"A ONE YEAR RANDOMIZED CLINICAL TRIAL ON THE EFFECT OF INTRACAMERAL LOW MOLECULAR WEIGHT HEPARIN ON POSTOPERATIVE INFLAMMATORY REACTION IN HIGH RISK CATARACT CASES"

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ABSTRACT

INTRODUCTION

Cataract surgery has a higher incidence and more pronounced postoperative inflammatory reaction in high risk groups such as congenital cataract, traumatic cataract, complicated cataract, diabetic patients with cataract and lens induced glaucoma. Despite the improvements in surgical technique, equipments and pharmacologic strategies, risk of postoperative inflammation related complications are still high in high risk cataract cases. Heparin surface modified lens was used for this purpose but it is very expensive. We studied the effect of intracameral low molecular weight heparin on postoperative inflammation after cataract surgery in high risk cataract cases and also the complications associated with its use.

MATERIALS AND METHOD

It is a randomized clinical trial in which forty patients with high risk cataract like patients with diabetes, complicated cataract, traumatic cataract, congenital cataract, steroid induced cataract and lens induced glaucoma undergoing small incision cataract surgery with posterior chamber intraocular lens implantation were randomly assigned into two groups, group A and group B. All patients in group A received low molecular weight heparin (enoxaparin) in the concentration of 40mg/0.4ml in 500ml in the irrigating solution and patients in group B received irrigating solution without low molecular weight heparin. The patients were examined postoperatively on day 1, day 7, day 30 and day 60 for anterior chamber cells and flare, vitreous haze, iris pigments on the surface of intraocular lens and posterior capsular opacification by SL 115 Classic Carl Zeiss slit lamp.

RESULTS

A statistically significant reduction in postoperative cells (P <0.001) and flare (P=0.001) and vitreous haze (P=0.001) was noted on day1 and day 7 in group with addition of low molecular weight heparin. At day 30 and day 60 no statistically significant reduction in post-operative cells and flare and vitreous haze was seen. Iris pigments on the surface of intraocular lens were significantly reduced (P<0.05) in all follow-ups in group with addition of low molecular weight heparin. There was no significant difference in development of posterior capsular opacification, pupillary membrane and posterior synechiae. None of the patients in either group developed optic capture. Intraoperative and postoperative complications related to low molecular weight heparin supplementation like hyphema and corneal opacity were not noted in any of the patients.

CONCLUSION

Low molecular weight heparin used in the concentration of 40mg/0.4ml in 500 ml irrigating solution reduces the early postoperative inflammation in high risk cataract cases with no adverse effects.

Key words: Postoperative inflammation, low molecular weight heparin, posterior capsular opacification, irrigating solution.

LIST OF ABBREVIATIONS USED

AC	-	Anterior Chamber
BAB	–	Blood Aqueous Barrier
BRB	_	Blood Retinal Barrier
BCVA	–	Best Corrected Visual Acuity
BSS	–	Balanced Salt Solution
CCC	–	Continuous Curvilinear Capsulorrhexis
CME	_	Cystoid Macular Edema
ECCE	–	Extracapsular Cataract Extraction
ICCE	_	Intracapsular Cataract Extraction
IOL	–	Intraocular Lens
IOP	–	Intraocular Pressure
LMWH	–	Low Molecular Weight Heparin
PCIOL	–	Posterior chamber intraocular lens
PCO	_	Posterior Capsular Opacification
PMMA	–	Polymethyl Methacrylate
ROS	_	Reactive oxygen species
SICS	–	Small Incision Cataract Surgery
SD	_	Standard Deviation

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INTRODUCTION

Cataract is defined as opacity within the natural clear lens inside the eye that reduces the amount of incoming light and results in deterioration of vision. Natural lens is a crystalline substance and a precise structure of water and protein to create a clear passage for light.

Cataract surgery has a higher incidence and more pronounced postoperative inflammatory reaction in high risk groups such as congenital cataract, traumatic cataract, complicated cataract, diabetic patients with cataract, steroid induced cataract and lens induced glaucoma. They are grouped under high risk because they have a significantly increased blood aqueous barrier (BAB) breakdown following cataract surgery when compared to normal eyes, leading to augmented protein leakage and cellular reactions in aqueous humor.

Postoperative inflammatory reaction is influenced by the surgical technique, intraoperative injury to adjacent structures such as the iris, remnants of retained cortical material and immunological reactions to the implanted intraocular lens [1].

During the past decade, major advances have occurred in cataract surgery techniques, equipments, and pharmacologic strategies that decrease the degree of postoperative inflammation following cataract surgery and reduce patient's risk for inflammation-related complications [1]. Ophthalmic topical preparations such as steroids and nonsteroidal anti-inflammatory drugs effectively reduce postoperative inflammation. Although the inflammatory complications in uncomplicated cataract extraction and intraocular lens (IOL) implantation are rare, but when it comes to high risk cataract cases the risk of postoperative inflammation related complications are still high.

Despite all these improvements some postoperative complications associated with polymethyl methacrylate intraocular lenses still remain [2]. The experience with uncoated polymethyl methacrylate intraocular lenses now span a period of almost 50 years and have demonstrated that though these intraocular lenses are relatively inert, they are not perfectly biocompatible, and result in postoperative inflammation [3]. Therefore a search is on to find a method to render these intraocular lenses more biocompatible to achieve minimal postoperative inflammation.

For over a decade intraocular lenses coated with heparin have been studied in both animal and human eyes. These studies showed that eyes implanted with heparin coated intraocular lenses showed a reduced incidence of inflammatory precipitates on its surface [4],[5] but heparin coated lenses are very expensive and not affordable by most of the patients.

A few studies have shown that low molecular weight heparin in irrigating solution during cataract surgery results in less disturbance of blood aqueous barrier (BAB) [6],[7] thereby decreasing the postoperative inflammation and also the complications arising due to increased postoperative inflammation. A low molecular weight heparin has anti-inflammatory, anti-proliferative and anti-coagulant properties. This modification is simple and can be done with no extra expenditure.

There are not many reports of similar studies in Indian population who have darkly pigmented irides. This prospective study was undertaken to evaluate the effect of intracameral low molecular weight heparin on postoperative inflammatory reaction after cataract surgery in high risk cataract cases. Low molecular weight heparin in the irrigation solution may be of tremendous value in decreasing postoperative

inflammation and cellular deposits on the intraocular lens surface which is a more economical option than heparin coated lenses.

OBJECTIVES OF THE STUDY

1. Primary Objective - To study the effect of low molecular weight heparin in the irrigating solution on postoperative inflammatory reaction in high risk cataract cases.
2. Secondary Objective - To study the postoperative complications of using low molecular weight heparin in the irrigating solution.

REVIEW OF LITERATURE

EVOLUTION OF CATARACT SURGERY AND INTRAOCULAR LENSES

History of cataract surgery

Cataract surgery is one of the oldest surgical procedures known, first documented in the fifth century BC [8]. The improvements in cataract surgery and the corresponding results over the past few decades have been nothing short of astounding.

Couching

In ancient times, cataracts were treated with a technique called couching. Sushruta practiced couching as early as 800 BC [8]. Couching could only be performed when the lens had become completely opaque, rigid, and heavy to the point that the supporting zonules had become fragile. The eye would then be struck with a blunt object with sufficient force to cause the zonules to break so that the lens would dislocate into the vitreous cavity, restoring limited but completely unfocused vision. Centuries later, the technique was modified so that a sharp fine instrument was inserted into the eye to break the zonules to cause the dislocation [8]. Serious complications were frequent, and there was no method for optical rehabilitation. So the patients were condemned to optical aphakia for the rest of their lives

Intracapsular cataract extraction (ICCE)

Samuel Sharp introduced intracapsular cataract extraction in 1753 [8]. After section and iridectomy, and with the pupil dilated, the lower part of the anterior capsule was grasped by forceps and by a variety of rocking manoeuvres the zonules were weakened and broken from the ciliary muscle (usually without rupture of the

capsule). The lens was then delivered upside down by an action known as tumbling. Excess pulling could cause either capsule rupture or vacuum at the vitreous face, which might rupture and cause macular edema and subsequent retinal detachment. In the Kirby technique (1955), the capsule was grasped near its upper pole and the lens slid out after breaking the upper zonules. Barraquer introduced Zonulysin (i.e. alpha chymotrypsin, a digestive proteolytic enzyme of bovine origin), which could be injected into the posterior chamber before either method, as an aid to easier and safer lens delivery.

The disadvantages of the intracapsular technique included vitreous loss, cystoid macular edema [8], retinal detachment, astigmatism and use of anterior chamber intraocular lens, also this technique could not be used in patients less than 30 yrs.

Extracapsular cataract extraction (ECCE)

In the mid eighteenth century, Daviel introduced the extracapsular method of cataract extraction of almost a century passed before this technique received widespread acceptance, although the lack of a method to clean out cortical material remained a problem. The anterior lens capsule was opened, either by toothed forceps (Arruga) or by being incorporated in a single action Graefe knife sweep through the cornea and lens capsule. Saline irrigation and pressure on the inferior cornea was used to express the lens nucleus via the large wound. The soft cortex was then flushed out from the pupillary plane using a silver canula and rubber bulb syringe. Atropine eyedrops were used pre operatively in order to improve visualization, and post operatively to avoid synechiae to the iris or capsule remnants. The synthesis of cortisone (1950) and antibiotics reduced the risks of iridocyclitis and infection. The

strong possibility of pupil block, iris bombe, and subsequent glaucoma was largely overcome by iridectomy which later became a standard part of all cataract procedures before the wound was closed with the conjunctival flap.

The first major advance was the development of techniques allowing the removal of the lens while leaving the lens capsule behind [9]. The intact capsule acted as a barrier preventing lens material from falling into the vitreous cavity. This allowed less advanced cataracts to be removed since any residual fragments could be removed at the time of surgery with aspiration and would not be retained in the vitreous, where they would incite inflammation. This change also resulted in the reduction of the wound down to approximately a quarter of a corneal circumference. The introduction of fine sutures around this time greatly enhanced the safety and quality of results.

The techniques and results of cataract surgery have changed dramatically during the past four decades. We have moved from intracapsular cataract extraction as the preferred technique to exclusively extracapsular procedures. Smaller incisions have become the standard, with phacoemulsification now being the method of choice for all surgeons. The most significant change marked by the modern era was the introduction of phacoemulsification surgery in 1967 by Dr. Charles Kelman [10].In this technique, ultrasonographic power is used to break the lens into minute fragments that can be aspirated. A combined ultrasonographic power, irrigation and aspiration hand piece allows the removal of any lens through a small incision.

Along with these advances, improved IOL materials and designs, especially well suited for use with smaller incisions. Advances in techniques and equipments have led to increased safety and efficiency. Viscoelastic agents have been developed synchronously with modern techniques, playing an integral role in the success of this

new technology. Improved surgical techniques for removing the anterior lens capsule have decreased the incidence of both intraoperative and postoperative complications.

EVOLUTION OF INTRAOCULAR LENS

The history of intraocular lenses has always been exciting often frustrating, but finally rewarding.

Although the current era of intraocular lenses dates back to 1949, the concept had occurred long before. It has been reported that Casanova reffered in his memoirs to the Italian oculist Tadini, who discussed with him the idea of implanting an artificial lens after a cataract extraction in 1764-1765. Around 1795, Cassamata attempted to introduce a glass lens into an eye after a cataract operation, but the lens immediately slid posteriorly towards the retina.

Posterior chamber lenses

The modern history of intraocular lenses began with the contributions of Ridley, who was inspired by a comment made by a medical student who, while observing Ridley close the incision after intracapsular cataract extraction, exclaimed that he had forgotten to replace the diseased lens with a new one. During the battle of Britain in World War II many plastic canopies of spitfire air planes were shattered by enemy gun fire. This plastic material (polymethyl methacrylate) occasionally lodged inside the eyes of pilots. It was noted that it resulted in little reaction to the plastic material, provided it did not move about inside the eye. Thus it occurred to Ridley that such a plastic substance might be used to replace the human lens.

The English ophthalmologist Harold Ridley is credited with the first successful human intraocular lens implants, starting in 1949 [11]. Ridley Lens was

abandoned because of a high incidence of complications (6% posterior dislocation, 10% glaucoma and intractable uveitis).

Anterior chamber lenses

After the failure of the Ridley lens, most surgeons turned their interest to the anterior chamber. There were two principle types of anterior chamber lenses, those with elastic supports and those with rigid supports. The prototype of anterior chamber lens with elastic supports was the Dannheim lens, and that of rigid support was the Strampelli lens. Barraques further modified the Dannheim lens. However these lenses were associated with a high incidence of bullous keratopathy, deformation of the pupil, ocular hypotony due to inadvertent cyclodialysis and corneal dystrophy, especially when larger lens were used [12]. Smaller lenses led to decentration during eye movements, causing irritation of the ciliary body and the angle structures. This resulted in peripheral anterior synechiae, secondary glaucoma and corneal dystrophy. Barraques finally had to explant most of these lenses. Choice persisted in his use of anterior chamber lenses and developed the first functional anterior chamber lens, later modified by Tennant and further modified by Charles Kelman [10].

Iris- supported lenses

Epstein of South Africa was the first to turn to the iris for support. He designed his collar-button lens. However, it was too heavy, and dislocated frequently. He then developed the Maltese cross design. This lens was modified by Richard Troutman and Richard Binkhorst and later manufactured by Mike Copeland. It was essentially a thinner maltese cross lens and was named the Copeland “Iris plane” lens. This had a higher incidence of cystoids edema and retrolenticular membranes. Binkhorst [9] first designed his iris clip lens in 1957 and inserted it in 1958. He made

eight modifications to his lens. Dislocations and corneal dystrophies still remained a major problem. In 1969, Worst, a pupil of Binkhorst, began to suture the lens to the iris in an effort to decrease the incidence of dislocations. The possibility of capsular support: as used by Ridley, had been abandoned until December 1963, when Binkhorst inserted an iris-clip lens after an extracapsular extraction in a traumatic cataract. The posterior loops get embedded in the adhesions between iris and the posterior capsule. Lens thus supported could not move inside the eye.

Binkhorst preferred the iridocapsular lens over the iris clip lens as there was less corneal endothelial damage there by combining the advantage of the iridocapsular lens with those of extracapsular extraction [13]. According to Binkhorst, the advantages included: a smaller incision, safer surgery due to less bulging of the vitreous and fewer cases of maculopathy. A definite disadvantage of extracapsular extraction was found to be the occurrence of secondary cataract. The frequency of needling however decreased considerably with increasing experience of the surgeon, especially in elderly patients.

These sequential events should remind us to accept changes with caution. After all, the implant and surgery is unintended to provide the patient good and safe vision for a life time.

There is also a tendency to divide the history of intraocular lenses into three eras, usually referred to as generations. The first generation was limited to Ridley's posterior chamber lens, the second generation to the anterior chamber angle fixated lenses, and the third generation to iris supported and iridocapsular lenses.

The credit for developing the first practical posterior chamber lens belongs to S Shearing and J Pearce [14],[15]. However modifications suggested by Sansky, Krantz and Simcoe, among others, helped to develop the currently available lens. Mazzoco is credited with the development of foldable posterior chamber intraocular lens. Numerous modifications, both major and minor, both useful and disastrous, have been made to these basic lens styles.

Currently, an intraocular lens is almost always implanted as a part of cataract surgery. The fact that cataract surgery has become the most frequently performed surgery in over 65 years age group is adequate proof of the visual rehabilitation that intraocular lens implantation affords. Although many uncontrolled studies seem to validate the safety and efficacy of cataract surgery with intraocular lens implantation compared to that without intraocular lens implantation, no large scale controlled study had irrefutably established this. On the other hand, clinical experience seems to provide overwhelming support for the superiority of intraocular lenses over other forms of aphakic optical correction.

INTRA-OCULAR LENS (IOL) MATERIALS AND HEPARIN SURFACE MODIFIED LENSES

Among the many critical issues in the ongoing pursuit of an ideal intraocular lens the importance of the material used seems to be paramount. The ideal implant material aims at the following properties.

- High optical quality
- High index of refraction
- Light weight
- Durability
- Ease of manufacture
- Lack of inflammatory reaction
- Lack of antigenicity
- Ease of sterilization

Despite the success of intraocular lens (IOL) implantation with the current materials, none of the IOLs can be said to be ideal. Most of them have been implanted in the current configuration for a relatively short time, and none long enough to determine lifetime stability and tolerance.

OPTIC MATERIALS

Polymethyl methacrylate (PMMA)

PMMA is a polymer of methylmethacrylate monomer. Monomer production begins with a reaction of acetone with hydrogen cyanide and then sulfuric acid. The resulting methacrylamide sulfate is reacted with methanol to yield methylmethacrylate. Various forms of PMMA are available commercially. Those used for lathe cut or compression molded intraocular lenses are of high molecular

weight PMMA, such as that manufactured by Imperial chemical industries (Perspex CQ). Injection molded intraocular lenses are made of lower molecular weight PMMA, such as that of Rohm and Haas (Plexiglass, Oroglass).

PMMA is a hard, transparent material with features that make it suitable for injection molding, lathing and polishing. It has been suggested that monomer excess or release from PMMA may be toxic to the tissues [16]. Monomer can be released from PMMA by heating, molding, grinding and other processes used in the manufacture of intraocular lenses.

Although the clinical experience of 40 years has shown PMMA to be bio-compatible, a cellular reaction can occur on the surface of even clinically well-tolerated intraocular lenses [16]. PMMA does not activate complement and induce chemotaxis of white blood cells as polypropylene and nylon loop materials. This property and the loss of "memory" (shape) of polypropylene loops within the eye have led to increased use of PMMA as the haptic material for one piece posterior chamber lenses.

Glass

Glass has been suggested as a material for the optical portion of intraocular lenses since the eighteenth century [17]. Glass has potential optical advantages over PMMA and may be sterilized by autoclaving. Its main disadvantage was its weight. A thin intraocular lens of high refractive index (1.62), held in a polyimide carrier was developed. However Nd: YAG laser capsulotomy causes severe cracking of the lens optic, therefore the material was withdrawn from use in the United States.

Silicone

The potential advantages of soft optic and haptic materials include autoclavability and decreased trauma to the intraocular structures. The chief reason for interest in them however has been the potential for insertion through a small incision, as in phacoemulsification.

Silicone lenses have been more widely used than hydrogels. They are cast or injection molded from silicone elastomers, which are lightweight polymers of organic silicone-oxygen compounds. They have a lower index of refraction than PMMA, requiring greater optic thickness. Because they are molded, no polishing is required, reducing potential toxicity from polishing compounds. They can be folded for small incision insertion, but have relatively low tensile strength, and must be handled carefully to avoid tearing. Discoloration of silicone lenses to a tan-brown color has been reported, although the color change does not appear to affect visual function [18].

Hydrogel

Most hydrogel lenses currently under study are polyhydroxy ethylmethacrylate (HEMA). They are lathe cut in the dry state and require polishing. They are hydrophilic, and are less damaging to the corneal endothelium on contact than other materials [19]. This material, like silicone, has low tensile strength and can be easily torn on insertion. Hydrogels may be implanted in the partly hydrated state and allowed to expand in the eye, thus allowing small incision insertion without folding. Clinical results and problems have been similar to those of silicone lenses, but some studies suggest that decentration is greater than that with PMMA lenses [20].

HAPTIC MATERIALS

Nylon

Nylon is a generic name for fiber polymers with repeating amide (-CONH-) groups, also known as polyamides. They are manufactured by several condensation processes and are named according to the number of carbon atoms in the monomer subunits. The most widely used material for intraocular lens loops are nylon 6 and nylon 66. The safety and durability of nylon have been questioned because of its tendency to slowly hydrolyze with gradual water absorption and to be broken down by proteolytic enzymes at amide sites. Degradation of nylon lens loops and fixation sutures has been well documented in clinical situations. For this reason, the polyamides have been replaced by PMMA and polypropylene.

Polypropylene

Polypropylene (Prolene) is a polymer of propylene, a derivative of propane. It may be clear or may be colored blue by a copper salt. The chief advantage of prolene over polyamides is its hydrophobic nature, making it highly resistant to hydrolysis. A potential problem with prolene when used in the eye as opposed to other body sites is its alteration by ultraviolet irradiation. Full spectrum ultraviolet light leads to significant loss of tensile strength. Surface degradation and fissuring of polypropylene lens loops have been noted but are not thought to cause clinical problems. Propylene and nylon have been shown to activate complement, initiating a pathway leading to neutrophil chemotaxis [21].

A case control study, as yet unconfirmed by further data, has shown the use of lenses with polypropylene haptics to increase the risk of endophthalmitis by 4 and 1⁄2 times over that of posterior chamber intraocular lenses with PMMA haptics. This is

consistent with the finding that bacteria can adhere better to polypropylene than to PMMA [22].

Polyethylene

Polyethylene terephthalate (Dacron) and polyethylene glycoterephthalate (Mersilene) are materials resistant to hydrolysis and to ultraviolet irradiation. They have been used as a mesh for iris fixation of intraocular lenses experimentally and are well tolerated [23]. Mersilene suture is softer than polypropylene and is non-biodegradable. It has been used in the closure of cataract wounds with comparable results to nylon, and may be useful for suturing intraocular lenses.

Metals

Metal looped iris supported lenses were introduced in the mid 1960's to avoid the problem of nylon degradation. Platinum-Iridium was well tolerated in extracapsular extraction. Titanium is lighter and has been used as a loop material. Stainless steel, nickel-iron alloy, has been used for limbus and iris fixation sutures.

All of the metal haptic materials have been abandoned because of high rates of complications when used with intracapsular cataract extraction and iris supported lenses.

SURFACE MODIFIED LENSES

Improvements in intraocular lens designs and surgical techniques have contributed to better clinical results of cataract surgery. Despite these results, there is increasing evidence of low grade inflammatory response to intraocular lens implants. Clinical studies and histological examination of enucleated human eye indicate that a foreign body reaction probably occurs in all eyes after intraocular lens implantation [24].There

is good reason to believe that this foreign body reaction contributes to clinical problems such as uveitis, synechiae formation and occurrence of cells and pigment deposits on the IOL surface. In some cases, the acute inflammatory reaction develops into a chronic postoperative anterior uveitis.

The reaction to a relatively inert foreign material such as PMMA starts with the deposition of protein on the surface of the IOL. The protein then undergoes some conformational changes. The proteinaceous surface attracts macrophages and inflammatory cells. Finally fibroblasts begin to accumulate. Several sophisticated chemical methods exist to modify this sequence of events by altering the surface of the polymer.

One method of surface modification is to graft a hydrogel to the surface of the PMMA by using radiation which makes the iris less susceptible to chafing.

Another process called surface passivation, makes the intraocular lens surface both hydrophobic and oleophobic. This lens seems to reduce the chance of endothelial damage compared to unmodified PMMA and may protect the blood aqueous barrier as measured by a reduced leakage of fluoroscein into the anterior chamber in comparison to unmodified PMMA.

