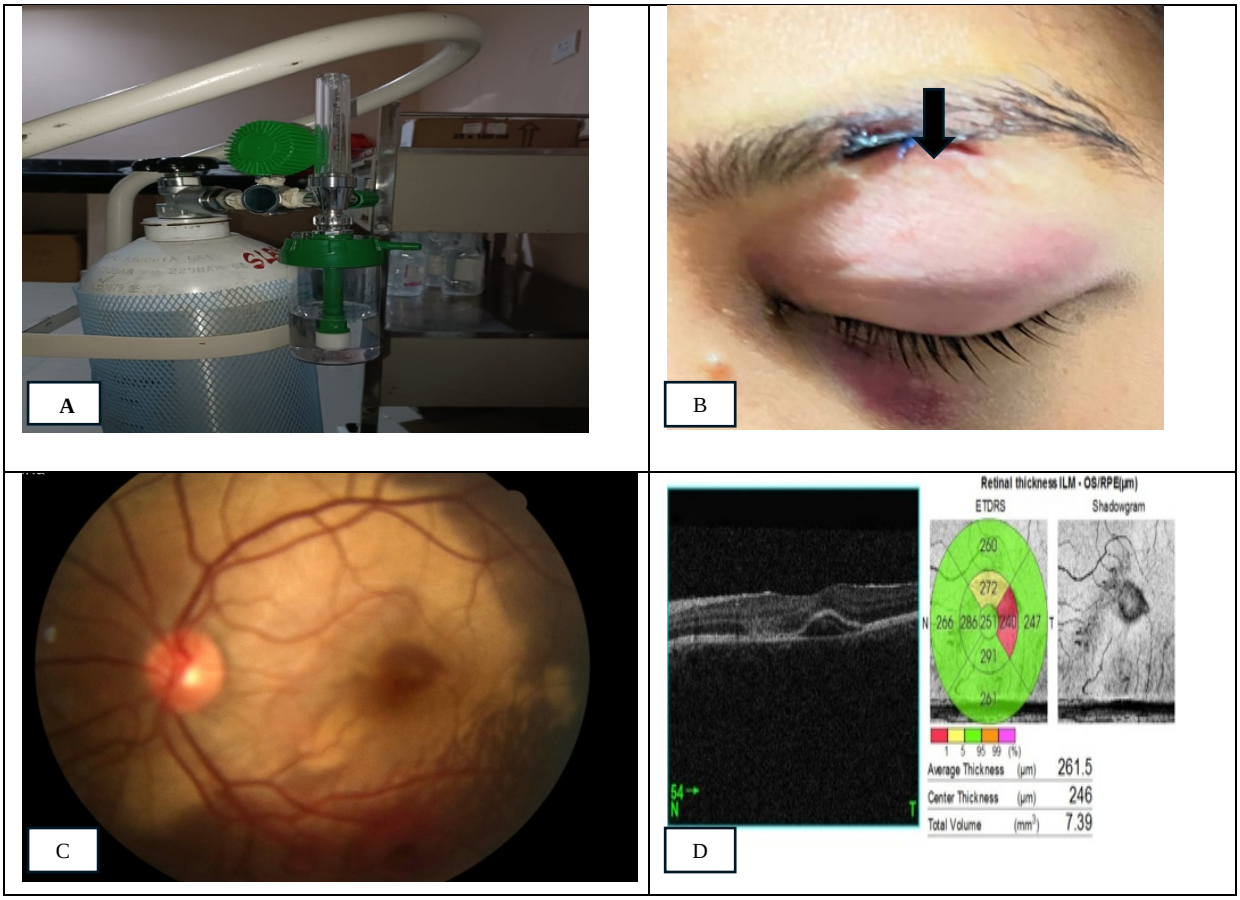


Figure.1: (A) Shows the oxygen cylinder with the arrow pointing toward the flow adjustment knob (B) shows the clinical image of the patient on the day of presentation showing periocular swelling with the arrow pointing towards the sutured laceration (C) shows the fundus image on the day of presentation showing retinal opacification with the characteristic cherry red spot (D) shows OCT image on presentation with disruption of the photoreceptor /EZ and subretinal fluid

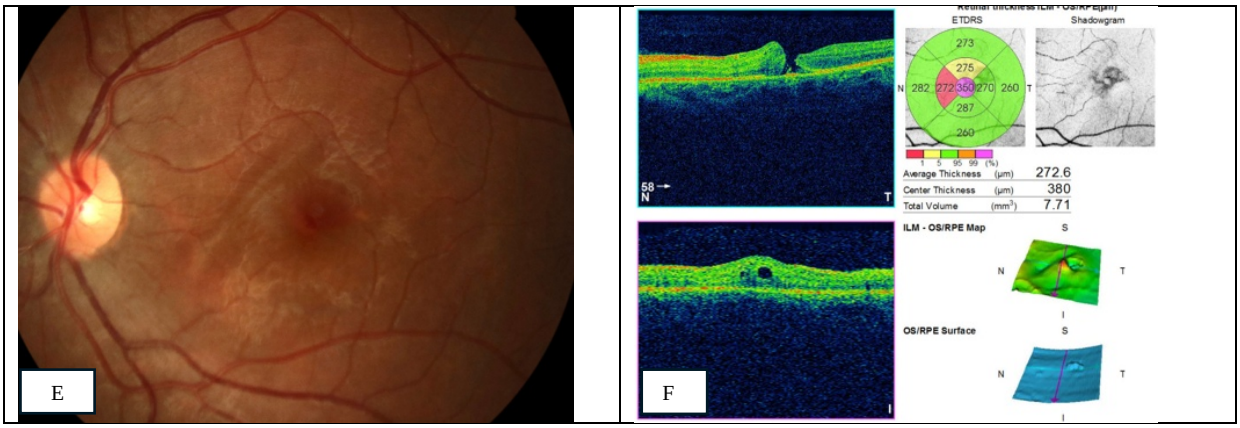


Figure 2 (E): Fundus image of the left eye after 2 weeks post trauma showing significant decrease in retinal opacification. (F):SD OCT of the left eye after 2 weeks showing a full thickness defect in the retinal layers suggestive of a macular hole.

Iatrogenic Rosette Cataract after Inadvertent Lenticular Needle Injury During Intra-Vitreal Anti –Vegf Injection: Managing Misfortunate Event into a Fortunate One

Dr. Praveen Panwar[1],MS, **Dr. Sheetal Sharma**[2],MS

[1] Associate Professor Deptt of Ophthalmology IGMC Shimla

[2] Senior ResidentDeptt of Ophthalmology IGMC Shimla

Abstract

Lens injury during anti – VEGF injections is a rare phenomenon and occur to the tune of 0.06%. Anti -VEGF have revolutionized the treatment in various ocular conditions including diabetic patients with macular edema. We are reporting a case of inadvertent lens injury during third time intravitreal injection of anti- VEGF lucentis for treating diabetic macular edema. Posterior capsule was breached and needle tract was seen in the lens with subsequent formation of rosette cataract, which was managed with phacoemulsification with special anticipation of complications. Slow motion phacoemulsification was carried out with low bottle height, no hydrodissection, only hydrodelineation , minimal nuclear rotation inside capsular bag and low vacuum settings thus, minimizing chamber fluctuation during the operation hence preventing enlargement of pre existing posterior capsular tear.

Key words: Anti-VEGF, non proliferative diabetic retinopathy (NPDR), phacoemulsification.

Introduction

Diabetic macular edema is the main cause of vision loss in a diabetic patient. Anti –VEGF have become the main modality of treatment for various intravitreal diseases including diabetic macular edema. Despite of proper surgical techniques of intravitreal injection various complications have been reported following injection like endophthalmitis, retinal detachment and lens injury. Incidence of lens injury while giving intravitreal injection is rare to the tune of only 0 – 0.06%.[1,2] Posterior capsular breach remains stable in some of the patients while in some patients it can progress to develop cataract of mainly posterior subcapsular variety in a rosette shape.

