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Al-Shifa Journal of Ophthalmology

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EDITORIAL

Oculoplastics and Glaucoma: Prostaglandin associated Periorbitopathy (PAP)

Tayyab Afghani

Life is full of surprises and so is Medicine. Sildenafil was originally marketed by Pfizer for hypertension and angina but then the "little blue pill" changed the world. Avastin-a drug that was approved by FDA for metastatic colorectal cancer found its way as a miraculous drug for chorioretinal proliferative disorders[1]. Latanoprost a prostaglandin analogue currently used as first line treatment for glaucoma is now also being marketed for lengthening of eyelashes[2].

Prostaglandin analogues associated periorbitopathy (PAP) is a recently described side effect of these antiglaucoma drugs[3]. Earlier reports implicated bimatoprost but lately PAP has been reported as a result of treatment with all topical prostaglandin analogues[4].

The clinical findings associated with PAP are upper eyelid ptosis, deepening of the upper lid sulcus, involution of dermatochalasis, periorbital fat atrophy, mild enophthalmos, inferior scleral show, increased prominence of lid vessels, and tight eyelids. In contrast to previous studies showing ptosis in PAP, relative upper eyelid retraction has recently been reported in most of their patients by Rabinowitz et al[5]. Other known side effects of prostaglandin analogues include lengthening of lashes and increased pigmentation of the iris (See a review article in this issue) and periorbital skin, which could possibly fit under the term PAP as well[6]. Another recent audible sign has been eyelid clicking that was noted intermittently and on each follow-up in each eye when the patient blinked[7].

The prevalence of PAP in Prostaglandin (PG) analogue treated eyes is not known, but anecdotal reports suggest that if we start looking for it, PAP can be identified in almost every patient. A new study by Shah et al[8] designed as a prospective cross-sectional survey using both external photography and external adnexal examination of 157 current, 15 past, and 171 never users of prostaglandin analogues showed that current PG users had a 230-fold increased risk of involution of dermatochalasis and a 249-fold increased risk of incremental loss of lower lid steatoblepharon (herniation of the orbital fat in eyelid). Additionally, upper lid ptosis, levator dysfunction, and lower lid retraction were also highly associated with current prostaglandin use. Levator muscle dysfunction leading to ptosis represent significant side effect that could impact an already compromised visual function in glaucoma patients. Surgery for these malpositions needs to be individualized. Overcorrection of ptosis may result in bleb exposure and the risk of blebitis or endophthalmitis[9].

Pharmacokinetic studies of a single topical administration of 0.1% bimatoprost in animals have shown that eyelid specimens contain more than 2,000 times higher concentrations of bimatoprost compared with aqueous and more than 16 times higher concentrations compared with iris and ciliary body[10]. Thus, there is significant periorbital absorption of prostaglandin analogue medication. Histopathology studies have confirmed that these drugs result in pre-aponeurotic and deep orbital fat atrophy which is most likely the main contributor responsible for the majority of PAP changes[11].

The management of PAP mainly revolves around discontinuation of eye drops, if possible. Otherwise change over from bimatoprost to latanoprost has also shown reversal of PAP to some extent[12]. While PAP implies pathology or a state of disease, others have reported these changes that can be perceived as an improvement in the overall appearance of the periorbital area beyond eyelash enhancement, induced by the topical application of bimatoprost ophthalmic solution, 0.03% (Latisse®, Allergan, Inc., Irvine, CA). This rejuvenating effect and overall improvement in the appearance of the periorbital area resulting from applying Latisse to the upper eyelid margins has been referred to as "chemical blepharoplasty"[13].

Currently, the use of prostaglandins for cosmetic management of facial fat is under investigation. A prostaglandin topical gel is being tested for dissolving submental fat. Similarly, many studies (including the one at Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan) are being performed currently to demonstrate the beneficial fat atrophy effect of prostaglandin analogues to counteract the changes occurring as a result of Thyroid associated orbitopathy. However so far no results have been published.

Thus, Prostaglandin analogues may produce undesirable effects for some while these may be beneficial cosmetically for others. Why not to change the term Prostaglandin-Associated Periorbitopathy (PAP) to Prostaglandin-Associated Periorbital Remodeling (PAPR).

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ORIGINAL ARTICLE

Deciding factors for patients to seek glaucoma specialist care

Yousaf Jamal Mahsood[1], Irfan Ullah[2], Muhammad Usman Arshad[2], Muhammad Zia-Ud-Din Khalil[3], Hamida Muneer[2], Farah Akhtar[2]

Abstract

Aims: To determine what are the factors which influence glaucoma patients to prefer specialized glaucoma clinic.

Study Design: Observational cross-sectional study.

Methods: A total of 400 patients were included in this study for a period of three months from 1st January 2016 to 31st March 2016. To avoid bias, patients were interviewed by a person who was not directly involved in their management. A short interview about the reasons why patients prefer glaucoma clinic was conducted and they were allowed to make a choice from the given options. A second choice was given only if the patient can't decide between two options. At the end they were asked about their satisfaction level from the quality of care they received.

Results: Of total 400 patients, 258 (64.5%) were males and 142 (35.5%) were females. When analyzed for the reasons of preferring the clinic, 145 (36.3%) opted for the option of free medicine availability followed by referral by other ophthalmologists in 125 (31.3%) cases. Among the remaining, 85 (21.3%) were self-referred, 34 (8.5%) preferred because of the competent glaucoma specialist and 05 (1.3%) cases opted better hospital staff. The satisfaction level of the patients was recorded as 330 (82.5%) were satisfied with the care they were receiving while 36 (09%) were not satisfied and 34 (8.5%) had no comments.

Conclusion: Economic status and proper in-time referral by other ophthalmologist are the main deciding factors in glaucoma management. *Al-Shifa Journal of Ophthalmology 2016; 12(2): 67-72.*

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Introduction:

Glaucoma is a diverse group of optic neuropathy with characteristic optic disc appearance and visual field changes.[1] Globally, it is the second leading cause of blindness after cataract but as cataract is a treatable problem with excellent results, this makes glaucoma the most common cause of irreversible blindness worldwide.[2] It is estimated that in 2010 about 4.4 million people were bilaterally blind from glaucoma but with increasing life-expectancy it is expected that this figure may rise to 5.9 million in 2020.[3]

Worldwide, about 3% of population above 40 years and 10% over 80 years of age was affected by glaucoma in 2010.[4,5] In 2010, approximately 60.5 million people were

affected from glaucoma globally and it is expected to rise to 80 million by 2020.[3] Till date the only treatment available for glaucoma is to control the intraocular pressure (IOP) which can be achieved either by medical, laser or surgical treatment.[6] However, not all these options are fit for all and needs to be tailored according to patient and glaucoma surgeon conditions and experience.

Glaucoma is usually treated by general ophthalmologist in our setup but now more and more ophthalmologists are encouraging these patients to be managed in glaucoma clinics. As the specialty of glaucoma is evolving, many ophthalmologists and even patients are now aware of the fact that these patients need an environment which provides best care for not only their eye problem but also psycho-social aspect of the disease process. In this effort, specialized glaucoma clinics have contributed a lot in achieving these goals. Our glaucoma clinic is one of the leading clinics in the country with more than 40,000 registered glaucoma patients who are being managed under keen supervision. We designed this study to look for the deciding factors among the glaucoma patients which influence them to get treatment in specialized glaucoma clinics.

Subjects and Methods:

This study was conducted from 1st January 2016 to 31st March 2016. Four hundred patients were interviewed and each of them was asked about the reason for preferring the specialized glaucoma clinic. To avoid bias, this interview was conducted by a third person who was not involved in the care of the patient. Patients were asked to make one choice of the given options and second choice was given only if patient couldn't decide between two options. In the end, patient satisfaction was asked and recorded on the proforma.

Results:

The data was analyzed by using SPSS software version 17. Means and frequencies were noted for the age and the options selected. Of total 400 patients, 258 (64.5%) were males and 142 (35.5%) were females (Table. I). Patients coming from different regions were in the following order: 294 (73.5%) from Punjab, 76 (19%) from Khyber Pakhtunkhwa, 19 (4.8%) from Federal and 11 (2.8%) from Azad Kashmir (Fig. 1). When analyzed for the reasons of preferring the clinic (Fig. 2), 145 (36.3%) opted for the option of free medicine availability followed by referral by other ophthalmologists in 125 (31.3%) cases. Among the remaining, 85 (21.3%) were self-referred, 34 (8.5%) preferred because of the competent glaucoma specialist and 05 (1.3%) cases opted better hospital staff. When patients gave second choice: Competent glaucoma specialist in 16 (4%), free medicine availability in 10 (2.5%) and self-referral in 9 (2.3%) were the common reasons. The satisfaction level of the patients (Fig. 3) was recorded as 330 (82.5%) were satisfied with the care they were receiving while 36 (09%) were not satisfied and 34 (8.5%) did not comment.

Table No. I: Gender distribution

Gender	Number (%)
Male	258 (64.5)
Female	142(35.5)

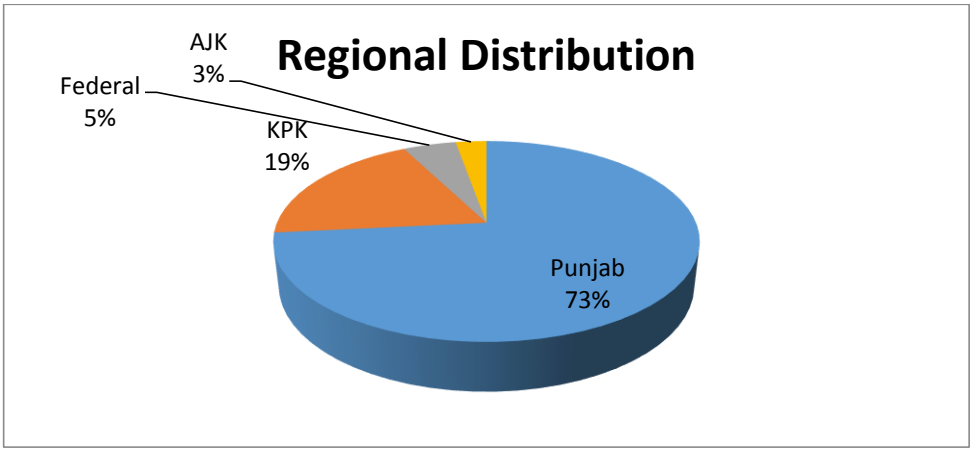

Figure No. 1: Regional distribution of glaucoma patients

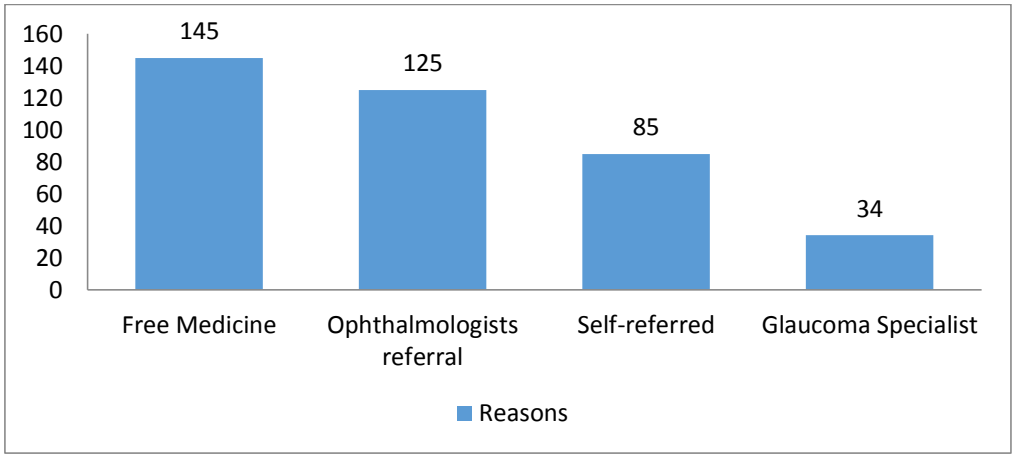

Figure No. 2: Reasons for preferring the glaucoma clinics in number

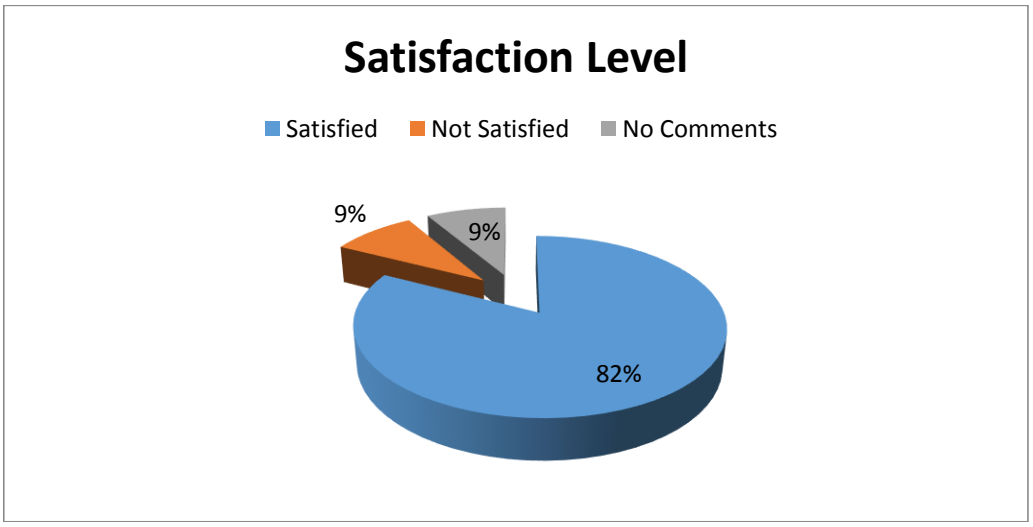

Figure No. 3: Satisfaction level of patients.

