"EFFECT OF HEPARINISED IRRIGATION SOLUTION ON POST OPERATIVE INFLAMMATION AFTER CATARACT SURGERY IN DIABETICS"

By

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In partial fulfilment of the requirements for the degree of

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I hereby declare that this dissertation entitled **"EFFECT OF HEPARINISED IRRIGATION SOLUTION ON POST OPERATIVE INFLAMMATION AFTER CATARACT SURGERY IN DIABETICS"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. NARENDRA.P. DATTI**, Professor, Department of Ophthalmology, Sri Devaraj Urs Medical College, Kolar, in partial fulfilment of University regulation for the award "**M.S. DEGREE IN OPHTHALMOLOGY**", the examination to be held in May 2017 by SDUAHER. This has not been submitted by me previously for the award of any degree or diploma from the university or any other university.

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Dr. BHAVYA REDDY.D

LIST OF ABBREVIATIONS

PMMA	Polymethylmethacrylate
T_2DM	Type 2 Diabetes Mellitus
BAB	Blood Aqueous Barrier
IOL	Intraocular lens
ACIOL	Anterior Chamber intraocular lens
Nd: YAG	Neodymium-doped yttrium aluminium garnet
HE MA	Hydroxyethylmethacrylate
ROS	Reactive oxygen species
CME	Cystoid Macular Edema
ICCE	Intracapsular cataract extraction
Mm	Millimeter
SUN	Standard Uveitis Nomenclature
Ml	Milliliter
Mg	Milligram
BRB	Blood Retinal Barrier
He-Ne	Helium-Neon
RBS	Random blood sugar

LIST OF ABBREVIATIONS

FBS	Fasting blood sugar
PPBS	Post prandial blood sugar
HIV	Human Immunodeficiency Virus
HBsAg	Hepatitis B surface Antigen
PCIOL	Posterior chamber intraocular lens
SICS	Small Incision Cataract Surgery
OPD	Outpatient department
IU	International Unit
BSS	Balanced salt solution
Pre-op	Pre-operative
Post-op	Post-operative
Std.	Standard
BCVA	Best corrected visual acuity
Hrs	Hours
e.g.	For example
I.P	In patient
O.P	Out patient
Dl	Deciliter
NO.	Number

ABSTRACT

Background: Post-operative inflammation after cataract surgery is invariably much higher among diabetic patients as they have significantly increased blood aqueous barrier breakdown when compared to normal eyes. Heparin surface modified lenses provide a greater degree of protection from the post-operative inflammation, but they are very expensive and not affordable by most of patients. Heparinised irrigation solution may be of tremendous value in decreasing postoperative inflammation and cellular deposits on the intraocular lens surface. This study was done to evaluate the effect of heparinised irrigating solution on the post-operative inflammation after cataract surgery in diabetics.

Aims and objectives:

1.To study the effect of heparinised irrigation solution on post-operative inflammation after cataract surgery in diabetics by recording flare, cells and pigments in the anterior chamber.

2.To study visual outcome in these patients.

Materials and methods: 130 diabetic patients with cataract attending Ophthalmology OPD to undergo cataract surgery between December 2014 and January 2016 were selected for this prospective study. Patients who met the inclusion/exclusion criteria were taken up for the study. Flare, cells, pigments on the lens and visual acuity were measured on day 1, day 7, day 28 and 8^{th} week post-operatively.

Results: There was a statistically significant reduction in the cells, flare and pigments in the anterior chamber in the early post-operative period in patients who received heparinised irrigating solution. ($P<0.05$). There was also a statistically significant improvement in the BVCA in early post-operative period in patients who received heparinised irrigating solution. ($P<0.05$).

Conclusion:

In this study, we used heparinised irrigation solution to see if heparin, which is a very economical drug, can be used as an alternative to heparin surface modified lenses in diabetics undergoing cataract surgery.

Hence, in our rural Indian population, heparinised irrigation solution may be a cost-effective and efficient alternative to heparin surface modified lenses to minimize post-operative inflammation in cataract surgery in diabetics.

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INTRODUCTION

Diabetes affects more than 120 million people worldwide. Population growth, ageing, urbanization, sedentary lifestyles and an increasing prevalence of obesity are increasing the number of people with diabetes mellitus. Several studies have shown diabetes to have 3-4-fold risk of developing cataracts among people less than 65 years of age and occur at an earlier age[1]

Overall, up to 20% of all cataract procedures are estimated to be performed for diabetic patients.[2]

Cataract surgery may be an ophthalmologist‘s delight, but post-operative inflammation is invariably his nightmare and this seems to be much higher among diabetic patients as they have significantly increased blood aqueous barrier breakdown when compared to normal eyes.[3,4,5]

When intraocular lenses first came into common use, problems associated with cataract surgery and intraocular lens implantation were poorly understood. In the early 1990‘s major improvements in the design of lenses, instruments and surgical techniques, all contributed to the excellent clinical results, which are observed today.

PMMA lenses have been used for around 50 years now and are the most widely used intra ocular lenses. Though PMMA is relatively inert, it tends to have some degree of inflammatory response post-operatively. Therefore, a search is on to find a method to render these 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. Heparin surface modified lenses provide a greater degree of protection from the post-operative inflammation, but they are very expensive and not affordable by most of patients.

A few studies have shown that heparinised intraocular infusion during cataract surgery reduces postoperative inflammation[6]. This modification is simple and can be done with no extra expenditure. However, there are no reports of similar studies in the Indian population which typically has darkly pigmented irides & increased incidence of T_2 DM. Heparinised irrigation solution may be of tremendous value in decreasing postoperative inflammation and cellular deposits on the intraocular lens surface. This study was done to evaluate the effect of heparinised irrigating solution on the post-operative inflammation after cataract surgery in diabetics.

OBJECTIVES OF THE STUDY

1. To study the effect of heparinised irrigation solution on post-operative inflammation after cataract surgery in diabetics by recording flare, cells and pigments in the anterior chamber.
2. To study visual outcome in these patients.

REVIEW OF LITERATURE

Cataract surgeries cause inflammation that results from trauma and immunological reactions to the implanted foreign body, that is intraocular lens .[1,3]

Severe post-operative inflammation can lead to cystoid macular edema, chronic uveitis, glaucoma and synechiae deteriorating the vision of the patient post operatively.[4,5]

The studies have shown that diabetic states of the patients was associated with a statistically significant increase in cells, flare and the pigmentary deposits on the intraocular lens on the first post-operative day.[3,6]

Diabetic eyes have many disturbances within anterior segment, such as bigger lens, a steeper anterior lens curvature, and a shallow anterior chamber, especially in eyes with diabetic retinopathy[6].

The breakdown of blood aqueous barrier (BAB) by surgical trauma produces postoperative inflammation with a pigment dispersion, a fibrinoid reaction and development of posterior synechiae[7].

The function of the BAB is a sensitive measure of surgical technique, since BAB disruption is a sign of intraocular inflammation. Quantitative and objective measurements of the postoperative inflammatory response in the anterior chamber indicate the quality of surgical methods and the biocompatibility of implanted materials. Even subclinical reactions should be examined since a persistent low-grade inflammation may induce cystoid macular edema and alterations of corneal endothelial function and intra-ocular pressure[8].

These factors make the eyes more susceptible to surgical trauma increasing the incidence of post-operative complications in the anterior and the posterior segment of the eye[4].

The function of the BAB is a sensitive measure of surgical technique, since BAB disruption is a sign of intraocular inflammation. Quantitative and objective measurements of the postoperative inflammatory response in the anterior chamber indicate the quality of surgical methods and the biocompatibility of implanted materials. Even subclinical reactions should be examined since a persistent low-grade inflammation may induce cystoid macular oedema and alterations of corneal endothelial function and intra-ocular pressure.

Studies have shown that adding heparin to the irrigating solution during cataract surgery results in less disturbance of the blood aqueous barrier (BAB) and helps prevent posterior capsule opacification postoperatively due to inflammation[6,9].

Previous studies demonstrated that adding heparin sodium to the irrigating solution decreased postoperative inflammatory and fibrinoid reactions and related complications such as synechiae, pupil irregularity, and IOL decentration[10].

Johnson et al reported that heparin injection into anterior chamber decreases fibrin clot formation in a rabbit model, but it had no effect on bleeding time[11].

EVOLUTION OF CATARACT SURGERY

The techniques of cataract extraction have evolved over several thousand years. Couching (pushing the lens into the vitreous) was used in India for almost 3000 years by Sushrutha . The technique is described in writing as early as the thirteenth century in the Arab book of Halifa[13]. 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.

In the mid eighteenth century, Daviel introduced the extracapsular method of cataract extraction and almost a century passed before this technique received widespread acceptance, although the lack of a method to clean the cortical material remained a problem.

Towards the end of eighteenth century, Samuel Sharp described intracapsular cataract extraction. In the early part of the twentieth century after Henry Smith, Eugene Kalt and Ignatio Barraquer introduced a methodology that led to safer results and the intracapsular cataract extraction replaced extracapsular surgery[14]. Other advances in the surgical treatment

of cataract included the use of sutures for wound closure and the introduction of topical anesthesia by Karl Kohler. By the end of the first half of the twentieth century, with the advent of alphachymotrypsin for chemical zonulolys, intracapsular extraction became the worldwide standard technique of cataract extraction for patients over the age of 40 years. The introduction of cryoextraction in the early 1960‘s cemented the preeminent position of the intracapsular techniques.

The disadvantages of the intracapsular technique included vitreous loss, cystoids macular edema, retinal detachment, astigmatism and use of anterior chamber intraocular lens[15]. Also, this technique could not be used in patients less than 30 yrs.

A revolution in cataract surgery occurred with the development of phacoemulsification by Charles Kelman in the 1960‘s[16]. Kelman not only invented a way of removing the cataract through a small incision, but also described a method for effectively removing the remaining cortical material. This paved the way for the reemergence of extracapsular cataract extraction as a safe alternative to intracapsular extraction.

Compared to intracapsular surgery, extracapsular cataract extraction has the advantage of lower rates of retinal detachment, cystoid macular edema, endophthalmitis, vitreocorneal adhesions, and vitreous loss. The extracapsular technique also permits the use of posterior chamber intraocular lens either primarily or secondarily. Extracapsular cataract extraction can be used in patients of any age and almost any kind of cataract. The disadvantages include the frequent need for posterior capsulotomy, greater technical difficulty and prolonged postoperative inflammation in the event of retained cortical material.

A major contribution to ophthalmic surgery occurred with the introduction of sodium hyaluronate for use in the eye in the late 1970s. It helps to form the anterior chamber and protects the endothelium from damage during expulsion of the nucleus during phacoemulsification and during insertion of intraocular lens.

Today, extra capsular cataract extraction, by its reduced incidence of retinal detachment and cystoid macular edema and is the cataract surgery of choice. The current techniques of extra capsular cataract extraction, combined with posterior chamber intraocular lens implantation, has the potential for creating excellent results.

Figure 1. HAROLD RIDLEY

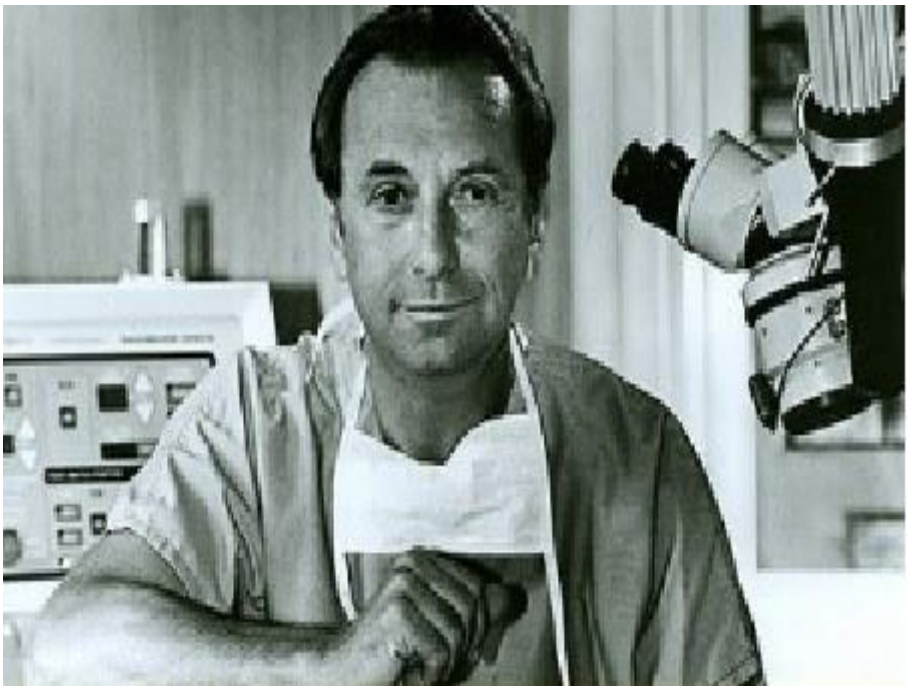


Figure 2. CHARLES KELMAN

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 referred 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 [17].

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 (polymethylmethacrylate) occasionally lodged inside the eyes of pilots. It was noted that the material incited little reaction to, 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 [18,19]. Ridley lens was abandoned because of a high incidence of complication (6% posterior dislocations, 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 principal 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 with 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 was use[20]. Smaller lenses led to decenteration during eye movements, causing irritation of the ciliary body and the angle structures. This resulted in peripheral anterior synechiae, secondary glaucoma and corneal dystrophy[21]. Barraques finally had to explant most of these lenses. Choyce 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 [17].

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 much 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 cystoid macular edema and retrolenticular membranes. Binkhorst 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 got 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 thereby combining the advantages of the iridocapsular lens with those of extra capsular extraction [22,23]. 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 occurence of secondary cataract. The frequency of needling however decreased considerably with increasing experience of the surgeon, especially in elderly patients [23].

These sequential events should remind us to accept changes with caution. After all, the implant and surgery is intended to provide the patient with 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 Pearc[24,25]. However modifications suggested by Sansky, Krantz and Simcoe, among others, helped to develop the currently available lens. Mazzocco 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 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 lenses implantation compared to that without intraocular lens implantation, no large scale, well controlled study has 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.

Figure 3 RIDLEY POSTERIOR CHAMBER LENS 1949

Figure 4. 3 POINT FIXATION ACIOL

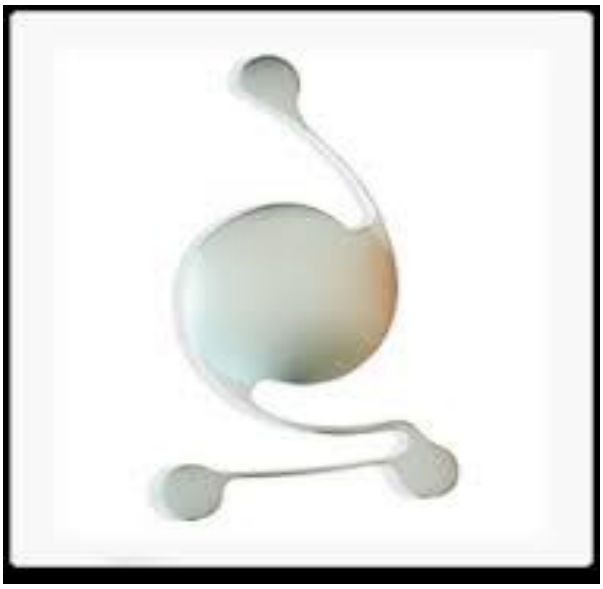


Figure 5. 4 POINT FIXATION ACIOL

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
- Lack of carcinogenicity
- 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

POLYMETHYLMETHACRYLATE (PMMA)

During World War II, Harold Ridley noted that intraocular foreign bodies of acrylic fragments from airplane canopies were well tolerated. He chose this material for the first successful intraocular lens implants, and has since been used for the optical portion of most intraocular lenses.

PMMA is a polymer of methylmethacrylate monomer. Monomer production begins with the 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[26]. Monomer can be released from PMMA by heating, molding, grinding and other processes used in the manufacture of intraocular lenses.

Release of monomer from PMMA became a concern with the introduction of the Nd:YAG laser for capsulotomy and its potential for damage to PMMA optics[27]. The

threshold for damage is lowest with injection molded lenses and much higher with lathe cut and cast molded lenses [28].

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[29]. PMMA does not activate complement and induce chemotaxis of white blood cells as polypropylene and nylon loop materials[29]. This property and the loss of ~~"~~memory" (Shape) or polypropylene loops within the eye have led to increased use of PMMA as the haptic material for one-piece posterior chamber lenses.

The PMMA used in intraocular lenses transmits a broader spectrum of light than does human crystalline lens. This allows transmission of near ultraviolet light, a possible source of retinal damage. Therefore, ultraviolet absorbing materials have been added to PMMA optics as covalently bound or entrapped chromophores.

The optical quality of PMMA lenses has been questioned in the past on the basis of manufacturing characteristics rather than materials[30]. A reappraisal showed marked improvements in resolution efficiency, and the optical quality of current lenses has been shown to hold up under in vivo conditions [31].

GLASS

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) glass, held in a polyimide carrier was developed [32]. 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. This may reduce surgical time, healing time and postoperative astigmatism.

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. Early silicone lenses were opalescent, but the more recent models are of comparable optical quality to PMMA[31]. They

are not fixated by fibrosis, although they may be associated with increased capsular fibrosis [33].

Difficulty with lens position and visibility has been a problem during air fluid exchange after vitrectomy in eyes with silicone lenses. Discoloration of silicone lenses to a tan-brown colour has been reported, although the colour change does not appear to affect visual function[40].

HYDROGEL

Most hydrogel lenses currently under study are polyhydroxyethylmethacrylate (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[33]. 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 decenteration is greater than that with PMMA lenses [34,35].

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 (Perlon, Supramid) 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 [36].

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 ½ times over that of posterior chamber intraocular lenses with PMMA haptics[37]. This is consistent with the finding that bacteria can adhere better to polypropylene than to PMMA[38].

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[39]. 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[40].Titanium is lighter than either and has been used as a loop material. Stainless steel, a 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 complication 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 eyes indicate that a foreign body reaction probably occurs in all eyes after intraocular lens implantation [41,42.] 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[43].

The reaction to 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 this makes the iris less susceptible to chafing[44.]

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 fluorescein into the anterior chamber in comparison to unmodified PMMA[45] .

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 [46]. Heparin surface modified lens has approximately 0.5 µgm 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[47.]

In-vitro experiments have shown reduced activation of human granulocytes after heparin surface modification of PMMA. A reduction of platelet adhesion and reduced growth of human fibroblasts also have been demonstrated[43]. 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[42]. A safety study with 56 patients followed for 1 year did not show any unexpected reactions or severe complications[25]. 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[43].

Literature on their use in eyes with a predisposition to increased activity is sparse. Two small series of mixed uveitides found little surface cell adhesion to the IOL, though implant precipitates were found in some eyes and synechiae to the IOL in several eyes including one case of iris bombe [49,50].

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 increased 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 pre-existing active uveitis, but also in cases involving other modes of blood ocular barrier breakdown, such as in proliferative diabetic retinopathy. 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[43]. 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 attendant 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 [47,51].