Heparin surface modified lens

A further approach is to bind heparin to the surface of the PMMA, which seems to reduce inflammatory cell reaction both in-vivo and in-vitro. Heparin surface modified intraocular lens has approximately 0.5µgm of heparin chemically bound to the surface of the intraocular lens. Heparin surface modification is a proprietary process in which PMMA surface is subjected to oxidative treatment to add negative

charges. Polyethylenimine is then electrostatically adsorbed and heparin is bound by a secondary amino-linkage giving a permanent chemical bonding uniformly over the entire PMMA lens surface.

In-vitro experiments have shown reduced activation of human granulocytes after heparin surface modification of PMMA [25]. A reduction of platelet adhesion and reduced growth of human fibroblasts also have been demonstrated. Experimental implantation in rabbit and monkey, as well as 3 month results of a comparative double-masked clinical trial involving 266 patients have indicated that this heparin surface modification of PMMA does reduce the signs of inflammation [26]. These studies indicate that the foreign body reaction to PMMA intraocular lens is substantially reduced by heparin surface modification. The incidence of posterior synechiae and pigment deposits with heparin surface modified lens was less than that with unmodified PMMA lens [27].

The causes of postoperative fibrinous uveitis are unclear, but following cataract surgery in eyes with active uveitis, distinct mechanisms may influence the anterior chamber response. A major cause is increased vascular permeability, seen in chronic uveitis and a further increase seen after cataract surgery, which allows release of large molecular weight proteins, notably fibrinogen into the anterior chamber. Postoperative fibrinous uveitis is seen not only in cases of preexisting active uveitis, but also in cases involving other modes of blood ocular barrier breakdown, such as in proliferative diabetic retinopathy, lens induced glaucoma. In eyes with uveitis, the postoperative period may be additionally complicated by increased inflammation resulting from active migration of inflammatory cells into the anterior chamber.

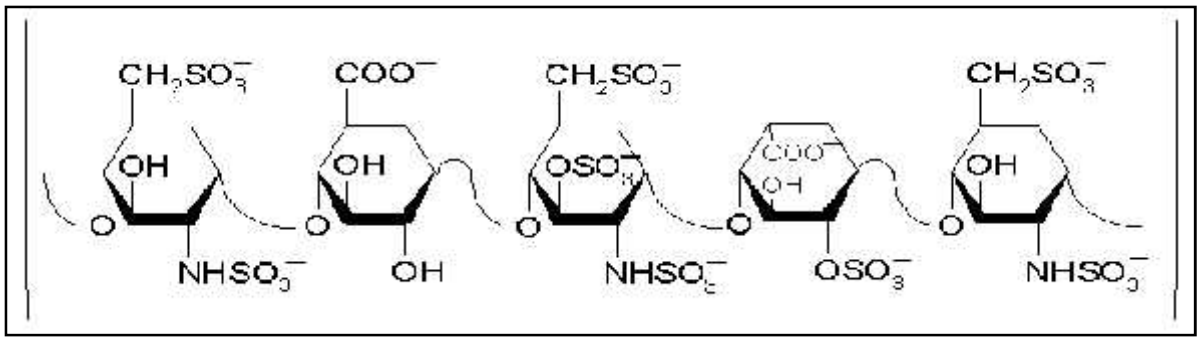
The use of a heparin surface modified IOL may have distinct advantages in this situation. Most significantly, it attracts fewer inflammatory cells. Though the IOL will not prevent or inhibit the development of fibrinous uveitis, the formation of adhesions to the IOL is retarded and hence posterior synechiae formation and its complications are less likely. Following the dissipation of postoperative uveitis, the coating of cells on the surface of a PMMA lens may persist for many months, with attendant visual problems. If cellular adhesion is reduced by implanting heparin surface modified lenses, the IOL will be clearer and the visual acuity enhanced.

Overall results suggest that heparin surface modification provided an impressive cell free IOL surface and greater protection from complications of inflammation than might be expected with unmodified lenses [27] but did not decrease post operative inflammation.

HEPARIN

Heparin was discovered by a medical student J Mc Lean, working at John Hopkins medical school in 1916. Heparin is a glycosaminoglycan found in the secretory granules of mast cells. These cells are abundant in the liver and the lung.

Figure 1: Structure of heparin



"Harpers illustrated Biochemistry 26th edition. Robert K Murray, Daryl K Granner, Peter A Mayes, Victor W Rodwell Pg 545".

Heparin is composed of an unknown number of sulfated D-glucosamine and D-glucuronic acid units linked through an oxygen bridge. The repeating disaccharide contains glucosamine (GlcN) and idoxuronic acids IdUA. The content of esterified sulfuric acid is very high and this makes heparin a strongly electronegative compound. Heparin is thus the strongest acid occurring in the body. The anticoagulant activity is attributed to its strong electronegative charge. It is available as the sodium salt. Commercial preparations are a mixture of molecules varying in molecular weight from 4000 to 40000 [28].

Low-Molecular-Weight (LMW) Heparin

As the name implies low-molecular-weight heparins are preparations that have lower average molecular weight than heparin. The average molecular weight of these LMW heparins typically ranges from 2,000 to 8,000 Da [29]. They are made by enzymatic or chemical controlled hydrolysis of unfractionated heparin. These molecules have very similar chemical structure as unfractionated heparin except for some changes that may have been introduced due to the enzymatic or chemical treatment. The mechanism of action of these drugs is the same as ordinary heparin.

Heparin depends for its anticoagulant action on the presence of a protein, antithrombin III, which is a naturally occurring inhibitor of thrombin and activated factor X in plasma. In the presence of heparin, antithrombin will become more active. The importance of inhibition of factor Xa is that, this factor is involved in both the intrinsic and extrinsic coagulation systems and heparin is effective in small quantities. At molecular level, the capacity of heparin to inhibit factor Xa has been found to depend on a specific pentasaccharide sequence which can be isolated in fragments of average molecular weight 5000 (Low molecular weight heparin). These fragments are too short to inhibit thrombin, which is the principal action of conventional heparin. Heparin also inhibits platelet aggregation [30].

In addition to its anticoagulant activity, heparin is known to have anti-inflammatory activity [30]. Matzner Y et al [31] demonstrated the effect of heparin on neutrophil chemotaxis in-vitro in the Boyden Chamber. This method enabled differentiation between the direct effects of heparin on neutrophil migration and locomotion, and its effects on chemotactic factors. Heparin inhibited both the random migration and directed locomotion of human neutrophils toward zymosan-activated

serum (ZAS) and F-met-leu-phe (FMLP). Inhibition was found to be dependent on the concentrations of the heparin and of the chemotactic factors. No specific binding of heparin to the neutrophils could be demonstrated, and heparin's inhibitory effects were eliminated by simple washing of the cells. When added directly to the chamber containing chemotactic factor, heparin inhibited the chemotactic activity of ZAS but not that of FMLP, suggesting a direct inhibitory effect against C5a, the principal chemotactic factor in ZAS. Experiments performed with low-molecular-weight heparin, N-desulfated heparin, dextran sulfate, chondroitin sulfate and dextran indicated that the inhibitory effects of heparin on neutrophil chemotaxis are not related to its anticoagulant activity, but probably depend on the degree of sulfation of the heparin molecule.

In a study by J Mansler et al [32] showed that heparin induces invitro apoptosis of human peripheral blood neutrophils. In addition, apoptosis may help to explain the anti-inflammatory effects resulting from interaction between vessel wall heparin sulphate and chemoattractant peripheral blood neutrophils.

Yet another study by Richard M et al [33] shows that heparin molecules can block neutrophil accumulation during acute inflammation, and suggests that this activity depends, at least in part, on the ability of these oligosaccharides to block L and P selectins, complement components and certain cytokines.

Paresh Dandona et al [34] investigated the effect of heparin on reactive oxygen species (ROS) generation by leucocytes. Heparin was injected intravenously at a dose of 10,000 units into eight normal subjects and blood samples were collected from the anticubital vein prior to and at 0,0.5,1,2 and 4 hrs. ROS generation was inhibited significantly in polymorphoneuclear cells and mononuclear cells. Since ROS are pro-

inflammatory and cause tissue damage, this study shows that it is possible that heparin may have anti-inflammatory effect in vivo.

Heparins ability to inhibit complement was described by Ecker and Gross in 1929 and several points of action have been identified. The rate limiting steps are suggested to be enhancement of C1INH in the classical pathway and prevention of formation of the amplification convertase of the alternate pathway [35]. The ability of heparin to inhibit the early steps in the cascade makes it attractive as a complement inhibitor.

Postoperative anterior chamber fibrin exudation is seen in several clinical settings, especially after vitrectomy surgery for proliferative diabetic retinopathy, proliferative vitreoretinopathy, ocular trauma or severe intraocular infection [36]. Fibrin has been noted to stimulate the transformation of retinal pigment epithelial cells into fibrocytic cells with migratory and contractile properties. The fibrin clot may also act as a scaffold for cellular proliferation and contraction. These properties of fibrin may predispose eyes with fibrin exudation to proliferative vitreoretinopathy and ultimately to retinal detachment. Fibrin exudation may also enhance wound healing leading to premature closure of filtering fistulas in glaucoma surgery.

Johnson et al [37] in his randomized study in 73 eyes showed that heparin supplementation in the vitretomy infusion solution. (10-IU/CC) resulted in statistically significant reduction in the post operative fibrin formation (P=0.04) but increased intra operative bleeding (P=0.02). In a similar study in rabbits Deborah A et al [38] studied the inhibition of intraocular fibrin formation following infusion of 5IU/ml of low molecular weight heparin sodium during lensectomy, vitrectomy and retinotomy. Surgery was performed on 18 eyes with 9 receiving heparin and 9 serving

as controls. There was a statistically significant decrease in fibrin formation in the study group.

Fibrin binding to corneal endothelium can cause cell damage and cell loss. Thrombin receptors on corneal endothelium have also been demonstrated, but the precise effect of these receptors are unknown. This might account for the increased corneal clarity in these studies with intraocular heparin infusion.

Absorption and pharmacokinetics

Heparin is not absorbed through the gastrointestinal mucosa and therefore is given parenterally. Administration is by continuous intravenous infusion or subcutaneous injection. The half life of heparin in plasma depends on the dose administered. When 100, 400 or 800 units/kg body weight of heparin is injected intravenously, the half life of the anticoagulant activity is approximately 1, 2.5 and 5 hours respectively. Heparin appears to be cleared and degraded primarily by the reticuloendothelial system. A small amount of non-degraded heparin also appears in urine. Low molecular weight heparins have longer biological half lives than do standard preparation of the drug. The therapeutic range for standard heparin is 0.3 - 0.7 U/ml in the plasma.

Adverse effects

Bleeding is the primary untoward effect of heparin. Recent studies suggest that major bleeding occurs in <3% of patients treated with intravenous heparin for venous thromboembolism. The incidence of bleeding is no worse for patients treated with low molecular weight heparin for this indication. The anticoagulant effect of heparin disappears within hours of discontinuation of the drug. Mild bleeding due to heparin usually can be controlled without administration of an antagonist.

Thrombocytopenia with arterial thromboemboli and hemorrhage is a further serious complication. This occurs in about 2-3% of patients who receive heparin for a week or more. It has an immunological pathogenesis and generally recurs on rechallenge. Other side effects include

- Osteoporosis – It is dose related and is seen with long term therapy.
- Hypersensitivity reactions and skin necrosis also is seen.
- Hyphema is the only complication reported in eyes.

CAUSES AND COMPLICATIONS OF POSTOPERATIVE INFLAMMATION

Cataract extraction is the single most common intraocular surgical procedure. Despite large numbers of patients undergoing this surgery, little research has been directed towards determining its effect on the anterior segment of the eye and the blood aqueous barrier.

Blood aqueous barrier

The eye is sequestrated from the blood by a permeability barrier that is both vascular and epithelial. Small lipophilic molecules pass through this barrier; relatively larger water soluble molecules are excluded. The protein content of the aqueous is thus less than 1% that of the plasma. The junctions between the endothelial cells of the iris capillaries represent the vascular part of this barrier. The permeability of macromolecules here is low. These iris capillaries stand in contrast to the fenestrated capillaries of the ciliary process. The epithelial part of the barrier in the ciliary process comprises the non-pigmented epithelial cells that are ringed with tight junctions. These tight junctions stamp the secretary nature of this epithelium, and their integrity is essential for the ordinary and normal formation of aqueous humor. The tight junction ensure the preservation of a solute gradient across the bilayer of ciliary

epithelia and, in addition, prevent the movement of membrane proteins past junctions, maintaining the symmetry of these transporters to ensure both the direction and content of proper secretion [39].

There are some situations when the breakdown of the blood-ocular barrier can occur, such as ocular injuries and ocular hypotonia. Many types of ocular injuries, such as surgical and non-surgical traumas, intraocular inflammation (e.g., uveitis, scleritis), vascular disorders (e.g., Coats disease, Eales disease), systemic disorders (e.g., diabetes) and intraocular tumors (e.g., retinoblastoma, uveal melanoma) can disturb the blood-ocular barrier, resulting in a variable inward movement of inflammatory cells and blood plasma constituents such as proteins, cytokines and growth factors.

Causes of breakdown of blood aqueous barrier after uneventful cataract surgery include

1. Surgical trauma and manipulations
2. High risk cataract cases with fragile blood aqueous barrier

- Diabetic patients with cataract
- Pediatric cataract
- Lens induced glaucoma
- Traumatic cataract
- Complicated cataract
- Steroid induced cataract

1. SURGICAL TRAUMA AND MANIPULATIONS.

Due to acute injury, there is vasodilatation of blood vessels in the iris and ciliary body. The increase in hydrostatic pressure by vasodilatation causes disruption of the blood aqueous barrier; vascular leakage, forcing the plasmoid aqueous into the posterior chamber. Anterior chamber cells are predominantly lymphocytes, but a significant number of neutrophils may also be present early in the course of the disease. Increased protein content in the anterior chamber is a manifestation of the breakdown of the blood-ocular barrier. There is approximately 7 gms of protein per 100 ml of blood, but only 11 mg of protein per 100 ml of aqueous. At the molecular level, these events are dictated by a host of plasma and cell derived vasoactive mediators including histamine, serotonin, neuropeptides, prostaglandins, kinins, complement fragments and coagulation cleavage products. These mediators promote fibrin deposition, clotting and fibroblast proliferation; that are the probable causes of fibrinous uveitis and posterior synechiae.

A number of studies have depicted the normal breakdown and recovery of the blood aqueous barrier following uneventful extracapsular cataract surgery with insertion of posterior chamber intraocular lens. Sanders D R et al [40] in a study conducted on 234 patients using fluorophotometric measurements found that in patients undergoing uneventful extracapsular cataract surgery with posterior chamber intraocular lens, the blood aqueous barrier became reestablished by 3 months.

VMG Ferguson et al [41] in a study on 130 patients examined the anterior segment and the degree of conjunctival injection by biomicroscopy. Anterior chamber cells and flare were graded on a scale of 0 to 3. This study showed that at 3 months after surgery 78.6% of all eyes had recovered to a normal blood aqueous barrier.

In yet another prospective study by Sanjay M Shah et al [42] photometry was used to document the recovery of the blood aqueous barrier in 27 normal eyes following cataract surgery. Aqueous flare and cells were highest on the first postoperative day, declining rapidly in the first week and returning to preoperative levels by 3 months.

2. HIGH RISK CATARACT CASES

DIABETES MELLITUS

Diabetes mellitus affects more than 120 million people worldwide and it is estimated that it will affect 220 million people by the year 2020. Both the Framingham eye study and the Health and Nutrition Examination Survey; the two largest and the most comprehensive prevalence studies to date, found a threefold to fourfold excess risk of cataract among diabetics less than 65 years of age [43].

Noyes [44] first described the association of uveitis and diabetes mellitus in a case report more than 100 years ago. This presumed association gained acceptance in 1885 when nine cases of iritis were found in 36 patients with diabetes mellitus.

Guy and associates [45] observed iritis in 30% of insulin dependent diabetic patients along with severe autonomic neuropathy as compared to 0.7% of control patients.

Diabetic vascular damage

Diabetic microangiopathy occurs throughout the body, but clinically is more apparent in the kidney and eyes, where it results in glomerulosclerosis and retinopathy respectively. Degree and duration of hyperglycemia appears to be the main factor responsible for the development of microangiopathy because intensive therapy with

strict control of blood sugar delays its onset and slows its progression, and even causes regression of microangiopathy. The precise biochemical mechanisms linking sustained hyperglycemia, basement membrane thickening caused by increased accumulation of extra cellular matrix protein and disturbed vascular functions are not yet fully understood. There is evidence that glucose induced increase in extra cellular matrix protein synthesis, possibly in concert with non-enzymatic glycosylation of proteins is involved.

In the retina, the cellular elements of retinal capillaries consist of endothelial cells and pericytes. The tight junctions of the endothelial cells constitute the inner blood retinal barrier. The pericytes are wrapped around the capillaries and are thought to be responsible for the structural integrity of the vessel wall. In normal healthy individuals, there is one pericyte to each endothelial cell, whereas in diabetic patients, there is a reduction in the number of pericytes. This reduction in pericytes is thought to be responsible for distension of capillary walls and breakdown of the blood retinal barrier leading to leakage of plasma constituents into the retina. A similar process occurs in the blood aqueous barrier [46].

In a study by Akitoshi Yo shida et al [47], the permeability of the blood ocular barrier was examined by fluorophotometry in adolescent and adult diabetic patients before the onset of retinopathy. Anterior chamber flare values, an index of the permeability of the blood aqueous barrier increased in the adolescent diabetic patient compared with the control and showed a significant positive correlation with glycosylated hemoglobin levels. Under normal conditions, the interendothelial junctions of the retinal vessels are known to be extremely tight, but the inter-endothelial junctions of the iris vessels are 10 times more permeable. They are known

as 'leaky' junctions. In this context, they have speculated as to whether changes in blood sugar levels in the course of a day in adolescents first impair the blood aqueous barrier, which is more fragile than the tighter blood retinal barrier. This indicates that assessment of blood aqueous barrier function may assist in the early assessment of diabetic retinopathy or may act as a predictive factor in suggesting the severity and progression of retinopathy.

A P Moriarty et al [48] studied 126 eyes of diabetic patients. Their results showed that (i) eyes with diabetes mellitus had a significantly increased blood aqueous barrier breakdown, when compared to normal eyes (ii) eyes with proliferative diabetic retinopathy had a significantly higher flare values than those with background diabetic retinopathy, no retinopathy or maculopathy (iii) eyes with regressed proliferative diabetic retinopathy had a significantly greater flare value than those with no diabetic retinopathy. Thus they suggested that diabetes mellitus may be associated with an increased blood aqueous barrier breakdown even before the onset of retinopathy, and that more severe proliferative forms may have a greater breakdown of blood retinal barrier.

VMG Ferguson et al [41] in his study showed that the presence of diabetes mellitus was related to excessive damage to the blood aqueous barrier immediately after surgery.

From the clinical point of view Cunliffe et al [49] found that diabetic patients had a higher incidence of inflammation and macular edema post intraocular lens implantation in comparison to age matched controls.

PEDIATRIC CATARACT

There are 1.5 million blind children (corrected visual acuity, 20/400 in the better eye) in the world and one million of them live in Asia. The prevalence of childhood cataract has been reported as 1 to 15 cases in 10,000 children in the developing countries. It is estimated that globally, there are 200,000 children blind from bilateral cataract [50].

Genetic factors

Several genes have been identified in association with congenital and pediatric cataracts. Genetically determined cataract is due to an anomaly in the chromosomal pattern of the individual. About one third of all congenital cataracts are hereditary. It may occur with or without microphthalmia, aniridia, anterior chamber developmental anomalies, retinal degenerations, other multisystem genetic disorders such as chromosome abnormalities, Lowe syndrome or neurofibromatosis type [51]. *PITX3* gene are reported to be responsible for some inherited cataracts in anterior segment mesenchymal dysgenesis [52]. Hereditary Mendelian cataract is inherited as autosomal dominant or autosomal-recessive or X-linked traits. Phenotypically, identical cataracts can result from mutations at different genetic loci and may have different inheritance patterns.

Maternal and fetal factors

Malnutrition during pregnancy or in early infancy has been associated with non-familial zonular cataract. Maternal infections like rubella, toxoplasmosis, and cytomegalo-inclusion etc., are also associated with congenital cataracts. Endocrine disturbance, abuses of alcohol or drugs (thalidomide, corticosteroids etc.) as well as exposure of radiation during pregnancy increases the risk of cataracts in their infants.

Intrauterine hypoxia in the last trimester of pregnancy, Lowe's syndrome, myotonia dystrophica, congenital icthyosis etc. are infantile factors to cause cataract in infants.

The specific characteristics of the pediatric eye especially in children less than two years of age are - 1) intra-operative: scleral collapse, vitreous pressure, highly elastic anterior and posterior capsule for continuous curvilinear capsulorhexis (CCC), miosis, fibrin release, etc. 2) post-operative: uveitis, visual axis opacification (VAO), secondary membrane formation, amblyopia, 3) long-term: growth of the eye and myopic shift.

Pediatric cataract surgery may result in preoperative and postoperative complications. The incidence of post-operative complications such as uveitis, secondary glaucoma and posterior capsular opacification is also much higher in the pediatric age groups compared to the adults[53]. Intraocular inflammation manifests itself as increased cells and flare, inflammatory precipitates on the IOL and the endothelium, formation of synechiae, and inflammatory cyclitic membranes. These reactions are associated with younger age and may be affected by surgical technique, intraoperative injury to adjacent structures such as iris, presence of antecedent ocular infection, and remnants of retained cortical material.

The fibrinoid reaction after pediatric cataract surgery is caused by the breakdown of the immature BAB and insufficient trabecular meshwork fibrinolytic activity. Secondary complications of severe fibrinoid reaction include pupillary membrane and opacification of the anterior hyaloid face. Therefore, measures to prevent or decrease inflammation in these eyes needs consideration.

Posterior capsular opacification is the most common complication after cataract surgery with or without IOL surgery in children. Pupillary capture occurs when a portion of the optic passes anterior to the iris. The incidence of pupillary capture is 8.5% to 33% [54]. Fixation of posterior chamber IOL in the capsular bag decreases the incidence of this complication.

LENS INDUCED GLAUCOMA

In India, 3.91% of the patients undergoing cataract surgery present with lens induced glaucoma. Even in developed countries, a significant number of patients have less than 20/200 vision when operated on for cataract [55]. This is mainly due to the general misbelief that cataract should be mature at the time of surgery to avoid complications.

Lens-induced glaucoma in the elderly can be subdivided into two major categories.