Discussion:

Pakistan is a developing country and is making progress in healthcare rapidly for past 2-3 decades. In past few years the patients' have got more concerned and educated about their health which has forced them to seek medical attention as early as possible. Patients have also made up their minds clear about choosing a setup where they can get the best care whether it is public sector, trusts, semi-private or private setups. Pakistan Institute of Community Ophthalmology conducted national survey on blindness and visual impairment and they reported that about 1.49 - 1.59 million of the population is blind and glaucoma is the 3rd leading cause in Pakistan.[7] The prevalence of blindness is 3-4 times more common in low economic regions and among them up to 75% is either treatable or preventable.[2,8]

Glaucoma clinic of Al-Shifa Trust Eye Hospital is dealing with varieties of glaucoma patients who are referred from all over the country to seek the best care. Although throughout the world many glaucoma patients are generally managed by general ophthalmologists but with the increasing burden and education of the patients, now they are being referred to glaucoma specialists or also called glaucoma surgeons and this we have noticed in our glaucoma clinic in recent past. So we moved on to the next step to look what are the deciding factors which bring these patients to the glaucoma specialists' care.

Glaucoma is life-long and therefore for obvious reason it is a costly disease. If it is diagnosed in early stages, then the treatment cost is lower and if it is diagnosed in late stages it adds to further economic burden. The cost burden is grossly divided into two i.e. direct (office visits, diagnostic, treatment) costs and indirect (loss of productivity, caregiver) costs. The results were quite astonishing for us because the most patients 145 (36.3%) preferred glaucoma clinic because of the free medicine availability at our institution. This showed that the affordability of patients to buy medicines and that too for life-long is really a big hurdle in our country to fight this disease. But when we searched the literature and after critical review we found that economic burden of glaucoma is a global issue and is affecting the economy of even the developed countries. And as the more the disease is diagnosed later, the more costly it becomes. Even in United States the direct medical costs of glaucoma treatment is estimated to be $2.9 billion annually and it alone contributes 30-50% of this cost.[9,10] Hence if the cost of medicines can be controlled then patients can get a good financial relief. When talking of indirect costs then it is more in advanced disease because of lack of productivity, accidents and caregiver issues, like in a European study the average healthcare cost for advanced glaucoma was 830 euros versus 2703 euros when given home help.[11] Other problems with poverty are lack of education and awareness, logistic problems and dependence which result in non-compliance of the patients. In glaucoma care, compliance is critical whether it is medical or regular follow-up and because these are adversely affected by poverty it eventually leads to compromise in care.

As more and more understanding of glaucoma is developing, more options of diagnosing and treating glaucoma are emerging. This has created awareness among the ophthalmologists that glaucoma should now be dealt by an ophthalmologist who is specially trained in this sub-specialty and who is aware of the latest developments in this field. So, now quite a number of ophthalmologists believe that these patients should be referred to the glaucoma specialists for best possible care and this is what we found in our study too. We found that 125 (31.3%) cases of our

glaucoma clinic were those who were being referred by other ophthalmologist from different parts of the country. This attitude should be encouraged because it benefits the patients and it will also decrease the economic burden on healthcare by not over or under diagnosing/treating them. To further develop this trend, we think it is the responsibility of glaucoma specialists to arrange activities which can highlight the need of the specialist care. This will allow more and more ophthalmologists to pursue glaucoma as a career and will help to decrease the burden on existing glaucoma specialists. Also we should ask the glaucoma patients to educate their families about the nature of the disease and get glaucoma screening because with the so much advancement in this field still more than 50% of the patients are undiagnosed even in developed countries and most common of them are family members of these patients.[12]

Another interesting fact we came to know from this study was that 85 (21.3%) cases were self-referred. These were those patients who were either under treatment of some other ophthalmologists or had family history. These patients opted glaucoma specialist care because of awareness of the nature of disease and need of specialized care. Unfortunately, due to our compromised socioeconomic conditions and lack of education we don't see these patients in huge numbers. For this reason, it is also our job to educate these patients on community level and run screening programs regularly to detect cases in early stages.

Glaucoma is a chronic irreversible but preventable disease if managed in early stages. Due to lack of patient awareness and proper counseling they think that the treatment is going to improve their vision but this is not the case. So this communication gap and unrealistic hopes of patients result in loss of patient satisfaction and looking for new physicians where their expectations can be met. That is why proper counseling of these patients is necessary to make them realistic in expectations. In this study we found that 330 (82.5%) of our patients were satisfied from the services they were receiving which is really appreciable. All credit goes to the members of our glaucoma clinic who realize the effectiveness of this aspect of the disease and take their time in patient education. What we believe is that while managing glaucoma patients the role of proper counseling is critical.

Conclusion:

From this study we conclude that the main decisive factors for glaucoma patients to seek glaucoma specialist attention are socioeconomic status followed by other ophthalmologists' referral and patients own awareness about the disease. For this we recommend that glaucoma medications should be brought to affordable prize either by special legislations, subsidy by government on these products or involving other non-government officials in helping the poor regions. Encouraging new ophthalmologist to take glaucoma as career field is also needed to decrease the burden. Also other factors like educating and proper counseling of these patients are as important as other factors. There are few limitations in the study like small sample size and level of patient education was not asked and we recommend that further workup on such topics is needed in future.

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ORIGINAL ARTICLE

Efficacy of subtenon anesthesia in manual small incision cataract surgery

Muhammad Zia-ud-Din Khalil[1], Irfan Ullah[2], Yousaf Jamal Mahsood[3], Tariq Shahnam[1], Hina Khan[1], Adnan Aslam Saleem[2]

Abstract

Objective: To evaluate the efficacy of subtenon anesthesia in manual small incision cataract surgery (MSICS).

Subjects and Method: This study was conducted at Ophthalmology Department, Hayatabad Medical Complex, Peshawar. Study design was descriptive case series and the duration of the study was six months in which a total of 194 patients were observed by using 56% efficacy, 95% confidence level and 7% margin of error, under WHO software for sample size. More over non-probability consecutive sampling technique was used for sample collection.

Results: In this study mean age was 59 years with standard deviation ± 5.59. Fifty eight percent patients were male and 42% patients were female. Efficacy of subtenon anesthesia among 194 patients was analyzed as subtenon anesthesia was effective in 40% patients and was not effective in 60% patients.

Conclusion: Sub-tenon's anesthesia is an effective and safe technique for manual small incision cataract surgery. Comparing this technique with peribulbar anesthesia there was no significant difference in terms of pain perception during surgery. *Al-Shifa Journal of Ophthalmology 2016; 12(2): 73-80.*

Introduction:

Subtenon's anesthesia is a technique of local anesthesia in which anesthetic is injected beyond the equator of the globe through a blunt cannula in the subtenon space and was first introduced by Scott Greenbaum in 1992 [1].

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Retrobulbar and peribulbar anesthesia are the most commonly used local anesthesia but carries risk of major complications like retrobulbar hemorrhage and globe perforation[2]. The incidence of orbital and systemic side effects with retrobulbar and peribulbar blocks in large series of studies was 0.8-2.8%[3]. Subtenon anesthesia is as effective as peri or retro bulbar anesthesia[2]. Subtenon anesthesia is reported to be safe and effective method for cataract surgery [4]. With analgesia, globe akinesia can also be achieved and it depends on the amount of the local anesthetic injected, with large amount of the anesthetic agent the akinesia is more as compared to a small amount[6]. Adequate akinesia is achieved in 88%[5] of patients and 56%[6] in another study. Subtenon anesthesia is getting popular among cataract surgeons as it provides good akinesia, better pain relief during surgery and a 50% reduction in posterior capsular rupture/vitreous loss as compared

to topical anesthesia[7]. Subtenon anesthesia is given by ophthalmologist under operating microscope[8].

The Manual Small Incision Cataract Surgery has been conventionally performed under peribulbar, retrobulbar anesthesia. Now there are some reports of the procedure being performed under subtenon and subconjunctival anesthesia too[8]. Due to low cost of consumables and no dependency on machine like Phacoemulsification with almost comparable results, Manual Small Incision Cataract Surgery has been rightly termed "Poor man Phaco". For the last decade Manual Small Incision Cataract Surgery is used more often in our region but most common technique of anesthesia is still peribulbar with only few surgeons shifting to Subtenon anesthesia. There are differences regarding the efficacy of subtenon anesthesia in different studies. I intended to determine the efficacy of Subtenon anesthesia in Manual Small Incision Cataract Surgery so that data can be provided to help to identify and to evolve better protocol of anesthesia for Manual Small Incision Cataract Surgery based on scientific regional evidence. Therefore, this study was designed to determine safety and efficacy of subtenon anesthesia in Manual Small Incision Cataract Surgery at our department.

Subjects and Methods:

This descriptive case series was conducted at Ophthalmology Department, Hayatabad Medical Complex Peshawar, over a period of 6 months. Sample Size was calculated to be 194, using 56% efficacy, 95% confidence level and 7% margin of error, under WHO software for sample size. Sampling technique was non-probability consecutive sampling.

Inclusion Criteria

1. Patient with senile Cataract.
2. Age above 40 and of either gender.

Exclusion Criteria

1. History of allergy to Xylocaine and bupivacaine.
2. History of convulsion.
3. Eyes with age related cataract but having Subluxated or dislocated lens.
4. People who preferred Phacoemulsification or conventional extra capsular cataract surgery.

Operational Definitions

Efficacy:

Adequate globe akinesia ten minutes after the subtenon injection was considered as an efficacious block.

Adequate globe akinesia

Globe movements of zero on scoring were considered as adequate akinesia. 'Akinesia' was scored on a scale designed to measure ocular movements in each quadrant (no movement=score 0, twitching of the globe=1, partial horizontal or vertical movement=2, full movement=3 in each quadrant, minimum score possible=0, maximum score possible=3×4=12)

Data collection procedure

Study was anticipated after having approval of Ethical Committee of our Institute. All patients admitted for cataract surgeries full filling the inclusion criteria was included in the study. An informed consent was taken from them. The preoperative assessment of the patient was done. Subtenon anesthesia was given on the operation table before initiating cataract surgery.

The eye to be operated was painted with povidone iodine. After draping, a lid speculum was applied and two drops of topical proparacaine was instilled. The patient was instructed to look upward and outward. Blunt Westcott's scissor was used to make a small nick in the conjunctiva and the tenon capsule was then skewed through the nick to create a path in the subtenon space. Conjunctival forceps was used to grip the conjunctiva

and a mixture of 2ml 2% xylocaine with adrenaline and 1 ml of bupivacaine was injected in the subtenon space with the help of irrigation aspiration cannula. Globe movements were seen after ten minutes of giving subtenon anesthesia for efficacy of the anesthesia.

Any adverse event (complication) during injection of Subtenon anesthesia and then during Manual Small Incision Cataract Surgery was reported. Senior Surgeons, with more than 10 years of surgical experience of performing Manual Small Incision Cataract Surgery, performed the surgeries.

Data analysis:

All the data was entered on a proforma. Data was analyzed using SPSS version 10. Mean ± SD was calculated for the numerical data like age. Frequency and percentages for the categorical data like gender and efficacy was calculated. Efficacy was stratified among age and gender to see the effect modification. All results were presented in the form of table and graph.

Results:

Age distribution among 194 patients was analyzed as 54(28%) patients were in age range 40-50 years, 66(34%) patients were in age range 51-60 years and 74(38%) patients were in age range 61-70 years. Mean age was 59 years with standard deviation ± 5.59 (Table No 1). Gender distribution among 194 patients was analyzed as 113(58%) patients were male and 81(42%) patients were female (Table No 2).

Movements of Globe among 194 patients were analyzed as 78(40%) patients didn't have globe movement, 19(10%) patients had twitching, 58(30%) patients had had partial movement, 39(20%) patients had full movement (Table No 3). Efficacy of subtenon anesthesia among 194 patients was analyzed as subtenon anesthesia was effective in 78(40%) patients and was not effective in 116(60%) patients (Table No 4). Stratification of efficacy of subtenon anesthesia with age and gender distribution is given in Table No 5, 6.

Table 1. Age Distribution
(n= 194)

AGE	FREQUENCY	PERCENTAGE
40-50 years	54	28%
51-60 years	66	34%
61-70 years	74	38%
Total	194	100%

Mean age was 59 years with standard deviation ± 5.59

Table 2. Gender Distribution
(n= 194)

AGE	FREQUENCY	PERCENTAGE
Male	113	58%
Female	81	42%
Total	194	100%

Table 3. Movements of globe
(n= 194)

MOVEMENTS OF GLOBE	FREQUENCY	PERCENTAGE
No Movement	78	40%
Twitching	19	10%
Partial movements	58	30%
Full movements	39	20%
Total	194	100%

Table 4. Efficacy of subtenon anesthesia
(n= 194)

EFFICACY	FREQUENCY	PERCENTAGE
Effective	78	40%
Not effective	116	60%
Total	194	100%

Table 5. Stratification of efficacy with age

EFFICACY	40-50 YEARS	51-60 YEARS	61-70 YEARS	TOTAL
Effective	22	26	30	78
Not effective	32	40	44	116
Total	54	66	74	194

Chi square test was applied in which P value was 0.003

Table 6. Stratification of efficacy with gender

EFFICACY	MALE	FEMALE	TOTAL
Effective	45	33	78
Not effective	68	48	116
Total	113	81	194

Chi square test was applied in which P value was 0.003

Discussion:

Ophthalmic surgery is one of the most frequent surgical procedures requiring anesthesia in developed countries. A mere decade or so ago most of the cataract surgeries were used to be performed under general anesthesia.[9,10] As the time passed by, new advances and developments in the

cataract surgeries were made. The time of surgery reduced and incision became small and now most of the surgeries are performed under safe and effective means of local anesthesia[11] and hence the unwanted effects that were associated with general anesthesia are no more there with local anesthesia.

There are different techniques of local anesthesia available for cataract surgeries. These are topical and regional. Regional includes needle blocks like retrobulbar, peribulbar, subconjunctival and subtenon blocks. Topical[6,7,12] types are free of serious and life threatening complications, can be used in selected cases[13] however they are lacking akinesia and a possible association between topical anesthesia and endophthalmitis has also been established[14] and also patients undergoing cataract surgery under topical anaesthesia experience more postoperative discomfort than patients receiving sub-Tenon's anaesthesia.[15] Subconjunctival block is pain free[16] provide anesthesia to the anterior segment and is not very popular.[17] Needle blocks like peribulbar and retrobulbar anesthesia provides excellent analgesia and akinesia however they are trickier and serious and life threatening complications can occur with these procedures. Therefore, these techniques require intravenous lines and presence of anesthetist and can be performed under the supervision of senior and experienced ophthalmic surgeon as suggested by joint report of royal college of anesthesia and royal college of ophthalmologists.[18] Subtenon technique is safe, effective and painless and is perfect block.[19,20] There is a statistically significant increased risk of serious complications with sharp needle anesthesia compared with subtenons technique.[21]

An ideal anesthetic technique must be safe from serious complications, effective in terms of providing good akinesia, analgesia and must not elevate intraocular pressure in order to provide optimal surgical conditions. In the above discussion it is already evident that subtenon is safer than peribulbar as for as serious complications are concerned and this study was aimed to compare the efficacy of subtenon with peribulbar anesthesia in terms of analgesia at the time of administration of anesthesia, during surgery and till 90 minutes after administration of anesthesia, akinesia 10 minutes after anesthesia administration and rise in intraocular pressure after anesthesia administration.