Few cases of such misfortunate events have been reported so far and to the best of our knowledge very few cases have discussed the details of management of such incidences. We are reporting the detailed management part of the patient with proper techniques of doing preoperative workup, low fluidics phacoemulsification with special care to minimize the complications as there is preexisting breach in the posterior capsule and successful placement of 3 piece IOL in the sulcus with good visual recovery.

Case description

53 year old male known diabetic has presented in out patient department (OPD) with rapid progression of visual loss in his left eye since 1 month. He was a diagnosed case of moderate non proliferative diabetic retinopathy

(NPDR) both eyes with centre involving cystoid macular edema in left eye. There was a history of 3 anti-VEGF intarvitreal injection given in left eye and last injection was given one month back.

His right eye vision was 20/20 and left eye vision was 20/200. His intraocular pressure in right eye and left eye was 17.1 mmHg and 17.6 mmHg (Schiotz tonometry) respectively. Slit lamp examinations of left eye clearly showed 3mm long needle tract on posterior aspect of lens on infero-temporal location along with rosette shape posterior sub capsular cataract nicely visible on retro-illumination (figure 1a, 1b). Rest of anterior segment examination was unremarkable in both eyes. OCT 3D macula of right eye showed normal CFT but it showed cystoid changes in left eye (fig. 2a,b,c& d). Exact macular thickness could not be measured in left eye because of media haze due to cataract. USG B scan of the left eye showed retina on and vitreous echo free. He had a good systemic glycemic control so he was planned for phacoemulsification in left eye with necessary preoperative workup. Patient was counseled in detail regarding pre-existing posterior capsular tear and visual outcome.

Patient was advised intra-vitreal dexamethasone implant for macular edema in left eye but he refused due to affordability issue and was given intra vitreal inj. kenacort 4mg / 0.1ml intraoperatvely. Phacoemulsification was performed under peribulbar anesthesia. Clear corneal incision was made and high molecular weight viscoelastic was injected into anterior chamber. Capsulorrhexis was made of size 0.5 mm smaller than usual one and well centered so as to place the lens in the sulcus or for the optic capture if size of rent increased during phaco maneuvers. OVD (ocular viscoelastic devise) was removed before doing hydro procedures to prevent the intracapsular pressure rise and subsequent extension of the tear.

Hydrodissection was avoided and soft hydrodelineation was performed to save the posterior capsular rent existing morphology as epi nuclear plate will cushion the nuclear maneuvers while doing phacoemulsification. Low fluidics phacoemulsification was done with avoiding nuclear rotation inside the bag in direct chop mode to avoid undue stress to the capsular bag and breached posterior capsule, thus avoiding any disturbance to anterior hyaloid face and subsequent prolapse of the vitreous and making further surgery a difficult one.

Nucleus was emulsified and aspirated and in irrigation and aspiration mode thick epinuclear plate was removed first by lifting it from capsular fornices and touching the posterior capsular ruptured area at the end. After cleaning up the cortical remnants we could see well circular posterior capsular rent in paracentral location which has not inadvertently increased in size during phaco emulsification. Care should be taken to avoid chamber fluctuation during any procedure by filling the anterior chamber with viscoelastics from paracentesis incision before removing phaco and coaxial irrigation aspiration handpiece.

The capsular bag was inflated with viscoelastic so as to compartmentalize the chamber and 3 piece IOL was implanted with heptics placed in the sulcus and optic captured to anterior capsulorrhexis margin (figure 3a). Any vitreous strands were checked at the end of the surgery with triamcinolone. By taking all these precautions vitreous did not prolapse and made the surgery uneventful . No vitreous strands were seen at the end of the surgery. Post operatively lens was well centered and visual acuity was regained to 20/120(fig. 3b). Patient was advised regular follow up for the management of macular edema and findings are depicted in figure 3 c, d & e.

Discussion

Iatrogenic crystalline lens injury due to needle tip contact or penetration is rare, with a reported incidence of 0.06%.[1,2] The site and the angle of the injection needle are important and are the main cause of lens injury. The needle used in intravitreal injection should puncture the pars plana which is generally 3.5 mm-4 mm posterior to the limbus. Injection close to the ciliary body would narrow the needle's movable range and the needle could easily touch the lens.

On the other hand, it might stimulate the ciliary body to cause pain, which will cause sudden movement of the operated eye, increase the difficulty of the operation and the risk of injury to adjacent structures especially lens. However, such misfortunate cases can be managed with proper techniques of phacoemulsification as we usually do in posterior polar variety of cataract. [2,3]Low flow phacoemulsification i.e. low fluidics settings like reduced bottle height, reduce flow rate and reduce vacuum settings to avoid undue pressure in the bag that might extend the preexisting rent.

In these cases phacoemulsification should be performed with all standard precautions as described above keeping in mind the preexisting defect in posterior capsule so that we can get successful outcomes. [2,3]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient concent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity can not be guaranteed.

Financial support and sponsorship

Nil

Conflict of interest

There are no conflicts of interest.

Correspondence to: Dr. Praveen Panwar , MS

Associate Professor Deptt. Of Ophthalmology

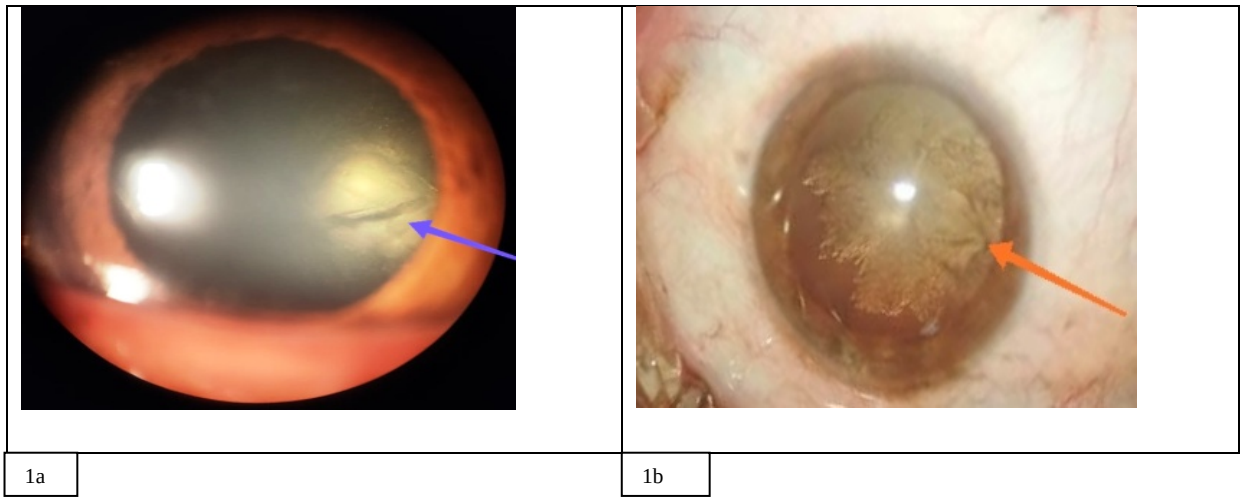
Indira Gandhi Maedical College Shimla, H.P. 171001