HEPARIN

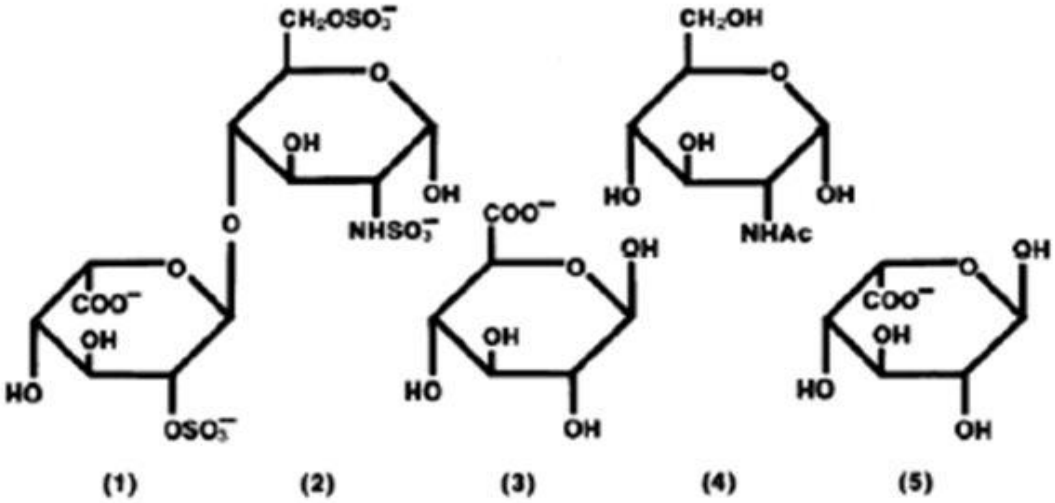


Figure 6. HEPARIN MOLECULE

Figure 7. UNFRACTIONATED HEPARIN

Heparin was discovered by a medical student J Mc Lean, working at Johns 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.

Heparin is composed of an unknown number of sulfated D-glucosamine and D-glucuronic acid units linked through an oxygen bridge. 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[52].

Heparin depends for its anticoagulant action on the presence in plasma a protein, antithrombin III, which is a naturally occurring inhibitor of thrombin and activated factor X. In the presence of heparin, antithrombin will become vastly 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. A molecular level, the capacity of heparin to inhibit factor Xa has been found to depend on a specific pentasacharide sequence which can be isolated in fragments of average molecular weight 5000 Daltons (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[53].

Postoperative anterior chamber fibrin exudation is seen in several clinical settings, especially after vasectomy surgery for proliferative diabetic retinopathy, proliferative vitreoretinopathy, ocular trauma or severe intraocular infection [54,55,56]. Fibrin has been noted to stimulate the transformation of retinal pigment epithelial cells into fibrocystic 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 [57,58].

Johnson et al in his randomized study in 73 eyes showed that heparin supplementation in the vitrectomy 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)58. In a similar study in rabbits Deborah A et al studied the inhibition of intraocular fibrin formation following infusion of 5 IU/ml of low molecule weight heparin sodium during lumpectomy, vasectomy 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 [59].

Fibrin binding to corneal endothelium can cause cell damage and cell loss [60]. Thrombin receptors on corneal endothelium have also been demonstrated, but the precise effect of these receptors are unknown [61,62]. This might account for the increased corneal clarity in these studies with intraocular heparin infusion.

In addition to its anticoagulant activity, heparin is known to have anti-inflammatory activity. In a study by J Mansler et al show that heparin induces apoptosis in vitro of human peripheral blood neutrophils. The known antiproliferative effect of heparin in several in vitro cell systems has therefore to be interpreted in this light. In addition, apoptosis may help to explain the anti-inflammatory effects resulting from interaction between vessel wall heparin sulphate and chemo attractant peripheral blood neutrophils [63]. Yet another study by Richard

Metal show 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 [64].

Paresh Dandona et all investigated the effect of heparin on reactive oxygen species (ROS) generation by leucocytes. Heparin was injected intravenously at a dose ofi 10,0000 units into eight normal subjects blood sampled were collected from the antecubital vein prior to and at 0,half,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 [65].

The ability of Heparin to inhibit complement was described by Ecker and Gross in 1929 and several points of action have been identified.

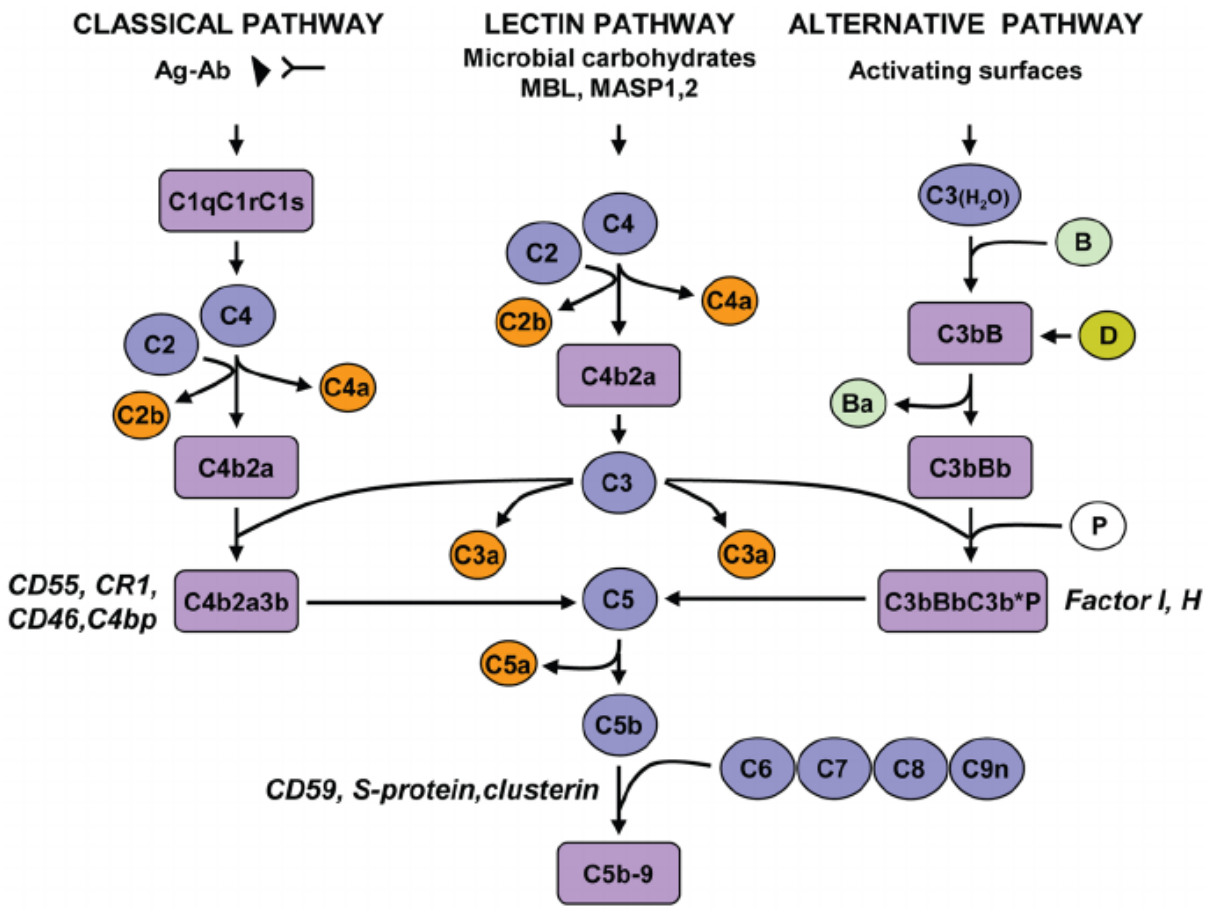


Figure 8. COMPLEMENT PATHWAY

The rate limiting steps are suggested to be enhancement of CHNH in the classical pathway and prevention of formation of the amplification convertase of the alternate pathway [67]. The ability of heparin to inhibit the early steps in the cascade makes it attractive as a complement inhibitor.

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 undegraded 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 to 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 haemorrhage 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.
- Other than bleeding, no other complication is reported in the eye.

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 if any research has been directed towards determining its effect on the anterior segment of the eye and the blood aqueous barrier. A number of studies have been done that describes the breakdown and re-establishment of the blood aqueous barrier in patients undergoing cataract surgery [68,69].

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 junctions 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 [70].

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

- Surgical trauma and manipulations
- Diabetes mellitus

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 gm 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[71].

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 Dretal in a study conducted on 234 patients using fluorophotometric measurements found that in patients undergoing uneventful extracapsular 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 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 73 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. 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[80]. 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 three fold to four fold excess risk of cataract among diabetics less than 65 years of age[72.]

Noyes 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.

Willington and Lawrence proposed that a specific kind of iritis is associated with uncontrolled diabetes mellitus. Guy and associates observed iritis in 30% of insulin dependent diabetic patients along with severe autonomic neuropathy as compared to 0.7% of control patients[73].

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 [74].

In the retina, the cellular elements of retinal capillaries consist of endothelial cells and pericytes. The tight junctions of the endothelial cells contribute 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 [75].A similar process occurs in the blood aqueous barrier.

The permeability of the blood ocular barrier was examined by fluorophotometry in adolescent and adult diabetic patients before the onset of retinopathy[76]. 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 inter-endothelial 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 diabetic retinopathy or may act as a predictive factor in suggesting the severity and progression of retinopathy.

A study of 126 eyes of diabetic patients 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[77].

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. The presence of diabetes mellitus is related to excessive damage to the blood aqueous barrier immediately after surgery[78].

Diabetic patients had a higher incidence of inflammation and macular edema post intraocular lens implantation kin comparison to age matched controls[79].

Increased post-operative inflammation is associated with various complications such as:

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

1. CYSTOID MACULAR EDEMA

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 with posterior chamber IOL implantation, the prevalence of clinically significant CME decreased to approximately 1%.

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 cystoids macular edema with permanent visual loss occurs in approximately 1% of patients undergoing extracapsular cataract extraction.

Cystoid macular edema is best visualized by careful slit lamp biomicroscopic examination contact 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 lager in the perifoveal region and become progressively smaller away from the center of the macula may be seen at the fovea. These limit the potential for visual recovery.

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

Pathogenesis

Irvine considered inflammation as one of the causes of decreased vision in patients with cystoid macular edema.

Eyes with CME often have signs of intraocular inflammation and evidence of blood ocular barrier breakdown during 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 cystoids 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 [80].

Other theories of cystoids macular edema include vitreous traction and vitreous-uveal traction [80]. In a study on 103 patients who underwent phacoemulsification found trend that those who had CME had higher anterior chamber flare and cell values, at 14, 30 and 60 days postoperatively[81]. 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 postoperative period onwards.

2. POSTERIOR CAPSULE OPACIFICATION

After cataract formation 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 in the bag IOL implantation with an intact posterior capsule[82].

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 may contain contractile elements (myofibroblasts) that cause the capsule to wrinkle [92].

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 cause opacities and fine wrinkles to form in the posterior capsule[89].

The first two problems can be dealt with by careful patient selection and good surgical technique[84]. 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.

Excessive post-operative inflammation also can result in posterior synechiae, pigments on intraocular lens surface and visual acuity problems[85].

MEASURMENT 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 inflamed 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.

Hence 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 humour. They are manufactured locally from the fixed tissue cells, or pass through the capillary walls from the blood into the tissues and thence 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 the 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 [86,87].

Anterior chamber cells are best seen by directing the slit beam obliquely across the eye and focusing posterior to the cornea using a 1 x 1mm slit beam under high magnification. 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 summarized the system proposed by Hogan and colleagues, the system proposed by Schlaegel and that proposed by Neusenblatt [87,88].

Using a wide beam with narrow 1 x 1mm slit

Table 1. GRADING SYSTEMS OF ANTERIOR CHAMBER CELLS.

SCHLAEGEL		HOGAN		NUSSENBLATT	
GRADE	CELLS	GRADE	CELLS	GRADE	CELLS
-	-	0	0	0	0
½	Rare(normal)	Rare cells	1-2		
-	-	Occasional cells	3-7		
-	-	-	-	Trace	1-5
1	Occasional cells	1+	7-10	1+	6-15
1 ½	2-7	1-2+	10-15	-	-
2	8-15	2+	15-20	2+	6-25
2$^{1/2}$	16-30	-	-	-	-
3	Too many to count	3+	20-50	3+	26-50
3$^{1/2}$	Too many to count	-	-	-	-
4	Most ever seen	4+	>50	4+	>50

Standardized nomenclatures have been employed to standardize the uniformity in reporting the gradation of clinical findings. Most commonly used nomenclatures were developed by the Standardization of Uveitis Nomenclature

(SUN) working group for grading inflammation in anterior and vitreous chambers. Observer can assess cells and flare in the anterior chamber using a slit lamp beam of

1 X 1 mm in height and width, when thrown at an angle of 45-60°. Based on the finding, the inflammation can be categorized from 0 to 4+ grade.

Table 2. The SUN working group grading system for anterior chamber cells

Grade	Cells in field
0	<1
0.5+	1-5
1+	6-15
2+	16-25
3+	26-50
4+	>50

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 as flare. There is approximately 1g of protein per 100ml of blood, but only 11mg of protein per 100 ml 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. Flare can be clinically graded on 0 to 4+ scale.

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 [86,87]

Table 3. GRADING SYSTEMS OF ANTERIOR CHAMBER FLARE

GRADE	SCHLAEGEL	HOGAN ET AL
0	Complete absence	
½	Faint(normal)	-
1	Very slight	Very slight
$1^{1/2}$	Mild	-
2	Mild to moderate	Moderate(iris and lens clear)
3	Moderate	Marked flare(iris and lens hazy)
4	Severe	Intense(fibrin, plastic aqueous)

Table 4. The SUN working group grading system for anterior chamber flare

Grade	Description
0	None
1+	Faint
2+	Moderate (iris and lens details clear)
3+	Marked (iris and lens details hazy)
4+	Intense (fibrin or plastic aqueous)

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. A technique ocular fluorophotometry uses the principle that fluorescein in the anterior chamber will bind to albumin and the amount of bound fluorescein will alter its polarization which can be measured by fluorophotometry.

OCULAR FLUOROPHOTOMETRY

Recently there have been considerable developments in the techniques and 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 and application to routine clinical practice is cumbersome and expensive.

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 humor 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:

(1) Permeability or diffusion coefficient of variant complexity,

(2) The ration of fluorescence between a normal and abnormal eye,

(3) A peak level of fluorescence or

(4) A percentage change from a previous value[86].

Fluorophotometry 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. A commercial machine has been produced which scans a small volume of the anterior chamber with a He-Ne laser and measures reflected light from the material within the anterior chamber by a sensitive photomultiplier[89].

LASER FLARE CELL METER

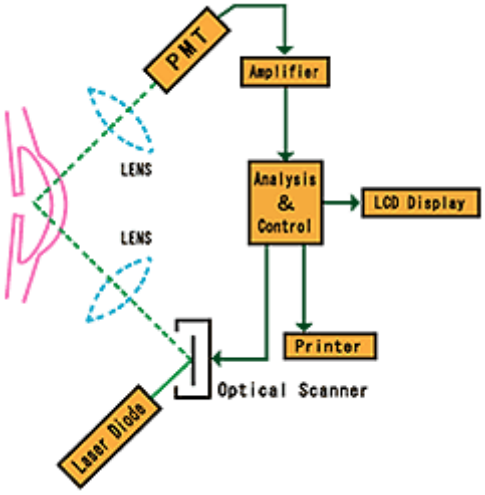


Figure 9. BLOCK DIAGRAM OF LASER FLARE CELL METER

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.

In a study done by Mitsuru SAWA et [90] , protein concentration measurement mode-a single photon sampling time was 1m sec and 10 consecutive samples were taken and mean calculated. To minimize signal contamination by back ground laser scattering, the laser beam was scanned vertically for a length of 0.6mm, covering the sampling window.

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[91]. They assessed the preoperative and postoperative anterior chamber reaction 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 ($P<.001$) 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 wigll be a useful tool in clinical and pharmacological research in the field.

Figure 10. LASER FLARE METER

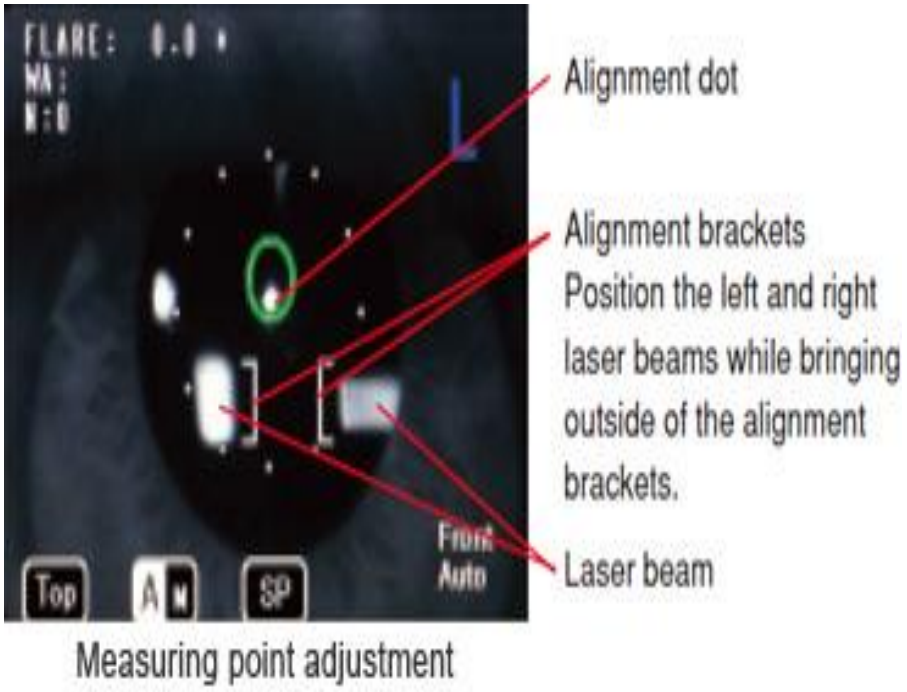


Figure 11. MEASURING POINT ADJUSTMENT OF FLARE CELL METER

MATERIALS AND METHODS

SOURCE OF DATA:

130 diabetic patients with cataract attending Ophthalmology OPD to undergo cataract surgery at R.L.JALAPPA HOSPITAL AND RESEARCH CENTRE, TAMAKA, KOLAR attached to SRI DEVARAJ URS MEDICAL COLLEGE between December 2014 and January 2016 were selected for this prospective study.

INCLUSION CRITERIA:

Senile cataract patients with diabetes mellitus.

EXCLUSION CRITERIA:

Patients with :

1. Pre-existing ocular inflammatory diseases.
2. Systemic anti-inflammatory medications prior to surgery.
3. Patients with bleeding tendencies.
4. Patients with complications during surgery.
5. Patients with poor mydriasis (<5mm). and complications during cataract surgery.