Our study shows that mean age was 59 years with standard deviation ± 5.59. Fifty eight percent patients were male and 42% patients were female. Efficacy of subtenon anesthesia among 194 patients was analyzed as subtenon anesthesia was effective in 40% patients and was not effective in 60% patients. Similar results were found in other studies as well.

Adequate akinesia is achieved in 88%[5] of patients and 56%[6] in another study. Subtenon anesthesia is getting popular among cataract surgeons as it provides good akinesia, better pain relief during surgery and a 50% reduction in posterior capsular rupture/vitreous loss as compared to topical anesthesia.[7] Subtenon anesthesia is given by ophthalmologist under operating microscope.[8]

Subtenon anesthesia was more comfortable for the patient at the time of anesthetic administration. They also had good analgesia intraoperatively, but the surgeon had to operate with incomplete akinesia, which some may find discomforting. The surgery was started immediately after administration of anesthesia in subtenon group. As lesser amount of the anesthetic agent was used for subtenon, the chances of adverse effects are also minimized. In a large hospital or in a community eye care setting, the cost would also be less. There

was no difference in positive pressure rise during surgery and postoperative pain between both the techniques of anesthesia. An audit of subtenon and peribulbar anesthesia for cataract surgery in UK demonstrated sub-Tenon's methods to be more effective than the peribulbar technique, with significantly fewer patients experiencing unacceptable levels of pain.[22] It was significantly less uncomfortable on administration than the peribulbar methods and reduced the interval between administration of anesthesia and surgery. On the range of 1-10, pain on administration of anesthetic had a mean of 2.4 for the peribulbar group and 1.4 for the subtenon group. This correlated with results of our study. The subtenon technique appeared to be the safest method of introducing anesthetic fluid into the retrobulbar space without the potential complication of a sharp needle injection. But a single case of globe perforation was reported in a patient who had underwent detachment surgery and had thinned sclera. It is likely that subtenon anesthesia offers a significantly reduced risk of complication such as scleral perforation, retro bulbar hemorrhage, optic nerve injury and injection of anesthetic solution into the subarachnoid space, as no sharp instrument is passed into the orbit. It should, however, be used with caution in patients with compromised and thin sclera.

A randomized study in Denmark comparing retrobulbar, subtenon and topical anesthesia for phacoemulsification found retrobulbar techniques had less discomfort/pain during surgery but patient preferred subtenon or topical anesthesia, as it did not involve the needle prick during anesthesia. [23]

Subtenon anesthesia has been found to be more comfortable for the patient, reliable, long lasting and with deeper anesthesia as compared to topical anesthesia for phacoemulsification patients. It was also more comfortable for the surgeon with better pupillary dilatation. A randomized trial in the UK found the difference between the pain score in the subtenon and topical groups to be highly statistically significant, with subtenon being more pain free, for phacoemulsification patients. Limitations of the study include subjective nature of the visual analog pain scales. But past studies and postoperative visual acuity results indicate that it would not be significant.[24]

The subtenon technique appeared to be the safest method of introducing anesthetic fluid into the retrobulbar space without the potential complication of a sharp needle injection. But a single case of globe perforation was reported in a patient who had underwent detachment surgery and had thinned sclera.[25]

Conclusion:

Sub-tenon's anesthesia is an effective and safe technique for manual small incision cataract surgery. Comparing this technique with peribulbar anesthesia there was no significant difference in terms of pain perception during surgery.

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ORIGINAL ARTICLE

Visual outcome after intraocular foreign body removal through pars plana vitrectomy

Bilal Khan[1], Irfan Aslam Khattak[2], Bilal Bashir[1], Zeeshan Tahir[1], Adnan Alam[1]

Abstract

Objective: To report the visual outcome after intraocular foreign body removal through pars plana vitrectomy in patients presenting to a tertiary care eye hospital.

Subjects and Methods: This cross sectional study was conducted in the Ophthalmology department,Lady Reading Hospital Peshawar from September 2013 to August 2014. After taking approval from the institutional research and ethical committee, patients who were operated for intra ocular foreign body removal through pars plana vitrectomy and were followed till the 10th post-operative day were included in the study. All other patients operated for foreign body removal without a pars plana vitrectomy were excluded from the study. All the results were analyzed by SPSS version 18 and results were represented in the form of graph and charts.

Results: Total 50 patients were included in this study in which males were 47(94%) while females were 3(6%) in number,with a male to female ratio of 15.66:1. All the patients were in the age range of 10 to 70 years having mean age of 38 ± 5 SD. Based on address, etiology and pre-operative symptoms, 35 patients were from Pakistan and 15 referred from Afghanistan, in which bomb blast injury (BBI) was the leading cause followed by injury due to hammering on metal piece, while ocular pain and visual loss were present in all (100 %) cases. Post-op visual improvement was noticed in 30 (60%) cases while it didn't improve in the remaining 20 (40%) cases.

Conclusion: Young to middle aged males in our region mostly suffer from injury of intraocular foreign bodies due to multiple causes including blasts, hammering, RTAs and firearms.If early intervention is carried out, majority of the patients will show improvement, provided the damage from IOFB is not too extensive. *Al-Shifa Journal of Ophthalmology 2016; 12(2): 81-87.*

Introduction

Intraocular foreign body (IOFB) is defined as any foreign material which is organic or inorganic in nature penetrating through the eye. After penetration, either the foreign body is retained inside eye due to its low velocity of impact or it pierces the eye and settles into the orbit, which is then called intra orbital foreign body. It is important from clinical point of view because it threatens the eye and vision, so it is an emergency and its removal is usually necessary. Intra ocular foreign bodies are classified into metallic and non-metallic types while metallic foreign bodies are again classified into magnetic and non-magnetic types, or toxic and non-toxic [1, 2]. Males suffer more from it as compared to females, mainly in young to middle aged group, which is the period of earning.Therefore, along with health, it also affects the profession and

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socioeconomic conditions of the population [3]. The commonest types of intra ocular foreign bodies are iron, aluminum, lead, concrete wood, glass, plastic or rock [4, 5].

IOFBscan result from multiple causes but in war and terrorism affected regions like Pakistan and Afghanistan, the most common cause is bomb blast injuries while other causes include fire arm injuries(FAIs), road traffic accidents (RTAs), hammering on metal piece, self-inflicted etc.[6,7]FB enters the eye through the sclera and cornea and then lodges in any of the ocular structures, which can generate important mechanical effects such as cataract formation, vitreous liquefaction, hemorrhage and retinal breaks and macular injury ultimately the end result is visual loss either partial or complete [8,9]. IOFB is diagnosed by history, examination and radiological investigations. Like all other traumatic cases evaluation begins with a thorough history, including setting of the trauma, time of injury, use of safety glasses, possible materials involved in the injury, and any events or interventions since the time of injury.Any ocular pain and visual loss should also be documented in detail. Then thorough ocular examination should follow, in which visual acuity, pupillary reaction, anterior segment and fundus examination are performed in order to know about the extent of the injury and location of IFB.[13] Ocular imaging is an essential part of evaluating a suspected retained intra ocular foreign body and should be considered in all open-globe traumatic injuries. Simple X rays can show us only the metallic foreign bodies in more detail along with the bones of orbit anatomy but the soft components of the orbit cannot be visualized. B Scan is a valuable tool that can augment the information obtained from other imaging modalities, although it must be used cautiously, as there is a risk of prolapsing the intraocular contents if inappropriate pressure is applied in the setting of an open-globe injury. Additional information about the intraocular status can be obtained simultaneously, including retinal and choroidal detachments, vitreous hemorrhage and posterior exit wounds.Computed tomography has become the modality of choice as it affords a high sensitivity, can accurately localize single or multiple IOFBs regardless of location, requires little patient cooperation, and does not cause globe manipulation. Magnetic resonance imaging can be used in specific cases in which a plastic or wooden intra ocular foreign body is suspected and not detected by other imaging modalities. It should only be used after the presence of metallic intra ocular foreign body has been excluded as the magnetic forces can alter the position of a metallic intra ocular foreign body and cause further injury to the eye [10, 11, 12].

Intervention for retained IOFB has many objectives, which include removal of foreign body from the eye and to prevent the complications from it. If there are increased chances of endophthalmitis, then immediate surgery is performed to remove the foreign body along with the vitrectomy (if it is present in the posterior segment), otherwise, surgery can be deferred for a few days to reduce the risk of intra operative hemorrhage. The wound should be closed as soon as possible because it decreases the chances of endophthalmitis [13,14,25,16]. Based on different types and location of IOFBs, Various procedures are used to remove the impacted intra ocular foreign body and decrease the complications which occur from it. If the IOFB is located in anterior chamber,a paracentesis is performed at 90-180^0 from where IOFB is located and not through the original wound. Viscoelastic should be used to reduce the risk of iatrogenic damage to the corneal endothelium and the lens. If there is cataract formation then lens extraction is done to have good fundus view, then foreign body is removed

followed by implantation of intraocular lens, if adequate capsular support is present[17]. For the removal of ferrous IOFB, intra ocular magnet is used while for nonmagnetic IOFBs, proper forceps may be used. Prophylactic chorioretinectomy is recommended for deep impact and full thickness folds in macula due to IOFB[18, 19,20,21,22].

Rationale of the current study is to know about the visual outcome after IOFB removal through pars plana vitrectomy. This study is important because our region has suffered from terrorism, and social crimes are more as compared to other countries. Moreover, protective measures are not undertaken at work, due to lack of awareness. Furthermore, the results of this study will be compared with international studies and this will show any deficiencies or limitations in the treatment of such patients in our setup.

Subjects and Methods:

This cross sectional study was conducted in Ophthalmology department,Lady Reading Hospital Peshawar from September 2013 to August 2014.

After taking approval from research and ethical committee of the hospital, patients of IOFB received through emergency were included in the study.A detailed history was taken about the cause, duration of injury and symptomology,followed by a clinical examination including visual acuity, pupillary reaction for checking RAPD, fundoscopy for foreign body, condition of macula and retina and B scan or CT scan of orbit in case of non-visualization of the retina due to cataract, hemorrhage etc. Hepatitis B, C and random blood sugar were performed along with arrangement for globe repair in the emergency and patients were discharged to home on treatment after short stay in the ward. Then after 2 weeks, patients were readmitted in the ward for definitive surgery.

After full preparation all the patients were operated through pars plana vitrectomy with removal of foreign body and ancillary treatment was also provided for conditions like retinal detachment etc when needed. Visual outcome of all patients was determined on 1st and 10th post op day. All the results were analyzed by SPSS version 18 and results were represented in the form of graph and charts

Results:

We included a total of 50 patients of IOFB, who were operated through pars plana vitrectomy in Ophthalmology department, Lady Reading Hospital Peshawar, among which majority were males i.e. 47 (94%),while only3(6%) were females(male to female ratio of 15.66:1). All the patients were in the age range of 10 to 70 years having mean age of 38 ± 5 SD. Regional distribution of the patients is shown in Table no 1. Regarding etiology, 30 (60 %) cases were due to Bomb Blast Injury, 14(285) from hammering on metal piece, while RTA and FAI caused 3 (12%) cases each (Fig no 1). Ocular pain and loss of vision partially or completely occurred in all (100 %) cases.

It was noted that 30 (60 %) eyes showed visual improvement and remaining 20 (40 %) did not improve (Fig no 2). 12 (24%) patients got visual improvement from counting fingers at the distance of 3 meters to 6/60 while 10 (20%) were from 6/60 to 6/18 and remaining 8(16%) had visual acuity > 6/18 at the 10 post op day (Fig no 3). Regarding etiology of no visual improvement, the most common cause were corneal opacities and maculopathy which were present in 5(10 %) cases for each, followed by traumatic optic neuropathy 4(8%), recurrent retinal detachment 3 (6%) and endophthalmitis in 2(4%) while the least common cause was an abandoned case. These causes are graphically shown in Fig no 4.