Mob. +919418454120

Email:praveendr97@gmail.com

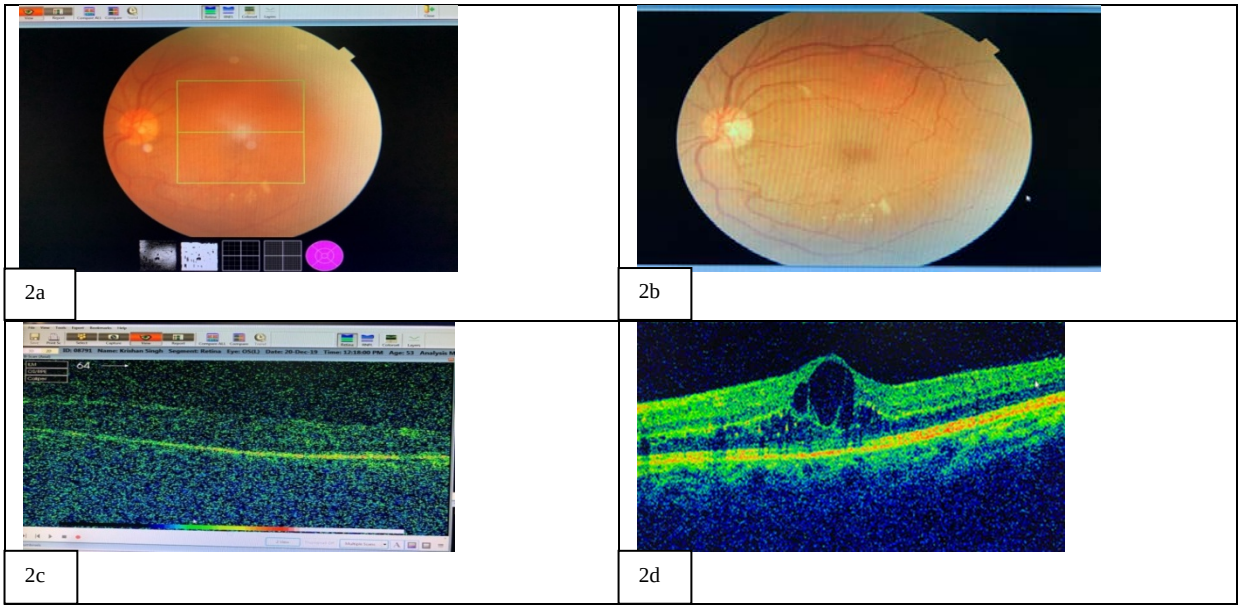
References

1. Meyer CH, Rodrigues EB, Michels S, Mennel S, Schmidt JC, Helb HM, Hager A, Martinazzo M, Farah ME (2010) Incidence of damage to the crystalline lens during intravitreal injections. J OculPharmacolTher 26:491–495.
2. Erdogan, G., Gunay, B.O., Unlu, C. et al. Management of iatrogenic crystalline lens injury occurred during intravitreal injection. IntOphthalmol 36**,** 527–530 (2016).
3. Saeed MU, Prasad S (2009) Management of cataract caused by inadvertent capsule penetration during intravitreal injection of ranibizumab. J Cataract Refract Surg 35:1857–1859.



1a 1b

Figure 1a Needle tract inside the lens and opacity formed due to injury from needle.**1b** Rosette shaped cataract with needle track in retro illumination view.



2a 2b 2c 2d

Figure 2:. Fundus and OCT pictures of the patient's left eye before and first post op day of cataract surgery.

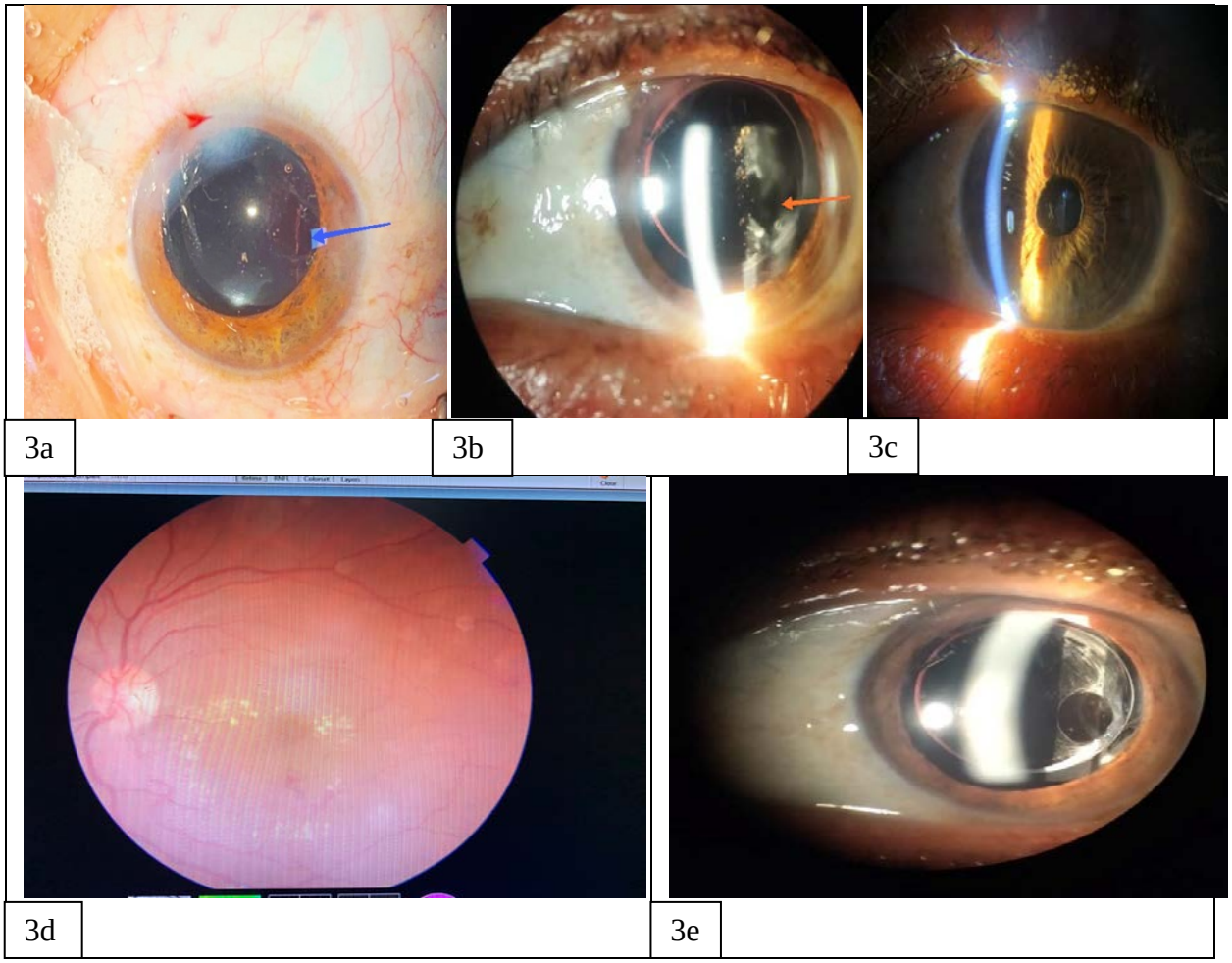


Figure 3a Intrao-perative picture showing well placed IOLin sulcus with optic capture and visible posterior capsular rent. **3b** Showing well centred IOL with PC rent post operated day1 on slit lamp. **3c & d** Slit lamp picture and fundus photograph of the patient 3 months down the line. **3e** Slit lamp picture of the patients operated eye showing undisturbed rent morphology and well centred lens after 6 months.

Conversion of complicated Phacoemulsification to Small Incision Cataract Surgery

Dr.R L Sharma[1], M.S., **Dr.Vinay Gupta**[2],MS, **Dr. Deepti Parmar**[3], MS, **Dr.Kalpana Sharma**[3],MS

[1] Prof and Head, Deptt of Ophthalmology, IGMC Shimla H.P.

[2] Associate Professor, Deptt of Ophthalmology, IGMC Shimla H.P.

[3] Assistant Professor, Deptt of Ophthalmology, IGMC Shimla H.P.

Abstract

Complications are unwanted and unpleasant situations during surgeries that occur as consequence of any procedure. They can totally be avoided if anyone stops doing surgery. It can be said that complications are part and parcel of surgery but they should be managed well. The modern day cataract surgery is very effective in visual restoration of cataract patients. Historically the techniques of cataract removal are intra and extra capsular surgeries (ICCE & ECCE), small incision and phaco surgery. Phacoemulsification is the best option in standard situation, but once complications occur during this surgery one falls back to complete the surgery by ICCE or ECCE with suturing. But one can convert complicated phaco surgery to SICS that will be better situation because SICS is without sutures. In patient with anticipated complications or otherwise, some modifications during the course of surgery or arising out of complications make it possible. One of the important step is to position the entry incision slight posterior to the limbus, that can be extended in complicated situation to convert to SICS.