Sample Size estimation:

	Heparin Group	Control Group
Flare	7.48+/- 3.30	9.47+/- 4.37

n=59+59=118

Considering 10% non response:

n=118+11.8=129.8=130(65+65)

METHOD OF COLLECTION OF DATA

130 patients fulfilling the criteria framed were included in this study after informed consent was taken. All the patients underwent similar protocol for standard cataract evaluation, which consisted of recording visual acuity, intraocular pressure by Applanation tonometer, slit lamp examination and fundus evaluation by direct and indirect ophthalmoscopy, lacrimal syringing and intraocular lens calculation by Sanders-Retzlaff-Kraff 2 method using Suoer Ophthalmic A Scan SW-1000.

Patients underwent standard pre-operative investigations - FBS, PPBS,HIV,HBsAg, urine protein and sugars along with systemic examination.

All patients received oral Tab Ciprofloxacin 500mg twice daily and Ciprofloxacin 0.3% eye drops hourly one day before the surgery. Preoperatively pupils were dilated with Tropicamide with Phenylephrine 0.5% or 1% drops along with Flurbiprofen 0.03% drops for all patients.

All patients underwent manual SICS with PCIOL(PMMA) implantation by a single experienced surgeon using the same technique under peribulbar anaesthesia.

Patients were randomised into 2 groups. Group 1-Study group (65 eyes) received heparin in irrigation solution during cataract surgery and Group 2-Control group (65 eyes) without heparin in irrigation solution by a person who had no interest in the study. Each patient was allotted a number according to the randomization table by the same person. Thereafter, the patient was identified by the surgeon and investigator solely on the number allotted. The presence of heparin in the irrigating fluid remained unknown to both the surgeon and investigator until final analysis was completed. The patient was blinded as the consent for adding heparin to the irrigating solution was taken pre-randomisation. The randomization code was opened only at the termination of the study.

At the beginning of surgery, 1000IU(1ml) heparin was added to 500 ml of balanced salt solution (irrigating solution) in a concentration of 10 IU/ml for study group. Control group received regular irrigating solution.

SURGICAL TECHNIQUE:

Procedure was started with a conjunctival flap made at superior part of the limbus. Scleral tunnel was constructed using a crescent knife and extended up to 1.0 mm into clear cornea. A 3.2 mm keratome was used to access the anterior chamber and the internal corneal incision was extended for about 0.5 mm more than the external scleral incision. The anterior chamber was deepened using a standard viscoelastic i.e. 2% hydrooxypropyl methylcellulose and continuous curvilinear capsulorrehexis of 5 - 6 mm was done using a bent 26 – gauge needle mounted on the irrigating infusion. The nucleus was delivered by sandwich method and the cortex was washed using a simcoe cannula. A 6 mm optic PMMA PC IOL was implanted in the capsular bag inflated by viscoelastic. The viscoelastic material was replaced by BSS solution .The integrity of the self-sealing scleral incision was ensured and the cut conjunctival flap was apposed using a forceps fitted to bipolar diathermy. In the event of any intraoperative complication the surgical technique was modified accordingly and the case was excluded from the study.

POST-OPERATIVE ASSESSMENT:

Post-operative medication consisted of moxifloxacin (0.5%) eye drops along with prednisolone acetate (1%) eye drops 8 times per day for the first week, after which it was tapered over 4 weeks for both groups. Oral antibiotics were continued for 5 days. Follow up on day 1, day 7, day 28 and 8^{th} week post-operatively included grading of flare, cells, pigments on the lens (from grade 0 to 4) and visual acuity using Snellen‘s chart. Slit lamp evaluation was done by an experienced examiner.

CELLS AND FLARE:

Slit lamp machine used was Topcon slit lamp SL-2G with light intensity and magnification at maximum at an angle of 45 to 60 degrees using a 1x1mm slit beam.

Cell and flare grading was done according to the SUN working group grading system of anterior chamber cells and flare.

GRADING OF PIGMENTS ON THE IOL SURFACE:

The pigments on the intraocular lens surface were examined semi-quantitatively using 3m long and 2 mm wide slit beam focused on 5 regions on the IOL surface as demonstrated in fig. 12 and average calculated.

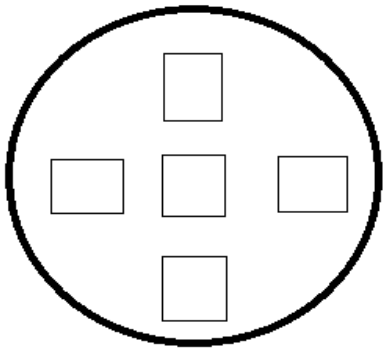


Figure 12 AREAS OF ASSESSMENT OF PIGMENT DEPOSITS ON IOL SURFACE

BCVA:

On each post-operative follow up, visual acuity was measured using Snellen‘s chart and the best corrected visual acuity was noted.

STATISTICAL ANALYSIS:

Data wias analysed using the statistical program for social sciences (SPSS) software. Comparison of visual outcome was done using Mann Whitney-U Test. Comparison of complications was done using Chi-square test. McNemar test was used to determine whether the values of a dichotomous variable changed significantly across two occasions of assessment. A probability value (p value) <0.05 was considered statistically significant.

RESULTS

BASELINE CHARACTERISTICS OF STUDY AND CONTROL GROUPS:

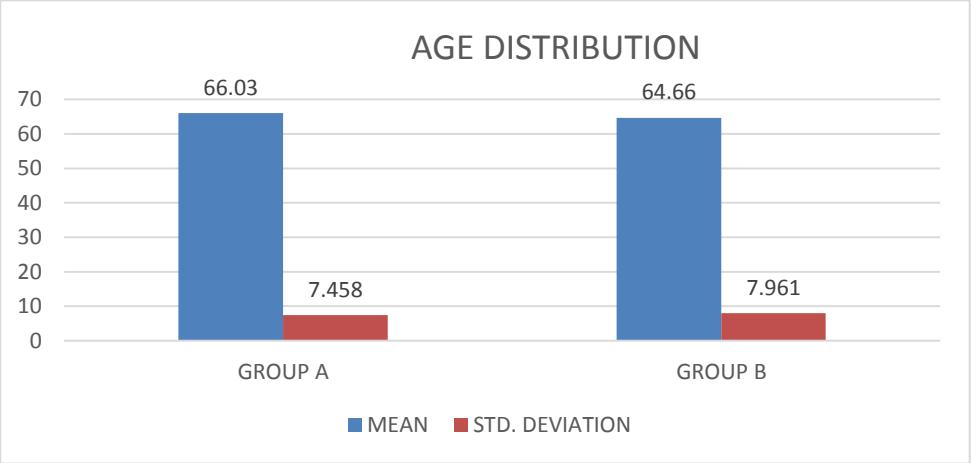
Age

The ages of the patients in the study group ranged from 51 to 85 with a mean of 66.06 and a standard deviation of 7.458.

The ages of the patients in the control group ranged from 52 to 84 with a mean of 64.66 and a standard deviation of 7.961.

Table 5. AGE DISTRIBUTION

	GROUP	MEAN	STD. DEVIATION	P VALUE
Age	A	66.03	7.458	**0.313**
	B	64.66	7.961	



GRAPH 1. AGE DISTRIBUTION

There was no statistical difference in age between the two groups.

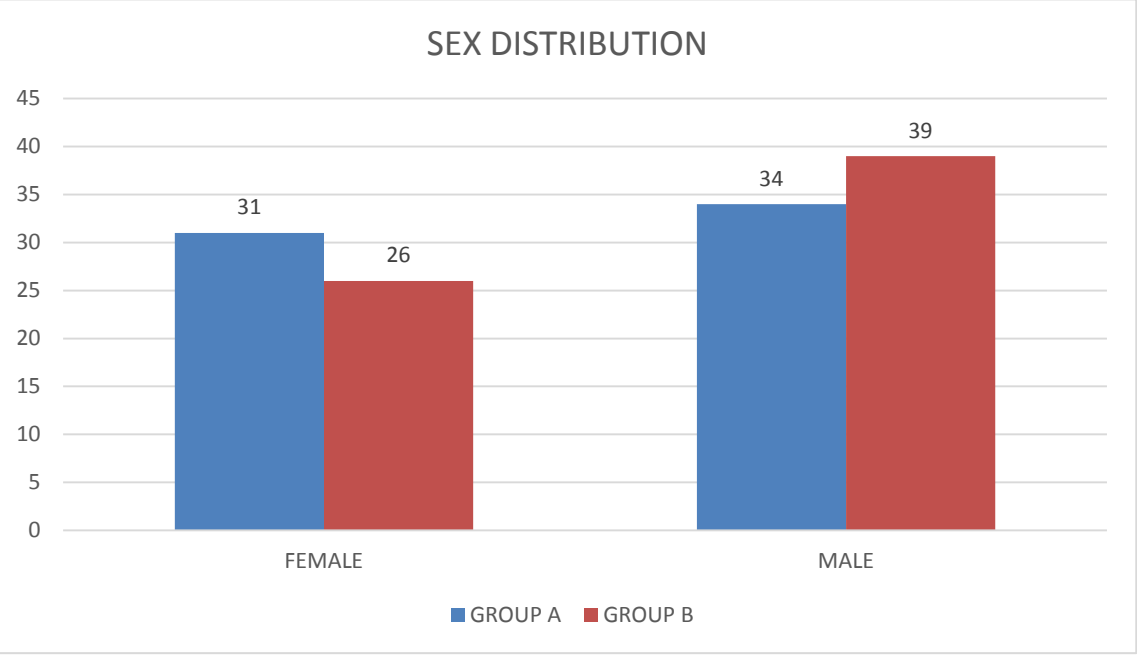
Sex

The study group had 31(47.7%) females and control group had 26 (41.9%) females.

The study group had 34(52.3%) males and control group had 39 (60%) males.

Table 6. SEX DISTRIBUTION

		GROUP		TOTAL	P VALUE
		A	B		
SEX	Female	31(47.69%)	26(40%)	57(43.84%)	**0.480**
	Male	34(52.30%)	39(60%)	73(56.15)	
Total		65	65	130	



GRAPH 2. SEX DISTRIBUTION

There was no statistical difference in the sex between the two groups.

Pre-operative FBS and PPBS:

The mean pre-operative FBS in study group was 95.89 with a standard deviation of 10.10.

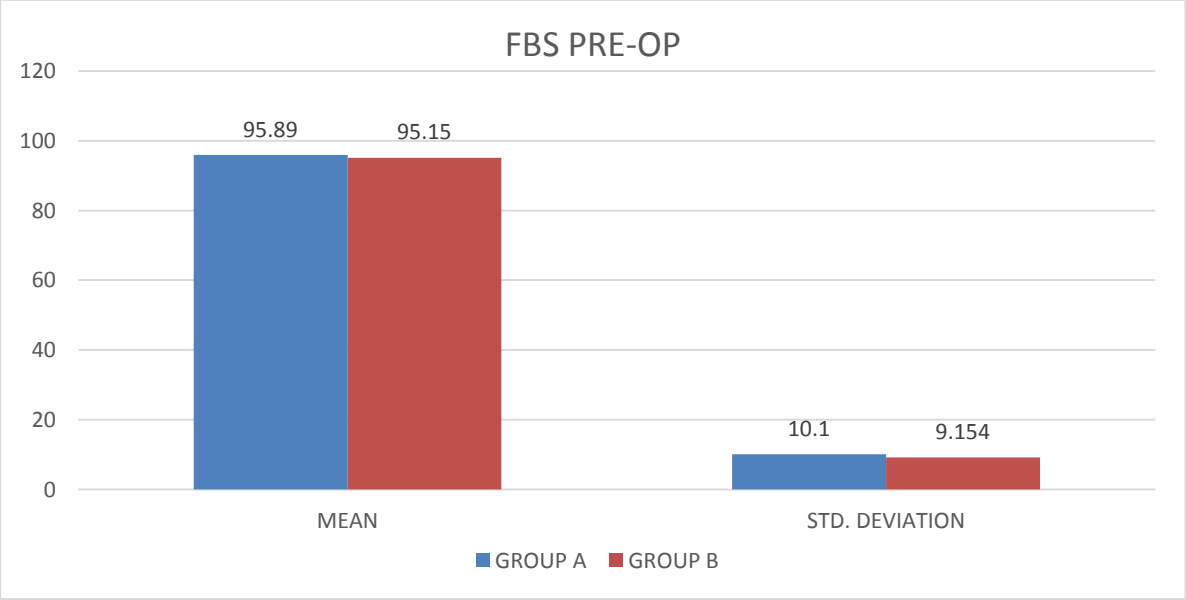
The mean pre-operative FBS the control group was 95.15 with a standard deviation of 9.154.

The mean pre-operative PPBS in study group was 127.26 with a standard deviation of 9.154.

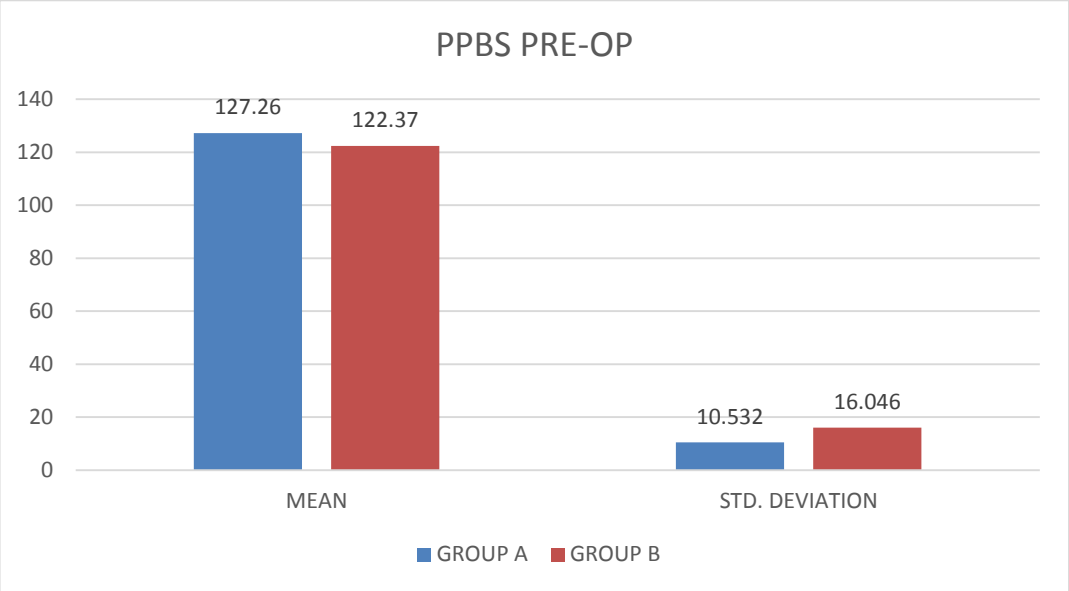
The mean pre-operative PPBS in the control group was 122.37 with a standard deviation of 16.046.

Table 7. PRE-OPERATIVE FBS AND PPBS

	GROUP	MEAN	STD. DEVIATION	P VALUE
FBS PRE-OP	A	95.89	10.100	**0.663**
	B	95.15	9.154	
PPBS PRE-OP	A	127.26	10.532	**0.042**
	B	122.37	16.046	



GRAPH 3. PRE-OP FBS



GRAPH 4. PRE-OP PPBS

There was no statistical difference in the pre-operative FBS and PPBS in the two groups.

Post-operative FBS and PPBS:

The mean post-operative FBS in the study group was 97.51 with a standard deviation of 19.030.

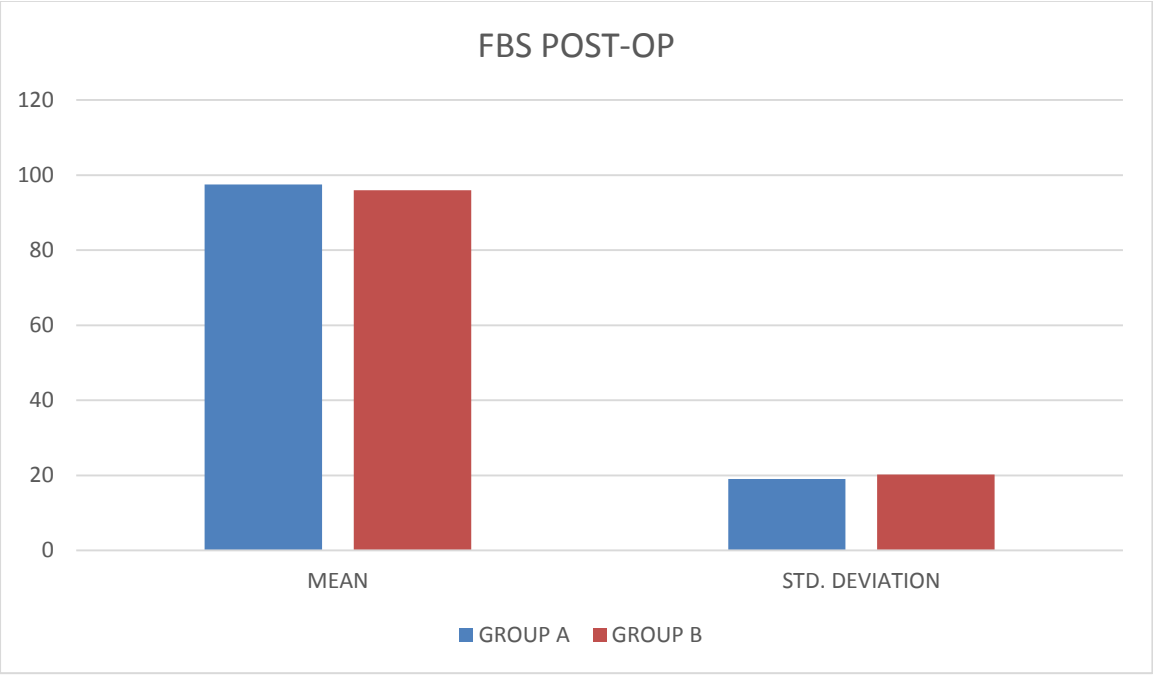
The mean post-operative FBS in the control group was 95.97 with a standard deviation of 20.214.