Table no 1: Distribution of patients according to region N=50

Address	No of pts	Percentage
Pakistan	35	70 %
Afghanistan	15	30 %

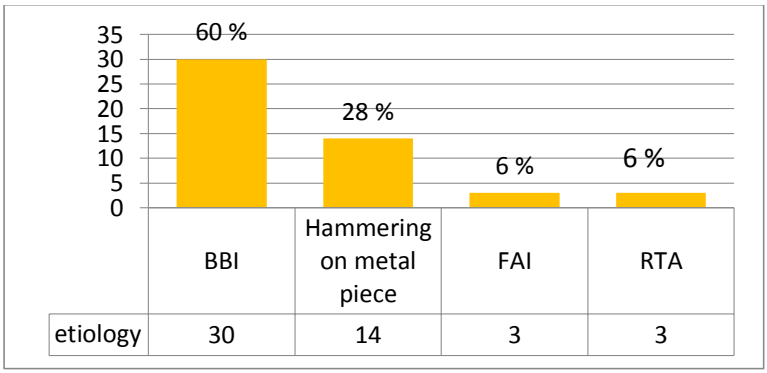

Fig no 1 - Etiology of intra ocular foreign body

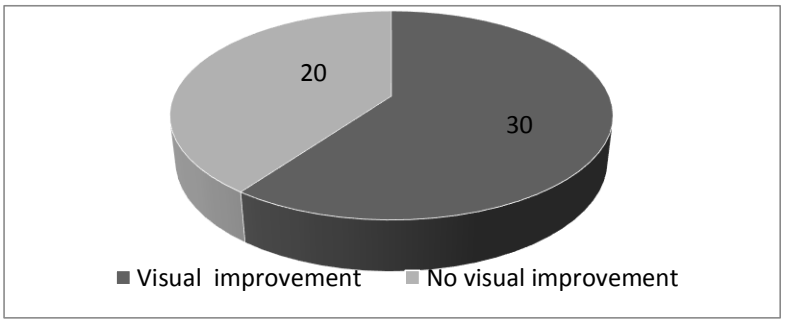

Fig no 2: Total visual outcome N=50

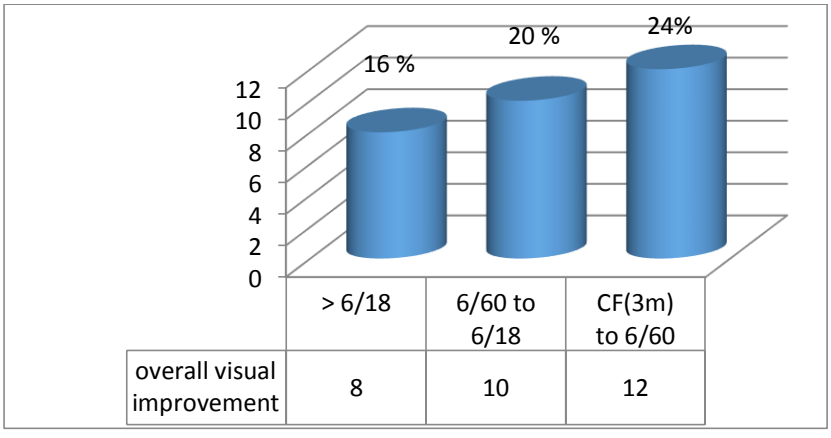

Fig no 3: Post-operative Visual Status N=50

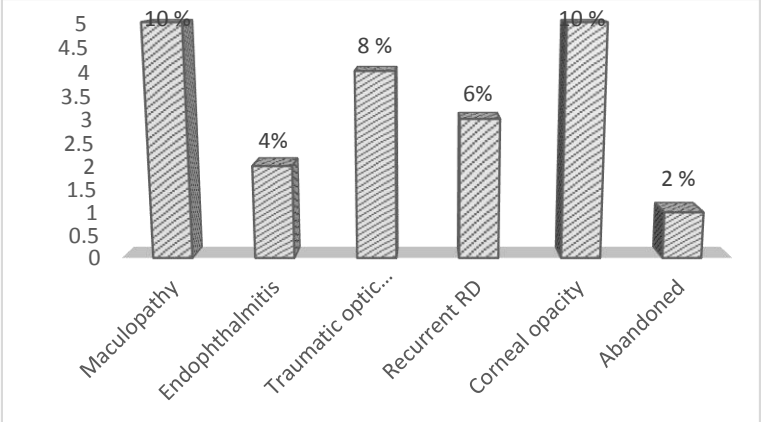

Fig no4: Causes of no visual improvement N= 50

Discussion

Patel SN et al [23]have documented in their study that the patients presented to them with IOFBS were in the age range of 6-69 years, while mean age of the patients was 33±5 SD, which shows resemblance to our study except that the mean age was slightly lower than our results. This is because in our study the major portion of patients were due to bomb blast injuries, fire arm injuries and road traffic accidents which can occur at any age[23].

Baber TF et al [6] and Costa MAN et al [7], Tach AL et al [8] have mentioned in their studies that males were predominantly affected from IOFB, which is obvious from the results of our study as well. Some international studies [15, 18, 19] have documented that females are affected more than males which is in contrast to our study. This is because of our Pathan culture, where females are mostly restricted to their homes due to parda system and males go out to earn for family and that is why they suffer more from IOFBs due to blast injuries, fire arm injuries and road traffic accidents.

Kelly WM et al [12], Chow DR et al [13], Kuhn F et al [14], Zhang Y et al [15] have documented that ocular pain and visual loss was present in all 100 % patients of intra ocular foreign bodies which shows resemblance to our study. When post operatively on 10th post op day final visual outcome was checked, we found that 30 (60 %) showed visual improvement and remaining 20 (40 %) did not improve. In comparison Mahmood H et al [24]reported a visual outcome slightly better than our study, which was 5 (71.42 %) out of 7 patients. Hiader SA et al [26] has determined the good visual outcome in 14 (73.68 %) out of 25 patients which is slightly better than our study.

Similarly, Greven CM [27] has showed better (80 %) results in terms of visual acuity post operatively as compared to us. The main reason for slight difference in post-operative visual improvement is that, in our study majority of the patients hadIOFBs due to blast injuries, road traffic accidents and fire arm injuries, which cause more damage to intra ocular structures like corneal opacities, maculopathy, retinal detachment, multiple entry wounds, secondary iritis and cataract,whichultimately lead to less visual improvement despite timely surgical intervention.

Conclusion:

In the regions suffering fromwar, social crimes, poverty and low education status, young to middle age males mostly suffer from injurieswith intraocular foreign bodies. Ocular pain and visual loss occur in almost all cases. If treated early, salvageable injured eyes of the patients with IOFBs show visual

improvement,while in caseswith more extensive trauma, visual outcome is poor.

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ORIGINAL ARTICLE

Comparative study of epi-off and epi-on Collagen Cross-Linkage in keratoconus patients

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ABSTRACT

Purpose: To evaluateepi-off and epi-on(trans-epi) collagen cross-linkage procedures in keratoconus patients.

Subjects and Methods: Eighty patients (102 eyes) with keratoconus were included in this prospective study from May 2014 to April 2015 in Amanat Eye Hospital,Rawalpindi.There were forty patients (51 eyes) with CXL epi-on procedure (Group I) and forty patients (51 eyes) with CXL epi-off procedure (Group II). Epi-off cxl procedure comprised isotonic riboflavin solution 0.1% with 20% dextran, whereas epi-on cxl procedure utilized hypotonic 0.25% riboflavin solution. The cornea was exposed to UVA 370 nm light for 3 minutes at an irradiance of 30mW/cm^2. After cxl procedure patients were then followed up at baseline, 3 months and 12 months respectively.

Results: In Group I, the mean age of patients was 21.83 years± 3.83 SD. There were 27 (67.5%) male and 13 (32.5%) female patients. The right eye was affected in 15 (37.5%) patients and left eye was affected in 14 (35%) patients. In Group II, the mean age of patients was 20.75years ± 4SD. There were 22 (55%) male and 18 (45%) female patients. The right eye was affected in 17 (42.5%) patients, left eye was affected in 12 (30%) patients.In both treatment groups there were insignificant difference in terms of improvement in best-corrected visual acuity and topographic parameters.

Conclusion: This study showed that there were insignificant differences between both cxl procedures. The added advantage of patient comfort, reduced post-operative infection and early visual recovery gave epi-on cxl the best treatment of choice. *Al-Shifa Journal of Ophthalmology 2016; 12(2): 88-96. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

Introduction:

Despite of extensive medical research, we could not still find out the etiology of keratoconus, although different researches prompt medical interventions to halt progression of keratoconus.[1,2]

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In keratoconus, there is weakness of collagen cross linkages in anterior stromal lamellae. The only way a procedure that strengthens collagen cross-linkages and stiffens cornea, thus halting progression of the disease is Collagen cross linkage (CXL, C3R). [3, 4]

In collagen cross-linkage riboflavin acts as dual function, photosensitizer activating the physical collagen cross-linking and as an absorbent of the UVA irradiation, averting damage to profound visual structures.[5, 6] Riboflavin with proper corneal stromal immersion plays an important role in collagen cross linkage procedure. In the absence of riboflavin, the ultraviolet radiations might disrupt

collagen fibers as opposed to facilitate cross-linking.[7]

Two unique procedures are adopted for intervention of this disease. Both methods, conventional cross-linkage (CXL, epi-off CXL) and trans-epithelial cross-linkage (epi-on CXL), used ultraviolet-A light and riboflavin drops. Epi-off cxl involved epithelium removal. Long-term clinical reports showed that this method halts the advancement of keratoconus [8–11] and to some extent improves refractive and topographic parameters.[12]

Recently introduced technique epi-on cxl that involves intact epithelium targets to reduce postoperative pain, chances of infections and early visual recovery.[13] Literature reports that confirm the effectiveness of both techniques.[14–17] These works found the procedures to be safe to the endothelium.[18, 19] However, further studies showed that the impact of epi-on irradiation was confined to superficial level limiting anterior stroma and that riboflavin penetration was not homogeneous with the epithelium in situ utilizing the same UVA power, concerning standard conventional treatment 3mW/cm^2.[20,21] In epi-off cxl procedure, isotonic riboflavin solution 0.1% with 20%dextran used in contrast with 0.25% hypotonic riboflavin solution.

The objective of this study was done to analyze the efficacy of the treatments on the basis of two homogeneous groups, visual outcomes and topographic parameters of patients with keratoconus.

Subjects and Methods:

Eighty patients (102 eyes) from May 2014 to April 2015 presented in outdoor patient department (OPD) of Amanat Eye Hospital, Rawalpindi were studied prospectively with age group 14 -31years. The study was conducted after approval of the ethical committee of the institution. Fully informed, understood and voluntary consent was obtained. Patients were informed regarding the benefits and hazards of the procedure. Confidentiality of the data was ensured.

There were forty patients (51 eyes) with epi-on cxl procedure (Group I) and forty patients (51 eyes) with epi-off cxl procedure (Group II). The inclusion criteria included 14-31 years of age, history of vigorous eye rubbing, intolerant to contact lenses, patients with complaint of unstable refraction, vision deterioration.Cases were classified on the basis of K-readings into mild<48D, moderate 48-54D and advanced keratoconus >54D.The exclusion criteria included systemic diseases affecting ocular conditions and corneal scarring.

Pre and post-operative testing included uncorrected distance visual acuity (UDVA), best-corrected distance visual acuity (CDVA), slit-lamp examination, corneal topography (Oculus Pentacam). UDVA and CDVA were recorded using Log MAR Early Treatment Diabetic Retinopathy Study. Pentacam topography evaluates corneal astigmatism and pachymetry.Pre-op and post op-data were recorded and clinical tests were repeated at baseline, three and 12 months following epi-on and epi-off cxl procedure.

Epi-off CXL technique involved epithelial debridement performed under topical anesthetic drops followed by instillation of isotonic riboflavin drops 0.1% in 20% dextran solution topically for 30 minutes. The cornea was exposed to UVA 370 nm light for 3 minutes at an irradiance of 30mW/cm^2, bandaged contact lenses were applied for 5 days after the procedure and then followed up at baseline,3 months and 12 months respectively.

Epi-on cxl group was treated using following technique. Firstly, cornea were exposed with topical anesthetic drops followed by instillation of hypotonic

riboflavin drops 0.25% solution for one hour without epithelial removal, then cornea was subjected to UVA radiation for 3 minutes with a wavelength of 370 nm at the intensity of 30mW/cm^2 within a circular diameter of 9 mm which increases collagen cross-linkages and stiffens the cornea. After cxl procedure, patients were then followed up at baseline, 3 months and 12 months respectively.

Results:

Eighty patients (102 eyes) presented with mean age (in years) ± SD as 21.29 ± 4.07. There were forty patients (51 eyes) with epi-on cxl procedure (Group I) and forty patients (51 eyes) with cxl epi-off procedure (Group II). In Group I, the mean age of patients (in years) ± SD was 21.83 ± 3.83 (range 14 to 31).

There were 27 (67.5%) male and 13 (32.5%) female patients. Right eye was affected in 15 (37.5%) patients, left eye was affected in 14 (35%) patients while there were 11 (27.5%) patients with both their eyes affected. In Group II, the mean age of patients (in years) ± SD was 20.75 ± 4.27(range 14-31).

There were 22 (55%) male and 18 (45%) female patients. The right eye was affected in 17 (42.5%) patients, left eye was affected in 12 (30%) patients while there were 11 (27.5%) patients with both their eyes affected.

The Independent Sample t-test reported no significant statistical difference between epi-on cxl and epi-off cxl procedure in terms of improvement in un-corrected visual acuity after three months, twelve months and between three to twelve months of treatment, with p values > 0.05.

There was also statistically insignificant difference among group 1(cxl epi-on) and group 2 (cxl epi-off) procedure on the basis of improvement in best corrected visual acuity with p-value > 0.05 (Table 1).

After stratification of keratoconus as mild, moderate and severe, Independent Samples t-test revealed that there were statistically insignificant difference between group 1(CXL epi-on) and group 2 (CXL epi-off) procedure in terms of improvement in astigmatism after three months, twelve months and between three to twelve months of treatment among all three grades of keratoconus, with p values > 0.05 (Table 2).