Keywords: Phacoemulsification, SICS, Surgically induced astigmatism.

Introduction

The site of incision in cataract surgery varies from purely scleral in standard SICS to clear corneal incision in phacoemusification. The clear corneal incision has the advantage of better AC approach during surgery but its limitation becomes apparent when it needs enlargement; either for implantation of rigid IOL or in complicated surgery, where suturing will be required and astigmatism will be significant. Similarly scleral incision has the advantage of lesser induced astigmatism, infections; despite large incision. But it makes surgery difficult particularly in hard cataracts, smaller pupil and deep set eyes.

The sclero-corneal tunnel gives the advantages of both the approaches with lesser surgical induced astigmatism (SIA) and better AC manipulations. Limbal incisions heal faster and resist more deformation pressure than cornea. [2] In small incision cataract surgery, superior and temporal approaches are comparable in terms of visual rehabilitation and induction of regular and irregular astigmatism. [3] SICS is significantly faster, less expensive, and less technology dependent than phacoemulsification [4] and could be a rescue surgery in complicated surgery.

Technique - Direct Stab Incision

The entry incision in cases of complicated cases or otherwise unexpected complication should be slightly posterior to limbus with minimum width 0f 2.5 to 3.2 mm. Such incision can be directly converted to SICS tunnel of 5.5 -6.5 mm if needed. The entry is made in such a way that tip of keratome (3.2mm) is inserted just posterior to the limbus and slowly pushed through the limbal tissue (Figure 1). Once the tip reaches in the cornea, the forward force is reduced and knife is slightly elevated initially to move along the corneal curvature and later dipped down into the anterior chamber to make a sharp and straight entry. The optimal incision depth is usually one-half of the thickness of the limbus or about 0.3-0.4 mm. The shape of external entry incision is straight or slightly curved and that of internal entry is straight (Figure 2). The position of stab incision is oblique in supero-temporal quadrant in right eye and supero- nasal in left eye taking 10:30 clock hour of limbus as centre point. Since more space is available on the sides rather than at 12 o'clock limbus, so surgical manipulation is easier on sides in the absence of superior rectus suture.

The anterior limit of the tunnel is 1-2 mm in the clear cornea making a total width of tunnel from 2.5-3.5 mm depending upon the desired length of tunnel keeping the length to breadth ratio of 2:1 in case extension is required. The direct stab incision passes through different tissue strengths of limbus and cornea which makes it self-sealing. It has better apposition due to the smoother opposing tunnel surfaces due to single initial stab. The tougher limbal tissue provides the external pressure to the outer incision at the same time aqueous pressure provides the internal sealing force to the inner incision.

Capsular Opening

The best capsular opening is a continuous curvilinear capsulorrhexis (CCC) as it guarantees the long-term, in the bag IOL; however any type of capsulotomy can be suitable for SICS conversion. But CCC is more difficult to learn and can cause zonular dehiscence during rotation in big nuclei and weaker zonules.

So during conversion from phaco to SICS when whole nucleus is in the bag, the rhexis should be either large in size or can be enlarged by giving relaxing cuts (2-3) on its margin with capsulotomy needle. It can be in the form of U shaped cuts (non-extending) or V cut deeper at zonular insertion (extends as radial tear) with tip of the needle and side of the needle tip respectively (Figures 3 and 4).

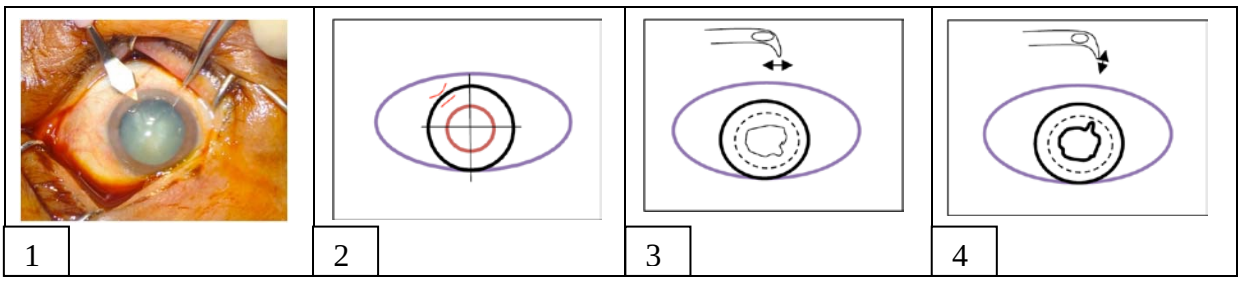


Figure 1 to 4 Direction and location of knife for oblique limbal stab incision, Deeper U and V-shaped extension cuts at rhexis edge (extending cuts).

The delivery of nucleus will be facilitated by anterior radial tear as it will reduce the stress on the zonules in complicated cases particularly when cortico-nuclear mass is formed during hydro-procedures or in hard nuclei. But this radial tear does not affect the surgery rather helps in delivery of nucleus, pushing the upper haptic of rigid IOL in the bag and facilitates sub-incision cortex removal. So an anterior radial tear can be a curse during phaco surgery but can turn up blessing in converted SICS.

Self Sealing Tunnel

The phaco is performed with the standard tunnel of 2.8 or 3.5 but it can be extended for SICS conversion with 5.5 mm blade to the desired length based on the nucleus size (Figures 5 and 6). Care is taken while extending the tunnel, the extension blade is positioned straight in the stab and globe should be stabilized, so that external incision doesn't tear away. The length of the self sealing incision varies from 6-6.5 mm for cortical cataract, and can be extended safely from 7 to 8 mm for brown and hard grade IV cataract but may require single 8 shaped suture (Figure 7).

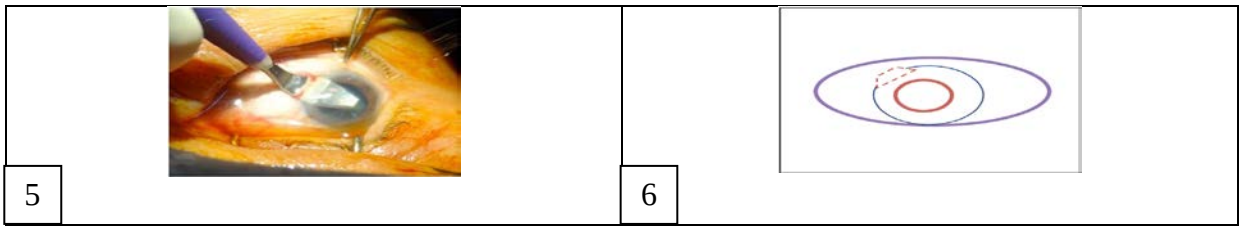


Figure 5-6 Tunnel extension of limbal incision for SICS, Extent of limbocorneal tunnel after extension at 9- 12 at clock hour position.

Precautions

- The instruments used for direct oblique tunnel construction such as keratome and 5.5 mm blade has to be sharp to avoid Descemet's detachment during entry and ragged cutting during tunnel extension.

- Visibility of keratome through the tissue during insertion is the rough guide to access the appropriate depth of the tunnel. Partial visibility of keratome during its passage through the sclero- limbal tissue will indicate the proper depth. If it is seen clearly then it is too superficial and might perforate outside; if it is invisible it is too deep to make premature entry into the anterior chamber.

- The position of tunnel has to be at least 1-1.5 mm in opaque limbal area and 1-2 mm in clear cornea; so that limbus makes part of the tunnel and attaining a total width of 2.5-3.5 mm.

- Extra care is taken while extending the stab tunnel as whole length of the tissue needs to be incised on both sides of the tunnel, contrary to the pre-formed cleavage in SICS tunnel. In order to ensure the

symmetrical outer (smiling) and inner (straight) incision, 5.5mm blade is gently pushed with its tip in AC and sides are extended by stabilizing the globe well.