The mean post-operative PPBS in the study group was 137.92 with a standard deviation of 22.39

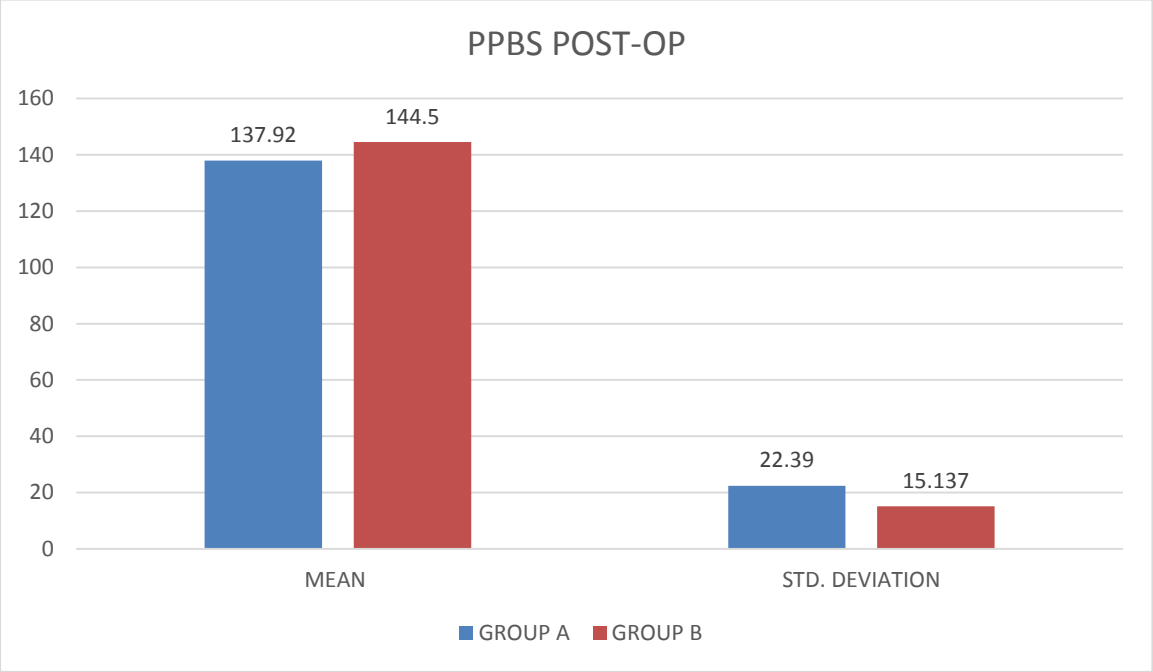
The mean post-operative PPBS in the control group was 144.5 with a standard deviation of 20.15.

Table 8. POST-OPERATIVE FBS AND PPBS

	GROUP	MEAN	STD. DEVIATION	P VALUE
FBS POST-OP	A	97.51	19.030	**0.656**
	B	95.97	20.214	
PPBS POST-OP	A	137.92	22.39	**0.084**
	B	144.5	20.15	



GRAPH 5. POST-OP FBS



GRAPH 6. POST-OP PPBS

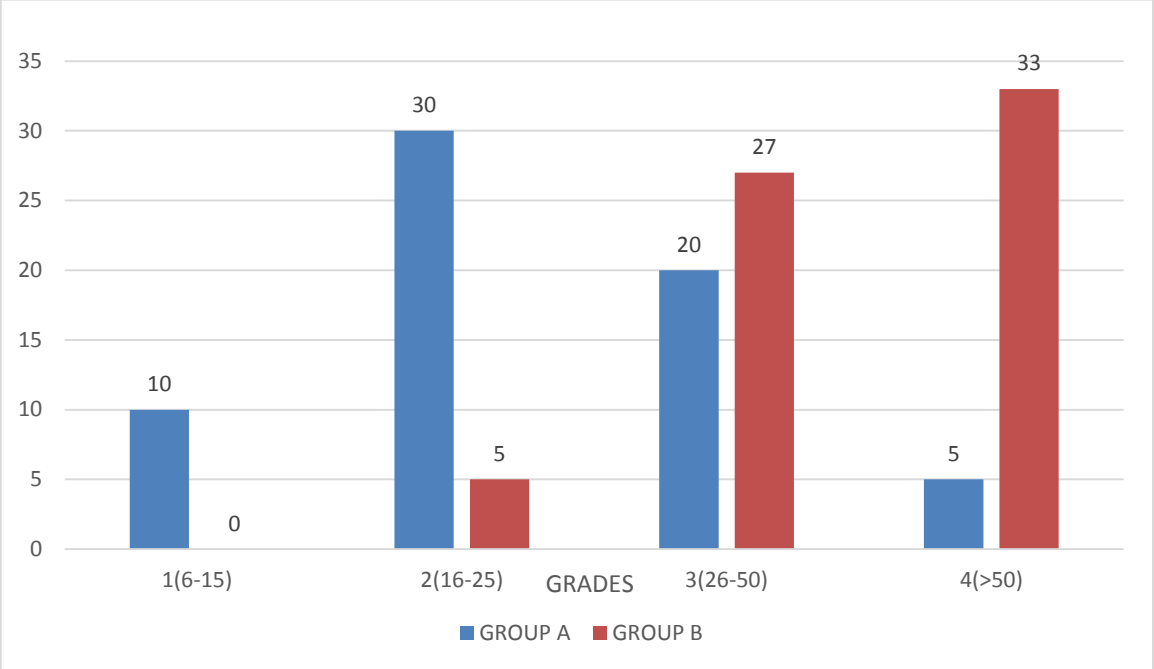
There was no statistical difference in the pre-operative FBS and PPBS in the two groups.

ASSESSMENT OF POST-OPERATIVE CELLS IN THE ANTERIOR CHAMBER IN STUDY AND CONTROL GROUPS:

The distribution of grading of cells (SUN Classification) in the study and control group is as shown below:

Table 9. POST OPERATIVE DAY 1 DISTRIBUTION OF CELLS

		GROUP		TOTAL	P VALUE
DAY 1	GRADE	A	B		
CELLS DAY1	1	10(15.38%)	0	10(7.67%)	**<0.001**
	2	30(46.15%)	5(7.69%)	35(53.84%)	
	3	20(30.76%)	27(41.53%)	47(72.30%)	
	4	5(7.69%)	33(50.76%)	38(58.46%)	
Total		65	65	65	130

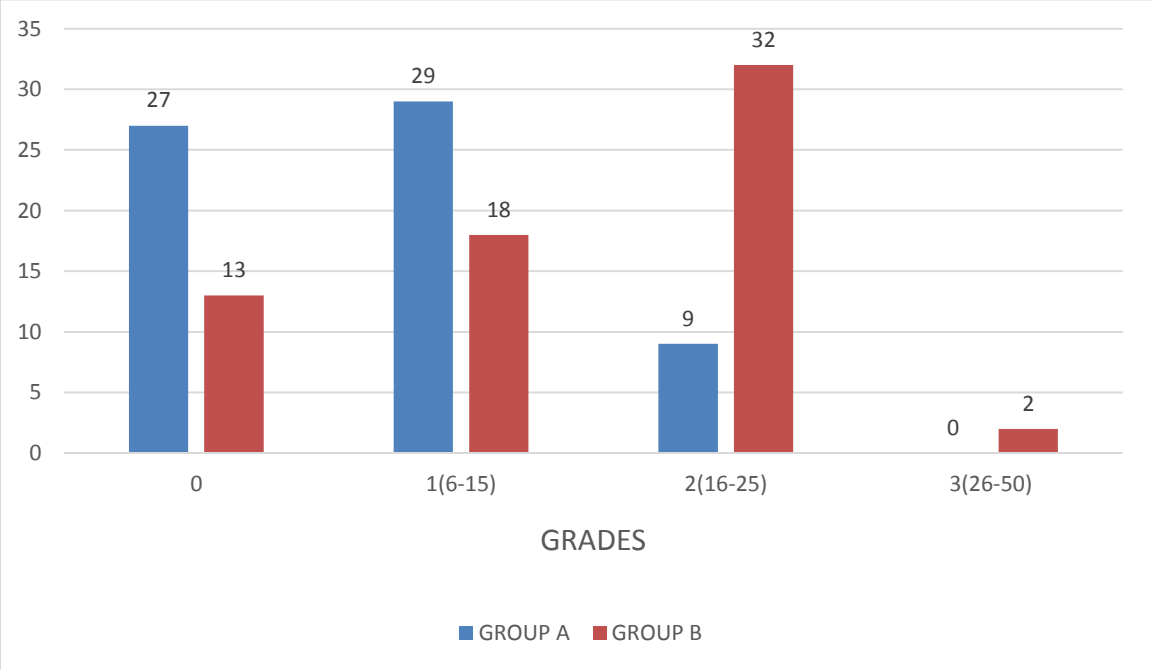


GRAPH 7. POST-OP DAY 1 DISTRIBUTION OF CELLS

There was a statistically significant reduction in the cells in the anterior chamber post-operatively on Day 1, in patients who received heparin in the irrigating solution. It was also noted that lesser number of cells (Grade 1-2) were seen in 40(61.53%) patients in the study group as compared to just 5(7.69%) patients in the control group.

Table 10. POST OPERATIVE DAY 7 DISTRIBUTION OF CELLS

	GRADE	GROUP		TOTAL	P VALUE
Day 7		A	B		
CELLS DAY 7	0	27(41.53%)	13(20%)	40(61.53%)	**<0.001**
	1	29(44.61%)	18(27.69%)	47(72.30%)	
	2	9(1.38%)	32(49.23%)	41(63.07%)	
	3	0	2(3%)	2(3%)	
Total		65	65	130	

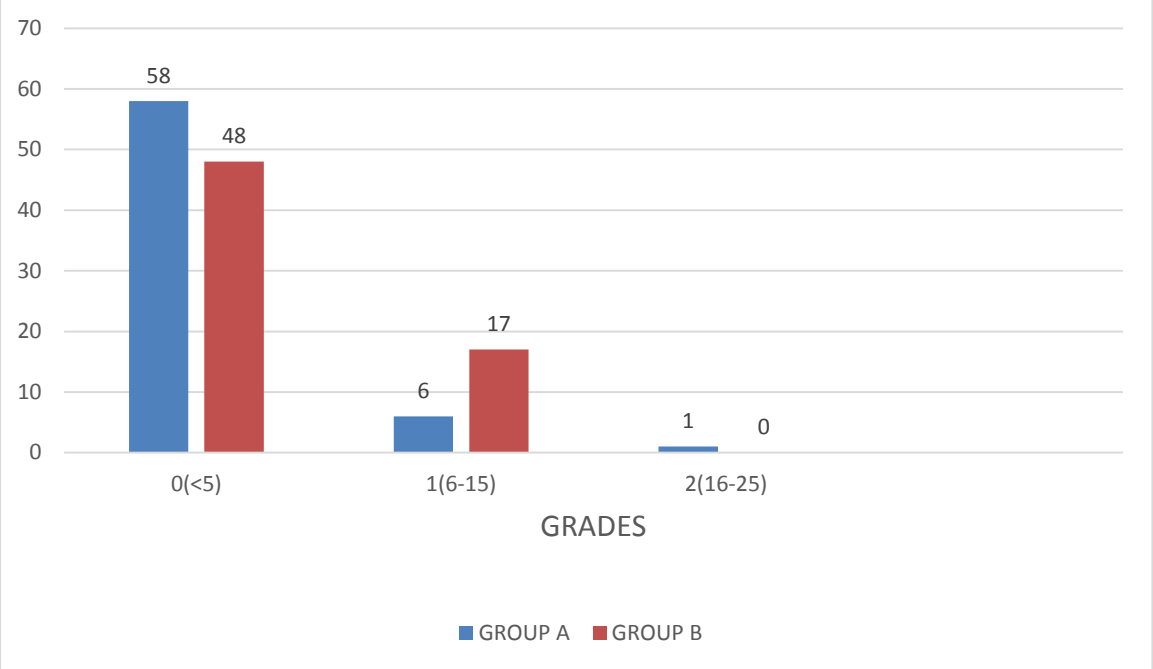


GRAPH 8. POST-OP DAY 7 DISTRIBUTION OF CELLS

There was a statistically significant reduction in the cells in the anterior chamber post-operatively on Day 7, in patients who received heparin in the irrigating solution. It was also noted that lesser number of cells (Grade 1-2) were seen in 56(86.15%) patients in the study group as compared to just 31(47.69%) patients in the control group.

Table 11. POST OPERATIVE 4TH WEEK DISTRIBUTION OF CELLS

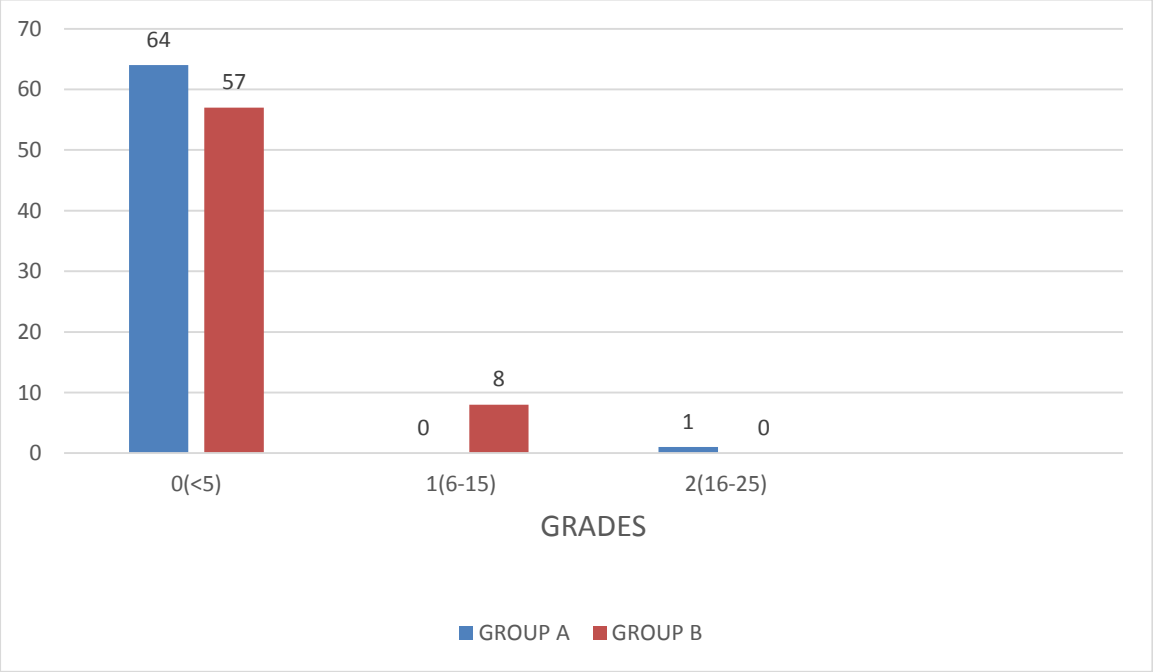
		GROUP		TOTAL	P VALUE
4th week	GRADE	A	B		
CELLS 4th WEEK	0	58(89.23%)	48(73.84%)	106(96.9%)	**0.057**
	1	6(9.2%)	17(26.15%)	23(35.3)	
	2	1(1.5%)	0	1(0.07%)	
Total		65	65	130	



GRAPH 9. POST-OP 4TH WEEK DISTRIBUTION OF CELLS

Table 12. POST OPERATIVE 8TH WEEK DISTRIBUTION OF CELLS

		GROUP			
8th week	GRADE	A	B	TOTAL	P VALUE
CELLS 8th WEEK	0	64 (98.46%)	57(87.69%)	121(93.07%)	**0.059**
	1	0	8(12.3%)	8(6.15%)	
	2	1(1.5%)	0	1(0.07%)	
Total		65	65	130	



GRAPH 10. POST-OP 8TH WEEK DISTRIBUTION OF CELLS

58 (89.23%) patients had no cells in the anterior chamber on post-operative 4th week and 64 (98.46%) patients had no cells in the anterior chamber on post-operative 8th week in the Study group compared to the control group, where 50 (76.92%) patients had no cells in the anterior chamber on post-operative 4th week and 57 (87.69%) patients had no cells in the anterior chamber on post-operative 8th week.

It was observed that:

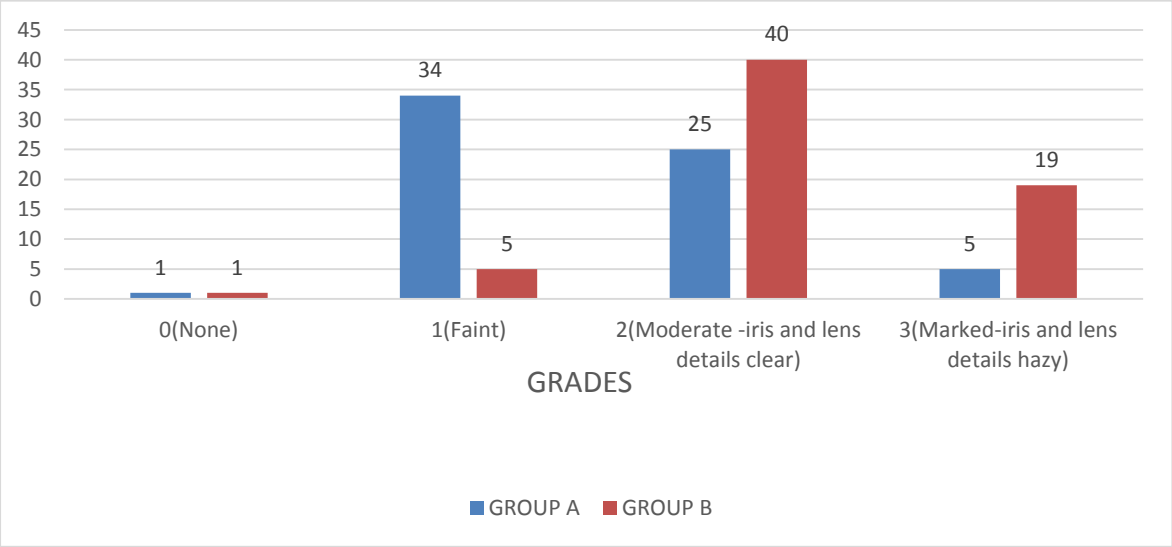
1) Study group had statistically significant (P<0.001) reduction in number of cells on Post-operative day 1.
2) Study group had statistically significant (P<0.001) reduction in number of cells on Post-operative day 7.
3) There was no statistically significant reduction in number of cells on Post-operative 4^{th} and 8^{th} week between both groups.