1. Due to blockage of outflow

a. Phacomorphic glaucoma

This type of glaucoma is characterized by the obstruction of the aqueous outflow by the apposition of the iris root to the trabecular meshwork. The most important predisposing factor is a shallow anterior chamber. Phacomorphic glaucoma often occurs from a mature cataract, but may also occur from spherophakia in Weill–Marchesani syndrome.

b. Ectopia lentis

It may present as an isolated inherited form such as ectopia lentis and ectopia lentis et papillae or may be associated with systemic disorders such as Marfan’s

syndrome, homocystinuria, Weill–Marchesani syndrome, hyperlysinemia, and sulfite oxidase deficiency. Dislocation of the crystalline lens may be secondary to trauma.

2. Due to blockage of the trabecular meshwork

a. Phacolytic glaucoma

This acute open-angle glaucoma is due to leakage of lenticular material from senile hypermature or Morgagnian cataract through an intact lens capsule. The original theory about the pathogenesis of this condition was that the macrophages were the major culprit of increase in IOP by blocking the trabecular meshwork. Later research by Epstein and colleagues, Yanoff and Scheie, and Dueker emphasized the role of heavy molecular proteins (HMW) leaking from the lens in the obstruction of the aqueous outflow and de-emphasized the role of the macrophages.

b. Lens-particle glaucoma

In contrast to phacolytic glaucoma, this form of lens-induced glaucoma is associated with a grossly disrupted capsule and the presence of obvious fragments of lens material in the anterior chamber. It may occur after cataract surgery, trauma to the lens, or Nd:YAG posterior capsulotomy.

c. Phacoanaphylactic glaucoma

Phacoanaphylactic glaucoma is an inflammatory reaction directed against lenticular antigens. The patient is sensitized to his own lens antigens and these proteins are kept in an immunologically privileged site within the lens capsule. After an eye surgery or other trauma to the lens capsule, these lens antigens are exposed to the circulation, they may be recognized as ‘foreign’ by the individual’s immune system and they incite an inflammatory response with elevation of the IOP due to involvement of the trabecular meshwork by the inflammation or by obstruction from

inflammatory cells. The time interval between the trauma and the onset of inflammation is 24 hours to 14 days. Pathologically, a granulomatous reaction is noted with polymorphonuclear, epithelioid and giant cells surrounding lenticular material. Phacoanaphylaxis is not the correct name of this condition since it is not an allergy. Eosinophils may be found but not immunoglobulin E (IgE). The mechanism causing the reaction seems to be an Arthus-type immune complex reaction mediated by IgG and the complement system.

Prajna RV et al [56] in their study on lens induced glaucomas found that the percentage of phacomorphic glaucomas (52.7%) is slightly higher than phacolytic (47.3%) and the latter is more common with increasing age probably due to aggregation of high molecular weight proteins in the crystalline lens over time. A significant risk of poor visual acuity was found when the duration between the onset of pain and surgery exceeded five days. Marginally significant risk of poor visual outcome was observed in cases of age higher than 60 years when compared with younger patients.

Pradhan D et al [57] dealt with the frequency and types of lens-induced glaucoma, the reasons for late presentation, and the outcome of current management. In this series, the final visual outcome was worse than in other studies, probably because the majority of the patients reported later than ten days after the onset of pain.

Cataract surgery is the final treatment for phacomorphic glaucoma and has more complications compared to other conditions associated with cataract. One of the most common postoperative complications of phacomorphic cataract surgery is fibrinous uveitis.

The pathogenesis of postoperative fibrinoid inflammation is unknown. Any defect in the blood.aqueous barrier, possibly due to intraocular inflammation, preoperative high intraocular pressure (IOP), or excessive eye manipulation during surgery may lead to a disturbance in coagulation and fibrinolytic pathway.

TRAUMATIC CATARACT

Ocular trauma is the leading cause of unilateral blindness all over the world. Traumatic cataract is common sequelae of ocular injuries in adults and children. The incidence of ocular injuries varies in different parts of the world. From India, the reported incidence is 20.53%.

Several mechanisms have been advocated in the pathogenesis of traumatic cataracts. Wolter [58] and Weidenthal and Schepens [59] have described the following main mechanisms responsible for ocular damage:

- Traumatic coup
- Traumatic countercoup
- Equatorial expansion of the globe
- Penetrating Trauma

Coup injury refers to direct injury to the lens epithelium and capsule, resulting in either an abrasion, which may create focal, or progressive cataract formation, or rupture of the lens capsule, which often leads to rapid opacification of the lens. Countercoup injury refers to damage as a result of shock waves. Blunt trauma to the orbit may cause shock waves to pass through the eye, disrupting the anterior or posterior lens capsule and thus resulting in contusion cataract formation. In blunt trauma, distortion of the globe in an anterior or posterior direction causes shortening of that meridian, with simultaneous equatorial scleral stretching. This may result in

capsular rupture at the equator, causing lens opacification, or zonular dehiscence, with consequent lens subluxation or complete dislocation. Equatorial expansion can also disrupt the anterior hyaloid face, allowing vitreous to enter the anterior chamber through the disrupted zonules. Penetrating trauma can cause total or localized cataracts. Penetrating trauma leading to capsular disruptions causes rapid opacification of the lens.

Based on lenticular opacity, the cataracts are classified as total, membranous, white soft, and rosette type. When there is no clear lens matter between the capsule and nucleus, the cataract was defined as total. When the capsule and organized matter are fused and formed a membrane of varying density, it is defined as a membranous cataract. When loose cortical material is found in the anterior chamber together with a ruptured lens capsule, the cataract is defined as white soft. A lens with a rosette pattern of opacity is classified as a rosette type cataract.

Many types of ocular injuries, such as surgical and non-surgical traumas, can disturb the blood-ocular barrier, resulting in a variable inward movement of inflammatory cells and blood plasma constituents such as proteins, cytokines and growth factors [60].

COMPLICATED CATARACT

Cataract consequent to any primary eye disease is described as complicated cataract. The lens is dependent on the health of the eye for its metabolism and so is affected when the eye cannot supply oxygen and nutrients, or when toxic substances are produced.

Chronic anterior uveitis is the most common cause. The incidence is related to the duration and activity of intraocular inflammation that results in prolonged breakdown of the blood–aqueous and/or blood–vitreous barrier and also related to chronic corticosteroid usage or more often from both. The incidence of cataract in uveitis varies from 57% in pars planitis to 78% in Fuchs heterochromic iridocyclitis (FHI) [61].

The earliest finding is a polychromatic lustre at the posterior pole of the lens which may not progress if the uveitis is arrested. If the inflammation persists, posterior and anterior opacities develop that may progress to maturity. The opacities appear to progress more rapidly in the presence of posterior synechiae.

In the majority of complicated cataracts, the presumed pathogenesis is a derangement of the metabolism of the lens by an interference with its permeability, or the diffusion into it, toxins either from an inflammatory focus or from products of degeneration caused by disease. Owing to the thinness of the posterior capsule and its lack of a supporting epithelial barrier, the earliest clinical changes were typically seen in the region of the posterior pole.

Testa et al [62] studying experimental anaphylactic uveitis came to the conclusion that uveitis, seems to be an unmasking factor for the lens protein sulfhydryl (SH) groups. An increase in the reactivity of the protein sulfhydryl groups together with a significant drop in the glutathione level were the first changes that occur in the lenses of eyes with mild uveitis, which still maintained lens transparency. Oxidation of the gamma crystalline fraction and the insoluble protein was found to occur some weeks later when loss of transparency was observed.

Barber postulated that this exposure allowed oxidation of -SH groups and the rearrangement and realignment of alpha, beta and gamma crystalline to insoluble proteins. These studies were, however thought to be remote from clinical situations.

Due to excessive breakdown of blood aqueous barrier, postoperative inflammation is more. This may vary in terms of severity or duration of inflammation. Associated with this is the development of cystoid macular edema, which may be treated by controlling the inflammation.

STEROID-INDUCED CATARACTS

The steroid induced cataracts are mainly posterior subcapsular cataracts. They exhibit three main distinctive characteristics: (i) association only with steroids possessing glucocorticoid activity, (ii) involvement of aberrant migrating lens epithelial cells, and (iii) a central posterior location. The first characteristic suggests a key role for glucocorticoid receptor activation and subsequent changes to the transcription of specific genes. Glucocorticoid receptor activation is associated in many cell types with proliferation, suppressed differentiation, a reduced susceptibility to apoptosis, altered transmembrane transport, and enhancement of reactive oxygen species activity.

Glucocorticoids may be capable of inducing changes to the transcription of genes in lens epithelial cells that are related to many of these cellular processes. Additionally, given that the glucocorticoid receptor can also cause wide-ranging indirect activities, glucocorticoids could also indirectly affect the lens through the responses of other cells within the ocular compartment and/or through effects on cells at more remote locations. These indirect mechanisms could be mediated through

alterations to the intraocular levels of growth factors that normally orchestrate lens development and maintain lens homeostasis.

Although the mechanism of steroid cataract induction remains unknown, glucocorticoid-induced gene transcription events in lens epithelial cells, and also other intraocular or systemic cells, likely interact to generate steroid cataracts.

COMPLICATIONS OF INCREASED POST-OPERATIVE INFLAMMATION

1. Cystoid macular edema.
2. Posterior capsule opacification.
3. Corneal edema and posterior synechiae.

1. Cystoid macular edema (CME)

Cystoid macular edema represents one of the most common causes of unexpected poor visual acuity after cataract surgery. Following intracapsular cataract extraction about 1% to 2% of the patients will have significant macular edema. Iris fixated IOLs implanted after ICCE were associated with a prevalence of CME of 2% to more than 5%. With extracapsular cataract extraction and phacoemulsification and posterior chamber IOLs the prevalence of clinically significant CME decreased to approximately 1% [63].

The usual onset of clinically significant macular edema is 4 to 12 weeks after uncomplicated cataract surgery, peaking at 4 to 6 weeks. The typical presentation is with poor postoperative central visual acuity followed by fluctuation in visual symptoms. Generally visual loss tends to be self-limiting; however chronic cystoid macular edema with permanent visual loss occurs in approximately 1% of patients undergoing extracapsular cataract extraction.

Cystoid macular edema is best visualized by slit lamp biomicroscopic examination using 78D or 90D lens. There is a loss of foveal depression. The perifoveal area may take on a yellow xanthophyllic colour. The macula appears thickened with translucent intraretinal cystoid spaces. The cystoid spaces are larger in the perifoveal region and become progressively smaller away from the center of the macula. In some patients, a shallow serous detachment of the macula may be seen. Epiretinal membranes and foveal cysts may be seen at the fovea. These limit the potential for visual recovery.

Fluorescein angiography shows capillary dilatation and leakage, later pooling in the outer plexiform layer (Henle's layer) of the retina, giving rise to the classic pataloid staining pattern in the perifoveal region.

Pathogenesis

Irvine [63] considered inflammation as one of the causes of decreased vision in patients with cystoid macular edema (CME). Eyes with CME often have signs of intraocular inflammation. Eyes with cystoid macular edema have evidence of blood ocular barrier breakdown on fluorophotometry. On histopathological examination, chronic inflammatory cells in the iris, ciliary body and retinal blood vessels may be seen. The iris is a metabolically active tissue, which is able to release a number of different inflammatory mediators. Prostaglandins were among the first inflammatory mediators to be implicated in the pathophysiology of cystoid macular edema.

The inflammatory mediators diffuse posteriorly into the vitreous cavity, as no significant diffusion barrier exists for the vitreous, where they result in the disruption of the blood retinal barrier. Immunohistochemical localization of the blood retinal barrier breakdown sites has shown that the barrier breakdown occurs primarily at the

inner blood retinal barrier. Vitreous fluorophotometry in aphakic cystoid macular edema suggests that backward diffusion may play a significant role in its development.

Other theories of cystoid macular edema include vitreous traction and vitreous-uveal traction. Paul G Ursel [63], in his study on 103 patients who underwent phacoemulsification found a trend that those who had CME had higher anterior chamber flare and cell values, at 14, 30 and 60 days postoperatively. This study also showed that the patients who had angiographically proven CME at 60 days have reduced visual acuity throughout the preceding postoperative period. Thus it was concluded that there was a trend for CME to be associated with blood aqueous barrier damage, and sensitive tests of visual acuity showed that even subclinical CME had a deleterious effect on the visual acuity from immediate post operative period onwards.

2. Posterior capsule opacification

Posterior capsule opacification is a major complication of intraocular lens (IOL) implantation after extracapsular cataract extraction. The incidence is in the range of 18 to 50% in adults followed for as long as 5 years. In infants and juveniles an opacification rate of 44% was found within 3 months of surgery, often with in the bag IOL implantation with an intact posterior capsule.

Posterior capsule opacification is caused by proliferation and migration of residual lens epithelial cells. They can produce visual loss through two mechanisms.

1. They can form swollen, abnormally shaped lens cells called Elschnig pearls, which migrate over the posterior capsule into the visual axis.

2. They can transform into fibroblasts, which contain contractile elements (Myofibroblasts) that cause the capsule to wrinkle.

Cell types other than lens epithelial cells may be involved in posterior capsular opacification. As extracapsular cataract extraction is always associated with breakdown of the blood aqueous barrier (maximum immediately after surgery); inflammatory cells, erythrocytes and many other components may be released from the blood into the aqueous humor. This elicits an inflammatory response, the severity of which may be increased by the implantation of an intraocular lens. This foreign body elicits a three stage immune response that involves many different cell types, which include polymorphonuclear leucocytes, giant cells and fibroblasts. As a result collagen is deposited on to the intraocular lens and the capsule, which causes opacities and fine wrinkles to form on the posterior capsule.

The first two problems can be dealt with by careful patient selection and good surgical technique. The excessive postoperative inflammation can be reduced by meticulous surgery and suitable drugs. Control of postoperative inflammation, will also help to keep the postoperative intraocular pressures under control.

MEASUREMENT OF ANTERIOR CHAMBER CELLS AND FLARE

The anterior chamber is easily examined with a slit lamp for signs of ocular inflammation because normally the anterior chamber is optically empty. The presence of cells or increased flare is the evidence of spill over from the inflammed iris or ciliary body. The inflammation begins in the iris and ciliary body and only when sufficient inflammatory cells accumulate within the tissues do the cells begin to enter the aqueous and become visible to the clinician.

Therefore anterior chamber inflammation is a convenient but somewhat indirect measure of the inflammatory reaction in the iris and ciliary body.

ANTERIOR CHAMBER CELLS

Cells from the inflammatory process in the iris and ciliary body pass either by diffusion or by active migration from the tissues into aqueous humor. They are manufactured locally from the fixed tissue cells, or pass through the capillary walls from the blood into the tissues and then into the aqueous humour. Cells from the ciliary body pass through the epithelial layers into the posterior chamber and then into the anterior chamber. They leave the eye through the angle structures and many cells undergo lysis.

Anterior chamber cells are primarily lymphocytes, but a significant number of neutrophils may be present early in the course of disease. It is seen that the size of the individual cells in the anterior chamber will decrease as the inflammation begins to resolve. This may occur before the number actually decreases. Inflammatory anterior chamber cells are white and should be differentiated from brown pigmented cells which may not indicate inflammation. Pigmented cells may be uveal cells, melanin containing macrophages, red blood cells, macrophages with blood pigment or even free pigment.

Anterior chamber cells are best seen by directing the slit beam obliquely across the eye and focusing posterior to the cornea. Neusenblatt suggests a 1 X 1mm slit beam. The cells between the lens and cornea in the slit beam should actually be counted and not estimated to make the grading more reliable and reproducible. There is considerable variation among physicians on the grading of the number of cells. The table summarizes the system proposed by Hogan and colleagues, the system proposed

by Schlaegel, the system proposed by Neusenblatt and that propose by SUN working group.

Figure 2: Grading of anterior chamber cells

Schlaegel		Hogan		Neusenblatt		SUN Working Group	
Grade	**Cells**	**Grade**	**Cells**	**Grade**	**Cells**	**Grade**	**Cells**
–	–	0	0	0	0	0	<1
	Rare (normal)	Rare cells	1–2	–	–		
–	–	Occasional cell	3-7	–	–		
–	–	–	–	Trace[‡]	1–5	Trace	1–5
1+	Occasional cell	1+	7–10	1+[‡]	6–15	1+	6–15
	2–7	1–2+	10–15	–	–		
2+	8–15	2+	15–20	2+	16–25	2+	16–25
	16–30	–	–	–	–		
3+	Too many to count	3+	20–50	3+	26–50	3+	26–50
	Too many to count	–	–	–	–		
4+	Most ever seen	4+	>50	4+	>50	4+	>50

Data from Schlaegel TF Jr. Essentials of uveitis. Boston: Little, Brown, 1967; 7; Hogan MJ, et al. Am J Ophthalmol 1959; 47: 155–70.

ANTERIOR CHAMBER FLARE

Increased protein content in the anterior chamber is a manifestation of a breakdown of blood ocular barrier. When the slit beam is obliquely carried across the anterior chamber, the ability to visualize the path of the beam is termed flare. There is approximately 1g of protein per 100ml of blood, but only 11mg of protein per 100ml of aqueous. A faint amount of flare is normal if a bright light is used. The amount of light scattering is proportional to the concentration of protein in a solution and hence more flare indicates increased protein in the anterior chamber fluid.

There is some disagreement as to whether the presence of flare by itself, without cells or other signs of active inflammation should be treated. Damaged blood vessels may be leaky for a long time after the active inflammation has resolved. Continued treatment with drugs such as corticosteroids probably does little to alter the repair of these vessels in the absence of active inflammation. There is no evidence that small amount of increased protein in the anterior chamber is detrimental to the eye and there appears to be no reason for continued therapy in this situation. The table summarizes the system proposed by Hogan and colleagues, the system proposed by Schlaegel, the system proposed by Neusenblatt and that proposed by SUN working group.

Figure 3: Grading of anterior chamber flare

Grade	Schlaegel	Hogan et al.	SUN Working Group
0	Complete absence		None
	Faint (normal)	–	
1+	Very slight (normal)	Very slight	Faint
	Mild	–	
2+	Mild to moderate	Moderate (iris and lens clear)	Moderate (iris and lens details clear)
3+	Moderate	Marked flare (iris and lens hazy)	Marked (iris and lens details hazy)
4+	Severe	Intense (fibrin, plastic aqueous)	Intense (fibrin or plastic aqueous)

Data from Schlaegel TF Jr. Essentials of uveitis. Boston: Little, Brown, 1967; 7; Hogan MJ, et al. Am J Ophthalmol 1959; 47: 155–70.

In addition to the subjective grading of flare it is possible to more accurately measure the degree of light scattering and quantify the amount of protein technique ocular fluorophotometery uses the principle that fluorescein in the anterior chamber will bind to albumin and the amount of bound fluorescein will alter the polarization of fluorescein which can be measured by fluorophotometry

OCULAR FLUOROPHOTOMETERY

Recently there have been considerable developments in the techniques potential uses of ocular fluorophotometry for the study of the physiological barriers that protect the eye from its external environment. Measurement of the Blood Aqueous Barrier (BAB) or blood retinal barrier (BRB) requires systemic administration of fluorescein either orally or intravenously.The development of the fluorotron master by Coherent Radiation has produced a fluorophotometer that is highly accurate, reliable, gives reproducible results and can measure fluorescence in any part of the eye. This machine has stood the test of time and has been accepted as the gold standard.

The clinical role of vitreous fluorophotometry has been established by work done in Chicago, Copenhagen and at Hammersmith Hospital in London. A single examination requires an hour with the patient, expensive equipment and a skilled operator as well as intravenous injection and at least two blood specimens, so its role is limited to clinical research.

Quantification of damage to the blood aqueous barrier has wide implication in anterior segment surgery and inflammatory eye disease. The BAB is much more permeable that the BRB and different problems are encountered in its measurement. In normal eyes the blood vessels contributing to the blood aqueous barrier appear to be about 10 times more permeable to fluorescein than those of BRB.

Intravenous fluorescein is rapidly bound to albumin in the plasma and also metabolized to fluorescein glucuronide, so that one hour later only about 17% of the dose is still present as free fluorescein. These metabolites have less fluorescence than free fluorescein (30% and 5% respectively) and are more water soluble, so that the

kinetics of their inward and outward transport across the BAB are different from those of free fluorescein. In normal eye most of the fluorescence in the aqueous humour after intravenous fluorescein is due to free fluorescein, principally leaking from the iris vessels, but in pathological eye this is no longer the case, as significant contribution can be made through the ciliary body and by the other metabolites. For this reason elegant equations to explain BAB in the normal eye cannot be applied.

BAB has been variously measured as a (1) permeability or diffusion coefficient of variant complexity, (2) the ratio of fluorescence between a normal and abnormal eye, (3) a peak level of fluorescence or (4) a percentage change from a previous value. Flurophotometry for measurement of BAB may be soon superseded by laser devices which measure the light scattering effect of cells and protein in the anterior chamber.

Laser flare cell meter

The measurement method is similar in principal to slit lamp microscopy. The instrument set up is comprised of a He-Ne laser slit lamp and binocular microscope, equipped with a photomultiplier and a personal computer which controls the system and analyses the data detected by the photomultiplier.

The power of the He-Ne laser and beam diameter is set. The anterior chamber is scanned using an optical scanner. Coaxial illuminating light used for the observation is turned off at the time of measurement by a synchronized lens shutter. Scattered light intensity in the aqueous is detected by the photon counting photomultiplier. The size of the sampling window is fixed and it is positioned in the center of the laser path.

There are two different modes during examination, a protein concentration measuring mode and a cell count mode. Protein concentration is measured first. Then the instrument set up is automatically converted to the cell count mode. It takes 0.5 seconds for each measurement mode and total measurement time was 1 second. When measurements are completed the results are displayed on a screen. Measurements are taken 5 times and average calculated

The reproducibility and validity of laser flare cell meter measurements as an objective method of assessing intraocular inflammation was studied by Akel E1-Maghrby et al [64]. They assessed the preoperative and postoperative anterior chamber reactions in a series of patients who had undergone cataract surgery. Two technicians did the laser flare measurements and clinical assessment of inflammation was recorded by a physician. The average cell and flare readings of the two technicians were nearly identical at every time point, showing the laser flare/ cell measurements to be highly reproducible. The correlations between laser flare/ cell measurement and clinical assessments at post operative time points were highly positive ($P<0.01$) demonstrating the validity of laser flare/ cell measurement.

This new method is non-invasive and enables us to make a quantitative evaluation of inflammation in the anterior segment of the eye. Therefore, it will be a useful tool in clinical and pharmacological research in the field.

VITREOUS HAZE

Vitreous haze is a better indicator of active inflammation than are vitreous cells, because it combines the optical effect of cellular infiltration and protein leakage. Nussenblatt developed a grading scale based on the view of the optic disc and posterior retina with the use of the indirect ophthalmoscope and a 20 diopter lens. It is

important to mentally correct for lens opacities, anterior segment inflammation, and corneal disease; however, the use of the indirect ophthalmoscope prevents mild media opacities from interfering with the grading. The use of photographic standards makes this system more reproducible than other subjective grading systems. In practice it is useful to have the standard color photographs in the examining room. One can then examine the patient's eye and look at the grading chart to select the standard that best matches the degree of haze.