Table 1:Un-corrected and best-corrected visual acuity after epi-on and epi-off CXL procedure

Visual Acuity	Type of Procedure	N	Improv-ed (n)	Stable (n)	Worsen-ed (n)	Mean Improvem-ent ± SD (in Log MAR units)	t (df)	p-value
UCVA after 3 months of treatment	On	51	11	40	0	0.05 ± 0.11	- 0.67 (100)	0.5
	Off	51	16	28	7	0.03 ± 0.20		
UCVA after 12 months of treatment	On	51	17	31	3	0.09 ± 0.19	- 0.84 (100)	0.4
	Off	51	16	27	8	0.06 ± 0.19		
UCVA between 3 to 12 months of treatment	On	51	10	35	6	0.04 ± 0.18	- 0.29 (100)	0.7
	Off	51	8	38	5	0.03 ± 0.15		
BCVA after 3 months of treatment	On	51	8	43	0	0.04 ± 0.11	0.73 (100)	0.47
	Off	51	7	41	3	0.03 ± 0.11		
BCVA after 12 months of treatment	On	51	15	35	1	0.09 ± 0.21	- 1.29 (100)	0.19
	Off	51	11	36	4	0.04 ± 0.20		
BCVA between 3 to 12 months of treatment	On	51	11	38	2	0.06 ± 0.16	- 1.08 (100)	0.28
	Off	51	7	40	4	0.02 ± 0.19		

Table 2:Astigmatism results on the basis of grades of keratoconus after epi-on and epi-off CXL procedure

Grades	Astigmatism	Type of Procedure	**N**	**Improved (n)**	**Stable (n)**	**Worse (n)**	**Mean Improvement ± SD**	**T (df)**	**p-value**
Mild (<48 D)	Astigmatism after 3 months of treatment	On	8	3	1	4	0.13 ± 0.86	-1.00 (34)	0.32
		Off	28	7	10	11	- 0.15 ± 0.64		
	Astigmatism after 12 months of treatment	On	8	3	2	3	0.15 ± 0.58	-1.49 (34)	0.15
		Off	28	6	9	13	- 0.21 ± 0.63		
	Astigmatism between 3 to 12 months of treatment	On	8	3	3	2	0.03 ± 0.49	-0.62 (34)	0.54
		Off	28	8	13	7	- 0.06 ± 0.35		
Moderate (48 – 54 D)	Astigmatism after 3 months of treatment	On	28	9	10	9	0.04 ± 0.59	0.98 (46)	0.33
		Off	20	9	4	7	0.26 ± 0.99		
	Astigmatism after 12 months of treatment	On	28	12	7	9	0.21 ± 0.99	0.25 (46)	0.81
		Off	20	9	4	7	0.27 ± 0.84		
	Astigmatism between 3 to 12 months of treatment	On	28	12	5	11	0.17 ± 0.82	0.67 (46)	0.50
		Off	20	9	1	10	0.01 ± 0.76		
Severe (>54 D)	Astigmatism after 3 months of treatment	On	15	8	0	7	0.20 ± 1.31	0.49 (16)	0.63
		Off	3	3	0	0	0.58 ± 0.38		
	Astigmatism after 12 months of treatment	On	15	8	1	6	0.92 ± 2.90	0.24 (16)	0.81
		Off	3	2	0	1	0.50 ± 1.39		
	Astigmatism between 3 to 12 months of treatment	On	15	7	3	5	0.72 ± 2.65	0.50 (16)	0.62
		Off	3	1	1	1	- 0.08 ± 1.13		

Table 3: The descriptive statistics of keratometric readings and astigmatism (in Diopters) after epi-on and epi-off cxl procedure

K Readings and Astigmatism (in Diopters)	Type of Procedure	N	Mean ± SD	Minimum	Maximum	Range
Pre-operative K Reading of Flat Meridian	On	51	46.55 ± 3.55	38.25	56.75	18.50
	Off	51	44.26 ± 2.06	41.00	51.75	10.75
K Reading of Flat Meridian after 3 Months of Treatment	On	51	46.74 ± 3.53	38.25	56.75	18.50
	Off	51	44.40 ± 2.02	41.00	51.50	10.50
Keratometric Reading of Flat Meridian after 12 Months of Treatment	On	51	46.80 ± 3.62	38.50	57.00	18.50
	Off	51	44.44 ± 1.99	41.25	52.00	10.75
Pre-operative Keratometric Reading of Steep Meridian	On	51	52.06 ± 4.56	42.00	63.00	21.00
	Off	51	48.24 ± 3.29	42.00	60.75	18.75
Keratometric Reading of Steep Meridian after 3 Months of Treatment	On	51	52.15 ± 4.63	42.50	63.50	21.00
	Off	51	48.34 ± 2.95	43.50	59.75	16.25
Keratometric Reading of Steep Meridian after 12 Months of Treatment	On	51	51.91 ± 4.63	42.50	63.25	20.75
	Off	51	48.40 ± 2.86	43.50	57.75	14.25
Pre-Operative Topographic Astigmatism	On	51	5.51 ± 2.58	1.25	12.50	11.25
	Off	51	3.98 ± 2.30	0.25	10.50	10.25
Topographic Astigmatism after 3 months of Treatment	On	51	5.41 ± 2.65	1.25	12.25	11.00
	Off	51	3.94 ± 2.00	0.50	9.50	9.00
Topographic Astigmatism after 12 months of Treatment	On	51	5.10 ± 2.42	0.75	12.00	11.25
	Off	51	3.96 ± 1.89	0.75	8.75	8.00

Discussion:

This study analyzed comparison of cxl procedure in two homogenous groups for treating keratoconus. Reported study of 26 eyes treated by epi-on cxl[22]showed insignificant increase in UDVA and CDVA in the first 3 months.[23]However this study showed no statistically significant difference between both cxl procedures on the basis of uncorrected visual improvement after three months, twelve months and between three to twelve months of treatment, as uncorrected visual acuity and best corrected visual acuity improves to 10(19.6%)and 11(21.5%)in epi- on technique (51eyes), whereas in case of epi-off cxl(51eyes) uncorrected and best corrected visual acuity improves to 8(15.6%) and 7(13.7%) respectively.

In 2003 another study reported on 22 patients presented with advanced keratoconus underwent collagen cross-

linking, followed by 2 to 4 years. There was improved visual acuity in 15 of 22 eyes and flattening of K-max by 2 diopters in 16 of 22 eyes with no progression of the disease.[24]However this one-year study followed up showed BCVA improved to 11 of 51 eyes in epi-on and 07 of 51 eyes in case of epi-off procedure with visual stability, 38 in epi-on and 40 in epi-off technique and worsening of the vision seen in 02 eyes with epi-on and 04 in epi-off cxl. The person who lost 2snellens line of BCVA was 18years old female who at baseline had UDVA of 20/60, a BCDVA of 20/30 and maximum K-value of 56.7D. After 12 months she was noted to had further deterioration of vision, UCDVA was 20/200,BCDVA was 20/80 and the maximum K value had increased slightly to 57.3D.

Magli et al study includes both cxl procedures, patients presented with homogeneous anatomical and topographic parameters with the stability of vision.[25]In this study, no patients needed re-treatment and both groups showed statistical insignificant improvement in visual acuity and topographic parameter with the p-value>0.05.

Wollensek et al[26]reported regression with reduction of maximum K readings by 2.01D after epithelial removal in 70% of eyes with mean follow-ups of 23.2 months. In this study we analyzed no change in mean keratometric readings in case of steep and flat meridian. However, topographic astigmatism improved in epi-on procedure than epi-off cxl procedure.
Recent studies by Bottos et al. reported that main barrier for cross-linking is epithelium.[27] The adversed event reported after cross-linking with less than 400 microns of corneal thickness may results in corneal edema due to ultraviolet effects to the corneal endothelium.[28]Therefore epi-on method (trans-epi) is safer on thin corneas with high K-readings. The main advantage of trans-epi cxl procedure is patient comfort, less post-operative pain and early visual recovery.

Several complications were reported in the literature, especially after epi-off cxl procedure such as corneal edema and endothelial damage.[29-31]In this study we observed significantly greater postoperative pain in the epi-off cxl group compared to epi-on cxl group because of epithelium debridement.

Despite an intensive search of literature, the current study is the first that describes and compares the results of cxl techniques performed on both groups of patients reporting effectiveness of epi-off and epi-on cxl techniques. However, limitations of my study were limited treated eyes and shorter follow-ups (12 months).

Conclusion:

One year followed-up study showed that in terms of visual outcomes and topographic parameters, there were statistically insignificant differences between both cxl procedures. However, the added advantage of patient comfort, reduced post-operative infection and early visual recovery gave epi-on cxl, the best treatment of choice.

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ORIGINAL ARTICLE

Clinical profile of keratoconus patients at a tertiary care eye hospital

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ABSTRACT

Objective: To describe clinical profile of keratoconus patients presenting at a tertiary care eye hospital.

Study Design: Cross sectional study.

Place and duration of study: Cornea clinic of Al-Shifa Trust Eye Hospital Rawalpindi from (15th Sep 2012 to 30th Nov and 1st Jan to 15th Apr 2013)

Subjects and Methods: One hundred patients were recruited from outpatient and cornea department of Al-Shifa Trust Eye Hospital using consecutive (non-probability) sampling technique. Detailed history, visual acuity and subjective refraction were done. Ophthalmic clinical examination using TOPCON- 3 F slit lamp and 90 D fundoscopy were performed under supervision while corneal thickness by TOPCON SP-2000P and corneal topography on HAAG-STREIT-CTK 922 were done by trained technicians. Clinical examination and findings on corneal topography (automated) and pachymetry were noted on proforma for data analysis.

Results: Mean age of the participants was 19.79 years (SD ±8.55), with an age range of 6 to 70 years. 63% were males while 37% were females. Mean spherical and cylindrical refractive error were -3.31DS (SD±3.80) and -3.02DC (SD±2.62) respectively. Mean of maximum keratometry reading (Kmax) was 59.41D (SD ± 12.5). Prominent corneal nerves was the commonest sign (96.1%) while 21.1 % patients belonged to Rawalpindi/Islamabad.

Conclusion: Our study revealed that keratoconus was more common in younger age group usually below 25 yrs, with higher prevalence in male. Prominent corneal nerves was the most consistent sign in these patients. Due to difference in socoeconmic status, lack of awareness and access to healthcare system; clinical profile of our keratoconus was not in complete agreement with international studies. *Al-Shifa Journal of Ophthalmology 2016; 12(2): 97-102.*

Introduction:

Keratoconus is a bilateral, asymmetrical non inflammatory ectatic corneal disease which causes progressive stromal thinning and weakening leads to corneal surface deformation[1.] Keratoconus affects all layers of corneabut corneal stromal thinning is the key feature. Various clinical signs includes Conical projection, Rizzuti's Sign, Munson sign, Vogt striae, Fleischer ring [2-6] and corneal scarring. Keratoconus is graded into mild, moderate, and advanced types depending on disease severity and its signs. Prevalence of keratoconus has been reported differently in different races[5].Keratoconus is more common in males[11,12]. Keratoconus usually presents around puberty and progresses more rapidly in younger patients[8.]

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Various risk factors have been proposed as a cause of keratoconus including eye rubbing, atopy, allergic conditions, contact lens use [10-12] and corneal dystrophies. Diagnosis is usually made on clinical examination and subclinical cases are detected by corneal topography[7]. Keratoconus severity percentage is called KCI%. Value >zero is assumed to be indicative of keratoconus. There are various imaging modalities used for the detection of keratoconus. They include Keratometry, Pachymetry Corneal cross linking (CXL) Intrastromal corneal ring segments (INTACS) Lamellar keratoplasty, deep anterior lamellar keratoplasty (DLAK).[7,8] and Penetrating keratoplasty (PKP)[9]. Patients may require contact lenses after grafting to improve vision[10].

Increasing prevalence of keratoconus in Saudi Arabia, New Zealand and Indian subcontinent[8] has been reported. Results of international studies cannot be generalized because of difference in socioeconomic status, lack of awareness and access to healthcare system. Unfortunately, there is limited research in this context in a developing country like Pakistan, hence the current research aims to identify the patients presenting at Al-Shifa Trust Eye Hospital, Rawalpindi which would help in better understanding of the pattern of disease presentation at a tertiary care hospital of Pakistan and to know if there is a difference in presentation of disease between local or international set ups.

Subjects and Methods:

It was a Cross sectional study carried out in outpatient department and cornea clinic of Al-Shifa Trust Eye Hospital Rawalpindi in duration of six months. Sample size was calculated on the basis of World Health Organization calculator with Level of confidence 95%, Margin of error 5%, P value 14.8% and D value 7%. 100 samples were dealt by non-probability (consecutive) sampling technique. Patients of all ages and any gender with keratoconus diagnosed on topography and clinically were included while patients with previous history of surgery, trauma, glaucoma were excluded from the study.
After approval from hospital ethical committee and informed consent from all patients, detailed history and visual acuity of these patients were measured at a distance of 6 meters by Snellen chart. Then this was converted to LogMAR and subjective refraction was done.

Patients fulfilling the inclusion criteria were subjected to ophthalmic clinical examination using TOPCON- 3 F slit lamp and 90 D fundoscopy performed personally under supervision while corneal thickness by TOPCON SP-2000P and corneal topography on HAAG-STREIT-CTK 922 was then done by trained technicians in this particular field. Patient's history, clinical examination and findings on corneal topography (automated) were then noted and subjected for analysis.

Data was analyzed using SPSS version17. Numerical variables like age, visual acuity, refraction, pachymetry, topographic values will be expressed as mean and standard deviation. Descriptive variables like gender, adress, location of cone, clinical profile will be expressed as frequency and percentages. Demographic and clinical presentations would be represented using bar graphs and pie charts

Results:

One hundered patients (180 eyes) were recruited consecutively from the cornea clinic over period of 6 months from 10th Sep 2012 to 10th Mar 2013.Ninety two (92%) patients had bilateral presentation while 8(8%) patients had unilateral presentation. 12 eyes of patients with bilateral keratoconus were not included as they had undergone surgery. The mean age of the participants was 19.79 years (SD ±8.55), with an age range of 6 to 70 years.

Sixty five(65%) patients belonged to Age group 0f 16-25years and 24(24%) between 5-15years. Among the participants, 63(63%) were males while 37(37%) were females. Mean visual acuity by Logmar was 0.61(SD± 0.54579) (Table 1). BCVA log MAR: Mean value was 0.49 (SD ± o.473) (Table 1). Mean refractive error was - 3.31DS (SD ±3.80) and -3.02DC (SD ± 2.62) (Table 1). Mean corneal thickness was 0.4181mm (SD± 0.151) (Table 1). Mean Kmax was 59.4D (SD± 12.5) (Table 1). Steep meridian value was 86.412(SD ± 39.68578) (Table 1). Prominent Corneal nerves was the most common presenting sign present in 173 (96.1%) patients. Rizzuti's sign was present in 95(52.8%) of the patients while corneal hydrops was the least common sign noted in only 5(2.8%) of participants. (Table 2). One hundred and thirty one(72.8%) patients had inferiorly located cone on topography while superior 23(12.8%) and central 21(11.7%) locations were less common (Table 3). 38(21.1%) patient belonged to Rawalpindi/Islamabad.