- Bleeding from the limbal vessels during extension does not interfere in surgery as blood does not enter through the self sealing tunnel. Rarely hyphema can occur from perforating vessels in tunnel, if it is positioned posteriorly or vessel comes on the way while extending the tunnel. In order to reduce the risk of postoperative hyphema ensure that there is no leakage of blood in AC at the end of surgery or one can inject an air bubble. Mild postoperative hyphema disappears in 1-2 days.

- Best way to deliver the nucleus is either by hydro- delivery or visco-delivery, if this is not possible vectis delivery is always possible by holding the eyeball in down gaze position. To avoid corneal endothelium damage during nucleus delivery, its rubbing with the cornea must be avoided by injecting viscoelastic in front of it and tunnel should be larger in big hard nuclei.

- Subconjunctival injection is given above the incision site that not only provides high concentration of drugs near the incision but ballooning conjunctiva also seals the entry (Figure 7).

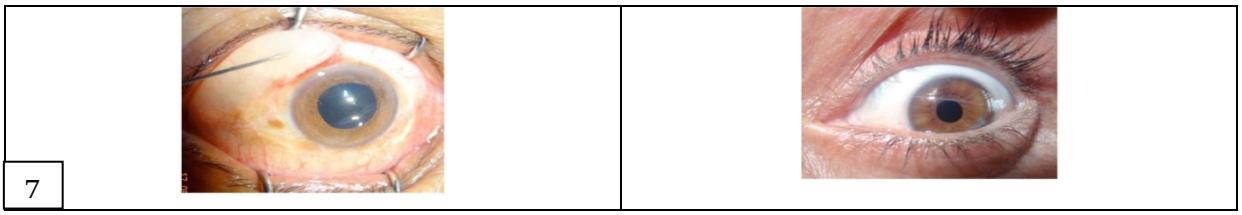


Figure 7 Subconjunctival injection at the end further help in sealing tunnel, minimal visible scar at four weeks post- operatively.

Discussion

Cataract is not only the leading cause of blindness in the world but it is also an important cause of low vision in both developed and developing countries. The trend in cataract surgery is now towards correction of low vision and any existing refractive error. Even where surgical services are available, low vision associated with cataracts may still be prevalent, as a result of long waiting for operations, cost, and lack of information and transportation problems.

The techniques of cataract surgery have been continuously evolving since its first description by Indian surgeon, Sushruta (6th century BCE). [5] Cataract surgery, using a temporal approach phaco- emulsification probe (in right hand) and chopper (in left hand) is being done across the world today. There could be some place for extra-capsular cataract extraction (ECCE) and intra-capsular cataract extraction (ICCE) but it is rarely performed that to in complicated situation. SICS is the simple, effective, cheap alter- native procedure for management of cataract in the developing world.

SICS is a technique that allows lots of flexibility depending upon the patient need and surgeon's comfort. It needs minimal instruments, no equipment dependence and is easy to learn, can be performed quickly and at very low cost. It has good post operative visual results with least complications in trained hands. The post-operative visual acuity at 12 weeks was 6/18 or better in 96% cases in SICS group and 98% cases in phaco group. The surgery can be performed without application of superior rectus suture (truly stitch less) or construction of conjunctival flap or cautery. [6] The one step incision tunnel is sealed equally well when extended; as the opposing surfaces are smoother for better sealing and healing.

The closure placement of the tunnel to the limbus also facilitates delivery of nucleus.

The technique of eliminating five surgical steps - superior rectus stitch, conjunctival flap, cautery, stab entry make conversion of all complicated phaco to SICS possible. Phaco performed through the stab tunnel is extended in complicated situation like PCR with 5.5 mm blade to the desired length without any suturing. The surgery is possible under topical anaesthesia or can be supplemented by lower dose trans-conjunctival peribulbar injection.

When incision is located superiorly, both gravity and eyelid blink tend to create a drag on the incision. These forces are better neutralized with temporal incision because it is not parallel to the vector of the forces. [7] One could find the conversion difficult in deep set eyes, narrow palpebral fissure, non dilating pupil, pseudoexfoliation, hypotony, bleeding tendencies as is true for other techniques.

The common complications in SICS is subconjunctival haemorrhage (16%) post-operatively as compared to 5% in phaco group. The subconjunctival bleeding is due to the posteriorly located incision, where conjunctival vessels are present and cautery was not used. The striate keratopathy (SK) is the commonest (21%) complication in phaco group and it is seen in 7% of SICS group. Posterior capsular rent is seen in 1% of cases in SICS group and 7% in phaco group. SK and posterior capsular rent was higher in phaco group due to higher use of energy and manipulation in harder cataract (advanced ISC or MSC). All complicated phaco are converted to SICS with IOL implantation without suture an advantage of this technique. Mild hyphema is seen in 2% cases in SICS but did not require surgical intervention. None of the patient in the two groups with oblique limbal stab incision had leaking anterior chamber or endophthalmitis. [8]

Clear corneal incision provides the benefits of shorter tunnel length, but will need suture if length of incision is extended beyond 3.2 mm and hence not suitable for direct SICS conversion. So a direct posterior limbal incision has the advantages of both like lesser astigmatism and extendible without suture.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity can not be guaranteed.

Financial support and sponsorship

Nil

Conflict of interest

There are no conflicts of interest.

Correspondence to: Dr. RL Sharma,MS

Prof and Head, Deptt of Ophthalmology IGMC Shimla H.P.

Mobile: +919418200098

Email: rls_10@rediffmail.com

References

1. Earnest P, Tipperman R, Eagle R. Is there a difference in incision healing based on locations? Journal of Cataract and Refractive Surgery 1998; 24: 482-6. http://dx.doi.org/10.1016/S0886-3350(98)80288-5
2. Oshika T, Sugita G, Tanabe T, Tomidokoro A, Amano S. Regular and irregular astigmatism after superior versus temporal scleral incision cataract surgery. Ophthalmology 2000; 107(11): 2049-53. http://dx.doi.org/10.1016/S0161-6420(00)00379-1
3. Ruit S, Tabin G, Chang D, Bajracharya L, Kline DC, Richheimer W, Shrestha M, Paudyal G. A prospective randomized clinical trial of phacoemulsification vs manual sutureless small-incision extra capsular cataract surgery in Nepal. Am J Ophthalmol. 2007; 143(1): 32-38. Epub 2006 Sep 5. http://dx.doi.org/10.1016/j.ajo.2006.07.023
4. Priya Vrat Sharma. Suruta-Sahit with English translation of text and alhaa's commentary along with critical notes. Vol I (Varanasi, India: Chaukhambha Visvabharati Oriental Publishers and Distributors, 2001; p. 202.
5. Sharma RL, and Praveen P. Minimal Duration Cataract Surgery (MDCS)-Small Incision Cataract Surgery (SICS) without superior rectus stitch, no conjunctival flap and no cauterization. Delhi Journal of Ophthalmology 2012; 275-8.
6. Ram Lal Sharma, Kalpana Sharma.Topical anaesthesia(vocal-focal) for small incision cataract surgery. International Journal of Ocular Oncology and Oculoplasty, July-September, 2017;3(3):222-225
7. Ram Lal Sharma, Deepti Mahajan and Kamlesh Sharma SICS Tunnel Construction with Oblique Limbal Stab Incision and its Effectiveness in Self-Sealing, Nucleus Delivery and Astigmatism - Minimal Duration Cataract Surgery Journal of Ocular Diseases and Therapeutics, 2014, 2, 55-63

Management of Age Related Senile Cataract and Aniridia with Aniridic Lens: A Case Report

Dr. Jitender Singh Roodkee[1]

[1]Block Medical Officer Ophthalmologist Civil Hospital Sundernagar Distt Mandi H P

Abstract

Aniridia is a condition characterized by a partial or complete absence of the iris. It can be either congenital or secondary to trauma. The absence of iris tissue can lead to glare and poor visual acuity, however it can be managed by implantation of aniridic intraocular lenses (IOL) in aphakic patients which can be either segmental or the Black diaphragm intra ocular lenses (BDIOL's) which have been tried as early as 1991. Aniridic IOL's are also available in different colors to match the iris of the opposite eye and provide good cosmesis. In this case manual small incision cataract surgery was performed and aniridic lens was implanted in the capsular bag with the main aim of reducing the symptoms of glare and also provide cosmesis.