No haze = 0

Slight blurring of optic disc margin = Trace

Slightly blurred optic nerve and vessels = +1

Moderately blurred optic nerve and vessels = +2

Optic nerve head border blurred but visible = +3

Optic nerve head obscured = +4

Figure 4: Grading of vitreous haze

(*From Nussenblatt RB, Palestine AG, Chan CC, et al. Standardization of vitreal inflammatory activity in intermediate and posterior uveitis. Ophthalmology 1985; 92: 467–71*.)

METHODOLOGY

The present study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on subjects with high risk cataract undergoing manual Small Incision Cataract Surgery (SICS) during the period of 1st January 2014 to 31st December 2014.

Study Design: One year randomized clinical trial

Duration: 1st January 2014 – 31st December 2014

METHOD OF COLLECTION OF DATA

Source of data

Patients with high risk cataract undergoing manual SICS at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi

Sample Size

A sample size of 40 cases (20 in each group).

Sampling procedure

A sample size of 40 cases was calculated using the formula

$$n = \frac{2(Z\alpha+Z\beta)^2 pq}{(p_1-p_2)^2}$$

Where n= sample size

$Z\alpha=1.96$

$Z\beta=0.84$

P_1= post operative inflammation in one group (without enoxaparin) =58%

P_2= post operative inflammation in 2nd group (with enoxaparin) =0%

P_1-P_2=effect size=58%

$$P = \frac{p_1 + p_2}{2}$$

$$q = 1 - p$$

SELECTION CRITERIA

Inclusion criteria:

Patients with,

1. Congenital/developmental cataract.
2. Lens induced glaucoma
3. Traumatic cataract
4. Diabetic patients with cataract.
5. Complicated cataract
6. Steroid induced cataract

Exclusion criteria:

Patients with,

1. Ocular surface disorders.
2. Bleeding dyscrasias or coagulopathies.
3. Ongoing anti coagulant therapy.

PROCEDURE:

The study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi during one year duration. Patients with high risk cataract as selected by the inclusion criteria were enrolled into the study after taking an informed and written consent. The study was approved by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belagavi.

All the enrolled patients were briefed about the nature of the study, the interventions used and a written informed consent was obtained (Annexure-I).

Further, demographic data of patients and detailed history was obtained by interviewing the participants and clinical examination and necessary investigations were recorded on predesigned and pretested proforma (Annexure-II).

Preliminary ophthalmological examination was done which included assessment of visual acuity, slit lamp examination and fundoscopy.

Investigations done:

1. Measurement of intra-ocular pressure (IOP).
2. Tests for lacrimal patency.
3. Blood pressure.
4. Random blood sugar.
5. Bleeding time, clotting time.
6. Prothrombin time, Activated partial thromboplastin time.
7. A-scan.
8. B-scan, if indicated.

The patients eligible for the study were randomly assigned into two groups using a computer generated random number table and each patient was allocated a number according to the randomization table.

- Group A- Irrigating solution with low molecular weight heparin (enoxaparin).
- Group B-Irrigating solution without low molecular weight heparin (enoxaparin).

A person not concerned with the study saw the randomization number and for patients in group A the same person added 40mg/0.4ml of enoxaparin in 500ml of

irrigating solution at the start of surgery. For patients in group B regular irrigating solution was used. The presence of enoxaparin in the irrigating solution was unknown to the investigator, the surgeon as well as the patient.

All the patients underwent manual small incision cataract surgery with posterior chamber polymethyl methacrylate (PMMA) IOL. One surgeon performed all the surgeries using the same standard technique. In too young patients, surgery was performed under general anesthesia, while adult patients were operated under peribulbar anesthesia.

Preoperative evaluation

The enrolled patients were admitted prior to surgery. A detailed history was elicited and recorded.

- Visual acuity, both unaided as well as aided using spectacles and pin hole was checked with Snellen's visual acuity chart.
- After pupillary dilatation the cataract was assessed and graded.
- A thorough posterior segment evaluation was done with direct and indirect ophthalmoscope
- Retinoscopy was performed.
- IOP was measured using a non-contact tonometer.
- Patency of lacrimal passages was checked using lacrimal sac syringing.

All patients received one hourly topical antibiotic (Gatifloxacin) eye drop one day prior to surgery. Tropicamide 0.8% and phenylephrine 5% eye drops were instilled for mydriasis, every 15 minutes, starting one hour prior to surgery. Systemic antibiotic (T. Ciprofloxacin 500 mg) was given one day prior to the surgery and on

the day of surgery. For congenital cataract patients, atropinization of pupil was done using 1% atropine eye ointment for 3 days prior to surgery.

Surgical technique

Under all aseptic precautions the eye to be operated was painted with povidine iodine and spirit and was draped. A wire speculum was placed and a superior rectus bridle suture was placed and secured. A fornix based conjunctival flap was made with corneoscleral scissors and hemostasis was achieved by wet field cautery.

The extent of incision was marked on the sclera with calipers and a 6.5 mm straight incision was made 1.5 mm posterior to the surgical limbus with 11 number surgical blade. Scleral tunnel was constructed using a crescent knife and dissection continued 1 mm into clear cornea. Anterior chamber was entered from the anterior limit of sclero corneal tunnel using a 3.2 mm entry keratome. Viscoelastic was injected into the anterior chamber. Capsulotomy was done by can opener technique. Hydrodissection was done. The tunnel was extended with keratome. Nucleus was prolapsed into anterior chamber (AC) and delivered out using sandwich technique. Cortical matter was aspirated using a classical simcoe cannula. A 6mm optic, Polymethyl methacrylate (PMMA), modified C loop IOL of appropriate power was implanted. Viscoelastic was aspirated with simcoe. AC formed with irrigating solution. Conjunctiva and Tenon's capsule were reposited back over the wound. Subconjunctival injection of dexamethasone and gentamycin was given. Eye padded and bandaged.

In case of pediatric cataracts, a 6mm scleral incision was taken 1.5 mm posterior to the surgical limbus with 11 number surgical blade. Scleral tunnel was constructed using a crescent knife and dissection continued 1 mm into clear cornea.

Anterior chamber was entered from the anterior limit of sclero corneal tunnel using a 3.2 mm entry keratome. Viscoelastic was injected into the anterior chamber. A capsulorrhexis was done. Hydrodissection was done. The tunnel was extended with keratome. Nucleus was aspirated with the simcoe canula. Remaining cortical matter was aspirated using a simcoe cannula. A 6mm optic, Polymethyl methacrylate (PMMA), modified C loop IOL of appropriate power was implanted. Posterior capsulorrhexis was done along with anterior vitrectomy. Viscoelastic was aspirated with simcoe. AC formed with irrigating solution and section sutured with 10-0 nylon. Subconjunctival injection of dexamethasone and gentamycin was given. Eye padded and bandaged.

Post operative care

Postoperative medication administered

- Prednisolone acetate 1% hourly for one week and tapered over 6 weeks,
- Antibiotic eye drops (gatifloxacin 0.4%) 6 hourly and
- Mydriatic eyedrops (Tropicamide 0.8% and phenylephrine 5%) once daily for one week.

Post operative assessment

The patients were assessed on 1^{st}, 7^{th}, 30^{th} day and 60^{th} day postoperatively. At each follow up, the patient underwent a detailed ophthalmological examination which included:

- Assessment of visual acuity, unaided and pin-hole visual acuity, using a Snellen's chart.
- Slit lamp examination for anterior chamber cells and flare, iris pigments on intraocular lens, posterior capsular opacification was done by a single

examiner using SL 115 Classic Carl Zeiss slit lamp biomicroscope.

- Intraocular pressure using non-contact tonometer.
- Fundoscopy was performed using direct and indirect ophthalmoscope.
- At the end of two months refraction was done and spectacle correction if any was given to the patient.

Assessment of aqueous cells

The light intensity and magnification of the slit lamp was maximal and with a 2×1mm slit the number of cells in anterior chamber was graded as follows.

No cells = 0

5-10 cells = +1

11-20 cells = +2

21-50 cells = +3

>50 cells = +4

Assessment of aqueous flare

The light intensity and magnification was maximal and with a 2×1mm slit placed obliquely to the plane of the iris to evaluate the degree of obscuration of iris details. The flare was assessed and graded as

Optically empty = 0

Faint- just detectable = +1

Moderate – iris details clear = +2

Marked – iris details hazy = +3

Intense with severe fibrinous exudates = +4

Assessment of vitreous haze

With the use of the indirect ophthalmoscope and a 20 diopter lens vitreous haze was graded as

No haze = 0

Slight blurring of optic disc margin = Trace

Slightly blurred optic nerve and vessels = +1

Moderately blurred optic nerve and vessels = +2

Optic nerve head border blurred but visible = +3

Optic nerve head obscured = +4

Assessment of pigments on the intraocular lens surface

The pigments and cells on the intraocular lens surface was examined semi-qualitatively using a beam 3mm long and 2 mm wide focused on 5 regions on the intraocular lens surface and the average calculated.

Statistical analysis

The data was entered into the Microsoft Excel Spreadsheet. The data was analyzed using SPSS statistical software version 20.0. The categorical data was expressed as rates, ratios and percentages and comparison was done using Fishers exact test and chi-square test. Continuous data was expressed as mean ± standard deviation and the comparison was done using independent sample t test. A probability ('p' value) of less than or equal to 0.05 at 95% confidence interval was considered as statistically significant.

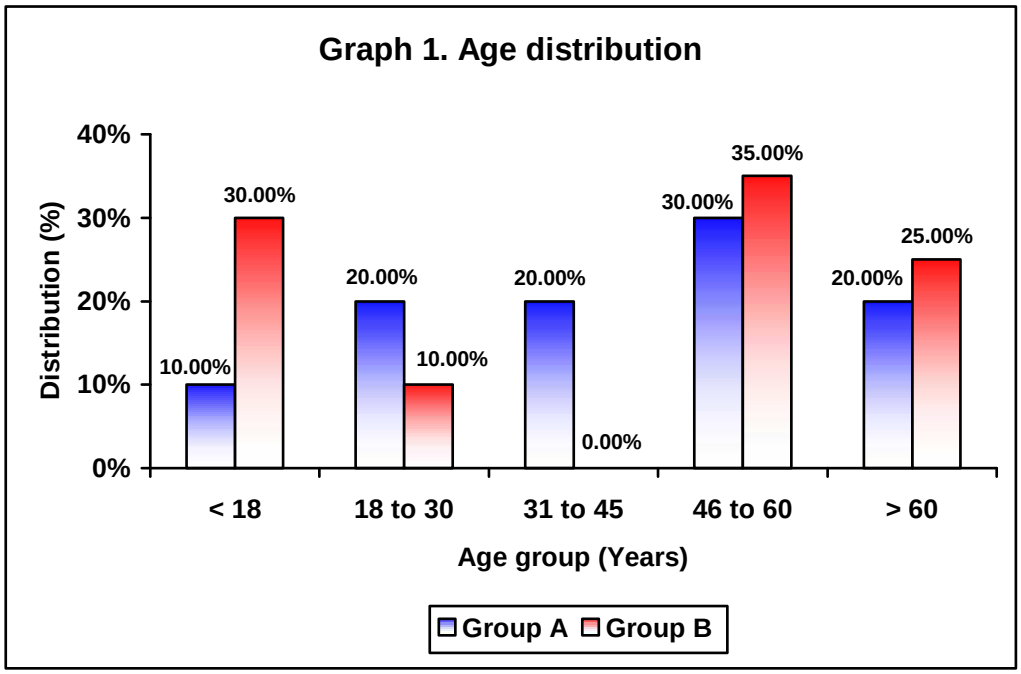
RESULTS

The present study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on subjects with high risk cataract undergoing manual SICS .The patients were divided into two groups that is Group A (irrigating solution with enoxaparin) and Group B (irrigating solution without enoxaparin). The data obtained was tabulated as below.

All calculations were performed using SPSS statistical software version 20.0.

Table 1. Age distribution

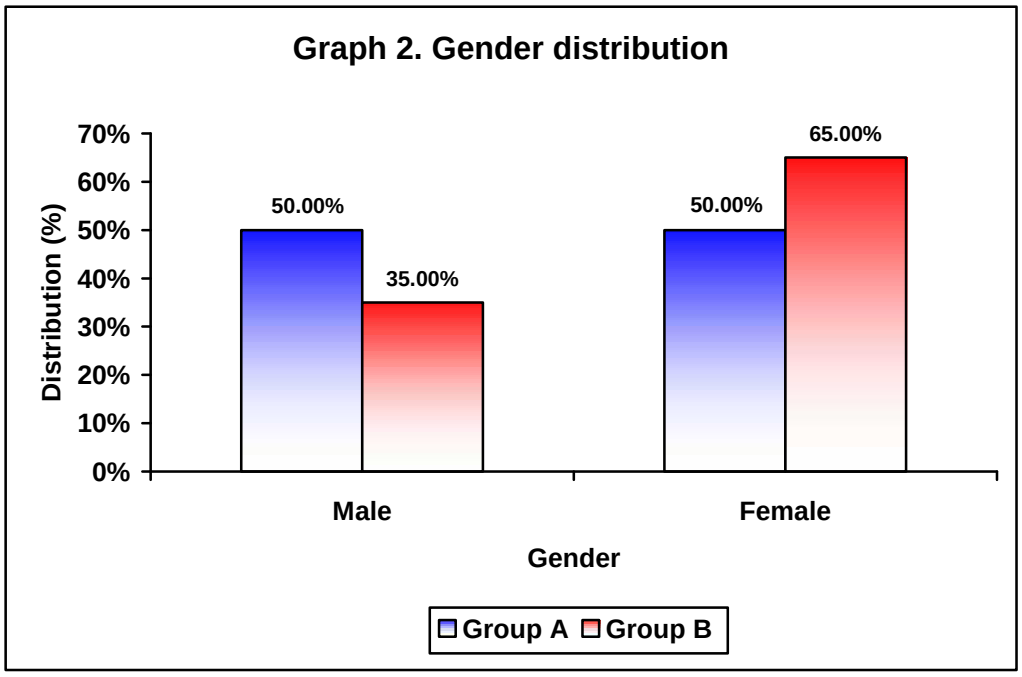
Age group (Years)	Group A (n=20)		Group B (n=20)	
	No.	%	No.	%
< 18	2	10.00	6	30.00
18 to 30	4	20.00	2	10.00
31 to 45	4	20.00	0	0.00
46 to 60	6	30.00	7	35.00
> 60	4	20.00	5	25.00
Total	**20**	**100.00**	**20**	**100.00**



In the present study the mean age in group A was 43.20 years with standard deviation (SD) of 20.41 and in group B the mean age was 41years with SD of 22.79. Majority of the patients in group A were in the range of 46-60 years that is 30%. Also in group B majority were in age group of 46-60 years that is 35%. There was no statistical difference in age between the 2 groups with p value of 0.750.

Table 2.Gender distribution

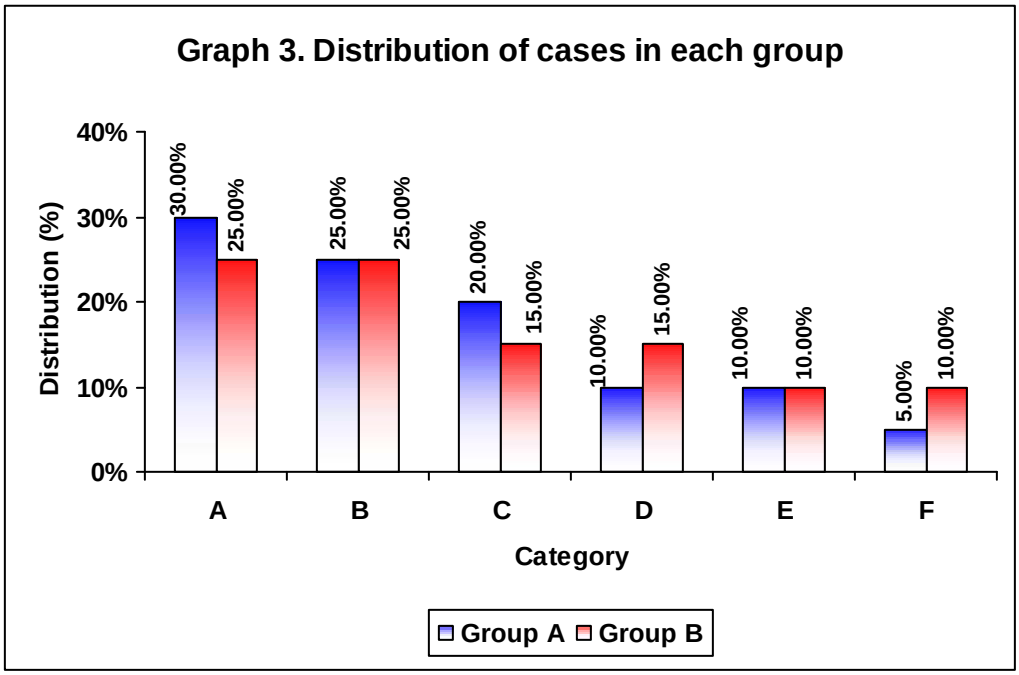
Sex	Group A (n=20)		Group B (n=20)	
	No.	**%**	**No.**	**%**
Male	10	50.00	7	35.00
Female	10	50.00	13	65.00
Total	**20**	**100.00**	**20**	**100.00**



In group A, 50% of patients were females and 50% were male with male:female ratio of 1:1. In group B, 35% were males and 65% were females with male:female ratio of 0.5:1. In both groups, sex distribution was comparable with p value of 0.262 which is statistically insignificant.

Table 3. Distribution of cases in each group

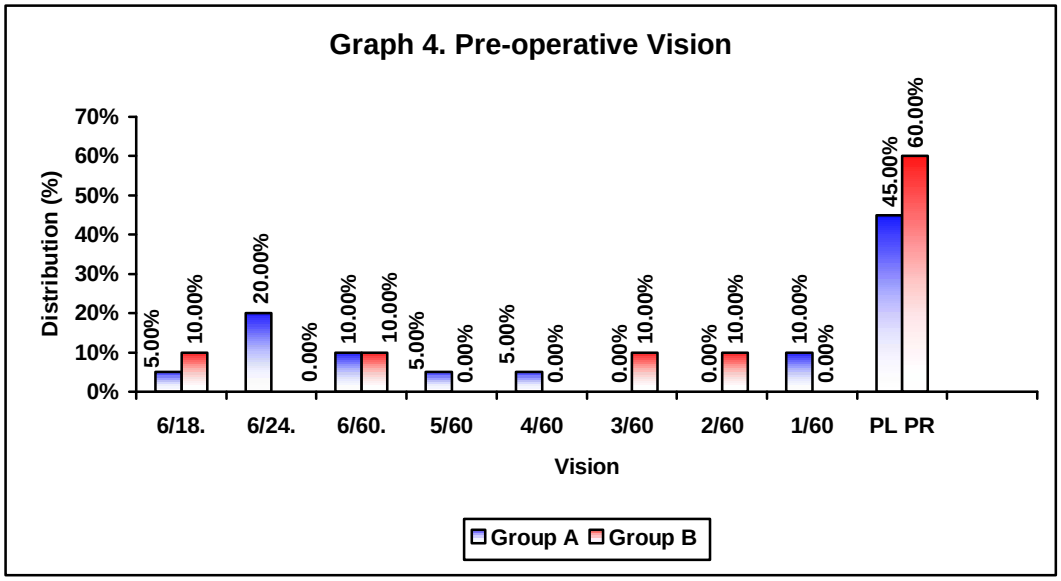
Category	Group A (n=20)		Group B (n=20)	
	No.	**%**	**No.**	**%**
A-Diabetic patients with cataract	6	30.00	5	25.00
B-Traumatic cataract	5	25.00	5	25.00
C-Complicated cataract	4	20.00	3	15.00
D-Congenital cataract	2	10.00	3	15.00
E-Steroid induced cataract	2	10.00	2	10.00
F-Lens induced glaucoma	1	5.00	2	10.00
Total	**20**	**100.00**	**20**	**100.00**



The distribution of different types of cataract in both the groups was comparable with p value of 1.Diabetic patients with cataract were 30% in group A and 25% in group B, traumatic cataract were 25% in each group. Complicated cataract was present in 20% of the patients in group A and 15% of the patients in group B. Steroid induced cataract was present in 10% of the patients in both the groups. Lens induced glaucoma was present in 5% of the patients in group A and 10% of the patients in group B.