TABLE 1: DESCRIPTIVE VARIABLES

VARIABLES	N	Mean	Std. Deviation
VA logMAR	180	.6100	.54579
BCVA logMAR	180	.4917	.47330
Spherical error(DS)	180	-3.3112	3.80835
Cylidrical error(DC)	180	-3.0289	2.62510
Cyl axis(degree)	180	88.0333	65.92877
Pachymetry(mm)	180	.4181	.15190
Kmax(Diopter)	180	59.4173	12.50055
Steep meridian(degree)	160	86.4125	39.68578

TABLE 2: CLINICAL SIGNS OF PARTICIPANTS

Clinical signs	Present (frequency)	Percentage	Not Present (frequency)	Percentage
Vogt's striae	42	23.3	138	76.7
Rizzuti's sign	95	52.8	85	47.2
Corneal nerves	173	96.1	7	3.9
Corneal scarring	22	12.2	158	87.8
Corneal hydrops	5	2.8	175	97.2
Fleshier's ring	71	39.4	109	60.6

TABLE 3: CONE LOCATION

Location	Frequency	Percent
CENTRAL	21	11.7
INFERIOR	131	72.8
NOT POSSIBLE	3	1.7
SUPERIOR	23	12.8
Total	**180**	**100.0**

Discussion:

This study showed that keratoconus was predominantly a bilateral condition which was prevalent in younger age groups usually below 25years of age. There was male predominance in our study. In present study 38(21.1%) patient belong to Rawalpindi/Islamabad. Mean values of visual acuity and Best corrected visual acuity (BCVA) by LogMAR was 0.61(SD± 0.54579) and 0.49 (SD ± o.473) respectively. Mean refractive error was -3.31DS (SD ±3.80) and -3.02 DC (SD ± 2.62). Mean corneal thickness and Kmax were 0.4181mm (SD± 0.151) 59.4D (SD± 12.5) respectively.

In a study conducted earlier mean age of patients was reported to be 29.5 ± 9.40 years[7] while median age was 24 years (15-36 years)[29] and this is comparable to our study. In a recent study, mean age in Asian subjects (27.6 ± 11.6 years)[25] was more than what we found in our study that was 19.79 years (SD ±8.55).This difference could be due difference in ethnicity as the previous study[7] included patients mostly of Chinese ethnicity. This difference of age of presentation in Pakistani population has also been reported in other local studies in which mean age of presentation was 17.41years with 94.11% age group between 8-29years[29], which is comparable to this present study in which mean age of presentation was between 5-25 years(89%).

Keratoconus has been reported to present at an earlier age in males than in females [23]. This relation of gender with age was not studied in our study. Male predominance has been reported in many international[13,14,15,16,29,26] and a local studywith 70.58%[29], and (87%)[17] and this predominance is also found in our study. Others report there was female predominance[18,19]. Association of Vernal keratoconjunctivitis (VKC) and keratoconus is reported previously[23]. Male predominance may be due to more VKC in males.

Clinically evident keratoconus was present in both eyes of 65 patients (56.0%) and unilateral keratoconus in 5 patients (4.3%)[7].In our study 92 patients had bilateral presentation of disease This was similar to another study in which unilateral keratoconus was reported to be 4.3%[7] and 4%[15].

In our study prominent corneal nerves was the most common sign present in 173(96.1%) of patients while in another study conical protrusion was the commonest sign (75.3%)[7].20% of patients developing corneal scarring[24] we had only 12.2 % patients with scarring[25]. This may be due to less severity of disease presentation in our population or an early

age of presentation and detection of disease. This result was very close (13%) to the study conducted in NewZealand[30].

In a study done previously the mean spherical error was (-3.64 ±4.30) and mean cylindrical error was (-4.01 ± 2.44)[27]. In our study mean refractive error was -3.31DS (SD ±3.80) and -3.02DC (SD ± 2.62). In our study cylindrical error was less while spherical errors were comparable to the mentioned study. This may be again due to an early age of presentation in our study population.Mean values of visual acuity and BCVA by Logmar were 0.61(SD± 0.54579) and 0.49 (SD ± o.473) respectively in our study compared to another study in which unaided VA (0.92 ±0.40), best corrected visual acuity (0.19 ± 0.25)[27]. Best corrected VA was better in our study. Millodot and Owens observed that the minimum pachymetric value was 452.6±60.9 μm in keratoconus eyes versus 546±23.7 in normal eyes[13]. In our study corneal thickness was 418 μm (SD± 0.151).This showed that in our population keratoconus eyes were thinner. This difference may be due to racial difference, association with VKC or other diseases. Decreased corneal thickness means more advanced KC but with more advanced KC visual acuity should also be less. This relationship of corneal thickness with visual acuity was not included in our study and needs further research.

In our study 131(72.8%) patients had inferiorly located cone on topography while superior 23(12.8%) and central 21(11.7%) locations were less common. This was in concordance with previously reported value of inferior cone location in 80% of keratoconus cases and central cone location in 15% of keratoconus cases[8].

In our patients keratoconus presented at an early age with corneal nerves as prominent clinical sign and decreased corneal thickness compared to western population. Gender distribution and bilaterality of disease and location of cone on topography is similar to that of western population.

Conclusion:

Our study revealed that there is male predominance with more prevalence of keratoconus in 2nd and 3rd decade of life. Prominent corneal nerves are most important clinical sign. In our patients, keratoconus presented at an early age with corneal nerves as prominent clinical sign and decreased corneal thickness compared to western population. Gender distribution and bilaterality of disease and location of cone on topography is similar to that of western population. Majority of patients belong to catchment area of hospital which may be due to limited access and this warrants further study. Also associated factors or ocular and systemic diseases association was not recorded and this should be probed in future studies.

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ORIGINAL ARTICLE

Frequency of ocular co-morbidity in patients with age related cataract

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ABSTRACT

Objective: To determine frequency of ocular co-morbidity in patients with age related cataract.

Material and Methods: This study was conducted at Eye Department, Lady Reading Hospital, Peshawar. It was a descriptive (cross sectional) study and the duration of the study was 6 months. The sample size (n = 156) was calculated by using WHO sample size calculator, where confidence level=95, absolute precision= 4.5 %, population proportion (P) of diabetic retinopathy in patients with age related cataract = 9 %. More over non probability consecutive sampling technique was used for sample collection.

Results: In this study mean age was 60 years with standard deviation ± 2.57. Fifty three percent patients were male and 47% patients were female. The incidence of ocular co-morbidity was 42% patients in which refractive error found in 43% patients, ARMD found in 14% patients, glaucoma found in 9% patients, diabetic retinopathy found in 7% patients.

Conclusion: Ocular comorbidities are highly prevalent among persons undergoing cataract surgery in this rural setting, and their presence is significantly associated with poorer visual outcomes. The fact that the great majority of comorbidities encountered in this program are treatable suggests that strategies to reduce their impact can be successful.*Al-Shifa Journal of Ophthalmology 2016; 12(2): 103-109.*

Introduction:

Visual impairment is a global health problem.[1] It is estimated that 37 million of the world population is blind and 124 million have severe visual impairment.[1] According to previous studies cataract is responsible for 50% of blindness worldwide.[2,]

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The number of people blind from cataract is expected to rise due to the increase in life expectancy.[3] Increasing age is also known to influence the visual acuity achieved after cataract surgery.[4]

Surgery is currently the only treatment option once the lens has opacified.[5] The indication for surgery is based on whether the patient's reduced visual function interferes with their quality of life.[6] There are three main forms of cataract extraction surgery: Extracapsular (ECCE), phacoemulsification (Phaco) and manual small incision (MSICS).[6] Each involves mechanical removal of the cataractous lens with subsequent Intraocular lens implantation.[6]

Cataract surgery yields excellent visual outcomes for the majority (71%) of patients.[7] The outcome of cataract surgery

is dependent on a complex interplay of systemic, ocular, operative and postoperative factors. The greatest influence on visual outcome is due to ocular comorbidity resulting in complex surgery and postoperative complications[8].

With the incidence of ocular diseases such as age-related macular degeneration, glaucoma and diabetes rising as populations around the world age, an increasing number of patients who require cataract surgery may present with complex situations.[8]
The rationale of the study was that ocular comorbidity has an impact on the final visual outcome for patients, many of whom may have unrealistic expectations from the surgery. Conversely, the preoperative examination for cataract surgery may serve as the only opportunity to diagnose and manage treatable ocular conditions. Also failure to recognize these conditions may result in complications during surgery. The study documented the frequency of ocular comorbidity in patients and has come up with recommendations to improve the preoperative detection and management of ocular comorbidities.

Subjects and Methods:

This was a descriptive cross sectional study carried out in the Eye Department of Lady Reading Hospital Peshawar. It was conducted in 6 months from January to July 2014. Sample size calculation was done using WHO sample size calculator, where Confidence level=95%, Absolute precision = 4.5 %, Population proportion (P) of diabetic retinopathy in patients with age related cataract = 9 % [9]. So the sample size= 156. It was a non-probability consecutive sampling.

Inclusion criteria was:
1. Adults with age related cataract of either gender.
2. Patients over 50 years of age.

Exclusion criteria was:
1. History of previous intraocular or refractive surgery.
2. Patients with dense cataract with no view of retina on slit lamp examination
3. History of systemic illness e.g. cardiovascular, renal or neurological disease.
4. Other causes of cataract such as trauma, use of oral steroids, etc.

An approval from the ethic committee of the hospital was sought. Each patient was included in the study through the outpatient department with age related cataract as examined on slit lamp biomicroscopy. An informed written consent was taken from the patient for inclusion into the study. A detailed history and systemic examination of the patient was carried out followed by visual acuity testing on a Snellen chart, refraction and routine ophthalmological (slit-lamp) examination including a fundus examination. This was allowed for detection of confounders which was excluded to control bias in the study results. The Examination of patients was done by an eye specialist.

The data was analyzed using SPSS (Statistical package for Social Sciences) version 10.0. Frequencies and percentages were calculated for categorical variables i.e. gender and ocular comorbidities (Refractive error, age related macular degeneration, glaucoma, diabetic retinopathy). Mean +/- standard deviation was computed for numeric variables i.e. age. Ocular comorbidity was stratified among age and gender to see the effect modifiers. All the results were presented in tables and graphs.

A separate data collection proforma was designed. Personal data, demographics, laterality, presence or absence and name of ocular comorbidity was consigned to the proforma.

Results:

Frequency of ocular co morbidity in patients with age related cataract and the results were analyzed.

Age distribution among 156 patients was analyzed. n=72(46%) patients were in age ranged from 51-60 years and n=84(54%) patients were above 60 years. Mean age was 60 years with standard deviation ± 2.57. 53% (n=83) patients were male while 47% (n=73) patients were female.

Ocular co-morbidity was found in n=66(42%) patients while no morbidity was found in n=90(58%) patients (table: 1). Out of those having co-morbid conditions, refractive error was found in 43 % of the patients, ARMD in n=9(14%), Glaucoma in n=6(9%) and Diabetic Retinopathy in n=5(7%) (table: 2).

Stratification of co morbidity condition with age distribution was analyzed. Out of 28 cases of refractive error, 11 patients were in age ranged from 51-60 years and 17 patients were above 60 years. In 9 cases of ARMD, 3 patients were in age ranged from 51-60 years and 6 patients were above 60 years. In 6 cases of glaucoma, 2 patients were in age ranged from 51-60 years and 4 patients were above 60 years. In 5 cases of diabetic retinopathy, 2 patients were in age ranged from 51-60 years and 3 patients were above 60 years. (table: 3)

Stratification of co morbidity condition with gender distribution was also analyzed. In 28 cases of refractive error, 16 patients were male and 12 patients were female. In 9 cases of ARMD, 5 patients were male and 4 patients were female. In 6 cases of glaucoma, 3 patients were male and 3 patients were female. In 5 cases of diabetic retinopathy, 3 patients were male and 2 patients were female. (as shown in table: 4)

Table no. 1. Ocular Co-Morbidity (n =156)

Ocular Co Morbidity	FREQUENCY	PERCENTAGE
Present	66	42%
Absent	90	58%
Total	**156**	**100%**

Table no 2.Co-morbidity condition (n = 66)

Co-morbidity Condition	Frequency	Percentage
Refractive error	28	43%
ARMD	9	14%
Glaucoma	6	9%
Diabetic Retinopathy	5	7%
Others	18	27%
Total	**66**	**100%**

Table no 3. Stratification of comorbidity condition with age distribution (n = 66)

Co Morbidity Condition	51-60 years	>60 years	TOTAL
Refractive error	11	17	28
ARMD	3	6	9
Glaucoma	2	4	6
Diabetic Retinopathy	2	3	5
Others	8	10	18
Total	26	40	**66**

Chi square test was applied in which P value was 0.003

TABLE NO 4. Stratification of co-morbidity condition with gender distribution (n = 66)

Co Morbidity Condition	Male	Female	TOTAL
Refractive error	16	12	28
ARMD	5	4	9
Glaucoma	3	3	6
Diabetic Retinopathy	3	2	5
Others	11	7	18
Total	38	28	**66**

Chi square test was applied in which P value was 0.002

Discussion:

Cataract remains the leading cause of blindness in the world[1] though studies have demonstrated excellent potential for return to normal vision with extraction of the cataractous lens in both the developed and developing worlds. In general, some 90% of persons undergoing cataract surgery may expect to achieve postoperative vision of 6/12 or better, and a similar proportion report the surgery to have been of subjective benefit. However, an important limitation on the excellent visual results usually associated with cataract surgery is the presence of ocular comorbidities.

Results similar results were found in other studies as Epidemiological studies are consistent in reporting an overall 26% to 49% incidence of ocular comorbidity in cataract patients.[9,10,11] Refractive error is the most common comorbidity (59.7%).[11]. Other conditions include Age related macular degeneration (ARMD) (17.3%) [12], glaucoma (10.6%) [9] and diabetic retinopathy (9 %) [9,13].

In the literature, ARMD is the most common comorbidity that decreases visual outcome after cataract surgery.[14] Progression of ARMD after cataract surgery has been suggested.[15] The increased risk of progression of diabetic retinopathy and development of macular oedema after cataract surgery in high risk patients is well known. [16] The ocular comorbidities that resulted in decreased VA were ARMD, degenerative myopia, diabetic retinopathy, hypertensive retinopathy, and central retinal vein occlusion.