Key words: Intra ocular lens, aniridia, aniridic IOL

Case Description

A 66 year old male, stone mason by profession presented with diminution of vision in both eyes four years. There was a history of trauma in both eyes few years back. He sustained a stone chisel while working on a stone to left eye and was operated for his left eye. He gave history of trauma multiple times in both eyes. His best corrected visual acuity was 5/60 in both eyes. Retinoscopy showed astigmatism of 12D in the left eye with 5/60 unaided and best corrected. There were corneal opacities in both eyes in the periphery with suture scar mark at 5 'O' clock position in the left eye. Central cornea was normal in both eyes. Further examination showed an irregular pupil with posterior synechiae in the right eye and complete aniridia in the left eye. Lens showed grade two nucleus sclerosis in both eyes. Intra ocular pressure and fundus were normal. Patient was counseled and advised implantation of aniridia IOL in the left eye and planned for manual small incision cataract surgery with aniridic IOL implantation in the left eye. Aniridic IOL was procured from Care Group company, name of IOL is QV lens and material is Polymethyl methacrylate (PMMA).

It's overall diameter was 12.5 mm and optic zone of 5.95mm. Biometry showed K1=38.37D, K2= 50.37 at 82 degrees and power of lens came 18D. We performed MSICS with an 8 mm temporal sclero corneal incision to neutralize corneal astigmatism. Oval continuous curvilinear capsulorehexis was done, nucleus was prolapsed and cortical matter was aspirated. The capsular bag was found intact and the aniridic lens was implanted in the bag (Figure c). Leading haptic went easily into the bag but the trailing one took many efforts. The tunnel was not sutured to minimize corneal astigmatism. On post op day 1, the best corrected visual acuity was 6/24 with minus lens of 4.50D sphere. On 45th day post operative vision was 6/18 with minus 3.50 D Cylinder at 90 degree

.

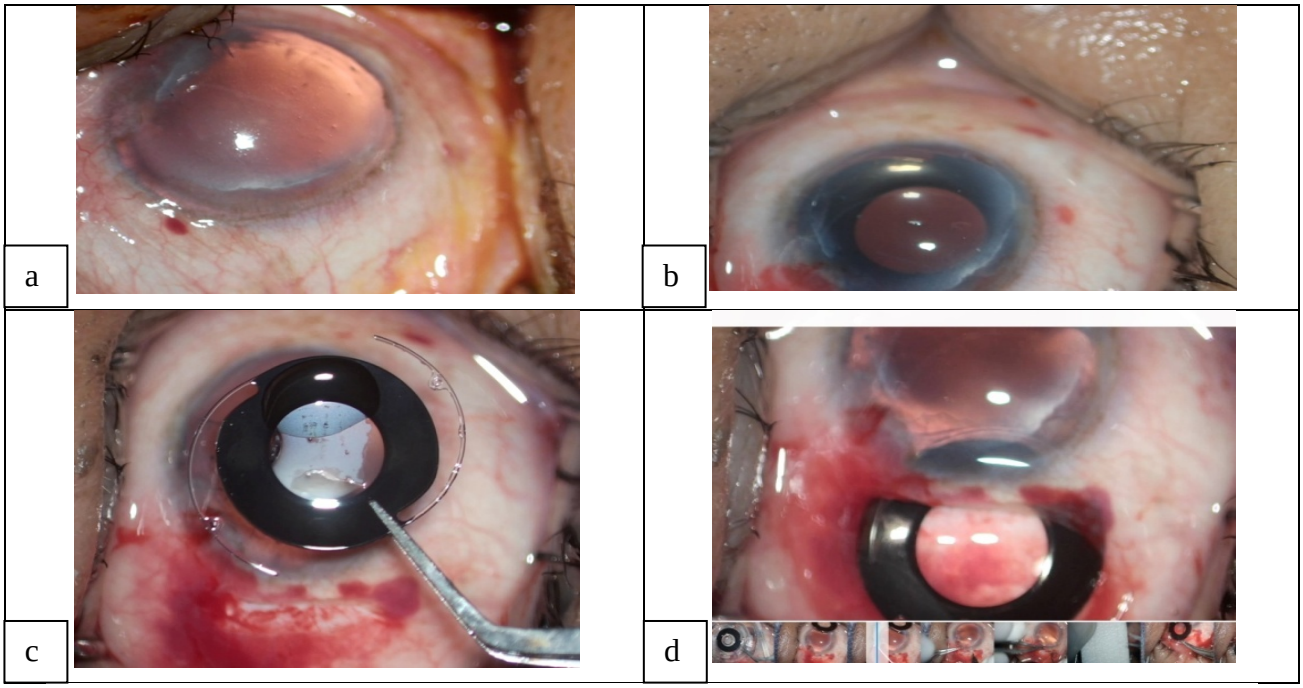


Figure: a, b, c, d Operative images

Discussion

The absence of iris can be either congenital or acquired.[1] These patients have symptoms of glare and photophobia especially in day light. Aniridic IOLs or segments is a great tool in reducing glare and photophobia. Also some patients are concerned about the color of the eyes, so it has an aesthetic value and provide reasonable cosmesis. These lenses are particularly useful when the loss of iris tissue is large and it cannot be repaired.

The aniridic IOL has a uniquely designed IOL with an optic and rigid haptics. The optic has a clear central zone and an opaque or tinted periphery. With the help of biometry we can get the spherical power of lens.

It can be implanted after doing an ECCE/ICCE in congenital aniridia, albinic eye, [7] traumatic iris defects or total traumatic aniridia, aphakia with iris absence in congenital and also in traumatic aphakia and iris absence. It can also be placed as scleral fixated IOL [1, 2]with traumatic aniridia with pars plana vitrectomy where lens complex is weak.[2, 4, 5]

Many surgeons have done this as a vitreo retinal procedure [5] (open globe surgery), [2, 4, 5] or post penetrating keratoplasty. In albinism eyes chances of glaucoma are more. [7] So the placement of IOL is important, if in sulcus then IOP monitoring is very important. But in this case the aniridic lens was implanted in the capsular bag. Thus implantation of aniridic IOL is a noble way to reduce the symptoms of photophobia glare and also preserve the aesthetic value.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity can not be guaranteed.

Financial support and sponsorship

Nil

Conflict of interest

There are no conflicts of interest.

Correspondence to: Dr. Jitender Singh Roodkee

Block Medical Officer Ophthalmologist

Civil Hospital Sundernagar Distt Mandi H P

Mobile: +919418161267

Email: jiturudkee1@gmail.com

References

1. Journal of American Association for Pediatric Ophthalmology and Strabismus Volume 12 issue 3, June2008,Pages 268-272 .

2. Combined aniridic intraocular lens implantation and vitreoretinal surgery. Hitendra Mehta, MS,Hijab Mehta, MS, Chaitra Jayadev, DOMS, and S Natarajan, DO.

3. Traumatic aniridia and aphakia after Artisan intraocular lens implantation. Sung Jin Lee .Affiliations expandPMID: 17586400DOI: 10.1016.

4. Thompson CG, Fawzy K, Bryce IG, Noble BA. Implantation of a black diaphragm intraocular lens for traumatic aniridia. J Cataract Refract Surg. 1999;25:808–13.
5. Wiechens B. Combined aniridia-intraocular lens implantation and pars plana vitrectomy in cases with total traumatic aniridia and retinal disorders. Available from: http://www.dog.org/2000/e-abstract_2000/71.html.
6. Tanzer DJ, Smith RE. Black iris-diaphragm intraocular lens for aniridia and aphakia D J Tanzer . RESmith. Affiliations expandPMID: **10569174**DOI: 10.1016/s0886-3350(99)00247-3
7. Davide Romano MD , Dominique BremondGignac MD , Miriam Barbany MD , Amna Rahman MS ,Laura Mauring MD, Francesco Semeraro MD,Artificial iris implantation in congenital aniridia: A systematic review .J CataractRefract Surg. 1999;25:1548–51.