Table 4. Pre-operative Vision

Vision	Group A (n=38)		Group B (n=35)	
	No.	**%**	**No.**	**%**
6/18.	1	5.00	2	10.00
6/24.	4	20.00	0	0.00
6/60.	2	10.00	2	10.00
5/60	1	5.00	0	0.00
4/60	1	5.00	0	0.00
3/60	0	0.00	2	10.00
2/60	0	0.00	2	10.00
1/60	2	10.00	0	0.00
PL PR	9	45.00	12	60.00
Total	**20**	**100.00**	**20**	**100.00**



In group A, majority of patients (45%) had just perception of light with accurate projection of rays (PL PR) followed by 20% with visual acuity of 6/24. In group B, also majority of patients (60%) had just PL PR followed by 10% each with visual acuity of 6/18, 6/60, 2/60 and3/60. Pre-operative vision in both groups was comparable with p value of 0.115

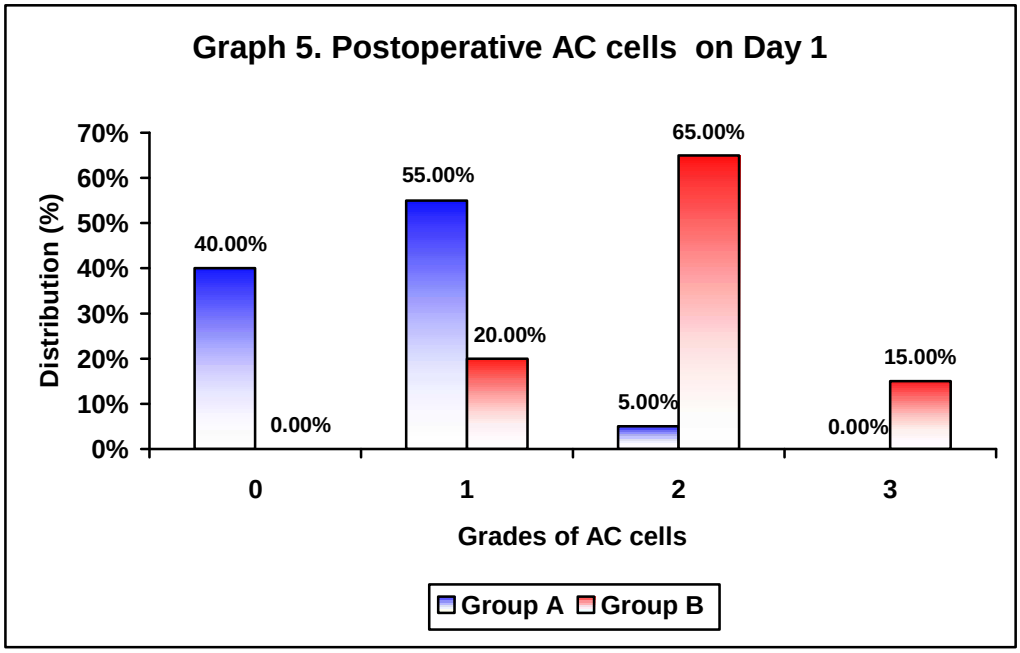
Table 5. Pre-operative IOP

Variables	Group A (n=20)		Group B (n=20)		p value
	Mean	SD	Mean	SD	
IOP (mm Hg)	16.50	6.69	16.78	7.03	0.896

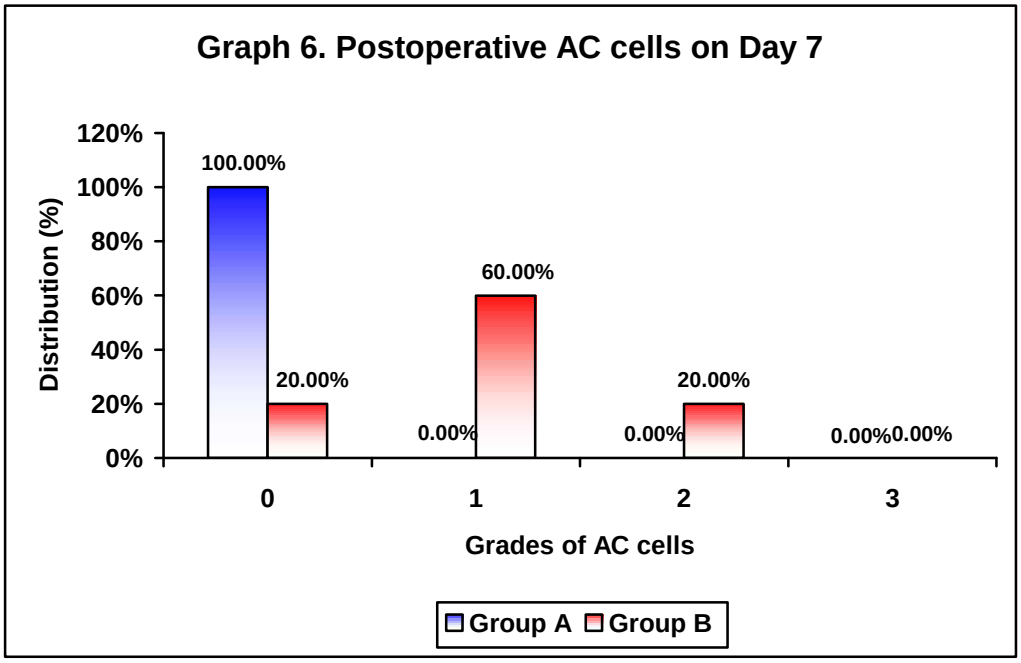
In group A, preoperative mean IOP was 16.50mmHg with SD of 6.69 mmHg and in group B, preoperative mean IOP was 16.78mmHg with SD of 7.03 mmHg Both the groups are comparable with p value of 0.896 which is statistically insignificant.

Table 6. Assessment of postoperative anterior chamber cells

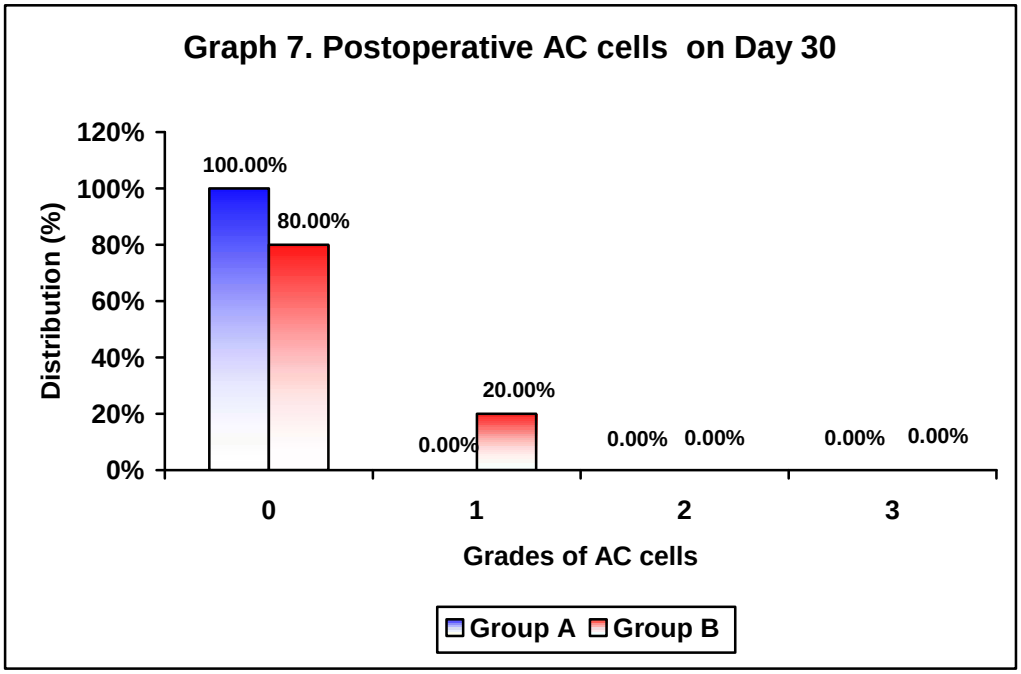
Intervals	Findings	Group A (n=38)		Group B (n=35)		p value
		No	**%**	**No**	**%**	
Day 1	0	8	40.00	0	0.00	**< 0.001**
	1	11	55.00	4	20.00	
	2	1	5.00	13	65.00	
	3	0	0.00	3	15.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 7	0	20	100.00	4	20.00	**< 0.001**
	1	0	0.00	12	60.00	
	2	0	0.00	4	20.00	
	3	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 30	0	20	100.00	16	80.00	**0.053**
	1	0	0.00	4	20.00	
	2	0	0.00	0	0.00	
	3	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 60	0	20	100.00	20	100.00	**-**
	1	0	0.00	0	0.00	
	2	0	0.00	0	0.00	
	3	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	



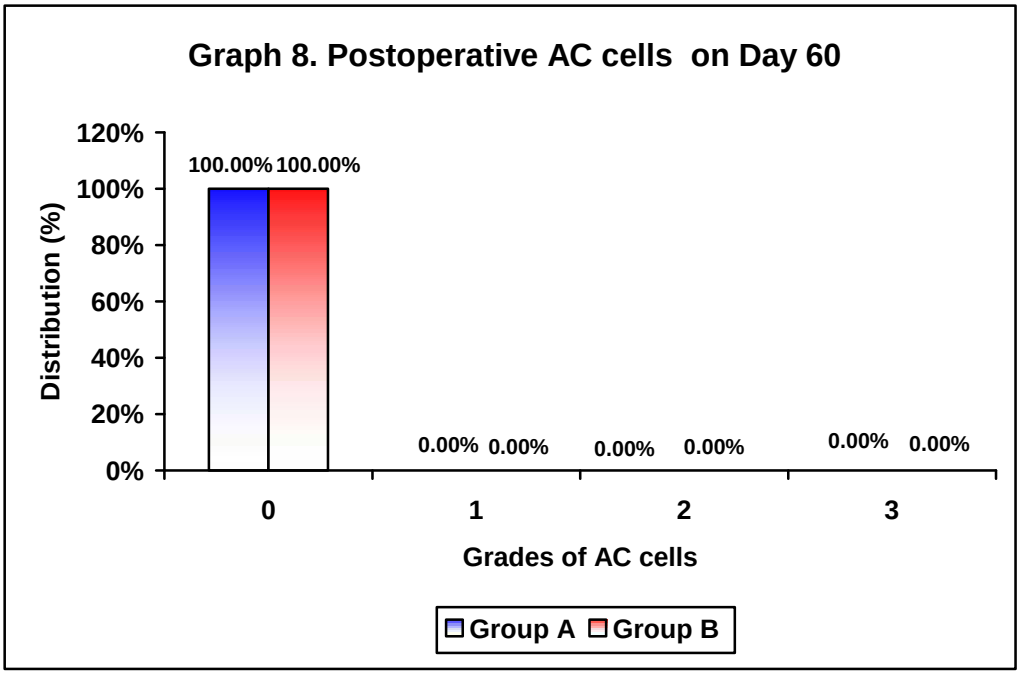
In group A, majority of patients (55%) were having grade 1 AC cells followed by 40% of the patients having no AC cells on day 1. In group B, majority of the patients (65%) were having grade 2 AC cells followed by 20% with grade 1 AC cells and 15 % grade 3 AC cells. In group A, there was significant reduction in AC cells compared to group B on day 1 with p value of <0.001



In group A, all patients had no AC cells on day 7. In group B, majority of the patients (60%) were having grade 1 AC cells followed by 20% each with grade 0 and grade 2 AC cells. In group A, there was significant reduction in AC cells compared to group B on day 7 with p value of <0.001.



In group A, none of the patients had AC cells on day 30. In group B, majority of the patients (80%) had no AC cells and 20% had grade 1 AC cells. There was no statistically significant difference between the two groups with a p value of 0.053.

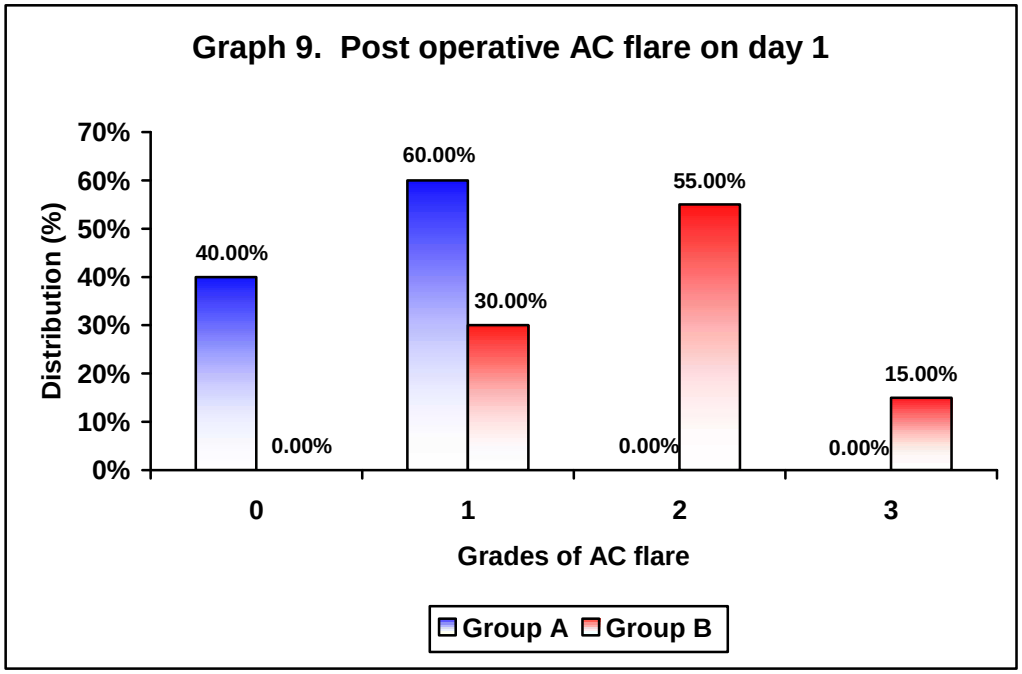


In both the groups none of the patients had AC cells on day 60. There was no statistically significant difference between the two groups.

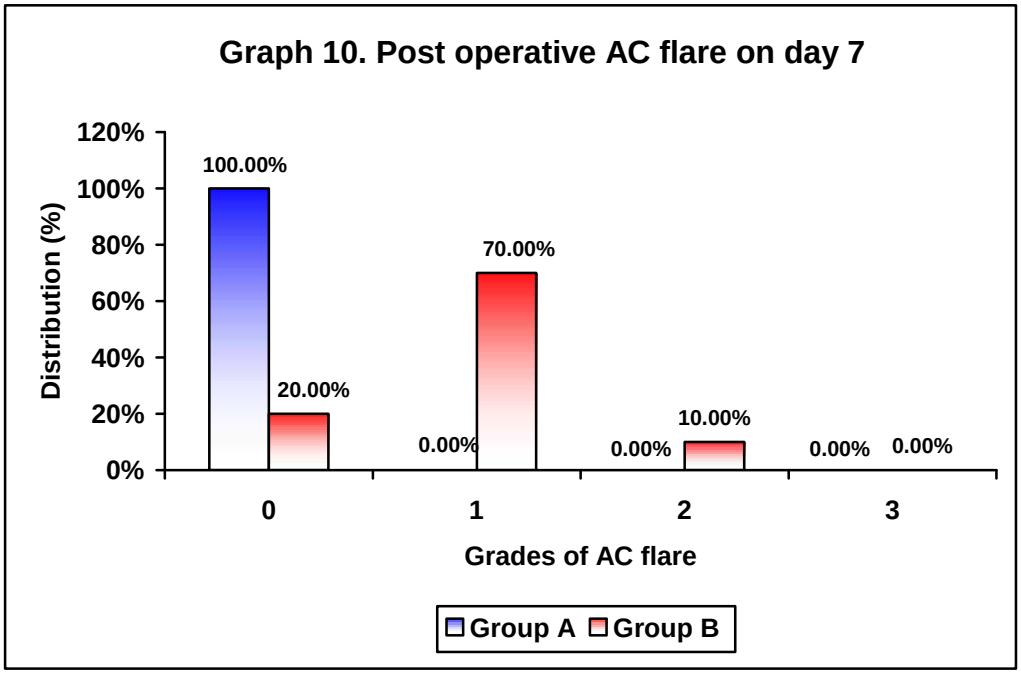
There was a statistically significant difference between the two groups with significant reduction in AC cells in group A on day 1 and day 7. However there was no significant difference in AC cells between the two groups on day 30 and 60.

Table 7. Assessment of post operative anterior chamber flare

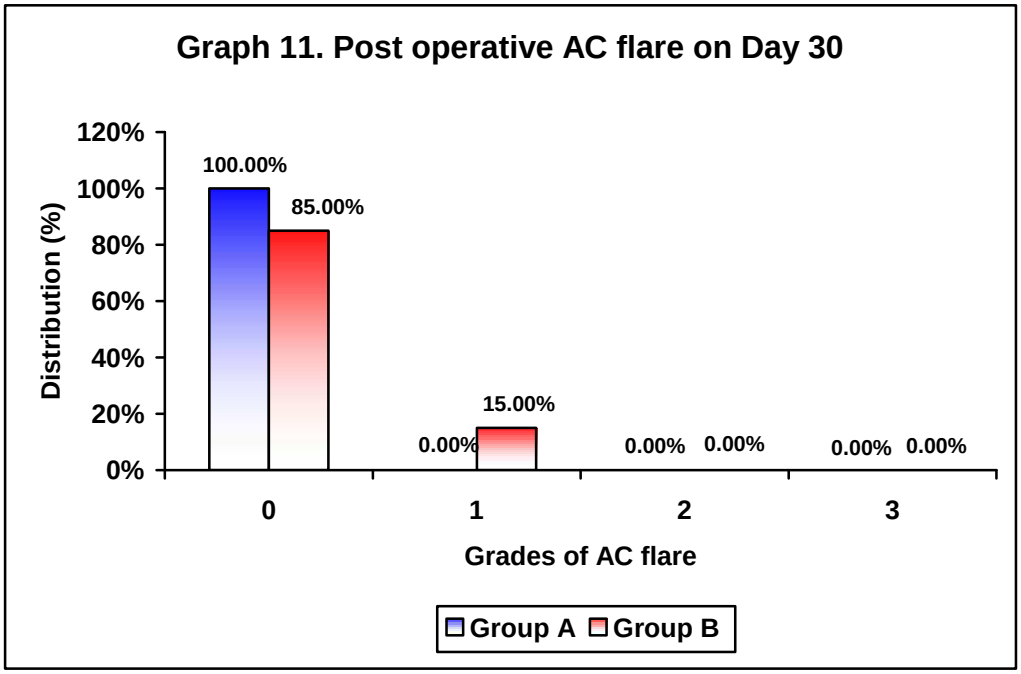
Intervals	Findings	Group A (n=38)		Group B (n=35)		p value
		No	**%**	**No**	**%**	
Day 1	0	8	40.00	0	0.00	**0.001**
	1	12	60.00	6	30.00	
	2	0	0.00	11	55.00	
	3	0	0.00	3	15.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 7	0	20	100.00	4	20.00	**0.001**
	1	0	0.00	14	70.00	
	2	0	0.00	2	10.00	
	3	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 30	0	20	100.00	17	85.00	**0.115**
	1	0	0.00	3	15.00	
	2	0	0.00	0	0.00	
	3	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 60	0	20	100.00	20	100.00	**-**
	1	0	0.00	0	0.00	
	2	0	0.00	0	0.00	
	3	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	



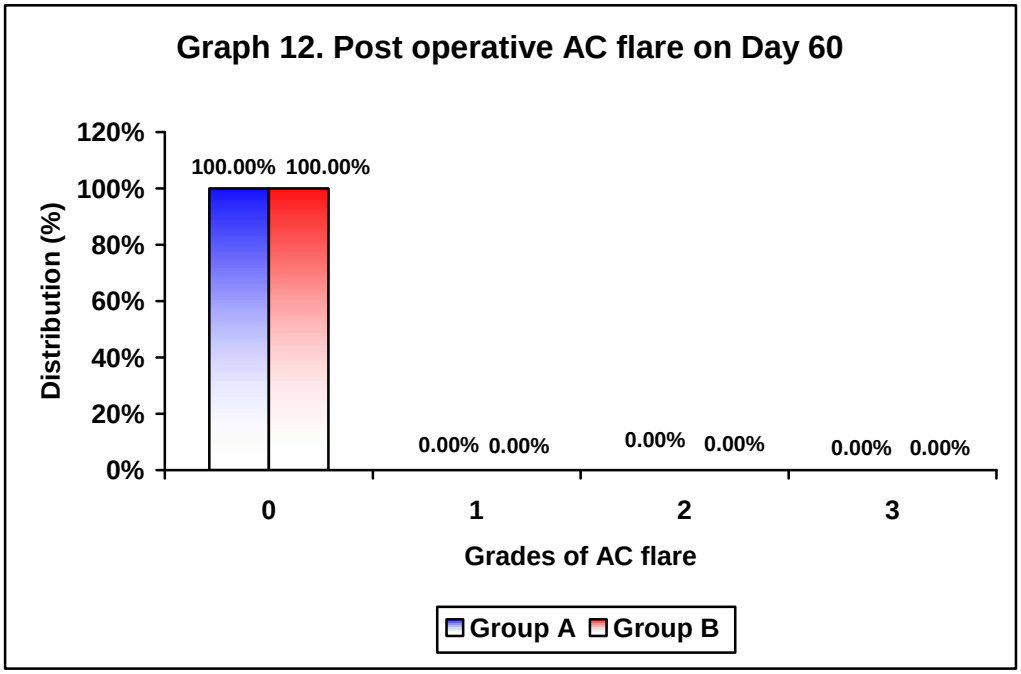
In group A, majority (60%) of patients had grade 1 AC flare on day 1. In group B, majority of the patients (55%) were having grade 2 AC flare followed by 30% with grade 1 and 15% grade 3 AC flare .There was a statistically significant difference between the two groups with p value of 0.001



In group A, none of the patients had AC flare on day 7. In group B, majority of the patients (70%) were having grade 1 AC flare followed by 10% grade 2 AC flare. There was a statistically significant difference between the two groups with p value of 0.001.



In group A, none of the patients had AC flare on day 30. In group B, majority of the patients (85%) had no AC flare and 15% had grade 1 AC flare. There was no statistically significant difference between the two groups with a P value of 0.115.

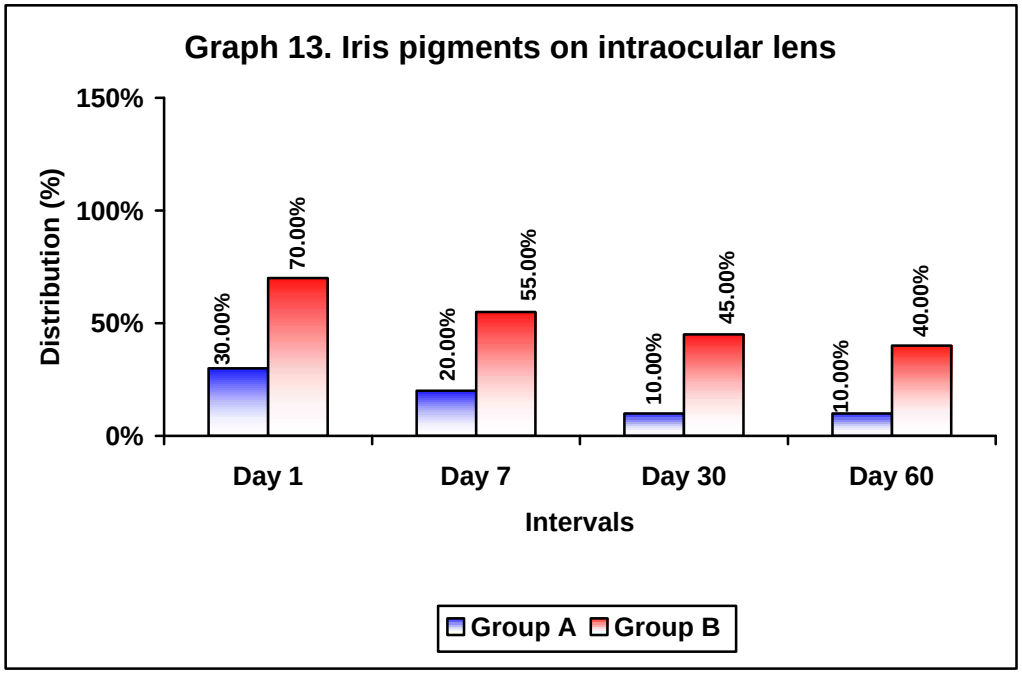


In both the groups none of the patients had AC flare on day 60. There was no statistically significant difference between the two groups.

There was a statistically significant difference between the two groups with significant reduction in AC flare in group A on day 1 and day 7. However there was no significant difference in AC flare between the two groups on day 30 and 60.