ASSESSMENT OF POST-OPERATIVE FLARE IN THE ANTERIOR CHAMBER IN STUDY AND CONTROL GROUPS:

The distribution of grading of cells (SUN Classification) in the study and control group is as shown below:

Table 13 POST-OPERATIVE DAY 1 DISTRIBUTION OF FLARE

		GROUP		TOTAL	P VALUE
DAY 1	GRADE	A	B		
FLARE DAY1	0	1(1.5%)	1(1.5%)	2(1.5%)	**<0.001**
	1	34(52.3%)	5(7.69%)	39(30%)	
	2	25(38.4%)	40(61.5%)	65(50%)	
	3	5(7.69%)	19(29.2%)	24(18.4%)	
Total		65	65	130	

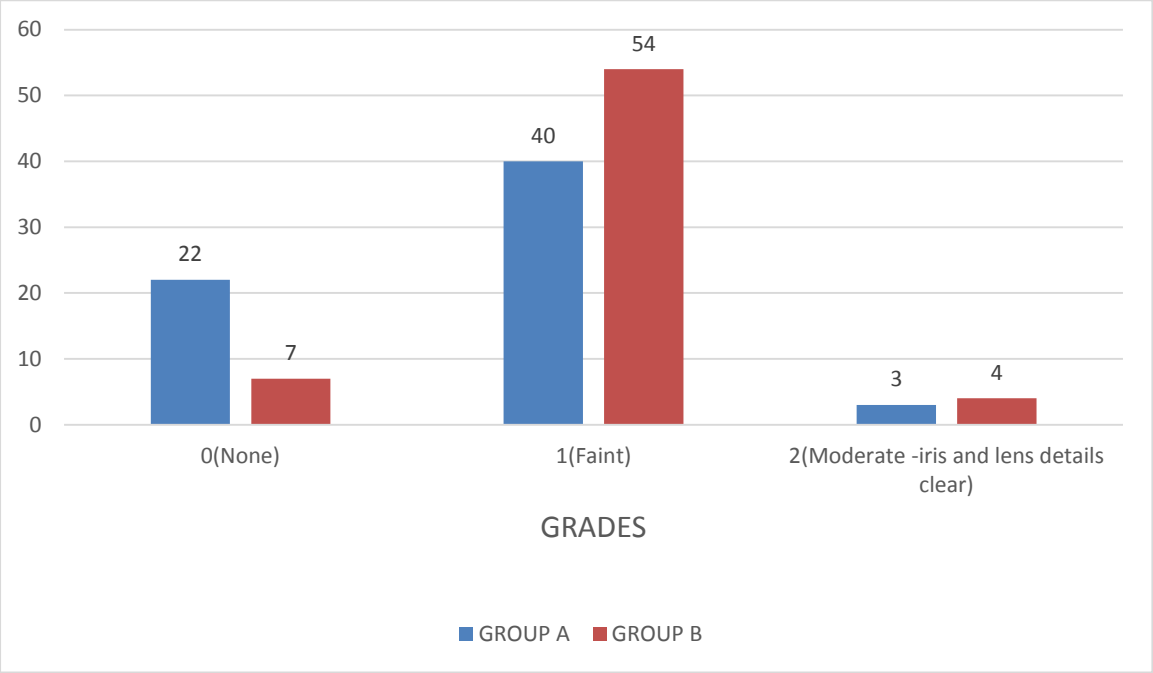


GRAPH 11. POST-OP DAY 1 DISTRIBUTION OF FLARE

There was a statistically significant reduction in the flare in the anterior chamber post-operatively on Day 1 in patients who received heparin in the irrigating solution. It was also noted that lesser grade of flare (Grade 1-2) was seen in 35(53.84%) patients in the study group as compared to just 6(9.23%) patients in the control group.

Table 14. POST OPERATIVE DAY 7 DISTRIBUTION OF FLARE

		GROUP			
Day 7		A	B	TOTAL	P VALUE
FLARE DAY 7	0	22(33.8%)	7(10.7%)	29(22.3%)	**0.007**
	1	40(61.5%)	54(15.38%)	94(72.3%)	
	2	3(4.6%)	4(6.1%)	7(5%.3)	
Total		65	65	130	

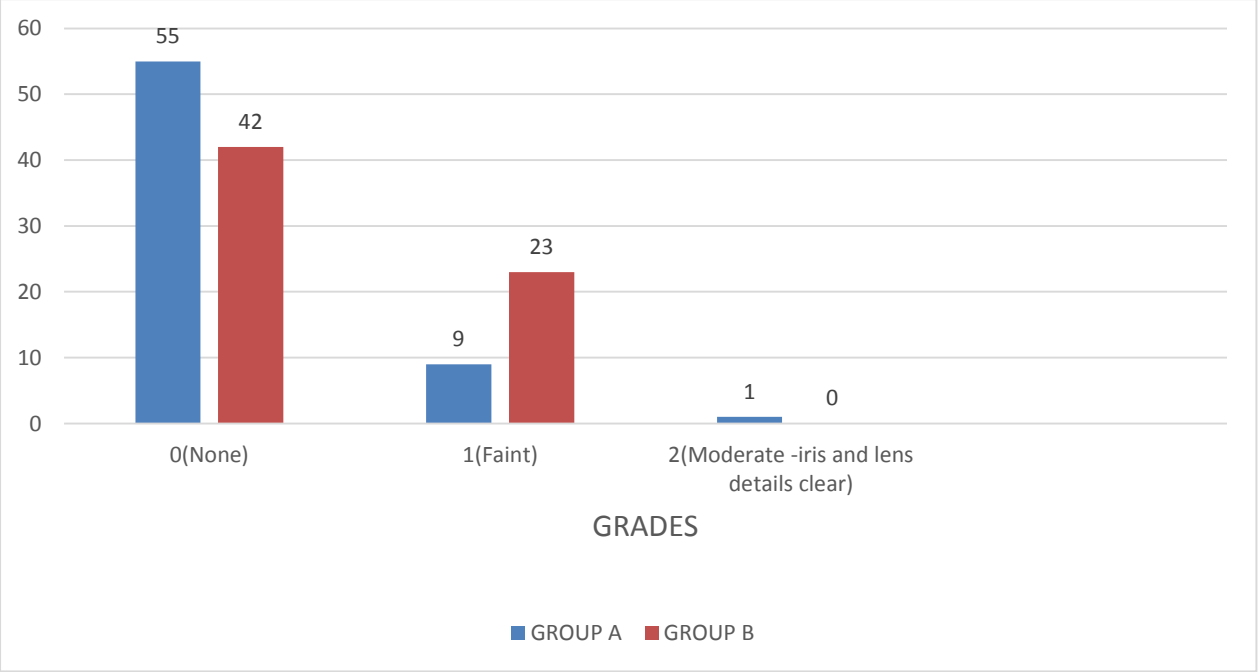


GRAPH 12. POST-OP DAY 7 DISTRIBUTION OF FLARE

On post-operative Day 7, it was seen that 22(33.85%) patients who had received heparin in the irrigating solution had no flare as compared to just 7(10.76%) patients from the control group.

Table 15. POST OPERATIVE 4TH WEEK DISTRIBUTION OF FLARE

		GROUP		TOTAL	P VALUE
4^{TH} WEEK	GRADE	A	B		
FLARE 4^{th} week	0	55(84.6%)	42(64.6%)	97(74.6%)	**0.012**
	1	9(13.8%)	23(35.3%)	32(24.6%)	
	2	1(1.5%)	0	1(0.7%)	
Total		65	65	130	

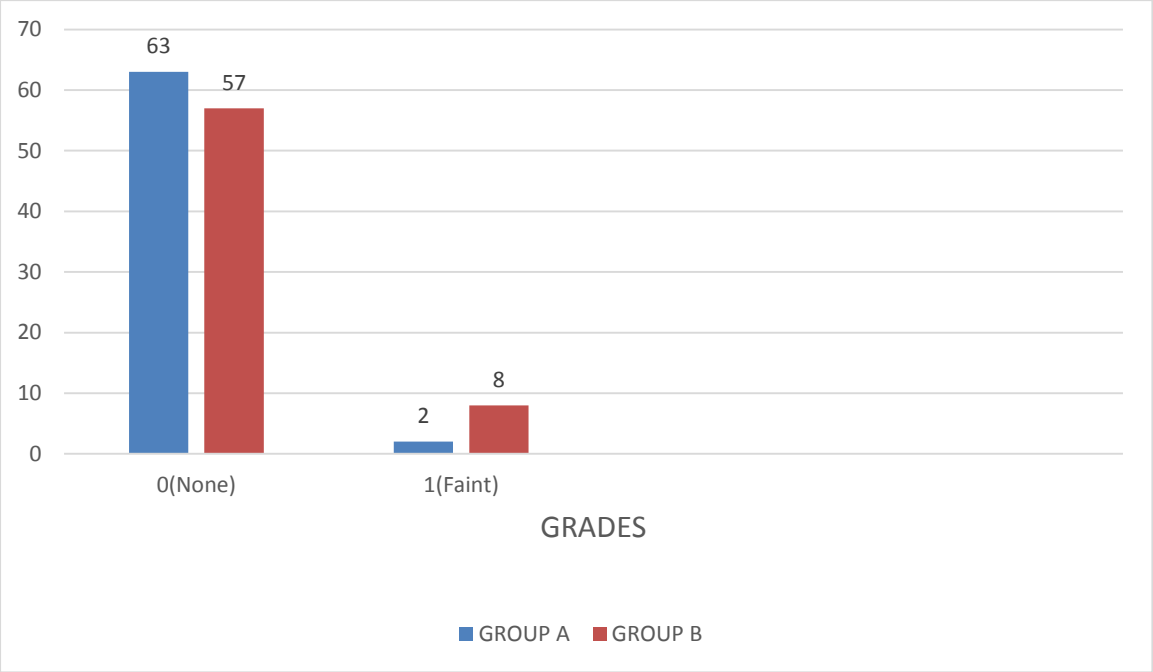


GRAPH 13. POST-OP 4TH WEEK DISTRIBUTION OF FLARE

On post-operative 4th week, it was seen that 55(84.61%) patients who had received heparin in the irrigating solution had no flare as compared to 42(64.61%) patients from the control group.

Table 16. POST OPERATIVE 8TH WEEK DISTRIBUTION OF FLARE

		GROUP		TOTAL	P VALUE
8th week		A	B		
FLARE 8TH WEEK	0	63(96%.9)	57(87.6%)	120(92.3%)	**0.058**
	1	2(3%)	8(12.3%)	10(7.6%)	
Total		65	65	130	



GRAPH 14. POST-OP 8TH WEEK DISTRIBUTION OF FLARE

On post-operative 8th week, it was seen that 63(96.92%) patients who had received heparin in the irrigating solution had no flare as compared to just 57(87.69%) patients from the control group.

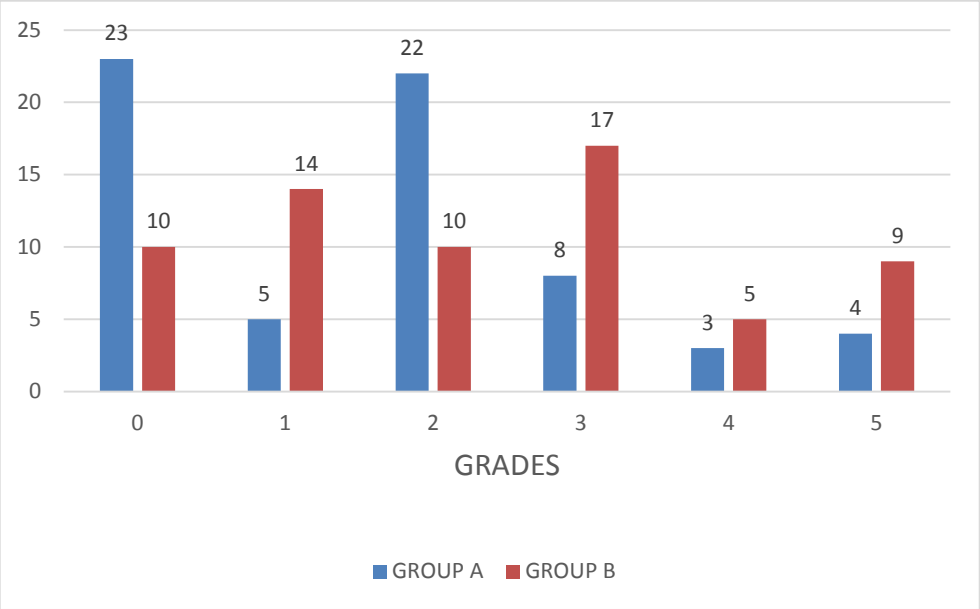
It was observed that:

1) Study group had statistically significant ($P<0.001$) reduction in grade of flare on Post-operative day 1, day 7, 4^{th} week in the study group.
2) There was no statistically significant reduction in flare on Post-operative 4^{th} and 8^{th} between both groups.

ASSESSMENT OF POST-OPERATIVE PIGMENTS IN STUDY AND CONTROL GROUPS:

Table 17. POST OPERATIVE DAY 1 DISTRIBUTION OF PIGMENTS ON IOL SURFACE

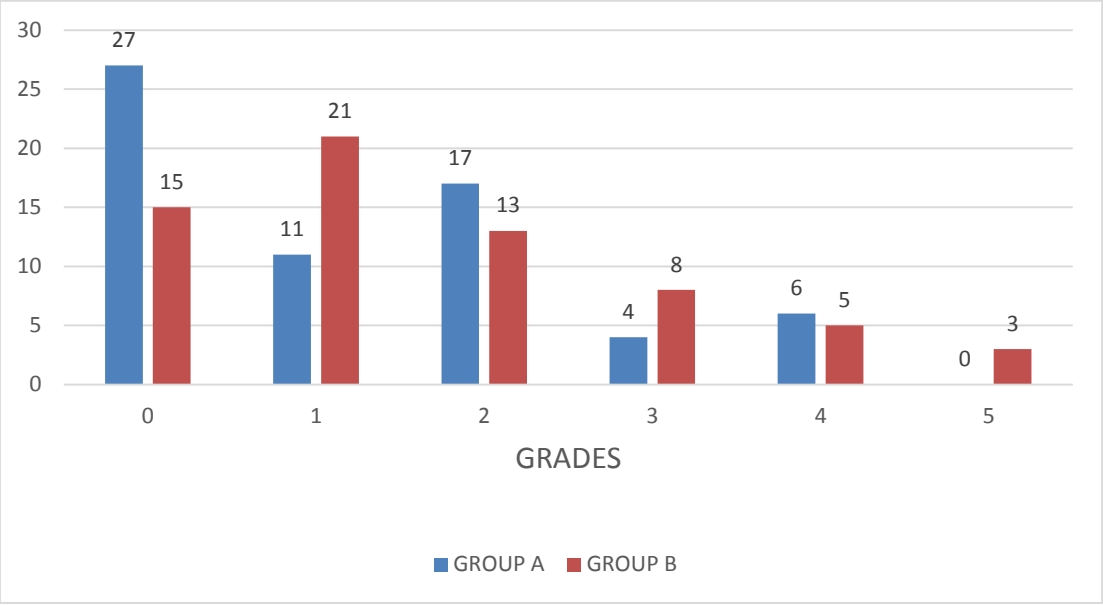
		GROUP		TOTAL	P VALUE
DAY 1	REGIONS ON IOL	A	B		
PIG DAY1	0	23(35.3%)	10(15.38%)	33(25.38%)	**0.002**
	1	5(7.69%)	14(21.5%)	19(14.61%)	
	2	22(33.8%)	10(15.38%)	22(16.9%)	
	3	8(12.3%)	17(26.15%)	25(19.23%)	
	4	3(4.6%)	5(7.69%)	8(6.1%)	
	5	4(6.1%)	9(13.8%)	13(10%)	
Total		65	65	130	



GRAPH 15. POST-OP DAY 1 DISTRIBUTION OF PIGMENTS ON IOL SURFACE

Table 18. POST OPERATIVE DAY 7 DISTRIBUTION OF PIGMENTS ON IOL SURFACE

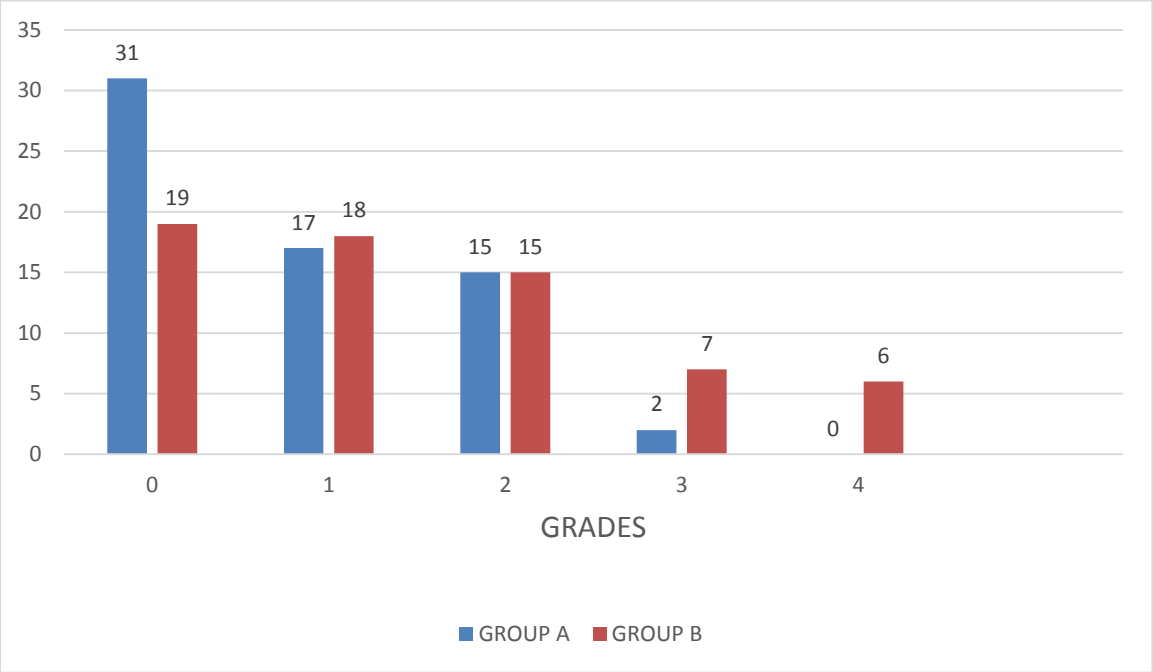
		GROUP		TOTAL	P VALUE
Day 7	REGIONS ON IOL	A	B		
PIG DAY7	0	27(41.53%)	15(23.07%)	42(32.30%)	**0.042**
	1	11(16.9%)	21(32.3%)	32(24.6%)	
	2	17(26.1%)	13(20%)	30(23.07%)	
	3	4(6.1%)	8(12.3%)	12(9.2%)	
	4	6(9.2%)	5(7.69%)	11(8.4%)	
	5	0(0%)	3(4.6%)	3(2.3%)	
Total		65	65	130	



GRAPH 16. Table 21 POST OPERATIVE DAY 7 DISTRIBUTION OF PIGMENTS ON IOL SURFACE

Table 19. POST OPERATIVE 4TH WEEK DISTRIBUTION OF PIGMENTS ON IOL SURFACE

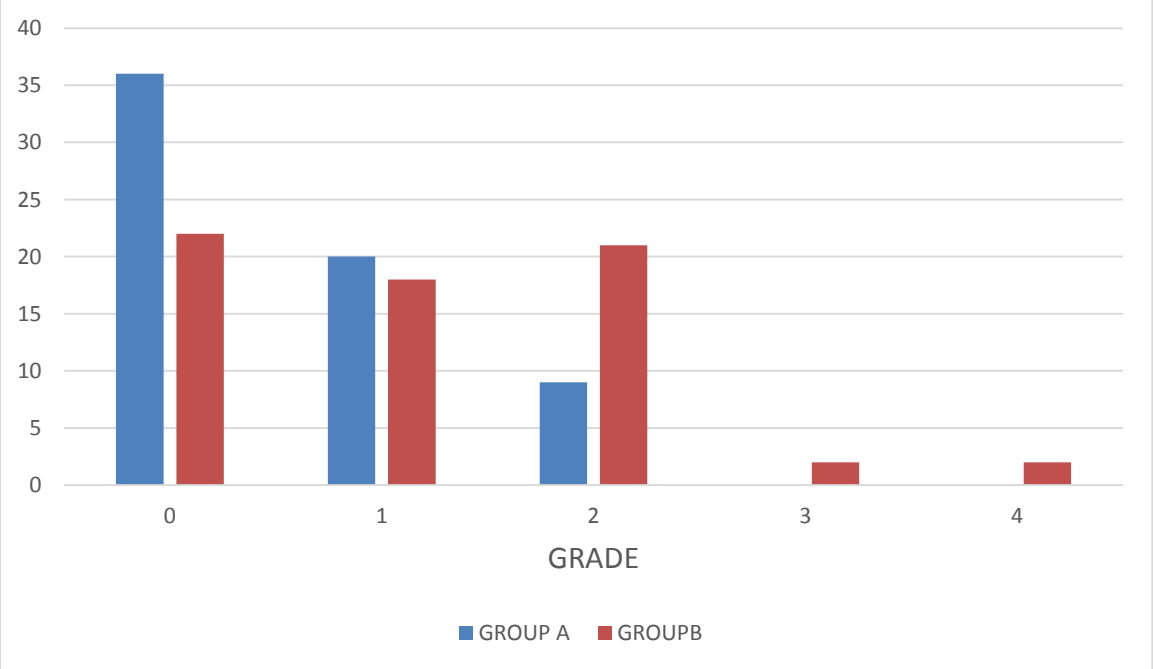
		GROUP		TOTAL	P VALUE
4th week	REGIONS ON IOL	A	B		
PIG 4TH WEEK	0	31(47.6%)	19(29.2%)	50(38.4%)	**0.060**
	1	17(23.1%)	18(27.6%)	35(26.9%)	
	2	15(23.07%)	15(23.07%)	30(23.0%)	
	3	2(3.0%)	7(10.7%)	9(6.9%)	
	4	0	6(9.2%)	6(4.6%)	
Total		65	65	130	