The 42% prevalence of comorbidities in operated eyes among our rural areas subjects is within the range of 26% to 49% reported for studies from the developed world.[17] Though there is limited data on comorbidities from rural Asia, our results are generally in line with those reported by Bourne et al from Bangladesh. Among operated eyes failing to achieve good (6/18) presenting vision, non-refractive comorbidities (Bangladesh 28%, current study 33%) were the second-leading cause, after refractive error (60% in Bangladesh, 72% in our study).[18] (Note that, due to the presence of both refractive and non-refractive comorbidities in several eyes in our studies, the sum exceeds 100%.) Among operated eyes, preoperative vision was strongly associated with the presence of comorbidities. Access to eye care, as indicated by having been fit for glasses (a service not currently offered by our program), was strongly protective against the presence of comorbidities in this cohort, with such persons having one third the odds of having an ocular comorbidity, after adjusting for age and gender. These glasses were largely for reading, and very few subjects brought their glasses to the postoperative examination, so it is unlikely that this effect was mediated through a reduction in refractive error, the most common comorbidity in operated eyes in this cohort.[19]

A principal aim of the current study was to identify strategies to reduce the impact of comorbidities in the context of local environment. Although preoperative vision was strongly associated with the presence of comorbidities, 86% of subjects were blind in the operative eye before surgery, so a strategy of not operating on subjects with poor vision would be ineffective and undesirable in this program. Similarly, though access to eye care outside of our program, as indicated by having been fit for glasses, had a protective effect on comorbidities in this cohort, only 40% of our subjects had ever received glasses. In this setting, regular access to eye care is unlikely to be available for the majority of patients.[15] Thus, it is quite possible that the figures given here represent an underestimate of the true burden of comorbid ocular disease. However, the current research was designed to elucidate the scope and impact of comorbidities potentially detectable by a well-trained ophthalmologist in a modestly equipped rural hospital, and not to constitute a prevalence study.

Despite its limitations, the current study remains one of the few to give information on the burden of ocular comorbidities among cataract-operated persons in rural areas. Our conclusion that these conditions are common and significantly associated with poor vision outcomes, and that the majority are treatable, has important implications for surgical programs in this region.

Conclusion:

Ocular comorbidities are highly prevalent among persons undergoing cataract surgery in this rural area setting, and their presence is significantly associated with poorer visual outcomes. The fact that the great majority of comorbidities encountered in this program are treatable suggests that strategies to reduce their impact can be successful.

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ORIGINAL ARTICLE

Causes, clinical behavior and final outcome of steroid induced glaucoma

Saima Jabeen[1], Yousaf Jamal Mahsood[2], Muhammad Sadiq Gul[3], Farah Akhtar[1]

Abstract

Objective: This study was aimed to evaluate the causes, disease pattern and effect of different treatment options on steroid induced glaucoma.

Study design: Observational cross-sectional study.

Methodology: Thirty six eyes of 18 patients, both genders with steroid induced glaucoma presenting to Glaucoma department of Al-Shifa Trust Eye Hospital were included in the study. The duration of the study was one year from May 2015 to April 2016. Patients with bilateral steroid induced glaucoma who had received treatment and were stable for at least six months were included in the study.

Results:A total 36 eyes of 18 patients were included in the study.Out of 18 patients 14 were males and 4 were females.Among 18 patients 14 (78.7%) had VKC, 2 (11.1%) had bilateral penetrating keratoplasty, 1 (5.5%) had retinitis pigmentosa, and 1 (5.5%) had vasculitis.The mean pretreatment IOP was 22.1 ±5.68 mm of Hg and post treatment IOP was 16.52±8.47 mmof Hg.The mean pre-treatment CD ratio was 0.725±0.275 and mean post treatment CD ratio was 0.75±0.267.

Conclusion: Vernal keratoconjunctivitis is the most common cause of steroid induced glaucoma in our clinical set up.Steroid induced rise in IOP can be effectively controlled with multiple treatment options.Majority of patients are stable on topical IOP lowering agents. *Al-Shifa Journal of Ophthalmology 2016; 12(2): 110-114.*

Introduction:

Increase in intraocular pressure can occur as an adverse effect of corticosteroid therapy. Topical, intravitreal, periocular, oral, intravenous and inhaled corticosteroids therapy, all can result an increased intraocular pressure.

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If ocular hypertension is of sufficient magnitude, for an adequate duration and not treated, subsequent damage to the optic nerve can develop and is called steroid induced glaucoma [1]. In 1950 Mclean reported the first case of steroid induced ocular hypertension induced by systemic therapy of Adrenocorticotrophic hormone (ACTH)[2]. Similarly, the another case of steroid induced ocular hypertension as a result of local administration of steroid was reported after four years by Francois [3].

Corticosteroid induced ocular hypertension occurs in 30% to 40% of the normotensive population [4]. Diurnal and daily fluctuation of intra ocular pressure is related to plasma cortisol levels [5]. All methods of steroid administration can result in elevation of intraocular pressure but most common route is topical corticosteroid application[6].

Steroid induced ocular hypertension begins within a few weeks of starting steroid therapy. The intraocular pressure lowers spontaneously to baseline on cessation of steroids in majority of cases. However, intraocular pressure remains elevated in some cases [7]. The purpose of this study is to describe the risk factors for developing steroid induced glaucoma and to evaluate the efficacy of different treatment options available for the management of steroid induced glaucoma.

Subjects and Methods:

Thirtysix eyes of 18 patients were included in the study. The duration of study was one year from May 2015 to April 2016. All patients with bilateral steroid induced glaucoma who presented to glaucoma department received treatment and were stable for at least 6 months were included in the study. Best corrected visual activity was recorded by using Snellen's chart and IOP was measured with Goldman applanation Tonometer.

All the data was analyzed in SPSS software version 17 with the help of tables and figures. Male to Female ratio was calculated. Paired T-test was applied to compare mean changes in IOP and CD ratio before and after treatment. Frequency was calculated for values like BCVA, reasons of steroid use, rout of steroid use and surgical intervention. A p-value of less than 0.05 was considered significant.

Results:

In this study we studied 36 eyes of 18 patients. Out of 18 patients 14 (77.7%) were males and 4 (22.2%) were females (Figure: 1). Patients included in this study had bilateral steroid induced glaucoma. BCVA of 8 (22.2 %) eyes was 6/6, 5 (25 %) had 6/18, 4 (11.11 %) had 6/36 at the end of 1 year (Table 1). Among 18 patients 14 (78.7%) had VKC, 2 (11.1%) had bilateral penetrating keratoplasty, 1 (5.5%) had retinitis pigmentosa, and 1 (5.5%) had vasculitis (Figure 2). In our study 15 (83.33%) patients used topical steroids, 2(11.11%) patients used oral steroids and one patient had history of IVTA. Among 36 eyes 10 (27.77%) eyes had trabeculectomy, 3 (8.33%) had DLCA, 2 (5.5%) eyes had both trabeculectomy and DLCA, 21 (58.33%) eyes were stable on topical medications. The mean pre-treatment CD ratio was 0.725±0.275 and mean post treatment CD ratio was 0.75±0.267 ((Table 2). The CD ratio was maintained over a period of one year. The mean pretreatment IOP was 22.1 ±5.68 mm of Hg and post treatment IOP was 16.52±8.47 mm of Hg (Table 3).

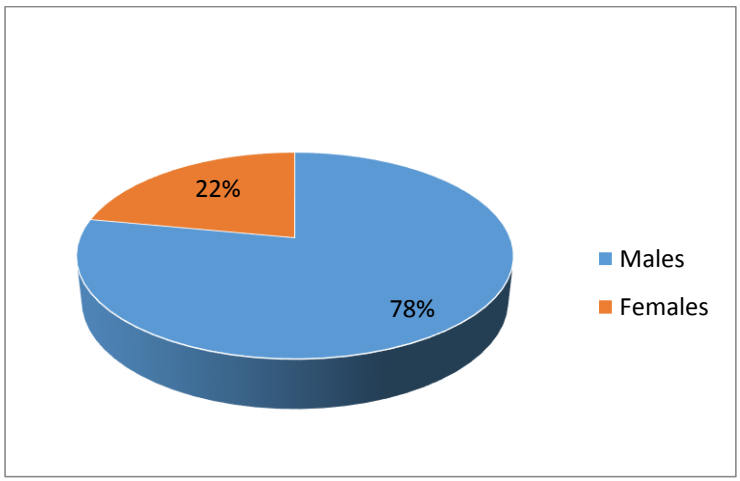

Figure 1: Gender distribution in percentage

Table 1:Visual outcome in patients after 1 year follow up

No.	VISION	No. of patients (%)
1	6/6	8 (22.22 %)
2	6/7.5	2 (5.55 %)
2	6/9	1 (2.7 %)
3	6/12	1 (2.7 %)
4	6/18	9 (25 %)
5	6/24	5 (13 %)
6	6/36	4 (11.11 %)
7	CF	3 (8.33 %)
8	PL -ive	3 (8.33 %)

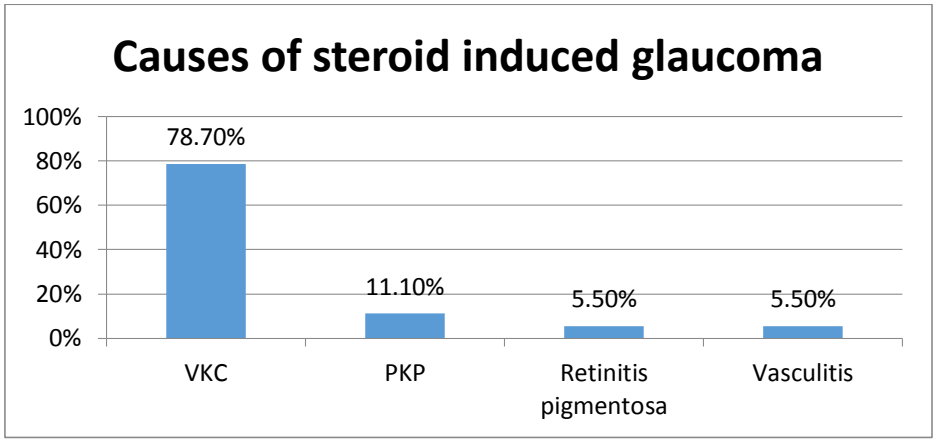

Figure 2: Causes of steroid induced glaucoma

Table 2: Changes in CD ratio

	MEAN PRE TREATMENT (SD)	MEAN POST TREATMENT (SD)	p-value
CD RATIO	0.725 ±0.275	0.75 ±0.267	0.0049

Table3:changes in IOP

	MEAN PRE TREATMENT (SD) In mm Hg	MEAN POST TREATMENT (SD) In mm Hg	p-value
IOP	22.11 ±5.68	16.52 ±8.47	0.00

Discussion:

Corticosteroid induced glaucoma is an iatrogenic secondary open angle glaucoma. Corticosteroids increase aqueous outflow resistance by inhibiting the degradation of extracellular matrix material in the trabecular meshwork.[8]. Corticosteroids inhibit the phagocytic activity of trabecular cells. It results in decreased facility of aqueous outflow due to accumulation of channel debris.[9]. Both topical and systemic administration of corticosteroids can result in elevation of IOP.

The aim of the study was to determine the causes of steroid induced glaucoma and to evaluate the difference between the pre-treatment and post treatment IOP and cup disc ratio. We also evaluated the efficacy of different treatment options for management of steroid induced glaucoma. In our study vernal keratoconjunctivitis appeared to be the most common cause of steroid induced glaucoma i.e. in 78.7 % cases. During the study we noticed that patients with vernal keratoconjunctivitis used topical steroids for a longer period of time.Patients continued to use topical steroids without regular follow ups because of the immediate relief in the symptoms.As a result of which corticosteroid induced rise in IOP was missed.Hence in our population injudicious use of steroids lead to steroid induced complications.

Marcus et al reported that 10-fold risk of developing corticosteroid induced glaucoma is present in patients with mixed form of VKC.He also reported 5.5% incidence of developing corticosteroid induced glaucoma in Asian children with severe VKC.[10].The Second cause of steroid induced glaucoma found in our study was bilateral penetrating keratoplasty i.e. 11.1 %.Erdurmus M et al has also reported overall frequency of steroid-induced IOP elevation after PKP in 73% of cases[11].Retinitis pigmentosa and Vasculitis was found in 5.5 % respectively. Tuncer S has also reported high incidence of IOP elevation after IVTA[12]. Both topical and systemic administration of steroids can result in elevation of IOP. In our study topical use of steroid was the leading cause of steroid induced glaucoma i.e. 14 (83.33%) patients. Francois at al described elevation of intraocular pressure as most common complication of topical corticosteroid application.[3]. Oral steroids were used in 2 (11.1%) and intravitreal steroids were used in 1 patient. In 1962 Mclean et al reported a rise in IOP due to systemic administration of corticosteroids [2]. S. Jain et al reported 1.1 % risk of IOP rise after IVTA.

In our study 21 eyes were stable on topical medications after 6 months.Topical IOP lowering agents were used as first line to control IOP and this was the most common treatment given to our patients. Trabeculectomy was done in 10 eyes.DLCA was done in 3 eyes.Two eyes were treated with both trabeculectomy and DLCA.

Limitations of our study include small sample size, lack of an ideal control group with which to compare the steroid responders.It was difficult to analyze the dosage and duration of corticosteroid

therapy due to patient's variable clinical course.

Conclusion:

In our study vernal keratoconjunctivitis appears to be the most common cause of steroid induced glaucoma.Steroid induced ocular hypertension can be controlled effectively with multiple therapies and topical IOP lowering agents are most commonly used and effective treatment option.Early diagnosis and prompt treatment helps in lowering intraocular pressure and stabilizes the cup disc ratio.

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REVIEW ARTICLE

Dilemma of Latanoprost induced hyperpigmentation-a review

Mahmood Ali[1], Muhammad Sadiq Gul[2], Farah Akhtar[1]

ABSTRACT:
The purpose of this review is to understand and evaluate prognosis, mechanism, pathogenesis and inhibition of latanoprost induced hyperpigmentation and other related side effects. Review of randomly selected studies by searching research data base like Medline PubMed and Google scholar on the subject by using words like latanoprost, hyperpigmentation, prostaglandins, glaucoma, histopathology and inhibition etc. Chronic use of latanoprost turns the color of iris darker in 11 to 23% of patients during one year of treatment. The exact mechanism and pathogenesis of iris hyperpigmentation is not completely known, although some in vitro studies showed that latanoprost may induce tyrosinase activity rather than increasing the mitotic index of the human melanoma cell lines. It is unclear that, whether latanoprost induced iris pigmentation is harmful or it is just cosmetic disadvantage of potential heterochromia between the eyes in unilaterally treated patients because the heterochromia is likely to be permanent, or very slowly reversible. In addition, it is unknown whether latanoprost causes increased pigmentation of the outflow pathways that might eventually lead to blockage and a type of pigmentary glaucoma.The adding of α-methyl-p-tyrosine completely prevented latanoprost-induced stimulation of melanin production in uveal melanocytes. It is concluded that latanoprost is well established and documented anti-glaucoma topical agent. The latanoprost induced hyperpigmentation is most popular and prominent side effect amongst others, which has clinical implications and has given a new mode and opened the doors of research for the researchers to further evaluate the latanoprost in this context. *Al-Shifa Journal of Ophthalmology 2016; 12(2): 115-122. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

Introduction:

Glaucoma is a group of ocular diseases which is often chronic and resulting in systematic damage of optic nerve leading to progressive and irreversible vision loss.