Table 8. Iris pigments on intraocular lens

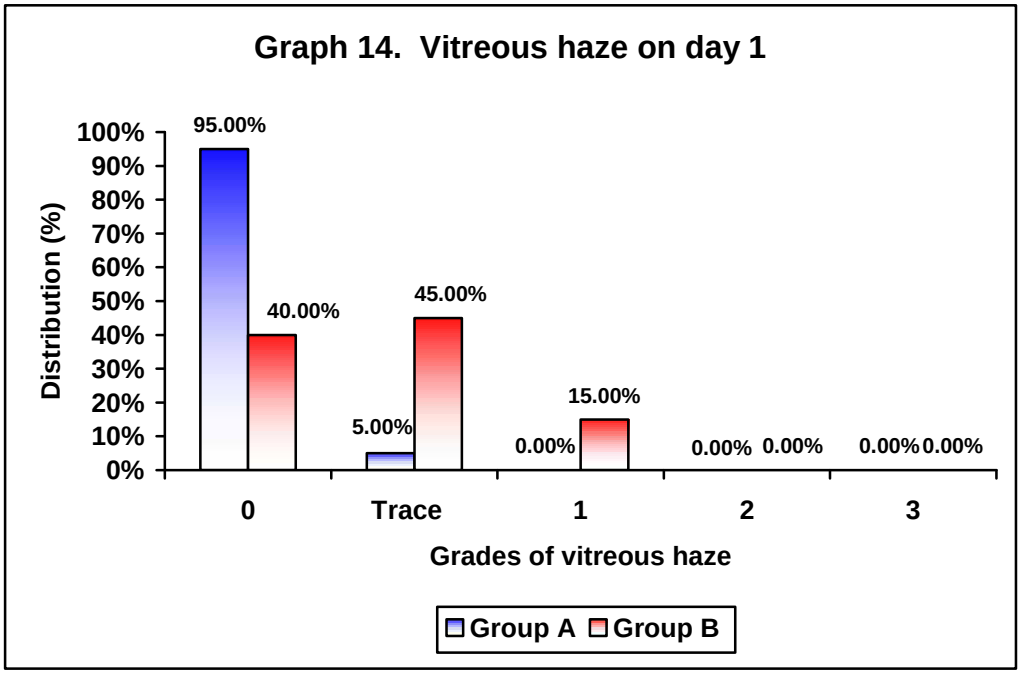
Intervals	Findings	Group A (n=38)		Group B (n=35)		p value
		No	**%**	**No**	**%**	
Day 1	Absent	14	70.00	6	30.00	**0.004**
	Present	6	30.00	14	70.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 7	Absent	16	80.00	9	45.00	**0.002**
	Present	4	20.00	11	55.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 30	Absent	18	90.00	11	55.00	**0.002**
	Present	2	10.00	9	45.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 60	Absent	18	90.00	12	60.00	**0.001**
	Present	2	10.00	8	40.00	
	Total	**20**	**100.00**	**20**	**100.00**	



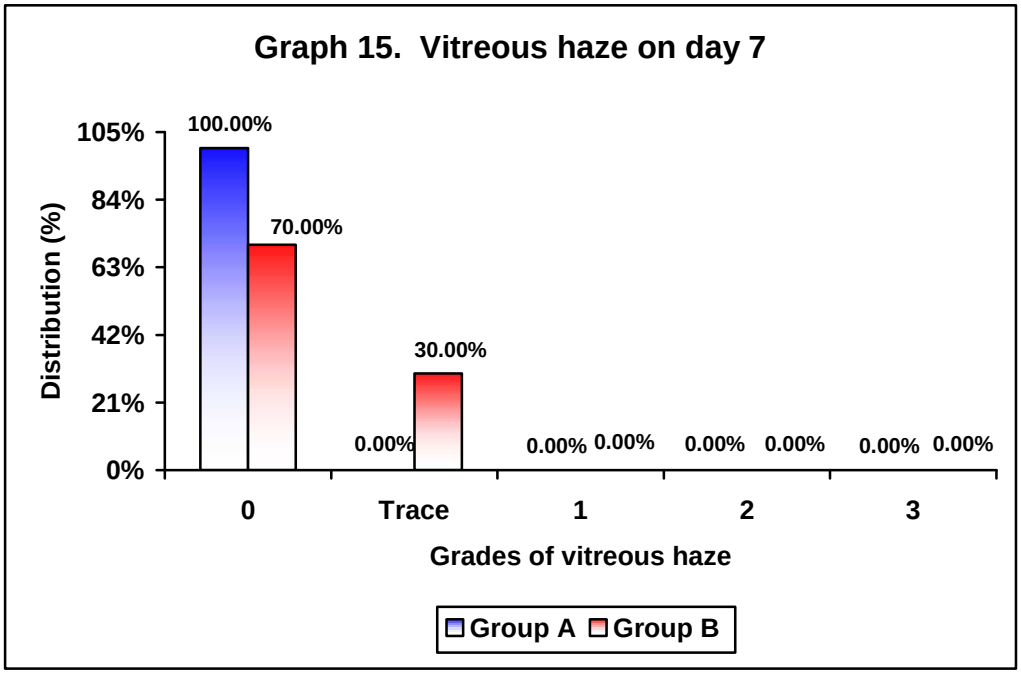
Iris pigments on intraocular lens were seen in 30 % of the patients in group A and 70% of the patients in group B on day 1 with p value of 0.004. On day 7, iris pigments on intraocular lens were noted in 20% of the patients in group A and 66% of the patients in group B with p value of 0.002. On day 30, iris pigments on intraocular lens were noted in 10% of the patients in group A and 46% of the patients in group B with p value of 0.002. On day 60, iris pigments on intraocular lens were noted in 10% of the patients in group A and 40% of the patients in group B with p value of 0.001. There was a statistically significant reduction in iris pigments on intraocular lens in group A when compared with group B.

Table 9. Vitreous haze

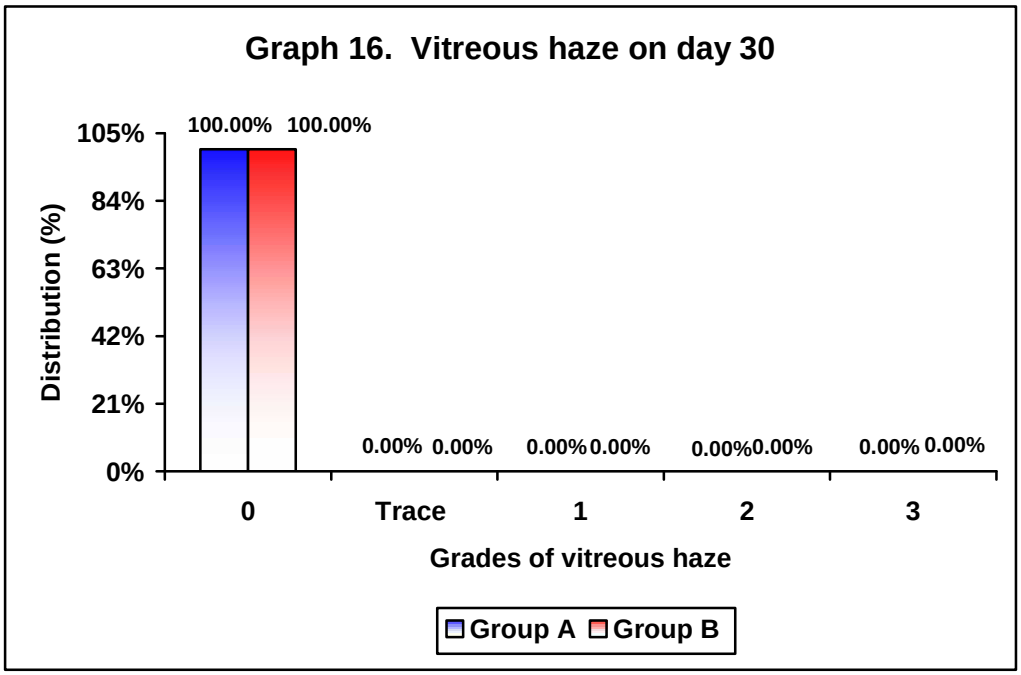
Intervals	Findings	Group A (n=38)		Group B (n=35)		p value
		No	%	No	%	
Day 1	0	19	95.00	8	40.00	**0.001**
	Trace	1	5.00	9	45.00	
	1	0	0.00	3	15.00	
	2	0	0.00	0	0.00	
	3	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 7	0	20	100.00	14	70.00	**0.010**
	Trace	0	0.00	6	30.00	
	1	0	0.00	0	0.00	
	2	0	0.00	0	0.00	
	3	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 30	0	20	100.00	20	100.00	**1.000**
	Trace	0	0.00	0	0.00	
	1	0	0.00	0	0.00	
	2	0	0.00	0	0.00	
	3	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 60	0	20	100.00	20	100.00	**1.000**
	Trace	0	0.00	0	0.00	
	1	0	0.00	0	0.00	
	2	0	0.00		0.00	
	3	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	



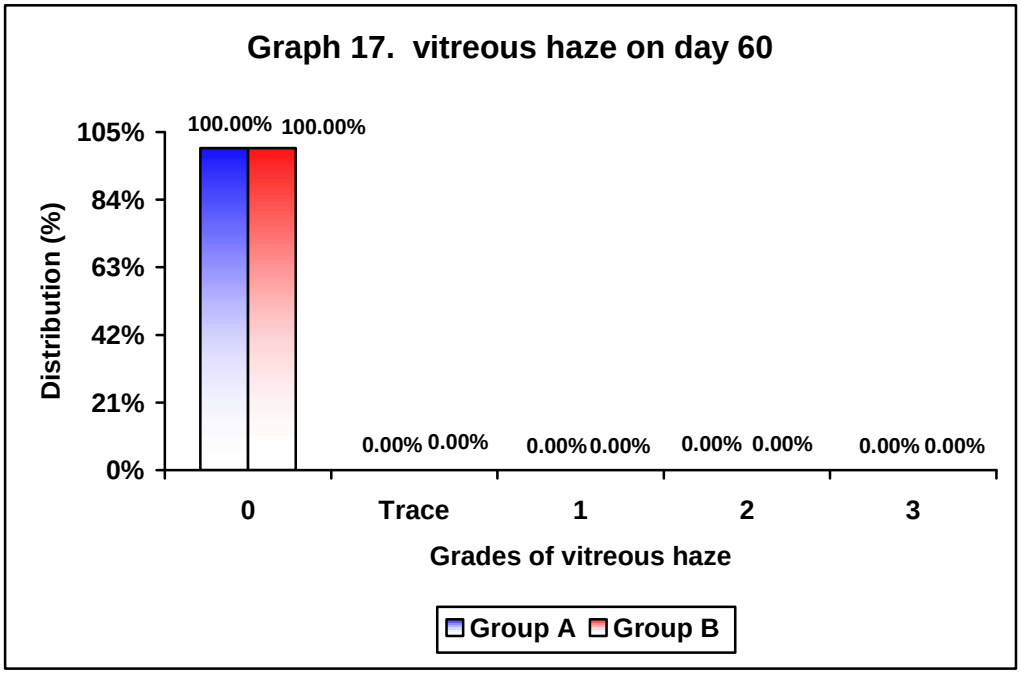
In group A, 95% of the patients had no vitreous haze on day 1 while 40% of the patients in group B had no vitreous haze. 5 % of the patients in group A had trace vitreous haze and 45% of the patients in group B had trace vitreous haze. None of the patients in group A had grade 1 vitreous haze while 15% of the patients in group B had grade 1 vitreous haze.



In group A, none of the patients had vitreous haze on day 7 while 30 % of the patients in group B had trace vitreous haze.



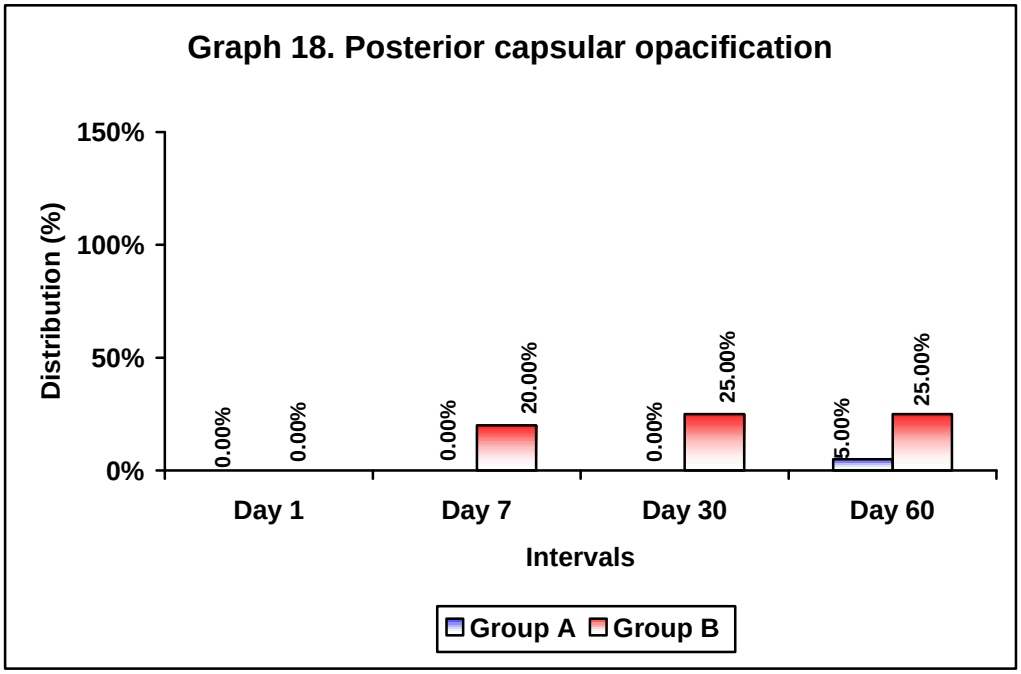
None of the patients in either group had vitreous haze on day 30



None of the patients in either group had vitreous haze on day 60

Table 10. Posterior capsular opacification (PCO)

Intervals	Findings	Group A (n=38)		Group B (n=35)		p value
		No	**%**	**No**	**%**	
Day 1	Absent	20	100.00	20	100.00	-
	Present	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 7	Absent	20	100.00	16	80.00	**0.053**
	Present	0	0.00	4	20.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 30	Absent	20	100.00	15	75.00	**0.024**
	Present	0	0.00	5	25.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 60	Absent	19	95.00	15	75.00	**0.091**
	Present	1	5.00	5	25.00	
	Total	**20**	**100.00**	**20**	**100.00**	



PCO was not seen in any of the patients in both the groups on day 1. On day 7 none of the patients in group A had developed PCO while 20% of the patients in group B had developed PCO. On day 30, none of the patients in group A had developed PCO while 25% of the patients in group B had developed PCO. On day 60, 5% of the patients in group A had developed PCO while 26% of the patients in group B had developed PCO. There was no statistically significant difference in development of PCO between the two groups in all follow-ups.

COMPARISON OF COMPLICATIONS AT DIFFERENT FOLLOW UP INTERVALS

1. Hyphema

Table 11. Hyphema

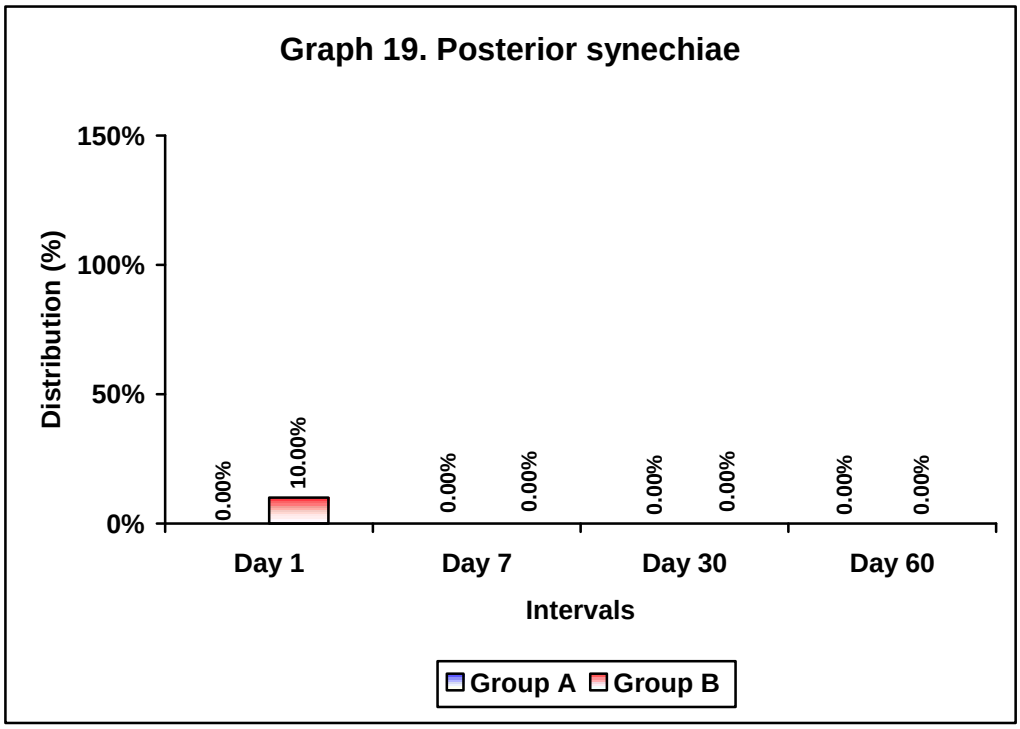
Intervals	Findings	Group A (n=38)		Group B (n=35)		p value
		No	%	No	%	
Day 1	0	20	100.00	20	100.00	-
	1	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 7	0	20	100.00	20	100.00	-
	1	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 30	0	20	100.00	20	100.00	-
	1	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 60	0	20	100.00	20	100.00	-
	1	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	

None of the patients in both the groups developed hyphema postoperatively.

2. Posterior synechiae

Table 12. Posterior synechiae

Intervals	Findings	Group A (n=38)		Group B (n=35)		p value
		No	%	No	%	
Day 1	Absent	20	100.00	18	90.00	**0.244**
	Present	0	0.00	2	10.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 7	Absent	20	100.00	20	90.00	-
	Present	0	0.00	0	10.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 30	Absent	20	100.00	20	90.00	-
	Present	0	0.00	0	10.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 60	Absent	20	100.00	20	90.00	-
	Present	0	0.00	0	10.00	
	Total	**20**	**100.00**	**20**	**100.00**	

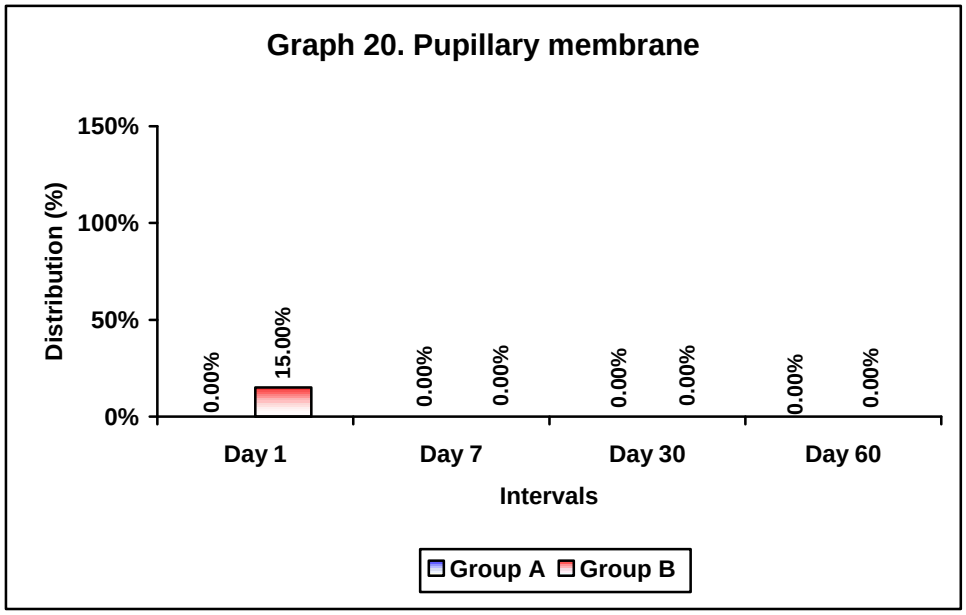


In group A, none of the patients developed posterior synechiae. In group B, 10% of the patients developed posterior synechiae on day 1.

3. Pupillary membrane

Table 13. Pupillary membrane

Intervals	Findings	Group A (n=38)		Group B (n=35)		p value
		No	%	No	%	
Day 1	Absent	20	90.00	17	85.00	**0.115**
	Present	0	0.00	3	15.00	
	Total	**18**	**90.00**	**20**	**100.00**	
Day 7	Absent	20	100.00	20	100.00	-
	Present	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 30	Absent	20	100.00	20	100.00	-
	Present	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 60	Absent	20	100.00	20	100.00	-
	Present	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	



In group A, none of the patients developed pupillary membrane. In group B, 15% of the patients developed pupillary membrane on day 1.

4. Optic capture

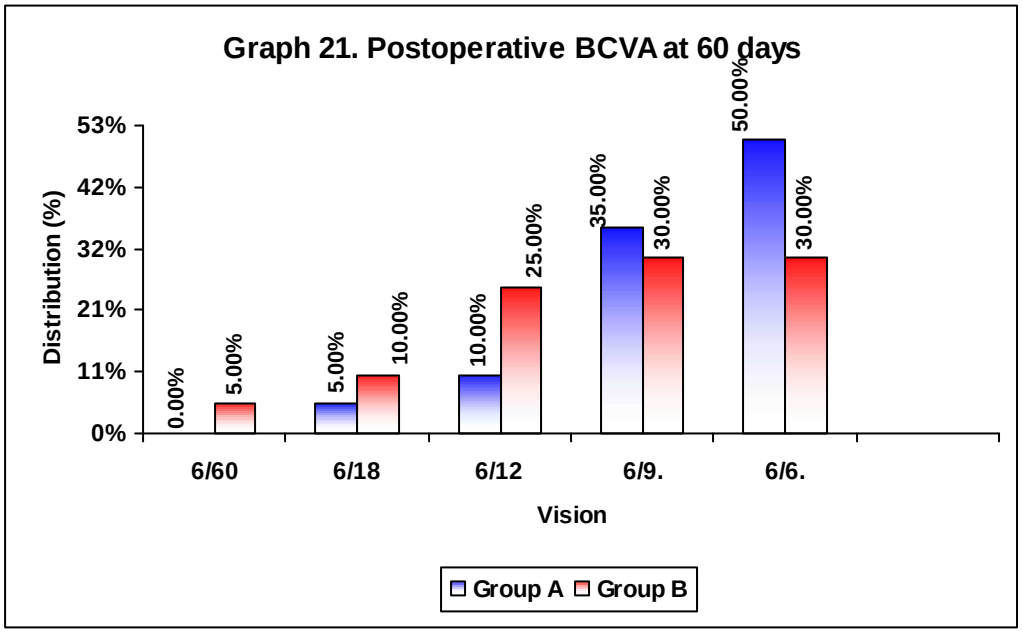
Table 14. Optic capture

Intervals	Findings	Group A (n=38)		Group B (n=35)		p value
		No	%	No	%	
Day 1	Absent	20	100.00	20	100.00	-
	Present	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 7	Absent	20	100.00	20	100.00	-
	Present	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 30	Absent	20	100.00	20	100.00	-
	Present	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	
Day 60	Absent	20	100.00	20	100.00	-
	Present	0	0.00	0	0.00	
	Total	**20**	**100.00**	**20**	**100.00**	

None of the patients in both the groups developed optic capture postoperatively.