GRAPH 17. POST OPERATIVE 4TH WEEK DISTRIBUTION OF PIGMENTS ON IOL SURFACE

Table 20. POST OPERATIVE 8TH WEEK DISTRIBUTION OF PIGMENTS ON IOL SURFACE

		GROUP		TOTAL	P VALUE
8^{th} week	REGIONS ON IOL	A	B		
PIG 8^{TH} WEEK	0	36(55.3%)	22(33.8%)	58(44.6%)	**0.065**
	1	20(30.7%)	18(27.6%)	38(29.23%)	
	2	9(13.8%)	21(32.3%)	30(23.07%)	
	3	0	2(3%)	2(1.5%)	
	4	0	2(3%)	2(1.5%)	
Total		65	65	130	



GRAPH 18. POST OPERATIVE 8TH WEEK DISTRIBUTION OF PIGMENTS ON IOL SURFACE

It was observed that :

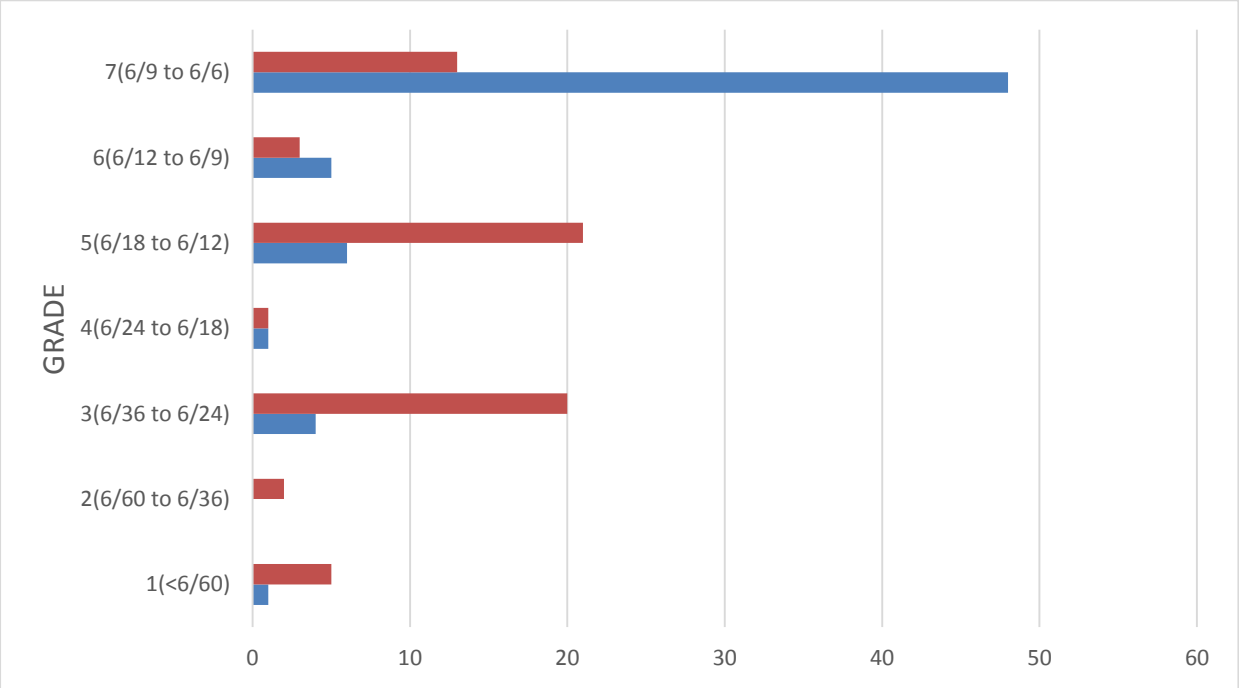
1)There was a statistically significant reduction in the pigments on the IOL surface on post-operative day1, day 7 in the study group.

2) There was no statistically significant reduction in pigments on the lens surface on Post-operative 4^{th} and 8^{th} week between both the groups.

ASSESSMENT OF POST-OPERATIVE BCVA IN STUDY AND CONTROL GROUPS:

Table 21. POST OPERATIVE DAY 1 DISTRIBUTION OF BCVA GRADES

		GROUP		TOTAL	P VALUE
DAY 1	GRADE	A	B		
BCVA1	1	1(1.5%)	5(7.69%)	6(4.6%)	**<0.001**
	2	0	2(3%)	2(1.5%)	
	3	4(6.1%)	20(30.76%)	24(18.4%)	
	4	1(1.5%)	1(1.5%)	2(1.5%)	
	5	6(9.2%)	21(32.3%)	27(20.7%)	
	6	5(7.2%)	3(4.6%)	8(6.1%)	
	7	48(73.8%)	13(0.2%)	61(46.9%)	
Total		65	65	130	

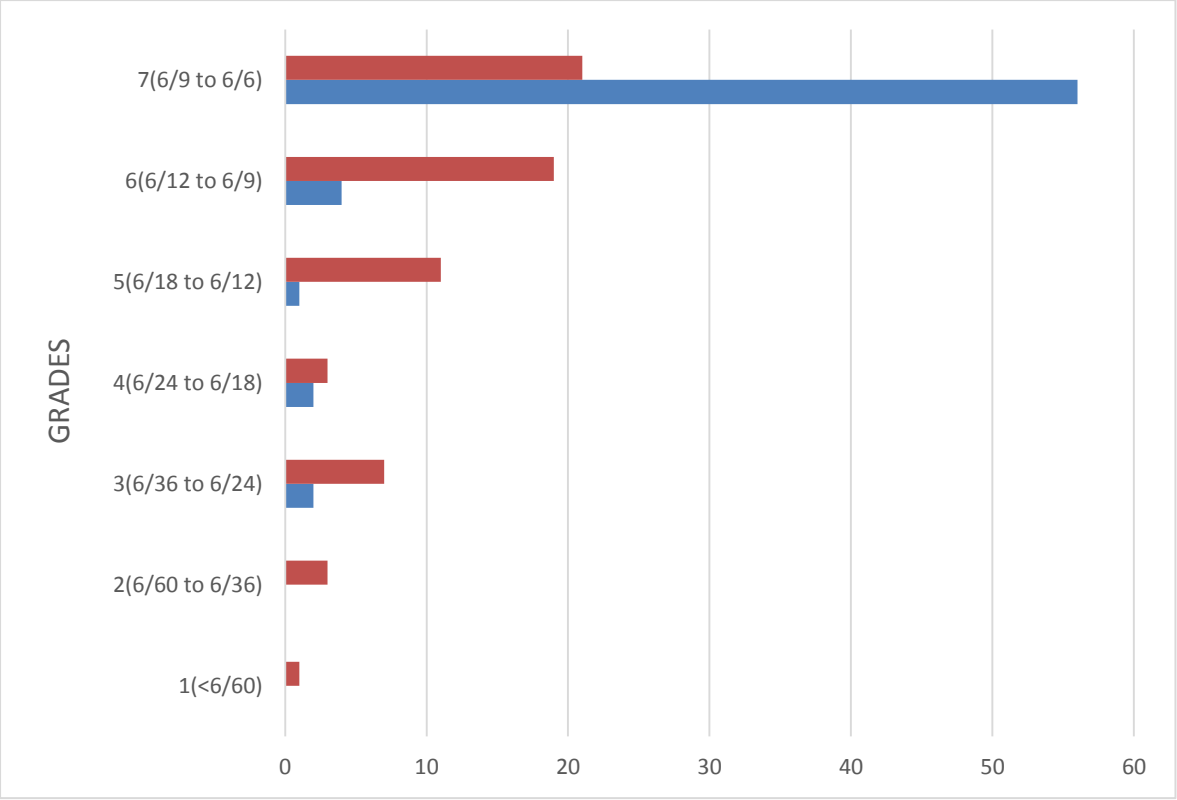


GRAPH 19. POST OPERATIVE DAY 1 DISTRIBUTION OF BCVA GRADES

There was a statistically significant improvement in the BCVA on post-operative Day 1 in patients who received heparin the irrigating solution compared to the control group.

Table 22. POST OPERATIVE DAY 7 DISTRIBUTION OF BCVA GRADES

		GROUP		TOTAL	P VALUE
Day 7	GRADE	A	B		
BCVA7	1	0	1(1.5%)	1(0.7%)	**<0.001**
	2	0	3(4.6%)	3(2.3%)	
	3	2(3%)	7(10.7%)	9(6.9%)	
	4	2(3%)	3(4.6%)	5(3.85%)	
	5	1(1.5%)	11(16.9%)	12(9.2%)	
	6	4(6.1%)	19(29.2%)	23(17.6%)	
	7	56(86.1%)	21(32.3%)	77(59.2%)	
Total		65	65	130	

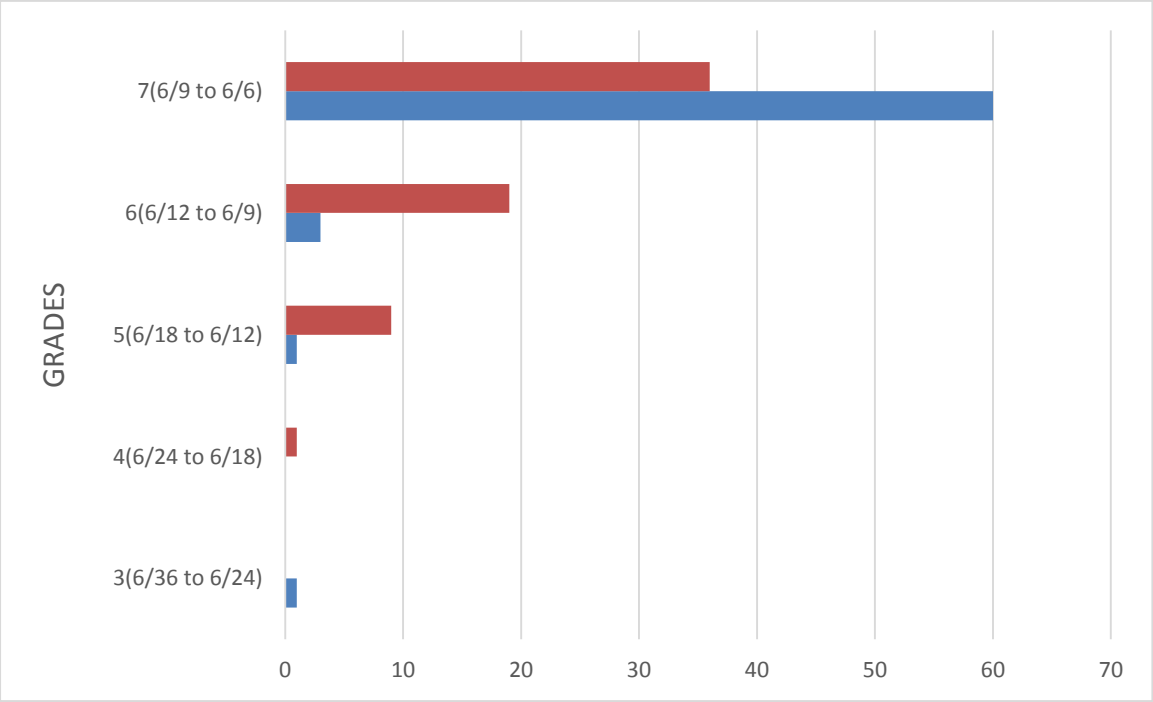


GRAPH 20. POST OPERATIVE DAY 7 DISTRIBUTION OF BCVA GRADES

There was a statistically significant improvement in the BCVA on post-operative Day 7 in patients who received heparin the irrigating solution compared to the control group.

Table 23. POST OPERATIVE 4TH WEEK DISTRIBUTION OF BCVA GRADES

		GROUP			
4th week	GRADE	A	B	TOTAL	P VALUE
BCVA 4th week	3	1(1.5%)	0	1(0.7%)	
	4	0	1(1.5%)	1(0.7%)	
	5	1(1.5%)	9(13.8%)	10(7.6%)	**0.061**
	6	3(4.6%)	19(29.2%)	22(20.7%)	
	7	60(92.3%)	36(55.3%)	96(73.8%)	
Total		65	65	130	

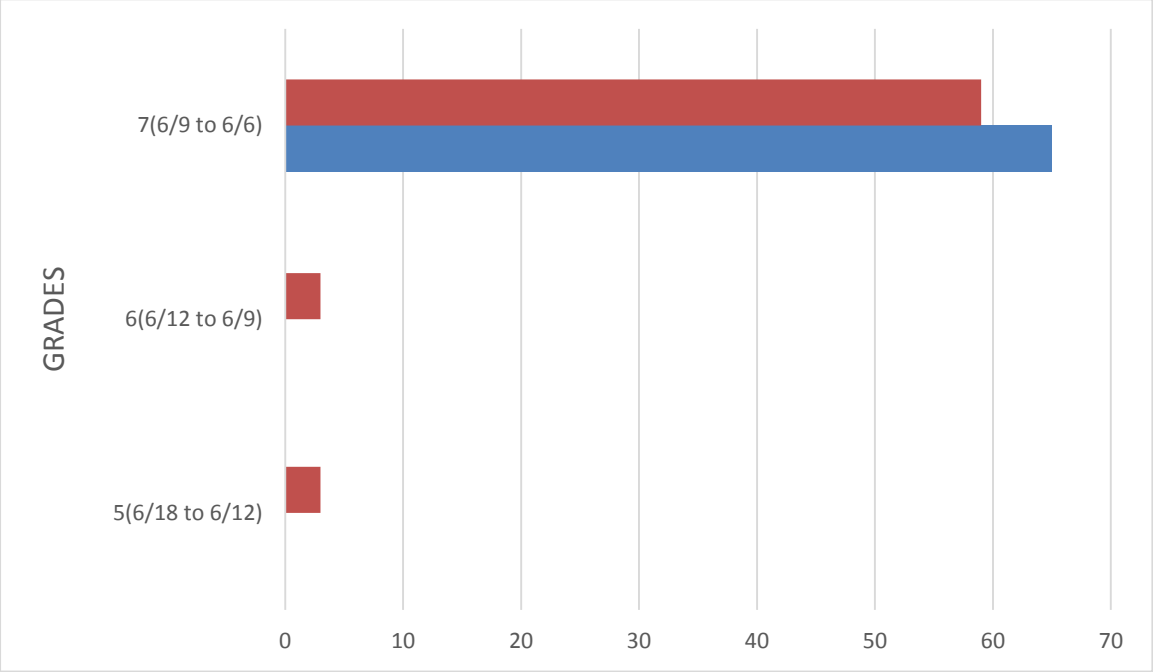


GRAPH 21. POST OPERATIVE 4TH WEEK DISTRIBUTION OF BCVA GRADES

There was a statistically significant improvement in the BCVA on post-operative 4th week in patients who received heparin the irrigating solution compared to the control group.

Table 24. POST OPERATIVE 8TH WEEK DISTRIBUTION OF BCVA GRADES

		GROUP		TOTAL	P VALUE
8th week	GRADE	A	B		
BCVA 8TH WEEK	4	0	3(4.6%)	3(2.3%)	**0.073**
	5	0	3(4.6%)	3(2.3%)	
	6	65(100%)	59(90.7%)	124(95.3%)	
Total		65	65	130	



GRAPH 22. POST OPERATIVE 8TH WEEK DISTRIBUTION OF BCVA GRADES

It was observed that :

1)There was a statistically significant improvement in the BCVA on post-operative day1, day 7 in the study group.

2) There was no statistically significant improvement in the BCVA on Post-operative 4^{th} and 8^{th} week between both the groups.

DISCUSSION

Standardized nomenclatures have been employed to standardize the uniformity in gradation of clinical findings. Most commonly used nomenclatures were developed by the Standardization of Uveitis Nomenclature (SUN) working group for grading inflammation in anterior and vitreous chambers. Observer can assess cells and flare present in the anterior chamber and vitreous humor which is a universally accepted method for quantifying inflammation in inflammatory eye diseases. This can be overcome by measuring the cells and flare by laser flaremetry. But it is expensive not widely available.

The baseline characteristics of the patients in the study and control groups were first analyzed to see if the groups were similar. Cases with intra operative complications like posterior capsular rent were also excluded from the study. Age and sex variation were found to be similar in both groups. Since the surgeon, type of surgery and IOL used were the same in both groups, we can conclude that any statistically significant difference in postoperative inflammation was due to the addition of heparin in the irrigating solution and not due to any baseline confounding factors.

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

CELLS:

In our study a statistically significant reduction in cells were noted on day1(P=<0.001) and day 7 (P=<0.001).

The anti-inflammatory effect of heparin on the cells was noted till day 7.

It was further noted that, 89.23% patients had no cells in the anterior chamber on post-operative 4th week and 98.46% patients had no cells in the anterior chamber on post-operative 8th week in the Study group compared to the control group, whereas 76.92% patients had no cells in the anterior chamber on post-operative 4th week and 87.69% patients had no cells in the anterior chamber on post-operative 8th week.

Our results are consistent with the findings or previous research:

Condon et al found that cellular deposits, seen with the slit lamp, were also found in significantly fewer patients who were implanted with heparin surface modified lenses at early follow-up visits[93].

In a study by **Bubanale et al**, A statistically significant reduction in postoperative cells was noted in group with addition of low molecular weight heparin (Enoxaparin) at days 1($p<0.001$) and 1 week ($p<0.001$), but there was no statistically significant reduction thereafter[94].

Kruger et al investigated the long-term effects of heparin sodium in the infusion solution during small incision cataract surgery[9]. The cell values were lower in the study group day 1, 3 and 7 postoperatively.

In a similar study by **Kohnen et al** reduced cell values were seen postoperatively on days 1 and 3[12].

Our findings suggest that heparin has a beneficial effect on early postoperative inflammation in terms of cellular reaction.