A Rare Case of Chronic Progressive External Ophthalmoplegia: A Case Report

Dr. Eathi Tuli[1],MS, **Dr. Aditya Kashyap**[2], MS, **Dr. Smriti Sharma**[3], MS, **Dr. Shaloo Negi**[3]MS

[1] Assistant Profesor Deptt. of Ophthalmolgy Pt. JLN Medical College Chamba H.P.

[2]Associate Profesor Deptt. of Ophthalmolgy Pt. JLN Medical College Chamba H.P.

[3]Senior Resident Deptt. of Ophthalmolgy Pt. JLN Medical College Chamba H.P.

Abstract

Chronic progressive external ophthalmoplegia (CPEO) describes an array of hereditary myopathies affecting extraocular muscles (EOMs), commonly manifesting as bilateral ptosis and ophthalmoplegia. It is bilateral symmetrical external ophthalmoplegia with sparing of pupils. We report a 36 year old male with severe ptosis without diplopia and with no history of fatiguability, fluctuations in drooping of eyelids. Ocular examination showed severe bilateral ptosis and marked limitation of conjugate gaze in all direction. Ice pack test was negative. Fundus examination was within normal limits.

Clinical presentation of Ptosis and ophthalmoplegia can be mimicked by neurogenic, neuromuscular junction and myogenic etiologies. Thus, it is crucial for ophthalmologist to have CPEO in their differential diagnoses to avoid unnecessary tests or delays in diagnosis.

Keywords: Chronic progressive external ophthalmoplegia (CPEO), ptosis, extraocular muscles (EOMs)

Introduction

CPEO is a hereditary myopathy affecting extraocular muscles (EOMs), commonly manifesting as bilateral ptosis and ophthalmoplegia.[1]As the name suggests, it is a chronic, progressive, bilateral, typically symmetrical, external ophthalmoplegia with sparing of pupils. CPEO can occur as isolated CPEO or in conjunction with other systemic findings (CPEO plus), which include hearing loss, neuropathy, ataxia and parkinsonism. Clinical presentation of ptosis and ophthalmoplegia can be mimicked by neurogenic, neuromuscular junction, and myogenic etiologies.[2] Thus, it is crucial for physicians to have CPEO in their differential diagnosis to avoid unnecessary tests or delays in diagnosis.

Case Report

A 38 year old male came to eye OPD with chief complaints of drooping of both the eye lids from past 6 years, which was gradual and progressive. Degree of ptosis bore no relationship to the time of day, with no history of fatiguability or variability. There was no history of breathlessness, muscle weakness, hearing loss or night blindness. There was no history of trauma or snake bite. Patient denied of diabetes, hypertension, tuberculosis, skeletal muscle weakness or other systemic disease. There was no family history of ptosis or squint.

Vision on initial examination was: BCVA 6/9 in both the eyes. Patient had severe ptosis with poor levator palpebrae superioris (LPS) action. The palpebral aperture measured 3.5mm on the right and 3mm on the left. Levator function measured 4.5 mm bilaterally. Marginal reflex distance (MRD10.5 min RE -1mm in the LE). Apart from position, lids were normal in appearance with no other cause for the ptosis.
There was restriction of extraocular movements (EOM) in all direction of gaze, complete external ophthalmoplegia. Anterior segment was within normal limits and pupillary reaction was brisk in both the eyes. There was no proptosis and both eyes were white and quiet with normal intraocular pressure and healthy fundus.

On the basis of history and examination, we had kept a differential diagnosis of CPEO, thyroid associated ophthalmopathy (TAO) and ocular myasthenia gravis. Ice pack test was performed which showed no improvement in ptosis. CBC, ESR, RBS and ECG, TFT were within normal limits. Patient was referred to higher centre for cosmetic correction of ptosis.

Figure: Image showing bilateral ocular involvement

Discussion

CPEO is a condition characterized by weakness of the eye muscles. The condition typically appears in adults between ages 18 and 40 years and slowly worsens over time.[1]

The first sign of CPEO is drooping of eyelids which can affect one or both eyes. Another characteristic feature of CPEO is weakness or paralysis of the EOMs that move the eye (ophthalmoplegia). The internal musculature of the eyes are characteristically unaffected and almost invariably the pupils react normally to light and accommodation.

Diplopia is often not present. [3] The head is thrown back because of the ptosis. Walsh, [4]reported that absence of diplopia is due to ptosis. On the other hand, Scott[5] reported diplopia does not develop because the visual axes are directed straightahead and others have reported that the slowly progressive nature of the muscle involvement permits adjustments which prevent diplopia. Other less ophthalmic manifestations include optic atrophy and pigmentary retinopathy. [6]

Myopathies are ubiquitous in mitochondrial disorders, and even asymptomatic patients will typically have significant muscle pathologies, hence muscle biopsy is diagnostic. The accumulation of enlarged mitochondria

produces a dark red staining of muscle fibres stained with gomori's trichome stain called as the "ragged red fibres".[7]

Pain, proptosis, periorbital swelling, lid lag/retraction and pupil involvement are not the symptoms of CPEO but indicate a different etiology[8]. Unilateral or rapidly progressive symptoms are also atypical and should prompt additional evaluation including neuro imaging. Detailed family history is important in identifying possible inherited conditions. There is no definitive cure for CPEO and control of symptoms can improve quality of life. [2]

Conclusion

The diagnosis of CPEO can be made by the history and eye findings, muscle biopsy and electromyography may help to confirm the diagnosis. To conclude CPEO is a rare mitochondrial myopathy, all the patients with slow progressive bilateral ptosis with external ophthalmoplegia should be investigated in terms of CPEO and awareness about classical clinical presentation can help the clinician to come to the diagnosis and to avoid unnecessary tests.

Declaration of Patient consent

Authors have certified that they have obtained appropriate consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil

Conflict of interest

There are no conflicts of interest.

Correspondence to: Dr. Eathi Tuli;Assistant Professor,
Department Of Ophthalmology,
Pt. JLN Medical College and Hosptial, Chamba, Himachal Pradesh
Mobile: 9602645411
Email:ethi.shree@gmail.com

References

1. Lee, A. G. &Brazis, P. W. Chronic progressive external ophthalmoplegia. Curr. Neurol. Neurosci. Rep. 2002; 2: 413–17.
2. Yu-Wai - M.P, Chronic Progressive External Ophthalmoplegia Secondary to Nuclear-Encoded Mitochondrial Genes in Mitochondrial Case Studies 2016; 159–169.
3. Kiloh, L. G. and S. Nevin Progressive Dystrophy of the External Ocular Muscles. Brain, 1951; 74:115-43.
4. Walsh,F.B. Clinical NeuroOphthalmology.Baltimore,Williams and wilikins,1957.
5. Scott, A. B. neurological Aspects of oculomotor disease. IntOphthal., Clin., 1964;4:711.
6. Tarnopolsky, M. Chronic Progressive External Ophthalmoplegia (CPEO).in Mitochondrial Case Studies 2016; 49-53
7. Yu-Wai –Man P, Gorman G.S, Taylor R.W, Turnbull D.M Diagnostic investigations of patients with chronic progressive external ophthalmoplegia. Br J Ophthalmology 2012; 96: 1536.
8. Richardson C, Smith T, Schaefer A, Turnbull D, Griffiths P, Ocular motility findings in chronic progressive external ophthalmoplegia. Eye 2005; 19:258-63.

Tackling Myopia-an Off-Beat Perspective

Dr. Shruti Anand , M.S. Assistant Professor Deptt of Ophthalmology Dr. RKGMC Hamirpur H.P.177001

Myopia has been classically defined as an ocular condition of short-sightedness. A problem in which the image falls just short of retina and lies in the homogenous space behind the lens. This problem has been effectively tackled by the application of concave lenses which by the property of divergence allow the image to be formed in its natural dwelling, the retina. So the person is ready to face a near perfect world.