Table 15. Postoperative best corrected visual acuity (BCVA) at 60 days

Vision	Group A (n=38)		Group B (n=35)	
	No.	%	No.	%
6/60	0	0.00	1	5.00
6/18.	1	5.00	2	10.00
6/12	2	10.00	5	25.00
6/9.	7	35.00	6	30.00
6/6	10	50.00	6	30.00
Total	**20**	**100.00**	**20**	**100.00**



In group A, majority of patients (50%) had BCVA of 6/6 at the end of 60 days, followed by 35% of the patients with visual acuity of 6/9, 10% of the patients had BCVA of 6/12 and 5% of the patients had BCVA of 6/18. In group B, 30% of the patients had BCVA of 6/9 and 6/6 each, followed by 25% of the patients with visual acuity of 6/12, 10% of the patients with BCVA of 6/18 and 5% of the patients with BCVA of 6/60. Postoperative BCVA in both groups was comparable with p value of 0.561

Table 16. Mean IOP 60 days post operatively

Variables	Group A (n=20)		Group B (n=20)		p value
	Mean	SD	Mean	SD	
IOP (mm Hg)	12.31	3.45	12.24	3.01	0.946

In group A, postoperative mean IOP was 12.31mmHg with SD of 3.45 and in group B, postoperative mean IOP was 12.24mmHg with SD of 3.01. There was no significant difference in IOP between the two groups with p value of 0.946 which is statistically insignificant.

DISCUSSION

The present study was conducted in the Department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on subjects with high risk cataract undergoing manual SICS. The patients were divided into two groups that is Group A (irrigating solution with enoxaparin) and Group B (irrigating solution without enoxaparin).

Extracapsular cataract extraction, as manual extraction or as phacoemulsification, with posterior chamber intraocular lens (PCIOL) implantation is widely accepted as the safest and most successful method of cataract surgery. Surgical trauma during cataract surgery causes breakdown of the blood aqueous barrier, leading to augmented protein leakage and cellular reaction in the aqueous humor. Ophthalmic topical preparations such as steroids and nonsteroidal anti-inflammatory drugs effectively reduce postoperative inflammation. Although the inflammatory complications of uncomplicated cataract extraction and IOL implantation are rare, inflammatory complications postoperatively in high risk cases are high.

Several recent laboratory studies have shown that heparin related compounds can reduce intraocular inflammation following intraocular surgery [37]. The use of heparin in ophthalmic surgery was first described by Johnson et al [37] who found that a single anterior chamber injection, heparin supplementation in the infusion solution, or a single intravenous injection resulted in a statistically significant reduction in postoperative intraocular fibrin formation in rabbits after vitrectomy and cyclocryotherapy. Heparin surface modification has been effective in reducing the inflammatory response to polymethyl methacrylate (PMMA) intraocular lens [3].

These heparin coated PMMA intraocular lens reduces the inflammatory deposits on the lens but does not have any effect on the blood aqueous barrier. The anti-inflammatory and anti-proliferative properties of heparin can be utilized by using it in the irrigating solution intraoperatively. This reduces the blood aqueous barrier breakdown along with decreasing the inflammatory deposits on the lens. Low molecular weight heparin has a lesser rate of bleeding with the same amount of anti-inflammatory and anti-proliferative effect. So by using low molecular weight heparin the advantages of heparin is maintained and the disadvantage is reduced.

Iverson et al [38] demonstrated that an infusion of low molecular weight heparin inhibits the development of fibrin after lensectomy, vitrectomy and retinotomy in rabbits. Heparin has been shown to induce apoptosis in human peripheral neutrophils which may help in explaining its anti-inflammatory effect [32]. Heparin also inhibits reactive oxygen species generation by mononuclear and polymorphonuclear leucocytes [34]. In addition, heparin possesses anti-inflammatory properties through its ability to inhibit activation of the complement system [35].

In this prospective study we have tested the hypothesis that low molecular weight heparin (enoxaparin) added to the irrigating solution reduces postoperative inflammation and pigment deposits on the intraocular lens surface. We have also studied about the complications associated with the use of low molecular weight heparin such as hyphema.

Low molecular weight heparin (enoxaparin) was added to the irrigating solution which has a potential to reduce the severity of postoperative fibrin formation after cataract surgery in eyes prone to postoperative inflammation. In our study postoperative inflammatory response in high risk groups was significantly reduced

when enoxaparin was added in the irrigating solution during surgery (group A) until 7^{th} postoperative day.

Postoperative inflammation was assessed by analyzing the anterior chamber cells and flare, vitreous haze and iris pigments on lens. All calculations were performed using SPSS statistical software version 20.0. A probability ('p' value) of less than or equal to 0.05 at 95% confidence interval was considered as statistically significant

The baseline characteristics of the patients in the study and control groups were first analyzed to see if the groups were similar.

In the present study, in both the groups majority of the patients were in the age group of 46 to 60 years. The mean age in group A was 43.20 years and in group B it was 41 years (P=0.750).

In group A, 50% of patients were females and 50% were male with male:female ratio of 1:1. In group B 35% were males and 65% were females with male:female ratio of 0.5:1. (P=0.262).

The distribution of different types of cataract in both the groups was as follows; diabetic patients with cataract were 30% in group A and 25% in group B, followed by traumatic cataract with 25% in each group. Complicated cataract was present in 20% of the patients in group A and 15% of the patients in group B. Steroid induced cataract was present in 10% of the patients in both the groups. Lens induced glaucoma was present in 5% of the patients in group A and 10% of the patients in group B. (P=1)

In group A majority of patients (45%) had just perception of light with accurate projection of rays followed by 20% of the patients with visual acuity of 6/24. In group B also majority of patients (60%) had just perception of light with accurate projection of rays followed by 10% of the patients each with visual acuity of 6/18, 6/60, 2/60 and 3/60. (P= 0.115).

In group A preoperative mean intraocular pressure (IOP) was 16.50mmHg with SD of 6.69mmHg and in group B preoperative mean IOP was 16.78mmHg with SD of 7.03mmHg. (P= 0.896).

The age, sex variation, distribution of cases in both the groups, preoperative vision and intraocular pressure were found to be similar in both groups. Both the groups were similar in all respects and any statistically significant difference in postoperative inflammation is due to the presence of low molecular weight heparin in the irrigating solution.

POST OPERATIVE CELLS, FLARE AND PIGMENT DEPOSITS ON THE INTRAOCULAR LENS.

Anterior chamber cells and flare:

In our study a statistically significant reduction in anterior chamber (AC) cells were noted in patients in whom low molecular weight heparin (enoxaparin) was used on day 1(P<0.001) and day 7 (P<0.001). We further noted that in patients who received low molecular weight heparin in the irrigation solution, 40% of the patients had no AC cells on day 1, 60% of the patients had lesser grade AC cells (Grade I to Grade II) and none of the patients had grade 3 AC cells. In the control group, 85% of the patients had grade I to Grade II AC cells and in 15% of the patients, grade 3 AC cells was noted on day 1. On day 7 none of the patients in whom low molecular

weight heparin was used in the irrigating solution had AC cells, in comparison with 80% of the patients in control group had grade I and grade II AC cells. From day 30 no significant difference was noted between the study and control groups.

In our study the assessment of flare in the early post operative period showed a statistically significant reduction on day 1 (P= 0.001) and day 7 (P=0.001) in the patients who had received enoxaparin in the irrigating solution. We further noted that in patients, who received low molecular weight heparin in the irrigation solution, 40% of the patients had no AC flare on day 1, 60% of the patients had grade I AC flare and none of the patients had grade 3 AC flare. In the control group, 85% of the patients had grade I to Grade II AC flare and in 15% of the patients, grade 3 AC flare was noted on day 1. On day 7 none of the patients in whom low molecular weight heparin was used in the irrigating solution had AC flare, in comparison 80% of the patients in control group had grade I and grade II AC flare. From day 30 no significant difference was noted between the study and control groups.

Our results are consistent with the findings of Kruger et al [7], in their study on long term effects of heparin sodium in the irrigating solution during small incision cataract surgery, the AC cells and flare values were lower in the study group on day 1,3 and 7 postoperatively. In a similar study by Kohnen et al[6], reduced cells and flare values were seen postoperatively on day 1 and 3.

The above two studies differ from our study in that though the cells and flare values were lower on day 1,3 and 7 the values were not statistically significant. This may be accounted for by the fact that our study included all high risk cataract cases like diabetic patients with cataract, traumatic cataract, steroid induced cataract, complicated cataract, congenital cataract and lens induced glaucoma in whom its

already been demonstrated in a number of studies that postoperative inflammation is increased. In the above two studies high risk cataract cases were excluded from the study. This could also possibly have resulted because of the difference in equipment used to quantify the cells and flare in the anterior chamber. The Kowa FC-1000 laser flare and cell photometer was used in the above studies, while we utilized a SL 115 Classic Carl Zeiss slit lamp to quantitate the cells.

Tirkey ER et al [65] studied the effect of low molecular weight heparin in high risk cases in which 80 eyes of 76 patients were included in the study. 40 eyes had intraocular infusion of enoxaparin (group-A) and 40 eyes were operated without intraocular enoxaparin (group-B). Both of the groups had high risk cases like congenital cataract, traumatic cataract, complicated cataract, lens induced glaucoma and diabetic patients with cataract. On day 1 and day 7 AC cells values were significantly lower in group with heparin infusion ($P<0.004$) and were very similar to flare value. None of the patients with enoxaparin in the irrigating solution had grade 4 AC cells while 2 patients in control group had grade 4 AC cells. Flare values were raised in the control group on day 1 and day 7 which was significant ($P<0.003$) with subsequent decrease thereafter. The results of this study are consistent with the results of our study.

Rumelt S et al [66] in their study on the use of intraoperative enoxaparin in the irrigating solution in pediatric cataract surgery found that in patients with enoxaparin in the irrigating solution had less than a mean of 10 cells in the anterior chamber while patients in whom enoxaparin was not used had more than a mean of 10 cells in the anterior chamber ($P<0.001$).

Caca I et al [67] studied the efficacy of enoxaparin in irrigating solution in

variable doses on postoperative inflammatory response in congenital cataract surgery and found that anti-inflammatory effect of enoxaparin varied with different dosage and least postoperative inflammation and related complications was seen in eyes that received 40mg enoxaparin in 500mL balanced salt solution.

Özkurt et al [68] in a study on pediatric cataract surgery found that addition of heparin to the irrigating BSS prevented early postoperative inflammatory reactions. In another study by Bayramlar et al [69] also showed that addition of heparin to the irrigating solution during surgery decreases postoperative fibrinoid reaction and late inflammatory complications.

However, Vasavada et al [70] in their study on pediatric cataract surgery found no significant reduction in postoperative inflammation on addition of low molecular weight heparin in irrigating solution.

In cases of phacomorphic glaucoma also low molecular weight heparin reduces the postoperative cells and flare and also fibrinous reaction when used in the concentration of 5 IU/L in 500 ml of Balanced Salt Solution [71].

Iris pigments on intraocular lens

A number of studies have demonstrated decreased pigments and cellular deposits on the intraocular lens surface in heparin surface modified lens. Heparin inhibits leucocyte migration and pigment deposition. Inflammatory cells originate from the uveal tissue, enter the anterior chamber and are frequently found over IOL surface.

Percival and Pai [25] placed a heparin surface-modified one-piece lens into the posterior chamber of 36 patients with cataracts associated with previous or chronic

recurrent uveitis. They found that recurrent inflammatory disease was present including an acute postoperative fibrin reaction, but the heparin coating appeared to provide a cell-free IOL surface in most eyes.

Alio et al [72] in a prospective study of cataract surgery in uveitic eyes compared four different types of IOL. Using hydrophobic acrylic, silicone, polymethyl methacrylate (PMMA), and heparin surface-modified PMMA lenses, they concluded that the acrylic IOLs had a better visual outcome and lower complication rate, whereas both acrylic and heparin surface-modified PMMA lenses had the lowest relapse rates.

In our study we noted a statistically significant decrease in pigments on the intraocular lens surface on the first postoperative day (P=0.004) in patients treated with enoxaparin in the irrigating solution. Our results are consistent with the published results of Kruger et al [7] who noticed that on the first postoperative day patients who received heparin had significantly less number of intraocular lens without cells on their surface, in comparison to the control group.

Tirkey ER et al [65] found that none of the patients treated with intraoperative heparin infusion had precipitates over the IOL (P<0.001) while 2 patients in control group had inflammatory precipitates over the IOL.

In our study we also noted a statistically significant reduction in pigments on the intraocular lens surface on day 7 (P=0.002), day 30 (P=0.002) and day 60 (P=0.001). It is known that the half life of heparin is not more than 5 hrs in the human body. However the anti-inflammatory and anti-proliferative property of heparin in the eye during surgery and the first 5 hours may be responsible for the decrease of long term residual pigments on the IOL.

POSTERIOR CAPSULAR OPACIFICATION (PCO)

In our study, PCO was not seen in any of the patients in both the groups on day 1. On day 7 none of the patients in group A had developed PCO while 20% of the patients in group B had developed PCO. On day 30 none of the patients in group A had developed PCO while 25% of the patients in group B had developed PCO. On day 60, 5% of the patients in group A had developed PCO while 26% of the patients in group B had developed PCO. There was decreased rate of PCO formation in group with addition of low molecular weight heparin and also the interval between cataract surgery and PCO formation was late, but it was not statistically significant.

Our study concurs with Knorr et al [73] who demonstrated anti-proliferative effect of low molecular weight heparin in cultured bovine lens epithelial cells. Zaturinsky et al [74] described reduced secondary cataract formation following extracapsular cataract extraction (ECCE) with heparin infusion.

Heparin is known to have anti-proliferative effects. It stabilizes the dividing lens epithelial cells at equators and prevents them to move onto the posterior capsule.

COMPLICATIONS ASSOCIATED WITH INTRACAMERAL LOW MOLECULAR WEIGHT HEPARIN (ENOXAPARIN)

Intraoperative or postoperative complications attributed to low molecular weight heparin supplementation was not observed in our study. None of the patients in either group developed hyphema similar to the results of most of the studies where hyphema was not noted on use of low molecular weight heparin. However in a case report by Sharan S et al [75] total hyphema was noted in a 73 year old patient who underwent trabeculectomy enhanced with 5-fluorouracil on the 4th postoperative day.

The patient was started on enoxaprin 1mg/kg to cover the risk of emboli from prosthetic valves. Enoxaparin, a low molecular weight heparin, inhibits thrombin directly and also acts on prothrombinase complex, that is, Factors Xa and Va, calcium and phospholipid (extrinsic pathway) and by releasing an endothelium-bound pool of tissue factor inhibitor.

In hyphemas, a fibrin–platelet clot is formed which reaches stability by day 5–7. These clots do not show any fibroblastic activity and finally is dissolved by the fibrinolytic system.

Total hyphema may have occurred because enoxaparin with its unpredictable and prolonged half-life might have caused hemorrhage when the clot was remodeled at day 4.

Johnson et al [37] in their study, used ordinary heparin at 10 IU/mL, which led to more frequent intraocular hemorrhage. However, Abdollahi A et al [71] used 5 IU/ml of low molecular weight heparin and there was no difference in rate of hyphema in the study and control group. The type and concentration of heparin are responsible for the occurrence of pre and postoperative intraocular hemorrhage. LMWH has higher anticoagulant activity than ordinary heparin as a result less hemorrhage occurs. This has been well demonstrated in patients who were treated with LMWH for deep vein thrombosis [29].

Posterior synechiae was noted in 2 patients (10%) in control group on the first postoperative day which was subsequently broken with the use of topical mydriatric, while none of the patients in group with addition of enoxaparin developed posterior synechiae. But the results are not statistically significant (P=0.244)

Our findings are consistent with the findings of Tirkey ER et al [65] who also found that none of the patients in whom low molecular weight heparin was used intraoperatively developed posterior synechiae.

Pupillary membrane was noted in 3 patients (15%) in control group on day 1 which later resolved by day 7, while none of the patients in group A (with addition of low molecular weight heparin) developed this complication. Tirkey ER et al[65] found that none of the patients in both the groups developed pupillary membrane.

Optic capture was not seen in any of the patients.

All corneas in study and control group remained clear for the entire follow up period.

Kruger et al [7] in a randomized prospective study in 50 patients and Kohnen et al [6] in a study on 72 patients did not experience any complications intraoperatively or postoperatively.

All these studies show that it is safe to use heparin sodium at a concentration of 10 IU/ml. Use of various concentrations of heparin or merely filling the anterior chamber with heparin sodium at the end of surgery may have a stronger and longer influence on the post operative inflammation. Patients predisposed to enhanced postoperative inflammation eg. Uveites, glaucoma, pediatric cataract, lens induced glaucoma, steroid induced cataract, and traumatic cataract might benefit from the addition of heparin in the irrigating solution.

ASSESSMEMT OF THE POSTOPERATIVE RE-ESTABILISHMENT OF THE BLOOD AQUEOUS BARRIER

In our study we found that following cataract surgery the anterior chamber cells and flare values were almost reduced to grade zero by the 8th week demonstrating that the blood aqueous barrier was re-established by 2 months postoperatively.

Sanders et al [40] studied 234 eyes of patients undergoing cataract surgery and found that the aqueous fluorescein concentrations decreased considerably by the 5th week postoperatively and blood aqueous barrier reestablishes by three months postoperatively.

VMG Ferguson et al [41] found that the blood aqueous barrier recovers rapidly during the first 6 weeks in eyes with uncomplicated cataract surgery and at 3 months a normal intact blood aqueous barrier was demonstrated by stable plateau levels of anterior chamber fluorescence in 69.0% of the eyes.

Shah SM et al [42] in their prospective study documented the re-establishment of the blood aqueous barrier following cataract surgery using laser photometry. They found that the aqueous flare and cells were highest on the 1st postoperative day, declining rapidly by the 7th day and returning to preoperative levels by 3 months.

Our study differed from the previous published results in that the blood aqueous barrier seems to be totally reestablished by the 2nd month in both groups. This could probably be accounted for by the difference in methods used to quantify the anterior chamber cells and flare. Our assessment was with a SL 115 Classic Carl Zeiss slit lamp while the above studies utilized the Kowa FC–1000 flare, cell photometer and ocular fluorophotometry which may be a more sensitive assessment.

CONCLUSION

In our study we conclude that:

- The postoperative anterior chamber cells and flare, vitreous haze and iris pigments on the surface of the intraocular lens were reduced significantly in the early postoperative period. (P value <0.05).
- There is no effect on the development of posterior capsular opacification (P value >0.05)
- Postoperative complications like hyphema, posterior synechaie, pupillary membrane and optic capture is insignificant (P value >0.05).
- Low molecular weight heparin is non-toxic to the corneal endothelium and is safe for use intracamerally.
- The blood aqueous barrier is re-established by 2 months of cataract surgery.

Thus, low molecular weight heparin used in the concentration of 40mg/0.4ml in 500 ml irrigating solution reduces the early postoperative inflammation in high risk cataract cases with no adverse effects.

However a larger sample size is required for conclusive evidence.

SUMMARY

Heparin surface modified lenses are advocated in general for patients with diabetes mellitus, uveitis and other conditions where a higher risk of postoperative inflammation is expected. However the cost of heparin surface modified lenses is about 4 times that of a good posterior chamber intraocular lens.

Knowing the benefits of heparin surface modified lenses we used low molecular weight heparin (Enoxaparin) in the irrigating solution to see if it can be used as an alternative to these expensive heparin surface modified lenses.

40 patients were randomized into two groups. One group received 40 mg/0.4ml of low molecular weight heparin in 500ml of irrigating solution, while the other did not. The effect of low molecular weight heparin in the irrigating solution was assessed postoperatively in terms of anterior chamber cells and flare, vitreous haze and iris pigments on the surface of the intraocular lens. The patients were followed up on day 1, 7, 30 and at 60 days postoperatively.

The re-establishment of the blood aqueous barrier was studied throughout the study up to 60 days. We used the SL 115 Classic Carl Zeiss slit lamp for assessment of every patient at each visit during the study.

We found that postoperative anterior chamber cells and flare, vitreous haze and pigment deposits on the intraocular lens surface were significantly reduced in the early postoperative period, in patients who received low molecular weight heparin in the irrigating solution (P value<0.05). Low molecular weight heparin did not have any effect on development of posterior capsular opacification (P value >0.05).

Our study demonstrated that the blood aqueous barrier was re-established by 60^{th} day postoperatively. Intraoperative and postoperative complications like hyphema, optic capture and posterior synechaie were not statistically significant. All the corneas in the study group remained clear postoperatively suggesting that the low molecular weight heparin is non-toxic to the corneal endothelium and can be used safely.

From our study we conclude that in the Indian population where heparin surface modified lenses are not affordable by most patients, low molecular weight heparin in the irrigating solution may be an economical and effective alternative in reducing postoperative inflammation especially in patients with diabetes, complicated cataract, traumatic cataract, congenital cataract, steroid induced cataract and lens induced glaucoma.

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ANNEXURE – I – CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

I.D. NO. ☐☐☐

Mr/Mrs/Ms _____You are invited to participate in our research study titled **" A ONE YEAR RANDOMIZED CLINICAL TRIAL ON THE EFFECT OF INTRACAMERAL LOW MOLECULAR WEIGHT HEPARIN ON POSTOPERATIVE INFLAMMATORY REACTION IN HIGH RISK CATARACT CASES."** conducted by Dr. Sneha Harogoppa, Post Graduate student in M.S. Ophthalmology, under the guidance of Dr. Shivanand C.Bubanale, Professor, Department of Ophthalmology,J N Medical College, Belagavi.

Respected Sir/Ma'am we request you to enroll yourself in our study as you are eligible for participation. Your participation in research is voluntary. If you decide to participate you are free to withdraw at any time.

Purpose of the Study: The purpose of research is to compare the effect of low molecular weight heparin in irrigating solution on post operative inflammatory reaction in high risk cataract surgery.

Procedure Involved: If you agree to enroll yourself in this study, you will be asked your present, past and family history. You will be clinically examined and relevant investigations will be done. Then manual small incision cataract surgery will be done with or without low molecular weight heparin in the irrigating solution. Selection of the procedure will be based on randomization chart, so you can be selected in either of the

groups. You would be asked to come for follow up on specified dates when your progress would be monitored, documented, and photographed.