FLARE:

In our study the assessment of flare in the early post-operative period showed a statistically significant reduction in flare value on day 1 (P valve <0.001) ,day 7 and 4th week in the patients who had received heparin sodium in the infusion solution. After 4th week, no significant difference was noted between the study and control groups. It is known that the half-life of heparin is not more than 5 hrs in the human body. This might account for its shorter duration of action.

Our results are consistent with some of the earlier published results. **Kohnen et al** found that on day 1 and 3 the flare values were significantly less in patients who had received

heparin sodium in the infusion solution (P value <0.001). There after he noted no significant effect[12].

Similarly, **Kruger et al** observed that the flare was significantly lower on days 1,3 and 7 postoperatively in the group that received heparin. Their next follow up at 3rd , 6th week and 1 year did not show any significance reduction in flare[9].

On post-operative Day 7, it was seen that 22(33.85%) patients who had received heparin in the irrigating solution had no flare as compared to just 7(10.76%) patients from the control group.

Bubanale et al noted a statistically significant reduction in postoperative flare was noted in group with addition of low molecular weight heparin (Enoxaparin) at days 1($p<0.001$) and 1 week ($p<0.001$), but there was no statistically significant reduction thereafter[94].

Baylamar et al stated that they found significantly less inflammation and synechiae formation compared to eyes that did not receive heparin[10].

PIGMENT DEPOSITS ON THE INTRAOCULAR LENS SURFACE:

In our study, we noted a decrease in pigments on the intraocular lens surface, which was found to be statistically significant on post operative day 1 and day 7. Our results were in agreement with the published results of **Kruger et al** who noticed that on the first and 7th postoperative day, patients who received heparin[9].

Our study was in concordance with a study by **Bubanale et al** who noted a statistically significant reduction in postoperative pigments on the IOL surface in group with addition of low molecular weight heparin at days 1($p<0.001$) and 1 week ($p<0.001$), except that our study did not show any significant decrease in IOL pigments after 7 days post-operatively, whereas **Bubanale et al** found significantly less number of pigments on intraocular lens surface till 8th week post-operatively. This can be accounted for by the longer duration of action of enoxaparin as compared to unfractionated heparin[94].

Özkurt et al in their study on pediatric cataract reported lesser pigment deposition, synechiae and pupillary membrane formation on post-operative day 7 [95].

Caca et al found that IOL pigment formation was significantly higher in group 1(without heparin) than that of group 2 and 3(with enoxaparin) in which there was no IOL precipitate ($P=0.048$)[96].

By the end of the 8th week, we noticed that a larger percentage of patients in the study group were free from any pigments on the IOL surface (55.38%) as compared to the control group (38.46%).

BCVA:

In our study, a statistically significant improvement was noted in the BCVA on post-operative days 1 and 7 in the study group (p value<0.001).

By the end of the 8th week, there was no statistically significant difference in the visual outcome between both groups. We have excluded patients with any pre-existing ocular inflammatory disease and diabetic retinopathy. All surgeries were performed by a single experienced surgeon. These factors could indicate that the improved visual acuity in the study group during the early post-operative can be attributed to the decrease in inflammation as a result of addition of heparin in the irrigating solution.

ASSESSMENT OF EFFECT OF DIABETIC STATUS ON POSTOPERATIVE INFLAMMATION IN PATIENTS WITH AND WITHOUT HEPARIN

Our study was undertaken in diabetic patients who had controlled blood sugar levels pre-operatively i.e., FBS<110 and PPBS<140 who did not have any evidence of diabetic retinopathy.

Our findings are consistent with those of **Masanori Ino-ue et al** post cataract surgery in diabetic patients[92].

Akitoshi Yoshiba et al demonstrated increased permeability of the blood aqueous barrier in adolescent diabetic patients and this showed a significant correlation with glycosylated hemoglobin levels[76].

ASSESSMENT OF POST-OPERATIVE INFLAMMATION WITHIN EACH GROUP:

In addition to statistically significant decrease in inflammation in the study group compared to control group, it was also noted that with each follow up, there was a consistent decrease of inflammation and improvement in visual acuity of both study as well as control groups.

COMPLICATIONS:

There were no intraoperative complications (e.g., hemorrhage, allergic reaction), which indicates that it is safe to use heparin sodium at a concentration of 10 IU/mL. This is in concordance with studies by **Kruger et al and Kohnen et al** in their respective studies, did not experience any complications intraoperatively or postoperatively.

CONCLUSION

In this study, we used heparinised irrigation solution to see if heparin, which is a very economical drug, can be used as an alternative to heparin surface modified lenses in diabetics undergoing cataract surgery.

We found that the post-operative cells, flare and pigment deposits on the IOL surface were significantly reduced, so better visual outcome was seen in early post-operative period in patients who received heparinised irrigation solution.

Hence, in our rural Indian population, heparinised irrigation solution may be a cost-effective and efficient alternative to heparin surface modified lenses to minimize post-operative inflammation in cataract surgery in diabetics.

SUMMARY

Diabetes Mellitus affects more than 120 million people worldwide and post-operative inflammation is invariably much higher among diabetic patients as they have significantly increased blood aqueous barrier breakdown when compared to normal eyes.

PMMA lenses have been the most widely used intra ocular lenses. Though PMMA is relatively inert, it tends to have some degree of inflammatory response post-operatively.

Heparin surface modified lenses provide a greater degree of protection from the post-operative inflammation, but due to technical reasons manufacture of these lenses has stopped and now they are not available. They also cost about 4-5 times more than regular PMMA lenses.

Heparinized irrigating fluid may be a simple and effective alternative. So the purpose of this study is to study the effect of heparin in irrigating solution during cataract surgery in diabetics.

130 diabetic patients with cataract were taken up for this study. Patients were randomised into 2 groups. Group 1-Study group (65 eyes) received 1000IU(1ml) heparin in irrigation solution during cataract surgery and Group 2-Control group (65 eyes) without heparin in irrigation solution.

All patients were evaluated in detail pre-operatively and all surgeries were performed by a single experienced surgeon.

Follow up on day 1, day 7, day 28 and 8th week post-operatively included grading of flare, cells, pigments on the lens (from grade 0 to 4) and visual acuity. All patients received identical post-operative treatment.

We found that the postoperative cells, flare and pigments on the intraocular lens surface were found to be significantly reduced in postoperative period in the study group, P value (<0.05). The early visual outcome was better in patients who received heparin in the irrigating solution. The re-establishment of the blood aqueous barrier after cataract surgery was noted at 2 months post-operatively in most patients as evidenced by disappearance of flare. There were no intraoperative or post-operative complications due to the use of heparin in the irrigation solution.

So it is evident that the addition of heparin to the irrigating solution during cataract surgery in diabetics is an affordable alternative to heparin surface modified lenses, especially in rural areas and in cataract camps.

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ANNEXURE I

PROFORMA

EFFECT OF HEPARINISED IRRIGATION SOLUTION ON POST OPERATIVE INFLAMMATION AFTER CATARACT SURGERY IN DIABETICS

Name: I.P. No.:

Age: O.P.No.:

Sex: Date of Admission:

Address: Date of Surgery

Date of Discharge:

PRE-OPERATIVE EVALUATION

Head Posture

Ocular Posture

OD: OS:

- Extra Ocular Movements
- Lids and Adnexa
- Conjunctiva
- Cornea
- Anterior chamber
- Iris
- Pupil
    1. Size
    2. Shape
    3. Reaction
- Lens
- Anterior Vitreous

- Visual Acuity (BCV A)

    1. Distant

    2. Near

    3. Refraction

- Intra Ocular Pressure (Applanation)
- Distant Direct Ophthalmoscopy
- Direct Ophthalmoscopy
- Indirect Ophthalmoscopy
- Keratometry

    K1

    K2

- Axial Length
- Intra Ocular Lens Power
- Lacrimal Syringing
- Lab Investigations:

    -Urine Albumin, Sugar and Microscopy

    -RBS, FBS, PPBS,HIV, HBsAg

GENERAL PHYSICAL EXAMINATION

Pallor Icterus Clubbing Cyanosis Oedema Lymphadenopathy

Pulse: Blood Pressure:

Cardiovascular System:

Respiratory System:

Gastro Intestinal System:

INTRAOPERATIVE NOTES :

TYPE OF SURGERY

POST OPERATIVE BLOOD SUGARS: **(mg/dl)**

1.FBS

DAY 7

DAY 28

8TH WEEK

2.PPBS

DAY 7

DAY 28

8TH WEEK

POST OPERATIVE COMPLICATIONS:

1.AQUEOUS CELLS **GRADE**

DAY 1

DAY 7

DAY 28

8TH WEEK

2.AQUEOUS FLARE **GRADE**

DAY 1

DAY 7

DAY 28

8th WEEK

POSTOPERATIVE OUTCOME: **SNELLEN'S GRADING**

BCVA

DAY 1

DAY 7

DAY 28

8th WEEK

ANNEXURE II INFORMED CONSENT FORM

EFFECT OF HEPARINISED IRRIGATION SOLUTION ON POST OPERATIVE INFLAMMATION AFTER CATARACT SURGERY IN DIABETICS

I, the undersigned, agree to participate in this study and authorize the collection and disclosure of my personal information as outlined in this consent form.

I understand the purpose of this study, the risks and benefits of the two techniques(using heparin in the irrigation solution and without heparin in irrigating solution during cataract surgery) ,method of randomization and the confidential nature of the information that will be collected and disclosed during the study. The information collected will be used only for research.

I have asked questions regarding various aspects of this study and my questions have been answered to my satisfaction.

I understand that I remain free to withdraw from this study at any time and this will not change my future care.

Participation in this study does not involve any extra cost to me.

Subject‘s name and signature /thumb impression Date:

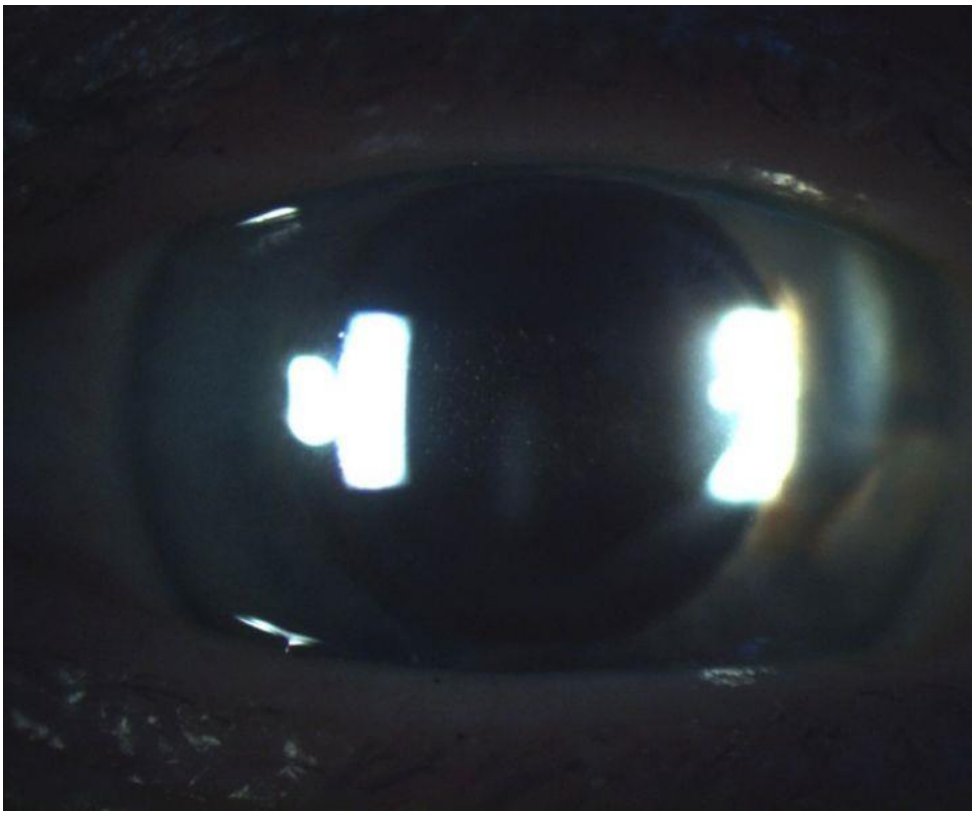
Name and signature of witness Date:

Name and signature of person obtaining consent Date:

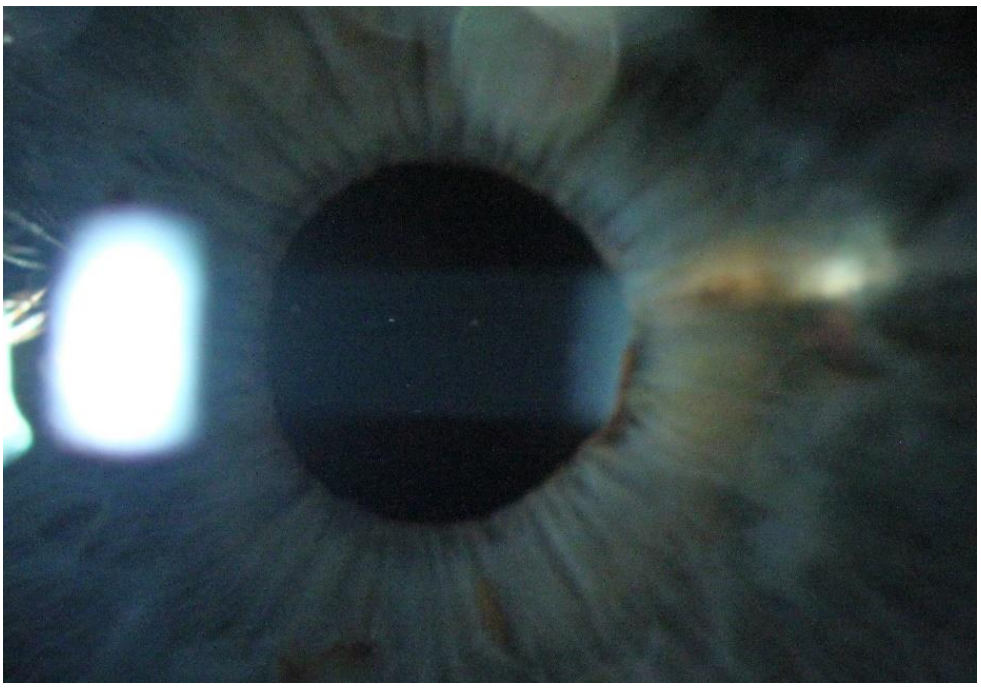
ANNEXURE III
PHOTOGRAPHS

PHOTOGRAPH 1 SLIT LAMP EXAMINATION

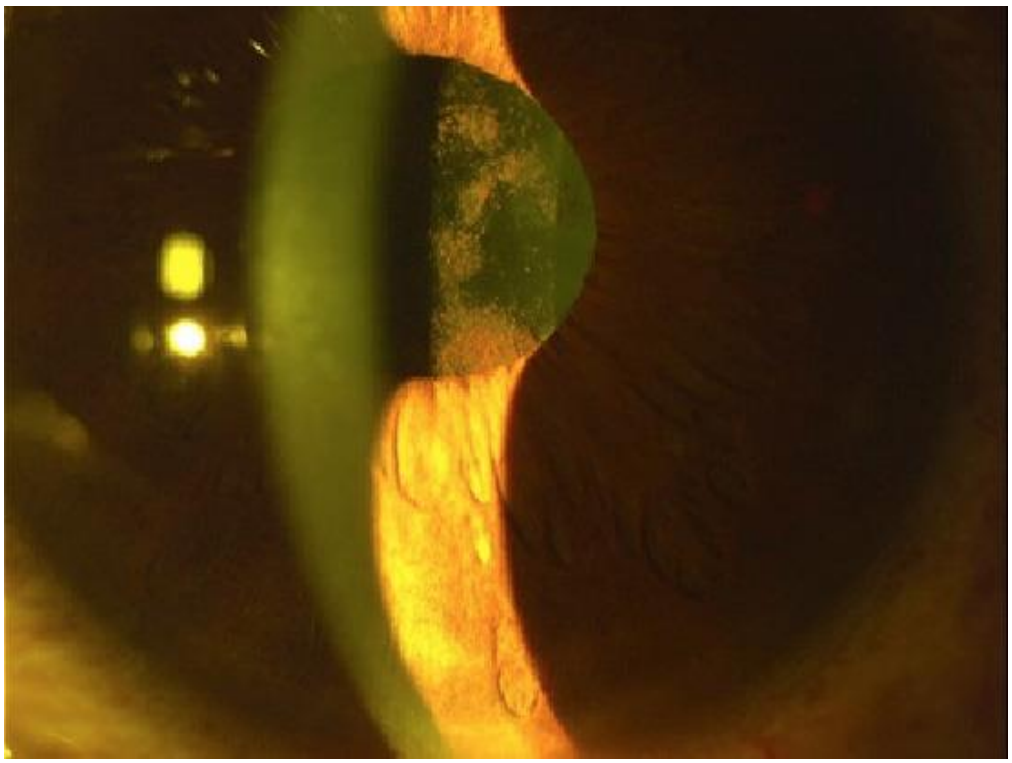
PHOTOGRAPH 2 SICS WITH PCIOL



PHOTOGRAPH 3 ANTERIOR CHAMBER CELLS



PHOTOGRAPH 4 ANTERIOR CHAMBER FLARE



PHOTOGRAPH 5 PIGMENT DEPOSITS ON IOL SURFACE

ANNEXURE IV

KEY TO MASTER CHART

Sl. No.: Serial number

IP.No.: Hospital number

IOL PIG: Intraocular lens Pigments

BCVA: Best corrected visual acuity

FBS: Fasting blood sugar

PPBS: Post prandial blood sugar

P: Parts

F: Female

M: Male

A: Group A

B: Group B

CF: Counting fingers

SL.NO.	IP NO.	AGE	SEX	STUDY/CONTROL	PRE-OP		DAY 1				DAY 7				4TH WEEK				8TH WEEK					
					FBS	PPBS	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	FBS	PPBS
1	986012	67	M	B	99	137	3	2	2	6/9P	0	0	3	6/9	0	0	4	6/6P	0	0	4	6/6P	112	130
2	5942	65	F	B	81	102	4	2	2	6/9	1	1	2	6/6P	0	0	2	6/6	0	0	2	6/6	131	210
3	962535	70	M	B	90	100	4	3	3	6/12P	2	1	1	6/9	0	0	1	6/9	0	0	1	6/9	110	142
4	984931	70	F	A	79	130	4	2	2	6/6P	2	2	1	6/6P	2	2	1	6/6P	2	1	1	6/6	86	103
5	984886	57	F	B	102	136	2	1	2	CF-5M	0	0	1	6/60	0	0	1	6/12P	0	0	2	6/6P	92	109
6	1002112	65	F	A	101	124	2	1	1	6/12	1	1	1	6/12	1	0	0	6/9	0	0	0	6/9	84	143
7	935687	70	F	B	90	110	3	2	2	6/6	2	1	1	6/6	0	0	1	6/6	0	0	2	6/6	99	156
8	1007392	60	M	B	99	120	3	2	0	6/12P	0	1	0	6/12	0	0	0	6/6P	0	0	0	6/6P	66	148
9	1008940	60	F	A	97	145	2	1	0	6/6P	1	1	0	6/6P	1	1	0	6/6P	0	0	0	6/6P	114	145
10	1015164	70	M	B	110	129	3	2	3	6/12P	0	1	2	6/12P	0	0	2	6/9	0	0	1	6/9	86	135
11	5094	60	M	B	102	130	3	2	3	6/24P	0	0	3	6/24	0	0	2	6/18	0	0	2	6/9	76	120
12	908957	70	F	A	90	119	1	0	1	6/6	0	0	2	6/6	0	0	1	6/6	0	0	1	6/6	68	108
13	3171	55	M	A	92	132	1	1	3	6/9	0	0	2	6/9	0	0	0	6/9	0	0	0	6/9	102	124
14	30651	51	M	A	110	142	2	1	2	6/6P	1	1	2	6/6P	0	0	2	6/6P	0	0	1	6/6P	104	145
15	44080	54	F	B	104	129	4	2	3	6/12P	1	1	1	6/12P	0	0	1	6/12P	0	0	1	6/6P	114	157
16	996358	61	M	A	107	131	2	1	2	6/9	0	0	3	6/9	0	0	0	6/9	0	0	0	6/9	130	109
17	1010609	71	M	A	102	129	1	1	0	6/6	0	0	0	6/6	0	0	0	6/6	0	0	0	6/6	128	162
18	999509	74	F	B	110	29	3	2	2	6/60	2	1	2	6/60	0	0	2	6/18	0	0	2	6/12	110	169
19	998607	64	M	A	105	131	2	1	2	6/6	0	0	2	6/6	0	0	2	6/6	0	0	1	6/6	108	156
20	3524	65	M	A	107	134	2	1	0	6/6P	1	1	0	6/6	0	0	0	6/6	0	0	0	6/6	109	157
21	28338	66	M	B	102	128	3	2	2	6/12P	2	1	2	6/9	1	1	2	6/9	1	0	2	6/9	92	135
22	7340	52	M	B	98	139	4	2	0	6/6P	2	1	0	6/6P	1	0	0	6/6P	0	0	0	6/6P	90	165
23	961641	55	M	B	102	109	3	2	1	6/6	0	0	2	6/6	0	0	2	6/6	0	0	1	6/6	76	159
24	991167	68	M	B	99	124	4	3	0	6/18	2	1	0	6/18	1	1	2	6/9	1	0	0	6/9	83	143
25	5870	69	F	A	79	115	1	1	3	6/12P	0	0	1	6/9	0	0	1	6/9	0	0	1	6/6	112	169
26	513	67	M	B	102	109	4	2	1	6/12P	2	1	0	6/12	1	1	0	6/9	1	0	0	6/9	86	138
27	5578	53	F	A	103	120	2	1	0	6/9	0	0	0	6/9	0	0	0	6/9	0	0	0	6/6	89	126