The physical handicap has been rectified, but what about the mental nearsightedness? This problem is not only prevalent in medicos with thick spectacles, but also who have been lucky enough to graduate without glasses adorning their noses.

We have been taught to identify and treat plethora of conditions not necessarily ocular but not equipped with social skills to take it easy and step out of our mental myopia

.

Often in social gatherings, most of us seek the company of fellow brethren. Even there the topic of our evening tete-a- tete will be a discourse on some patient encountered and problems faced in our clinical settings. We don't look beyond medicine. The company of our familiar colleagues somehow pacifies our minds and we never feel the urge to reach out and meet plethora of people who constitute our society. A very welcoming change bearing in mind the fact that such fruitful associations are bound to affect us not only mentally but also socially. Not only it will broaden our horizons, but a polite hello and just loosening a bit will give us recognition which most of us crave for, even if we never accept this hard fact.

The present scenario in society is of distrust. The patient is suspicious of the treating physician, is he trying to fleece me? And we as doctors are obsessed with the deliberation, will he sue me? Loosen up a bit, develop communication skills. Explain the procedure and the possible complications and give yourself a break. You are not God! By the time Indian medical graduate settles in his life, he is in late thirties or early forties with the most productive years having just flown away.

So, go beyond the shackles of myopia that bind you. In the journey of professional excellence, don't let go of your passions and hobbies. Life is beautiful and we do not require our concave lenses rectify our mental myopia.

Correspondence to:Dr. Shruti Anand, MS

Assistant Professor Deptt of Ophthalmology

Dr.RKGMC Hamirpur H.P.-177001

An Ode of an Eye Surgeon to Fundus Calls…

Dr. Mukta Sharma, MS, Senior Resident Deptt of Ophthalmology Dr.RKGMC, Hamirpur,HP 177001

Fundus refers to the retina of the eye where vasculature can be seen
Its importance in prognosis and diagnosis has always been seen
In each and every patient coming to us Fundus examination is must
All the other Departments rely on it before starting the treatment
Our visit to their department is thus very frequent
First and foremost is the call from Pediatrics for ROP screening
In this case we have to hear the neonate screaming
Even the OBG people are there to impress For every PIH patient they want us to confess
No matter what, Medicine JRs cannot do without a Fundus call
And seeing their number of calls,we get a haul
To see bedside calls forHypertensive and Diabetic Retinopathy, Papilloedema or Headache
We surely get a backache How can we forget the Surgery/Ortho SR
They are under obligation because the bedside call has been advised on their case sheets by Medicine JR
ENT people are no less For every Epistaxis they want us to assess
Oh how can we forget Psychiatry, as their patients are often blurry
So they too consider it mandatory
Last but not the least, Dermatology Department which share a special bond with Ophthalmology
They also get the Fundus examined Otherwise to put a patient on T.HCQS is restricted
Even patients with SLE , Herpes Zoster, Leprsoy, Sarcoidosis, Neurofibromatosis are referred
Otherwise their treatment is deferred
So my dear colleagues,we are here to provide you with the insight
Before you set the patient right

Correspondence to: Dr. Mukta Sharma, MS

Senior Resident Deptt of Ophthalmology

Dr.RKGMC Hamirpur H.P.-177001

PG Corner

1. KF ring is seen in (besides Wilson disease)?
    A) Splenic infarction
    B) Chronic lymphocytic leukaemia
    C) Amiodarone therapy
    D) Osteosarcoma
2. Increase in intraocular pressure on up gaze in thyroid eye disease is known as ?
    A) Sattler sign
    B) Payne trouseau sign
    C) Lowy sign
    D) Ballet sign
3. Long term Trifluridine therapy can cause ?
    A) Glaucoma
    B) Cataract
    C) Punctal stenosis
    D) Diplopia
4. Lacteocrumenesia is also called ?
    A) Capsular bag shrinkage syndrome
    B) Capsular bag breaking syndrome
    C) Capsular bag rupture syndrome
    D) Capsular bag distension syndrome
5. -2D sphere/+2D cyl at 90degree. The above prescription is ?
    A) Simple myopic with the rule
    B) Simple Hypermetropic against the rule
    C) Compound Myopic with the rule
    D) Mixed Hypermetropic against the rule

6. Christmas Eye is also known as
    A) Festival keratitis
    B) Harvesters keratitis
    C) Plumber keratitis
    D) None of the above
7. Transformation Plate on Ishihara chart (Standard 38 Plate) is
    A) Plate no 1
    B) Plate no 2-9
    C) Plate no 10-17
    D) Plate no 18-22

8. Vesmodegib is used to treat

A) Keratoacanthoma

B) Inverted follicular keratosis

C) Basal cell carcinoma

D) Squamous cell carcinoma

9. Smith and Kirchner clinical diagnostic criteria is for

A) Idiopathic intracranial hypertension

B) Vogt koyanagiharada syndrome

C) Thyroid eye disease

D)Mucormycosis

10. Omega Sign on OCT is seen in

A) Compound Hamartoma of retina and retinal pigment epithelium

B) Retained subretinalPerflurocarbon liquid

C) Both

D) None

E) Polypoidal choroidal Vasculopathy

Answers will be shared in next issue.

Correspondence:Dr. Anubhav Chauhan, MS, Assistant Professor

Deptt of Ophthalmology , SLBSGMC Mandi at Ner Chowk H.P

Moble: +919816991482, Email: chauhan.anubhav2@gmail.com

Raymed

100% Vegan | 30 GUMMIES

Vitamax®

G-U-M-M-I-E-S

Lutein 4 mg, Astaxanthin 1600 mcg,
Zeaxanthin 800 mcg, Vitamin A 499.8 mcg,
Vitamin C 30 mg, Vitamin E 5.04 mg, Docosahexaenoic acid (DHA) 100 mg

PROTECTION FROM DIGITAL LIGHT-GREAT EYESIGHT

Protect your eyes with the NEW AGE SUPPLEMENT

A Complete Nutritional Supplement

- Helps reduce eye strain & fatigue
- Protects from blue light damage
- Supports long term eye & vision health

GUMMIES *A new dosage form*

Deliciously healthy

Convenient dosage form

Tempting taste, color and appearance

Raymed

Raymed Pharmaceuticals Limited
Corporate Office: SCO-859, Manimajra, Chandigarh
E-mail : admin@raymedindia.com, Website : www.raymedindia.com

Raymed

MADE IN TURKEY IMPORTED MADE IN TURKEY

Aquaray®

Ocular Wipes
Ocular Care Gel
Ocular Cleanser

Tea Tree Oil
with Sodium Hyaluronate

Complete Ocular Protection Starts With.... **Eyelid Hygiene**

Aquaray Ocular Wipes

- Reduce Inflammation and Itching
- Get rid of demodese mites from the eyelid margin & relieve the symptoms of chronic blepharitis[1,2]

STERILE

Aquaray Ocular Cleanser

- Relives itching & irritation, quick relief in symptoms of blepharitis
- Nourish surrounding soft skin around eye

No Irritation pH ≥ 7

Aquaray Ocular Care Gel

- Effective anti bacterial and anti fungal agent
- Treats superficial corneal inflammation or damage caused by dust, scratching or mechanical damage during surgery[1,2,3,4,5]

Indications Puffy Eyes | Eye infection | Dry eye | Pre-post surgery

1. Cont Lens Anterior Eye. 2022 Jul 13;101733.doi: 10.1018/j-clae.2022.101733 2. Ophthalmol Ther. 2019 Jun; 8(2): 313-321. doi: 10.1007/s40123-019-0182-x 3.Parassitol Res. 2017; 116(3): 997-1001. doi: 10.1007/sDD436-017-5377-2
4. Ann Palliat Med;9(3):927-939. doi: 10.21037/apm-20-695 5. Eye Vis(Lond). 2019; 6:6. doi: 10.1186/s40662-019-0131-8

Raymed

Raymed Pharmaceuticals Limited
Corporate Office : SCO 859, NAC Manimajra, Chandigarh
E-Mail : info@raymedindia.com, Website : www.raymedindia.com

Scan to learn more