Risks and Benefits: There are no major risks involved with the use of intracameral low molecular weight heparin. Some of the complications involved with the use of intracameral low molecular weight heparin such as intraoperative hemorrhage and postoperative hyphema are rare. For which all necessary precautions would be taken. Your participation may benefit you and others by establishing certain facts about the study.

Alternatives: If you are not willing to participate you will be treated according to the existing protocol & it will not affect your relationship with this hospital.

Costs for participating in this research: There will not be any extra cost incurred by you. You will, however, have to pay for the investigations which are part of the existing management protocol for the condition. There is no commitment for any reimbursement or any other compensation.

Privacy and Confidentiality: Your privacy is guaranteed. However, your medical records can be directly accessed and reviewed by authorized individuals or by the ethics committee. Records, which could reveal your identity, will be kept confidential. Personal data will remain anonymous if data is being published or written as a dissertation.

Authorization to Publish Results: When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity.

Compensation: In the event of injury related to the study, treatment will be made available through KLES Dr.Prabhakar Kore Hospital & MRC, Belagavi. There is no compensation or payment for such medical treatment by law. The doctors and the staff will provide facilities and medical attention to you.

Questions

If you have any questions about the research you may please contact:

1. Investigator, Dr. Sneha Harogoppa,
   Post Graduate student
   Department of Ophthalmology, JNMC, Belagavi.
   Contact No. 9742352674

2. Guide, Dr. Shivanand C.Bubanale,
   Professor,
   Department of Ophthalmology,JNMC, Belagavi.
   Contact No. 9448219777

3. Dr. Ganga.S. pilli.
   Chairman, Institutional Ethics Committee.
   JNMC, Belagavi
   Contact No.9448863866

Consent for participation in research trial

I, Mr./Mrs. _____ Voluntarily agree for the participation as a subject of this study. By signing this consent form, I am not giving up any of the legal rights. I may withdraw from the study at anytime. I am signing the consent form after having read or been read for me in my own vernacular language, including the risks and the benefits and having all my questions answered.

Patient's Name : _____

Signature or the Left Thumb Print of patient: _____

Witness name: _____

Signature or the left thumb print of witness:

Investigators Name: _____

Signature of Investigator: _____

Name of the guide: _____

Signature of the guide: _____

Date: Place:

Assent for participation in research trial

I, Mr./Mrs. _____ parent/guardian of _____

Voluntarily agree for the participation of my child as a subject of this study. By signing this consent form, I am not giving up any of the legal rights. I may withdraw my child from the study at anytime. I am signing the consent form after having read or been read for me in my own vernacular language, including the risks and the benefits and having all my questions answered.

Parent's /guardian Name : _____

Signature or the Left Thumb Print of parent/guardian: _____

Witness name: _____

Signature or the left thumb print of witness:_____

Investigators Name: _____

Signature of Investigator: _____

Name of the guide: _____

Signature of the guide: _____

Date: Place:

ANNEXURE – II - PROFORMA

IP NO: **OP NO:**

NAME:

(FIRST NAME)	(MIDDLE NAME)	(SURNAME)

AGE: (in years)

SEX: 1.Male. 2. Female

ADDRESS:

TELEPHONE NO.

RELIGION:

DATE OF ADMISSION:

DATE OF SURGERY:

DATE OF DISCHARGE:

PROVISIONAL DIAGNOSIS:

PROPOSED SURGERY

HAS INFORMED CONSENT BEEN TAKEN?

1. Yes 2. no

FINAL RESULT INFORMATION:

1. Ineligible
2. Eligible, refusal
3. Eligible, participating

ID NO:

SURGEON'S NAME:

SURGEON'S SIGNATURE:

DATE:

CHIEF COMPLAINTS:

Diminution of vision - Right eye ☐ Duration-

Left eye ☐

HISTORY OF PRESENTING ILLNESS:

1. Diminution of vision-

Gradual	☐	Sudden	☐
Progressive	☐	Static	☐
Painless	☐	Painful	☐

(1. YES 2. NO) RE LE

2. Diplopia/polyopia: ☐ ☐
3. Colored halos: ☐ ☐
4. History of black spots in front of eyes: ☐ ☐
5. History of photophobia: ☐ ☐
6. History of watering/discharge: ☐ ☐
7. History of redness ☐ ☐
8. History of trauma: ☐ ☐

If present, duration- months/years.

9. History of bleeding tendencies: ☐ ☐
10. History of wearing spectacles

If 1, then a. distant b. near c. both ☐

Duration -

PAST HISTORY: 1.Yes 2. No (If 1, then duration)

	RE	LE
Intra-ocular Surgery		
Trauma		
Other		

Diabetes	
Hypertension	
Bleeding disorders	
Others	

Drug history:

PERSONAL HISTORY: ☐

1. Significant 2. Insignificant

FAMILY HISTORY: ☐

1. Significant 2. Insignificant

GENERAL PHYSICAL EXAMINATION

Vitals

Pulse (per min) ☐☐☐

Blood Pressure (systolic/diastolic)(mm of hg) ☐☐☐/☐☐☐

Temperature ☐ (1=Febrile; 2=Afebrile)

Respiratory Rate (per ☐☐☐ min)

(1=Yes; 2=No)

Pallor		Clubbing	
Icterus		Lymphadenopathy	
Cyanosis		Oedema	

SYSTEMIC EXAMINATION:

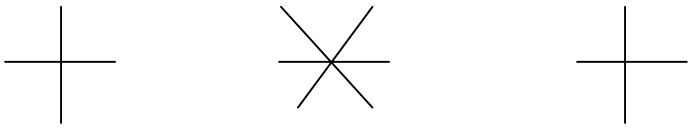
1. Normal 2. Abnormal (if 2 then specify)

Respiratory system		
Cardiovascular system		
Per abdomen		
Central nervous system		

OCULAR EXAMINATION

1. Head posture ☐ (1=Erect; 2=Tilted)
2. Facial symmetry ☐ (1=Symmetrical; 2=Asymmetrical)
3. Visual axes ☐ (1=Parallel; 2=Deviated.if 2, then a. esotropia b. exotropia

4. Extra-ocular movements OD BINOCULAR OS



5. Vision

	RE	LE
Distant		
Pin-hole		
Near		
With spectacles		

Retinoscopy: OD OS

Refraction

	RE				LE			
	Sphere	Cylinder	Axis	Vision	Sphere	Cylinder	Axis	Vision
Distance								
Near								

6. Anterior segment examination

	RE	LE
Adnexa (1=Normal; 2=Abnormal) If 2, specify		
Conjunctiva		
Cornea [1=Clear. 2=edematous. 3=other] If 3, specify		
Sclera (1=Normal; 2=Abnormal) If 2, specify		
Anterior chamber a. Depth (1=Normal depth; 2=shallow; 3=deep) b. others-specify		
Iris (1=Normal; 2=Atrophic patches; 3=other) If 3, specify		
Pupil • Size (1=normal; 2=constricted; 3=dilated) • Reactions: o Direct o Indirect (1=present; 2=absent; 3=sluggish)		
Lens (1=Clear; 2=Cataract,3=peudophakia, if 2 then specify the type)		

7. Fundus

	RE	LE
Glow		
Media		
Disc • Size • Margins • CDR • NRR		
Blood vessels		
Background		
Macula		

INVESTIGATIONS

1. Tonometry

	RE	LE
IOP (mm Hg)		

2. Lacrimal sac

RE	LE

3.A-scan

K_1-

K_2-

Axl-

PCIOL-

4. B- scan-

5. Random blood sugar ☐☐☐ mg/dl

6 .BT - ☐ (1. Normal. 2. Abnormal)

7 .CT- ☐

8. PT – ☐

9. aPTT- ☐

FINAL DIAGNOSIS:

DETAILS OF SURGERY

Type of surgery-

Date of surgery-

Name of surgeon-

Pre-op medications-

Anesthesia-

Post operative medications-

Day 1-

Day 7-

Day 30-

Day 60 –

POST OPERATIVE EVALUATION OF INFLAMMATION

1.

Symptoms	Pain	Watering	Visual acuity
Day 1			
Day 7			
Day 30			
Day 60			

2.

LID ODEMA	Day 1	Day 7	Day 30	Day 60
present				
absent				

3.

CONJUNCTIVAL CONGESTION	Day 1	Day 7	Day 30	Day 60
None 0				
Mild 1(some vessels injected)				
Moderate 2 (diffuse injection)				
Severe 3 (intense injection)				

4.

CILIARY FLUSH	Day 1	Day 7	Day 30	Day 60
None 0				
Mild 1(some vessels injected)				
Moderate 2 (diffuse injection)				
Severe 3 (intense injection)				

5.

CORNEA	Day 1	Day 7	Day 30	Day 60
Microcystic Odema				
Descemet's folds				
Keratic precipitates				

6.

ANTERIOR CHAMBER FLARE	Day 1	Day 7	Day30	Day 60
Grade 0 (absent)				
Grade 1(faint, barely detectable)				
Grade 2 (moderate, iris and lens details clear)				
Grade3(marked, iris and lens details hazy)				
Grade 4(intense flare, fibrinous aqueous)				

7.

ANTERIOR CHAMBER CELLS	Day 1	Day 7	Day 30	Day 60
Grade 0(0)				
Grade 1 (5-10)				
Grade 2 (10-20)				
Grade 3 (20-50)				
Grade 4 (>50)				

8.

HYPHEMA	Day 1	Day 7	Day 30	Day 60
Present				
Absent				

9.

PUPILS	Day 1	Day 7	Day 30	Day 60
Synechaie				
Pupillary membrane				
Optic capture				

10.

Iris pigments on intraocular lens	Day 1	Day 7	Day 30	Day 60
Present				
Absent				

11

Posterior capsular opacifiation	Day 1	Day 7	Day 30	Day 60
Present				
Absent				

12

VITREOUS HAZE	Day 1	Day 7	Day 30	Day 60
Grade 0 (No Haze)				
Trace (Slight blurring of optic disc margin)				
Grade 1 (Slightly blurred optic nerve and vessels)				

Grade 2 (Moderately blurred optic nerve and vessels)				
Grade 3 (Optic nerve head border blurred but visible)				
Grade 4 (Optic nerve head obscured)				

Days	Visual acuity			Intraocular pressure (mmHg)
	Distant	pin hole	near	
Day 1				
Day 7				
Day 30				
Day 60				

Refraction

	RE				LE			
	Sphere	Cylinder	Axis	Vision	Sphere	Cylinder	Axis	Vision
Distance								
Near								

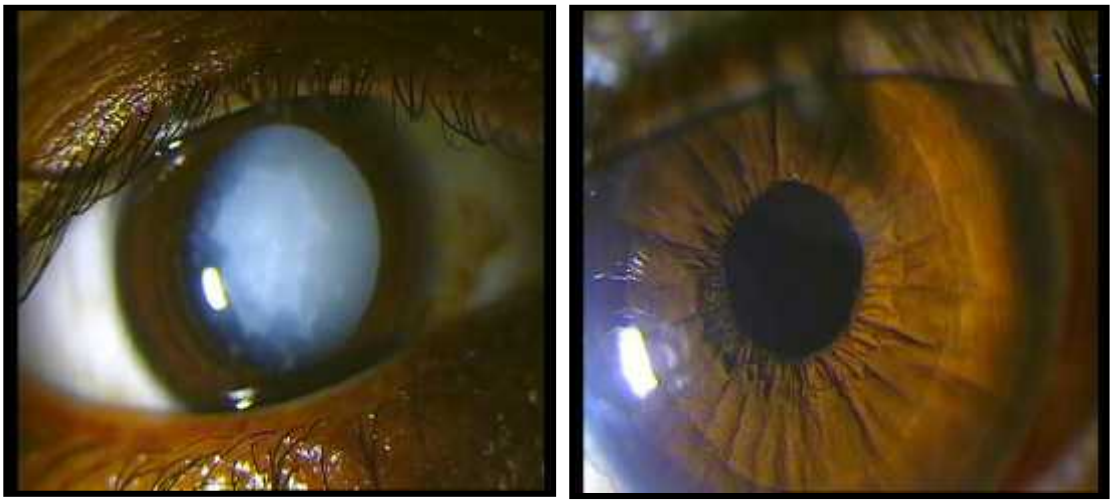
ANNEXURE – III – PHOTOGRAPHS

Photograph 1: Slit lamp examination

Photograph 2: Operation theatre

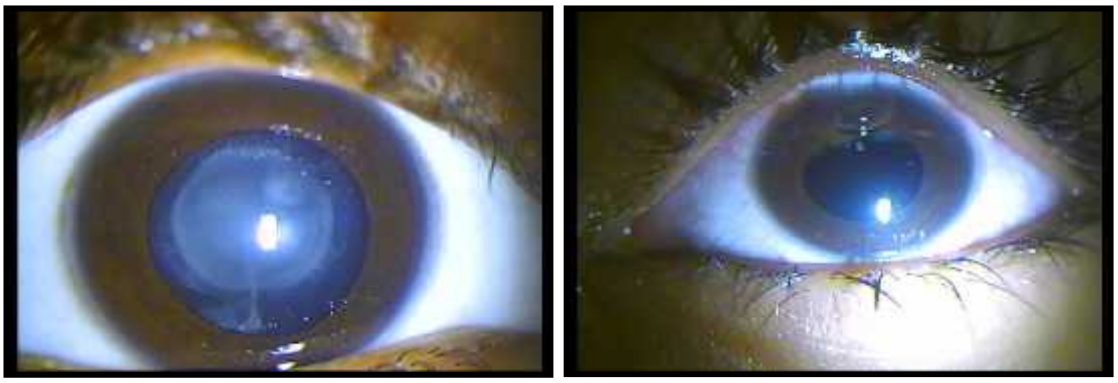
Photograph 3: Irrigating solution

Photograph 4: Low molecular weight heparin



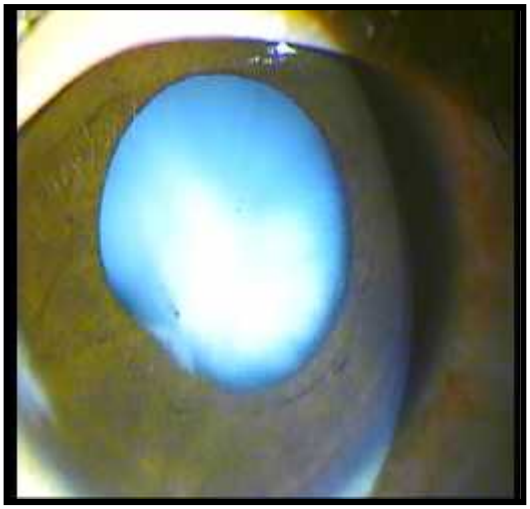
(a) **(b)**

Photograph 5: Left Eye complicated cataract secondary to electric shock in Group A a) Pre-Op b) Post Op



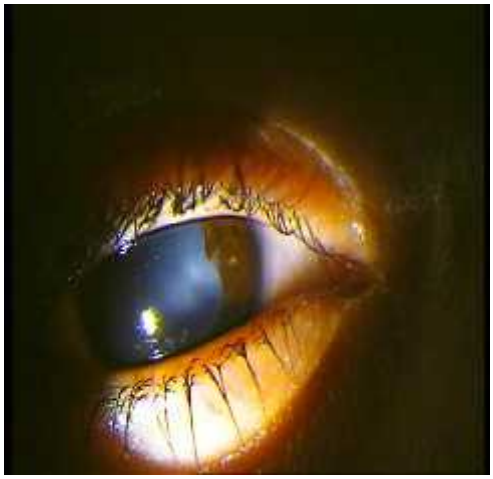
(a) **(b)**

Photograph 6: Right Eye zonular cataract in Group B. a) Pre-Op b) Post-Op



(a) **(b)**

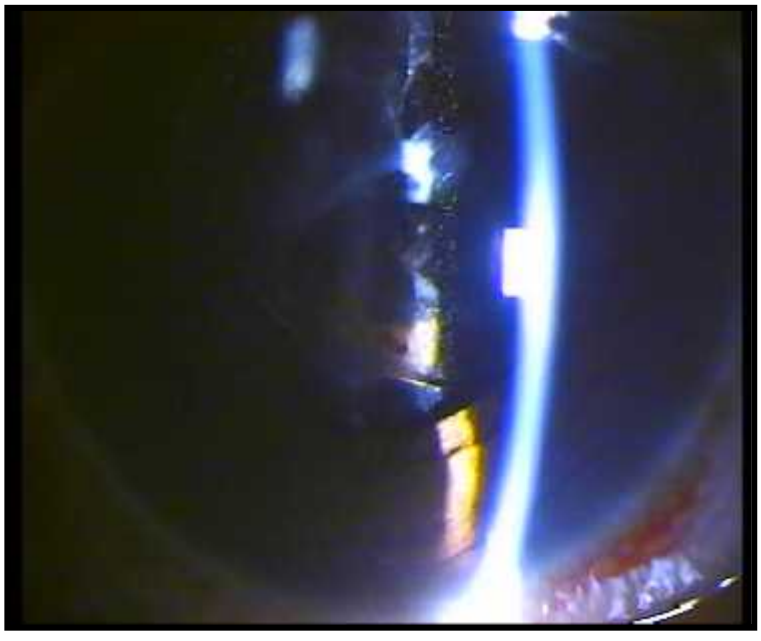
Photograph 7: Left Eye complicated cataract in Group A a) Pre-Op b) Post-Op



(a) **(b)**

Photograph 8: Right Eye traumatic cataract with entry wound at 3 O'clock position in Group B a) Pre-Op b) Post-Op

Photograph 9: Post-op clear cornea with quiet anterior chamber in a patient in Group A



Photograph 10: Post-op pupillary membrane with Iris Pigments on intraocular lens in a patient in Group B

ANNEXURE – V- KEY TO MASTER CHART

AC	-	Anterior chamber
Category A	-	Diabetic patients with cataract
Category B	-	Traumatic cataract
Category C	-	Complicated cataract
Category D	-	Congenital/developmental cataract
Category E	-	Steroid induced cataract
Category F	-	Lens induced glaucoma
IOP	-	Intraocular pressure
PCO	-	Posterior capsular opacification

SL NO	IP NO	AGE	SEX	GROUP	CATEGORY	EYE	PRE-OP		POST - OP																																								
									DAY ONE									DAY SEVEN									DAY THIRTY									DAY SIXTY										
							VISION	IOP	AC Cells	AC Flare	Iris pigments on IOL	Vitreous haze	Hyphema	Posterior Synechiae	Pupillary membrane	Optic capture	PCO	AC Cells	AC Flare	Iris pigments on IOL	Vitreous haze	Hyphema	Posterior Synechiae	Pupillary membrane	Optic capture	PCO	AC Cells	AC Flare	Iris pigments on IOL	Vitreous haze	Hyphema	Posterior Synechiae	Pupillary membrane	Optic capture	PCO	AC Cells	FLARE	Iris pigments on IOL	Vitreous haze	Hyphema	Posterior Synechiae	Pupillary membrane	Optic capture	PCO	VISION	IOP
1	568042	65	F	B	E	LE	6/60.	15.8	2	2	1	1	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/9.	13.7
2	569281	32	F	A	F	LE	PL PR	43.4	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	7.2
3	569738	24	M	A	C	RE	PL PR	14.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	8
4	570432	3	M	A	B	RE	PL PR	10	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	6/18.	8
5	571621	44	F	A	E	LE	6/24.	15.9	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	10.6
6	571755	55	M	B	F	RE	PL PR	41.5	2	2	1	1	0	1	1	0	0	1	1	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	6/9.	10
7	579645	50	M	A	A	RE	6/18.	18.9	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	6/9.	11.2
8	583821	49	F	B	A	RE	3/60.	12.9	2	2	1	1	0	0	0	0	0	1	1	1	1	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	6/9.	8
9	584024	54	F	B	A	LE	PL PR	13.4	2	2	1	1	0	0	0	0	0	1	1	0	1	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	6/6.	13.4
10	587244	64	F	A	C	LE	1/60.	17.3	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/12.	15.9
11	590203	35	F	A	B	RE	PL PR	15.9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/9.	13.7
12	590191	60	F	A	A	LE	6/60.	12.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/12.	12.2
13	593378	58	F	A	A	LE	1/60.	17.3	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	15.9
14	572174	13	M	B	B	RE	PL PR	17.3	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/60.	12.2
15	591308	5	F	B	D	LE	PL PR	11.6	2	1	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	6/18.	8.2
16	596411	12	F	A	D	LE	6/24.	15.2	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	6/19.	14.6
17	671670	12	F	B	D	RE	6/18.	16.1	2	2	1	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	6/12.	15.8
18	621789	78	M	A	A	RE	PL PR	12.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/9.	10.1
19	629103	67	F	B	A	RE	PL PR	14.6	2	2	1	1	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	10.8
20	601245	50	F	B	F	LE	PL PR	26.6	3	3	1	2	0	1	1	0	0	2	2	1	1	0	0	1	0	1	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	1	6/12.	12.2
21	599678	65	F	B	C	LE	2/60.	12.2	2	2	0	1	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/12.	10.8
22	604053	49	M	B	C	LE	6/18.	17.3	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	13.4
23	620645	12	M	B	B	LE	PL PR	7.6	3	3	1	2	0	0	0	0	0	2	2	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	6/6.	8
24	602130	73	M	A	A	LE	6/60.	15.9	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/9.	11.2
25	621327	29	M	A	B	LE	PL PR	17.3	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	16.2
26	621345	50	M	A	C	RE	4/60.	17.3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/9.	10.2
27	612487	42	M	A	B	RE	6/24.	15.9	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	8.4
28	617728	14	M	B	B	RE	PL PR	10.2	3	3	1	2	0	0	0	0	0	2	1	1	1	0	0	0	0	1	1	0	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	1	6/6.	9.2
29	637163	51	M	B	B	RE	6/60.	17.3	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	10.6
30	625553	65	F	A	C	RE	PL PR	14.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	13.2
31	626623	17	F	B	A	LE	3/60.	17.3	2	2	1	0	0	0	0	0	0	2	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	6/9.	16.8
32	601307	65	F	B	A	RE	PL PR	20.1	2	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/18.	18.9
33	646515	30	F	B	C	RE	PL PR	17.3	2	2	1	1	0	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/9.	15.1
34	648203	25	M	A	E	RE	6/24.	14.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	11.2
35	645720	20	F	B	D	RE	PL PR	17.3	2	2	1	0	0	0	0	0	0	1	1	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	1	6/12.	13.6
36	652199	20	F	A	D	LE	PL PR	14.6	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/9.	12.2
37	650789	50	M	A	B	RE	PL PR	14.6	2	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	15.2
38	576233	55	M	B	B	LE	PL PR	14.6	1	1	1	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/12.	10.2
39	671939	50	F	B	A	RE	1/60.	12.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/6.	20.9
40	655695	72	F	B	E	LE	2/60.	14.6	2	2	1	1	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6/9.	13.8