SL.NO.	IP NO.	AGE	SEX	STUDY/CONTROL	PRE-OP		DAY 1				DAY 7				4TH WEEK				8TH WEEK					
					FBS	PPBS	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	FBS	PPBS
28	983875	56	M	B	100	129	4	2	2	CF-5M	2	1	2	6/36P	0	1	2	6/12	0	0	0	6/9P	76	132
29	37828	72	M	B	102	129	3	2	1	6/18P	1	1	1	6/18P	0	0	1	6/18P	0	0	0	6/12	99	131
30	9565	73	M	B	110	119	4	3	3	6/24P	1	1	1	6/24P	0	0	1	6/9	0	0	0	6/9	104	162
31	1018396	63	M	A	90	104	2	2	0	6/9	1	1	0	6/9	0	0	0	6/9	0	0	0	6/9	114	127
32	36340	62	M	B	97	132	2	1	2	6/12P	2	1	0	6/12P	1	0	0	6/6P	0	0	0	6/6P	76	136
33	122056	57	M	A	103	140	1	1	1	6/6	0	0	1	6/6	0	0	0	6/6	0	0	0	6/6	85	140
34	88598	63	M	A	104	112	4	3	5	6/24	2	1	3	6/18P	0	0	2	6/9P	0	0	2	6/9	66	163
35	929663	62	F	B	99	116	2	2	3	6/12P	1	2	2	6/12	1	1	1	6/12	0	1	1	6/12	114	201
36	42278	58	F	B	98	124	4	2	2	6/12P	2	1	0	6/12	0	1	0	6/12	0	0	0	6/12	76	142
37	90740	75	M	B	102	136	3	2	4	6/9P	0	0	5	6/9P	0	0	4	6/9P	0	0	4	6/9P	52	138
38	99706	61	M	B	105	118	3	2	1	6/12P	1	1	1	6/12	1	0	1	6/9	0	0	1	6/9	114	142
39	85721	61	F	B	98	126	3	2	1	6/24P	1	1	2	6/12P	0	1	1	6/6P	0	0	1	6/6P	109	148
40	11384	62	M	B	87	112	2	1	2	6/6	0	0	1	6/6	0	1	1	6/6	0	1	1	6/6	90	136
41	161840	65	M	A	69	108	2	1	0	6/12P	1	1	0	6/9	1	0	0	6/9	0	0	0	6/9	82	120
42	88147	66	M	A	103	130	2	1	2	6/9P	1	1	1	6/9P	0	1	1	6/9P	0	0	0	6/6P	104	148
43	38806	59	M	A	98	146	2	1	0	6/12	0	0	0	6/9	0	0	0	6/9	0	0	0	6/9	120	136
44	78284	72	F	B	88	132	3	0	0	6/9P	1	1	0	6/9	0	0	0	6/6P	0	0	0	6/6P	108	132
45	50535	77	M	B	109	128	4	3	4	6/12P	1	1	4	6/12	0	0	3	6/9	0	0	2	6/9	106	138
46	86754	69	F	B	78	116	4	2	1	6/36	2	1	1	6/9P	0	1	1	6/9P	0	0	2	6/9P	98	129
47	72845	83	M	B	88	110	3	2	3	6/24P	2	1	2	6/9	1	0	1	6/9	0	0	1	6/9	99	1400
48	19978	68	M	B	93	106	3	2	5	6/12P	2	1	5	6/12	0	0	4	6/9	0	0	2	6/9	95	143
49	38476	66	M	B	102	130	4	2	3	6/24P	2	1	2	6/12	0	0	1	6/12	0	1	2	6/9	83	163
50	91157	78	F	A	100	142	3	1	0	6/6P	0	0	0	6/6P	0	0	0	6/6P	0	0	0	6/6P	80	160
51	927767	81	M	A	99	138	1	1	0	6/12P	0	0	0	6/9P	0	0	0	6/9P	0	0	0	6/9P	121	12817
52	931100	64	F	B	88	116	4	3	2	6/12P	2	1	1	6/9	0	0	2	6/6	0	0	1	6/6	87	122
53	857803	60	F	B	83	140	4	3	0	6/6P	0	1	0	6/6P	0	0	0	6/6P	0	0	0	6/6P	98	120

SL.NO.	IP NO.	AGE	SEX	STUDY/CONTROL	PRE-OP		DAY 1				DAY 7				4TH WEEK				8TH WEEK					
					FBS	PPBS	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	FBS	PPBS
54	858651	61	F	A	92	132	1	1	0	6/12P	0	0	0	6/9	0	0	0	6/9	0	0	0	6/9	104	131
55	908906	64	F	B	102	122	4	2	2	CF-5M	0	0	1	6/36	0	0	0	6/12	0	0	0	6/12	109	132
56	893206	70	M	A	78	124	4	3	2	6/6P	1	1	2	6/6P	0	0	2	6/6P	0	0	1	6/6P	92	154
57	878213	75	F	A	100	128	3	2	0	6/6	0	0	0	6/6	0	0	0	6/6	0	0	0	6/6	97	132
58	908957	67	F	A	93	116	3	2	0	6/12	1	1	0	6/12	0	1	0	6/9	0	1	0	6/6	93	138
59	932576	64	M	B	85	132	4	3	2	6/60	2	1	1	6/24P	0	0	1	6/9P	0	0	1	6/6P	112	152
60	944690	66	M	A	104	140	2	1	0	6/12P	0	0	0	6/12P	0	0	0	6/6P	0	0	0	6/6P	87	159
61	947460	84	F	B	110	130	4	2	0	HM+	2	1	0	CF-4M	0	0	0	6/18P	0	0	0	6/18P	80	135
62	947046	59	M	B	89	126	4	3	2	6/6P	2	1	1	6/6	0	1	1	6/6	0	0	0	6/6	84	151
63	917774	60	M	B	90	140	4	2	1	6/6P	2	1	1	6/6P	0	1	1	6/6P	0	0	2	6/6P	90	180
64	920725	62	F	A	102	112	3	2	3	6/12P	0	0	2	6/9	0	0	2	6/9	0	0	2	6/9	92	195
65	956743	77	M	A	98	110	2	1	2	6/6P	1	1	2	6/6P	0	0	1	6/6P	0	0	1	6/6P	99	127
66	170861	67	M	B	90	109	4	3	4	6/6P	2	1	4	6/6P	0	1	3	6/6	0	1	2	6/6	76	139
67	176533	67	F	B	94	114	4	3	3	6/12P	1	1	2	6/12	1	0	2	6/12	1	0	0	6/9P	108	142
68	917203	84	F	B	86	136	4	3	0	6/24P	1	1	0	6/12	0	0	0	6/9	0	0	0	6/9	112	150
69	917838	75	M	A	111	120	2	1	2	6/6P	0	0	0	6/6P	0	0	0	6/6P	0	0	0	6/6P	104	162
70	809264	74	M	A	90	126	4	2	0	6/9	1	1	0	6/9	1	0	0	6/9	0	0	0	6/9	131	136
71	914600	78	F	B	102	130	4	3	0	6/12P	2	1	0	6/12P	1	1	0	6/9P	1	0	0	6/9P	118	152
72	903554	59	M	A	101	140	3	1	0	6/9	0	0	0	6/9	0	0	0	6/9	0	0	0	6/9	96	138
73	889947	81	F	A	95	125	3	2	2	6/24P	1	1	1	6/24P	0	0	1	6/24P	0	0	1	6/12	110	135
74	946251	75	F	A	79	115	3	2	2	6/6P	1	1	1	6/6P	0	0	1	6/6P	0	0	1	6/6P	103	142
75	725327	67	M	A	88	118	2	1	2	6/9	0	0	1	6/9	0	0	2	6/9	0	0	1	6/6	116	156
76	733234	65	M	B	85	110	4	3	5	6/36	2	2	4	6/24	1	0	3	6/9	1	0	2	6/9	92	152
77	739673	70	F	B	110	108	4	3	3	6/12P	2	2	3	6/12	1	1	3	6/12	0	1	2	6/6P	91	160
78	739669	70	M	A	84	136	2	2	3	6/6P	1	1	2	6/6P	0	1	1	6/6P	0	0	1	6/6P	99	154
79	758909	57	F	A	102	120	1	1	2	6/36	0	0	2	6/24	0	0	2	6/6	0	0	1	6/6	107	168
80	760861	65	F	A	103	122	3	2	2	6/9	1	1	1	6/9	0	0	1	6/9	0	0	1	6/9	84	126

SL.NO.	IP NO.	AGE	SEX	STUDY/CONTROL	PRE-OP		DAY 1				DAY 7				4TH WEEK				8TH WEEK					
					FBS	PPBS	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	FBS	PPBS
81	762809	70	F	A	90	130	2	2	1	6/6P	1	1	0	6/6P	0	0	0	6/6P	0	0	0	6/6P	90	100
82	780839	60	M	B	84	140	3	2	0	6/24P	2	1	0	6/12	0	0	0	6/9	0	0	0	6/6P	113	146
83	780810	60	M	A	76	138	3	2	4	6/6	2	1	4	6/6	0	0	2	6/6	0	0	1	6/6	88	99
84	780845	70	F	A	106	118	1	1	5	6/9	0	0	4	6/9	0	0	2	6/9	0	0	2	6/9	98	126
85	782147	60	F	A	90	136	2	1	0	6/6P	0	0	0	6/6P	0	0	0	6/6P	0	0	0	6/6P	95	174
86	782162	70	M	A	107	134	3	2	2	6/9	2	2	2	6/9	0	0	2	6/9	0	0	1	6/9	91	125
87	782136	55	F	B	94	132	3	1	0	6/36	2	1	0	6/36	0	0	0	6/18	0	0	0	6/18	106	109
88	782152	51	M	A	100	128	4	3	0	6/6P	1	1	0	6/6P	0	0	0	6/6P	0	0	0	6/6P	115	163
89	782156	54	M	B	76	130	3	2	3	6/12P	1	1	3	6/12P	0	1	4	6/12P	0	0	2	6/9P	124	142
90	782154	61	F	A	83	140	3	2	3	6/6P	2	1	4	6/6P	0	0	3	6/6P	0	0	2	6/6P	90	125
91	3236789	71	M	A	93	126	3	3	1	6/9	0	0	0	6/9	0	0	0	6/9	0	0	0	6/6	94	163
92	300651	74	F	B	92	118	3	2	0	6/24P	1	1	0	6/9	0	0	0	6/9	0	0	0	6/9	1	128
93	902182	64	F	A	96	119	3	2	4	6/6P	2	1	4	6/6P	0	1	3	6/6P	0	0	2	6/6P	8	1151
94	321086	65	M	A	110	112	2	2	2	6/36	0	1	3	6/9	0	0	2	6/9	0	0	2	6/9	95	131
95	783103	66	F	A	97	140	3	2	0	6/6	1	1	0	6/6	0	0	0	6/6	0	0	0	6/6	90	1100
96	323451	52	F	A	104	136	2	2	2	6/6P	0	1	2	6/6P	0	0	1	6/6	0	0	2	6/6	118	102
97	723612	55	M	A	94	140	3	2	0	6/6P	1	1	0	6/6P	0	1	0	6/6P	0	0	0	6/6P	106	127
98	34061	68	M	B	79	120	4	2	1	6/24P	3	1	0	6/12	1	1	0	6/12	0	1	0	6/9P	113	109
99	647592	69	M	A	83	122	3	2	2	6/9(P)	1	1	2	6/6	0	0	1	6/6	0	0	1	6/6	104	106
100	430015	67	M	A	107	123	3	3	5	6/6P	2	1	4	6/6P	1	1	2	6/6P	0	0	1	6/6P	107	124
101	312851	53	F	B	105	140	3	2	4	6/36	1	1	4	6/12	0	0	3	6/12	0	0	1	6/9P	102	142
102	318350	56	M	B	94	136	3	2	5	6/24P	0	1	5	6/12P	0	0	4	6/9	0	0	3	6/9	104	198
103	793518	72	F	B	105	128	3	2	2	6/12P	1	1	1	6/9	0	0	2	6/9	1	0	1	6/9	124	106
104	320813	73	F	A	84	120	2	1	2	6/9	0	1	1	6/9	0	0	0	6/9	0	0	0	6/9	121	165
105	324531	63	M	B	79	108	3	2	5	6/36	0	1	4	6/12	0	1	3	6/12	0	0	2	6/9	96	166
106	700374	62	F	A	106	105	3	2	3	6/6P	2	1	2	6/6P	0	1	2	6/6P	0	0	0	6/6P	86	128
107	904283	57	M	B	83	109	4	3	5	6/24P	0	1	3	6/24P	0	0	4	6/12	0	0	3	6/9P	89	132

SL.NO.	IP NO.	AGE	SEX	STUDY/CONTROL	PRE-OP		DAY 1				DAY 7				4TH WEEK				8TH WEEK					
					FBS	PPBS	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	CELLS	FLARE	IOL PIG	BCVA	FBS	PPBS
108	321749	63	M	B	101	120	4	2	0	6/6P	1	1	0	6/6P	1	1	0	6/6P	0	1	0	6/6P	66	126
109	308251	62	M	A	110	136	2	1	2	6/9	0	1	2	6/9	0	0	1	6/9	0	0	0	6/9	73	138
110	324189	58	M	B	93	130	4	3	3	6/24P	3	2	2	6/24P	0	0	1	6/12	0	1	1	6/12	90	162
111	763812	75	F	B	82	135	3	2	0	6/12P	2	1	0	6/12P	0	1	0	6/12P	0	0	0	6/9P	72	154
112	963420	61	M	A	108	132	2	1	0	6/6P	1	1	0	6/6P	0	0	0	6/6P	0	0	0	6/6P	92	145
113	331931	61	F	A	94	125	2	1	2	CF-5M	1	1	1	6/24P	0	0	1	6/12P	0	0	1	6/9P	69	148
114	309715	62	F	A	94	126	2	1	0	6/9	1	1	0	6/9	0	0	1	6/9	0	0	2	6/9	108	121
115	365810	65	M	B	80	138	3	2	5	6/24P	2	1	3	6/12	0	1	2	6/12	0	0	2	6/9P	92	143
116	983536	65	M	A	103	132	2	1	2	6/36	0	1	2	6/9	0	0	1	6/9	0	0	0	6/9	107	108
117	983526	75	M	A	90	135	2	1	3	6/6P	1	1	2	6/6P	0	0	1	6/6P	0	0	1	6/6P	105	116
118	984988	70	F	B	89	138	3	2	5	6/9	2	1	3	6/9	0	1	3	6/9	0	0	1	6/9	113	178
119	987149	70	F	A	79	126	3	2	0	6/6P	1	1	0	6/6P	0	0	0	6/6P	0	0	0	6/6P	126	200
120	987216	65	F	A	105	140	2	1	2	6/9	1	1	0	6/9	0	0	0	6/9	0	0	0	6/9	96	140
121	987218	65	M	B	93	125	4	3	5	CF-5M	2	1	3	6/24P	0	1	2	6/18	0	0	0	6/9P	100	156
122	990100	52	M	B	92	128	4	2	0	6/36	2	1	0	6/12P	1	1	2	6/9	1	0	2	6/9	109	167
123	990102	50	F	B	99	103	4	3	4	6/9	2	1	1	6/9	0	0	1	6/9	0	0	1	6/6	120	152
124	990116	53	M	B	100	117	3	2	1	6/24P	1	1	1	6/9P	0	0	0	6/9P	0	0	1	6/6P	114	109
125	992292	85	F	A	80	126	3	2	5	6/6P	1	1	3	6/6P	0	1	2	6/6	0	0	2	6/6	107	132
126	979233	62	M	B	104	128	2	1	0	6/6	1	1	0	6/6	0	0	0	6/6	0	0	0	6/6	122	114
127	994247	65	F	A	83	106	1	1	0	6/9	1	1	0	6/9	1	0	0	6/9	0	0	0	6/6	95	103
128	994261	60	F	B	101	124	4	3	5	6/12P	2	1	2	6/12P	0	0	2	6/9P	0	0	1	6/9	89	142
129	996834	80	F	A	101	127	2	2	4	6/6P	1	2	4	6/6P	0	0	2	6/6P	0	0	1	6/6P	74	157
130	955721	68	M	A	102	138	2	2	3	6/9	2	1	2	6/6	0	0	1	6/6	0	0	0	6/6	70	152