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It is often diagnosed in an advanced state because of lack of symptoms or insidious symptoms which may develop very slowly[1]. It is one of the leading cause of irreversible visual loss and blindness and responsible for approximately 15% of blindness worldwide, and it is estimated that 6.7 million of the 67 million people affected by glaucoma worldwide are bilaterally blind[2]. Asia alone contributes for 60% of the total world glaucoma cases[3]. According to National Health Survey of Pakistan (1987-88), prevalence of blindness in Pakistan is 1.78% (2.5 millions) and glaucoma is the 4th most common cause of blindness that accounts for 3.9% of total blinds in Pakistan[4].

Depending on the mechanism of aqueous outflow impairment with respect to the anterior chamber angle configuration, glaucoma is classified as open or closed angle glaucoma. Open angle glaucoma (OAG) is by far more common (75%) and it is estimated that by the year 2020 it will affect 60 million people worldwide[5].

Glaucoma can also be described as a group of optic neuropathies which are progressive in which optic nerve axons are injured, cell membranes of retinal ganglion are reduced and permanent and gradual vision loss. Reduction of intraocular pressure is the only effective and approved way to treat glaucoma[6]. Above 21mm Hg intra ocular pressure damage to the eye can begin. In addition, as in open angle glaucoma, visual damage can also occur if pressures are below 20 mm Hg with progressive cupping and atrophy of the optic nerve and loss of the visual field[7]. Relief of the excess pressure is effected by various types of treatments. These treatments range from drugs to surgical procedures and implants which are used to relieve the excess pressure[8].

Topical antiglaucoma therapy occupies the first place in the treatment regimen and mostly it controls intra ocular pressure effectively and prevents further damage to the optic nerve. All of the drugs lower intra ocular pressure mainly by two ways, either by increasing outflow of aqueous humor or by decreasing its production[9]. There are five groups generally used as an antiglaucoma drugs in order to lower the intra ocular pressure which includes β-blockers, α-agonists, parasympathomimetics, carbonic anhydrase inhibitors (CAI's), and Prostaglandin analogues[10].

The use of prostaglandin analogues as a first choice of antiglaucoma treatment is increasing because of their high efficacy, lack of systemic side effects and just once daily administration[11]. Latanoprost is an ester prodrug and analogue of a prostaglandin F2-alpha isopropyl, which is rapidly hydrolyzed in the cornea to a biologically active latanoprost acid by the action of esterases. Chronic use of latanoprost turns the color of iris darker and may cause other side effects related to hyperpigmentation. The Purpose of this review is to understand and evaluate prognosis, mechanism, pathogenesis and inhibition of latanoprost induced hyperpigmentation and other related side effects.

Methodology:

Review of randomly selected studies by searching research data base like Medline PubMed and Google scholar on the subject by using words like latanoprost, hyperpigmentation, prostaglandins, glaucoma, histopathology and inhibition etc.

Results and Discussion:

Latanoprost is an ester prodrug and analogue of a prostaglandin F2-alpha isopropyl, which is rapidly hydrolyzed in the cornea to a biologically active latanoprost acid by the action of esterases. When latanoprost is administered topically into the eye, the cornea acts like a slow release depot to the anterior segment. After one hour of administration of latanoprost, maximum concentration is available in the iris followed by anterior chamber and the ciliary body with elimination half-life of 3 to 4 hours. Analytical experiments showed that it does not reach to the posterior segment[12]. It is a selective agonist of prostanoid FP receptor. Due to its unique mechanism to decrease intra ocular pressure, it can be combined with other antiglaucoma drugs like tomolol, epinephrine, pilocarpine and acetazolamide[13].

Increase in the ocular aqueous outflow through uveoscleral pathway is considered as the possible mechanism of latanoprost. Although it is not clear but it is thought

that they may bind to the ciliary body receptors and up regulate metalloproteinases which in turn remodel extracellular matrix and consequently increase the permeability of aqueous humor[14]. Once daily administration of 0.005% latanoprost exhibited superior intra ocular pressure lowering efficacy as compared to beta blocker timolol and prostaglandin analogue unoprostone and similar efficacy as exihibited by newly identified prostaglandin analogues bimatoprost and travoprost as confirmed in japan and other countries worldwide[15].

Conjunctival hyperemia is a subject of concern for both ophthalmologist and patients. It may compromise the outcome of filtration surgery or it may lead to non-compliance due to cosmetic problem. A results of study conducted by Robert M. Feldman at University of Texas Health Sciences Center at Houston showed the incidence of hyperemia in as many as 50% of patients treated with travoprost and as few as 5% of patients treated with latanoprost. This variation of incidence of hyperemia and intra ocular pressure lowering effect is linked with the difference of chemical structure of these drugs[16].

Chronic use of latanoprost turns the color of iris darker in 11 to 23% of patients during one year of treatment. Typically, a concentric increase of the iris pigmentation appears after 6 months of treatment[17]. The treatment of latanoprost turned peripheral lighter color of the iris to uniformly distributed dark brown color[18]. Camras etal concluded that this iris color darkening is irreversible and does not change even after discontinuation of the treatment for several years[19]. During one year of the treatment, the latanoprost induced hyperpigmentation was seen in 12, 23 and 11% of patients in the USA, United Kingdom (UK) and Scandinavia, respectively. Green-brown, yellow-brown and blue/grey-brown eyes showed highest incidence of hyperpigmentation[20]. While according to another study, use of latanoprost for at least twelve months induced hyperpigmentation in approximately 50% of the treated eyes of Japanese patients which is a considerably higher percentage than that reported in Caucasians[21].Tatsuya Chiba et al conducted a 12-month prospective study on the occurrence of latanoprost-induced iridial pigmentation and eyelash change in Japanese patients with glaucoma. The results of their study showed that the incidence of hyperpigmentation of the iris was 6.3% at 1 month, 15.7% at 3 months, 37.8% at 6 months, and 56.5% at 12 months. The incidence of eyelash change was 0% at 1 month, 33.8% at 3 months, 44.4% at 6 months, and 46.2% at 12 months. None of the investigated parameters except age affected the iridial pigmentation/eyelash change[22].

Latanoprost induced iris hyperpigmentation in children is an important issue. Although a very little data is available on the use of latanoprost in children. Sandra M. Brown reported a 13 months old child with elevated intra ocular pressure. Initially 0.5% timolol once daily was started but due to unsatisfactory results after few weeks timolol was discontinued. Latanoprost 0.005% once daily then started and it showed successful lowering of intra ocular pressure. After few months of treatment with latanoprost, iris darkening was noted by child's mother. The author said that, "To my knowledge, this is the first reported case in which a pediatric patient with blue-gray eyes with minimal brown pigment developed iris color change after 5 months of treatment with latanoprost. This corresponds to the time course in adults, most of whom developed increased pigment in the first 6 months of treatment"[23].

The exact mechanism and pathogenesis of iris hyperpigmentation is not completely

known, although some in vitro studies showed that latanoprost may induce tyrosinase activity rather than increasing the mitotic index of the human melanoma cell lines. So it is suggested that in vivo iris hyperpigmentation is due to elevated tyrosinase activity but not as a result of increased cell division[24]. James D et al also conducted a study to understand the exact mechanism of hyperpigmentation by studying induction of Tyrosinase Gene Transcription in Human Iris Organ Cultures Exposed to Latanoprost. They concluded that latanoprost induced hyperpigmentation of iris is due to induction of tyrosinase expression[25].

A comparative study of specimens of iris darkened by latanoprost and untreated controls by Arranz-Marquez et al concluded that latanoprost induced hyperpigmented irides had an increased number of melanocytes within transnuclear inclusions, nuclear invaginations, prominent nucleoli, and mitotic figures suggestive of atypia. The Authors also found increased number of melanin granules in the vascular walls and an increased number of melanocytes and free melanin granules in the stroma compared with controls[26].

It is unclear that, whether latanoprost induced iris pigmentation is harmful or it is just cosmetic disadvantage of potential heterochromia between the eyes in unilaterally treated patients because the heterochromia is likely to be permanent, or very slowly reversible. In addition, it is unknown whether latanoprost causes increased pigmentation of the outflow pathways that might eventually lead to blockage and a type of pigmentary glaucoma[27]. Ian Grierson et al reported in a study that increased production of melanin contents with stromal release of granules could cause uveitis, exacerbate primary or secondary glaucoma, or lead to precancerous changes. They reported while studying morphologic and ultrastructural features of a specimen of the iris taken from a patient whose brown-green iris darkened while participating in the phase 3 trial of latanoprost in Sweden[28]. Later in another study Grierson I et al described that according to all evidences gathered from clinical, in vivo and in vitro studies latanoprost does not induce melanocyte proliferation. There were no any latanoprost induced pathological changes reported in morphological studies of human peripheral iridectomy specimens and there was no evidence of melanin granules blocking the outflow pathways in treated patients. Iris melanocytes melanogenesis stimulation is may be due to tyrosinase hyperactivity which in turn appears to account for induction of melanin production[29].

Michael S Kook et al reported a case that a 62-year-old Korean woman with normal-tension glaucoma developed bilateral increased eyelid skin pigmentation 4 months after beginning treatment with latanoprost in both eyes. They concluded that an increase in eyelid skin pigmentation is a possible complication of topical latanoprost therapy, and the cessation of the drug can result in loss of induced pigmentation in humans[30].Recently in 2011 Rhona C. Digger responded to a case study and said that prostaglandin induced periocular hyperpigmentation is now a well-documented phenomenon but this case was unusual, as the pigmentation occurred within a juxta-ocular skin graft placed after removal of a malignant melanoma[31]. This case was earlier reported by Daniel Calladine et al in 2007 and they commented that “A 68-year-old woman was diagnosed with primary open-angle glaucoma in September 2002. Topical latanoprost was commenced in both eyes, with a good control of intraocular pressure. In April 2005, a malignant melanoma was surgically excised from the left side of the patient's face and skin was grafted to this area from her neck behind the ear. In

September 2005, severe darkening of the skin graft was noted together with subtle bilateral periocular hyperpigmentation and eyelid-margin hyperemia. Her medication was switched from latanoprost to topical brinzolamide in both eyes with a good control of the intraocular pressure. One month after stopping latanoprost, the skin graft had lightened significantly and the subtle bilateral periocular hyperpigmentation and eyelid-margin hyperemia had resolved"[32].

Periocular hyperpigmentation is well documented side effect of latanoprost. This side effect may have some positive implications and usage in dermatological sciences. Recently Amir Hossein Siadat et al conducted a study to evaluate the safety and efficacy of latanoprost plus fractionated CO_2 laser on the repigmentation of hypopigmented scars in patients. Hypopigmented scarring is a common complication and fractionated CO_2 laser can be used to treat hypopigmented scars. Patients with hypopigmented scars were divided into two groups. The patients in group A were treated fractional CO_2 laser plus latanoprost 0.005% and those of group B fractionated CO_2 laser plus placebo (distilled water). The results showed that more than 50% improvement in hypopigmentation was seen in the patients in group A. So the authors concluded that topical latanoprost along with fractional CO_2 laser can be used as a safe and efficacious method to treat hypopigmented scars[33].

A histopathological study conducted by Daniel M. Albert et al concluded that there is no histopathological evidence of premalignant changes in latanoprost treated darkened irides. The latanoprost-induced iris color changes are due to a thickening of the anterior border layer and an increased amount of melanin in the anterior border layer and within the stromal melanocytes[34].

It is still the subject of interest to know the effect of hyperpigmentation on ocular pharmacokinetics and toxicity of other drugs or the effect of drug binding to pigment or pigmented tissues on the pharmacokinetics of Trans-scleral drug delivery. In this context Narayan P. S. Cheruvu et al investigated "Effect of Eye Pigmentation on Trans-scleral Drug Delivery" and concluded that trans-scleral retinal and vitreal drug delivery of lipophilic drug (celecoxib) is significantly lower in pigmented eye than in non-pigmented. This difference is may be due to increased binding of drug to melanin and its accumulation or retention in the melanin-rich choroid-RPE of pigmented eyes of the test animal[35].

Other side effects related to latanoprost are hypertrichosis of eyelashes and hyperpigmentation in the region of treatment, eyelids and periocular skin. It may also cause ocular inflammation and mild delayed uveitis. Clinically symptomatic and angiographically documented cystoid macular edema (CME) associated with the use of latanoprost in pseudophakic eyes after uncomplicated cataract surgery has been reported[36, 37, 38]. In addition latanoprost induced deepening of the upper eyelid sulcus (DUES), upper eyelid ptosis, flattening of the lower eyelid bags, inferior scleral show, and supplemental side effects (eye lid pigmentation and poliosis) around the eyelids; however, the rates of such occurrence might be relatively low as reported by Shunsuke Nakakura et al[39.]

In a study conducted by Filippo Drago et al to investigate the melanin production, its contents and activity of tyrosinase enzyme of cultured uveal melanocytes after adding latanoprost with or without α-methyl-p-tyrosine (a tyrosinase inhibitor). The results showed that latanoprost stimulated melanin content, melanin production and tyrosinase activity in uveal melanocytes. The adding of α-methyl-p-tyrosine

completely prevented latanoprost-induced stimulation of melanin production in uveal melanocytes[40].

Conclusion:

It is concluded in the light of reported studies that latanoprost is well established and documented anti-glaucoma topical agent. The latanoprost induced hyperpigmentation is most popular and prominent side effect amongst others, which has clinical implications and opened the doors of research for the researchers to further evaluate the latanoprost in this context. Multiple studies have been conducted in various parts of the world to evaluate hyperpigmentation to address different aspects of the safety and efficacy of latanoprost but still it is a dilemma which needs further clarification. Although the mechanism and prognosis of hyperpigmentation has been thoroughly studied which helped researchers to find out the ways to reverse or inhibit drug induced hyperpigmentation. Some in vitro studies claimed the successful inhibition by using α-methyl-p-tyrosine but in vivo studies are required to confirm the claim.

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