"COMPARISON BETWEEN TOPICAL NEPAFENAC AND FLURBIPROFEN IN MAINTAINING INTRAOPERATIVE MYDRIASIS AND CONTROLLING POSTOPERATVE INFLAMMATION IN CATARACT SURGERY"

By

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In partial fulfillment of the requirements for the degree of

MASTER OF SURGERY

IN

OPHTHALMOLOGY

Under the guidance of

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LIST OF ABBREVATIONS

SL NO	ABBREVATIONS	FULL FORM
1	ICCE	Intra capsular cataract extraction
2	ECCE	Extra capsular cataract extraction
3	SICS	Small incision cataract surgery
4	MSICS	Manual small incision cataract surgery
5	MICS	Micro incision cataract surgery
6	IOL	Intraocular lens
7	AC	Anterior chamber
8	PCIOL	Posterior Chamber Intraocular lens
9	NSAIDS	Non Steroidal Anti-inflammatory Drugs
10	IOP	Intraocular pressure
11	AL	Axial length
12.	US	Ultrasound
13.	PC	Posterior Chamber
14.	BC	Before Christ
15.	PMMA	Poly Methyl Metacrylate
16.	SUN	Standard Uveitis Nomenclature
17.	CME	Cystoid Macular Edema
18.	COX	Cyclooxygenase

ABSTRACT

NEED FOR THE STUDY: Preoperative dilation of pupil is one of the requisites for performing an uncomplicated cataract surgery. Intraoperative miosis is one the many challenges which a surgeon can encounter during cataract surgery. Routinely tropicamide with phenylephrine is used for preoperative dilatation of pupil,but intraoperative miosis is the complication.Preoperative use of NSAIDS like nepefenac,flurbiprofen,ketorolac has been found useful for maintaining intra operative mydriasis and controlling postoperative inflammation by blocking prostaglandin synthesis.This study is taken up in our setup to compare the efficacy of flurbiprofen and Nepafenac

OBJECTIVES

1. To measure the horizontal and vertical pupil diameters preoperatively and intraoperatively in Nepafenac group using Castroviejo's callipers.
2. To measure the horizontal and vertical pupil diameters preoperatively and intraoperatively in Flurbiprofen group using Castroviejo's callipers.
3. To compare the preoperative and intraoperative horizontal and vertical pupil diameters between Nepafenac group and Flubiprofen group.
4. To assess and compare the postoperative inflammation between the two groups by slit lamp biomicroscopy.

Methods: This prospective comparative study was performed on 110 patients, 55 were allocated in each group and were given either of the topical NSAID's Nepafenac or Flurbiprofen prior to cataract surgery. Pupillary diameter was measured at the beginning and at the end of the surgery and the values were compared between the groups. Postoperative inflammation was also compared between both the groups.

Results: The mean pupillary diameter of the two groups were comparable at the beginning of surgery . The difference in horizontal papillary diametres between both the groups was statistically significant (P = 0.04) ($p<0.05$)at the end of surgery. The difference in vertical pupillary diameters between both the groups was statistically significant (P = 0.000) ($p<0.05$) at the end of surgery The mean change in the pupillary diameter was more in flurbiprofen group when compared to nepafenac group.There was statistically significant difference among both the groups in maintenance of intraoperative mydriasis .The comparison of postoperative inflammation was also statistically different between both the groups. Postoperative flare on day 1 was compared between both groups (0.35±0.48 in Nepafenac group and 0.59±0.53 in Flurbiprofen group) and it was found to be statistically significant (P = 0.02) ($p < 0.05$). The postoperative cells on day 1 was compared between both groups (0.35±0.48 in Nepafenac group and 0.79±0.41 in Flurbiprofen group) and there was significant difference found statistically (P = 0.00) ($p < 0.05$).

Conclusions: Pre-operative Nepafenac was found to be better than flurbiprofen in maintaining intraoperative mydriasis and controlling postoperative inflammation

Keywords: Cataract surgery , Small Incision Cataract Surgery,nepafenac , flurbiprofen , intraoperative miosis, postoperative inflammation

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF GRAPHS

LIST OF PHOTOGRAPHS

INTRODUCTION

INTRODUCTION

Senile cataract is the leading cause of avoidable blindness throughout the world.It is estimated that 39.1% of global blindness is caused by cataract.[1]

The definitive treatment of cataract is the surgical removal of the cataractous lens and its replacement with an intraocular lens (IOL). Extracapsular cataract extraction with posterior chamber intraocular lens implantation (PCIOL) was the most frequent surgical technique until the past decade.The use of a smaller incision with the advantages of faster rehabilitation, less astigmatism and better postoperative vision without spectacles led to phacoemulsification becoming the preferred technique where resources are available. However, cost, both in terms of equipment and training has limited its use in the developing world. Thus, there is a dichotomy with different standards of care between the developed and the developing world.

Maintaining the pupil size is an essential prerequisite for uneventful cataract surgery. In Small Incision Cataract Surgery(SICS) all the manipulations are done in the posterior chamber (PC) of eye, the visibility of which can be increased by pupillary dilatation (mydriasis).

Preoperative dilatation is usually achieved by Cyclopentolate 1% eye drops or Tropicamide 0.8% with Phenylephrine 5% eye drops. However, inspite of adequate dilatation of pupil with mydriatics, intraoperative miosis is one of the challenges which a surgeon can encounter during cataract surgery leading to difficulty in performing precise anterior capsulorrhexis and IOL implantation, with high risk of posterior capsular rent,vitreous loss, postoperative uveitis and cystoid macular edema.

Non-Steroidal Anti-Inflammatory drugs(NSAIDs) like Nepafenac ,Flurbiprofen and Ketorolac are effective in maintaining intraoperative mydriasis and controlling postoperative inflammation.[2]

Surgical trauma triggers the inflammatory cascade with release of Cyclooxygenase enzymes (COX-1 and COX-2) producing excessive quantities of prostaglandins in the anterior chamber, leading to miosis, inflammation and disruption of blood-aqueous barrier.NSAIDs inhibit cyclooxygenase enzyme, thereby interfering with endogenous prostaglandin production, thus preventing intraoperative miosis and controlling postoperative inflammation.[3]

However there are only a few studies comparing the effectiveness of Nepafenac 0.1% and Flurbiprofen 0.03% in maintaining intraoperative mydriasis and controlling postoperative inflammation. This study was conducted to compare the effect of topical Nepafenac 0.1% vs Flurbiprofen 0.03% on the pupil size intraoperatively and the postoperative inflammation in cataract surgery.

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REVIEW OF LITERATURE

ANATOMY

IRIS

The iris is the most anterior portion of the uveal tract. It lies in the frontal plane of the eye between the anterior and posterior chamber and is bathed on both surfaces by the aqueous. It is continuous peripherally with the anterior aspect of the mid point of the ciliary body and in this way an anterior band of the ciliary body and the scleral spur into which it is inserted, and contribute to the boundaries of the anterior chamber at the drainage angle.

MACROSCOPIC APPEARANCE

ANTERIOR SURFACE

The anterior surface of the iris is generally richly textured, but in the darker races, where iris pigment is increased, the surface is smooth and velvety and the texture is masked.

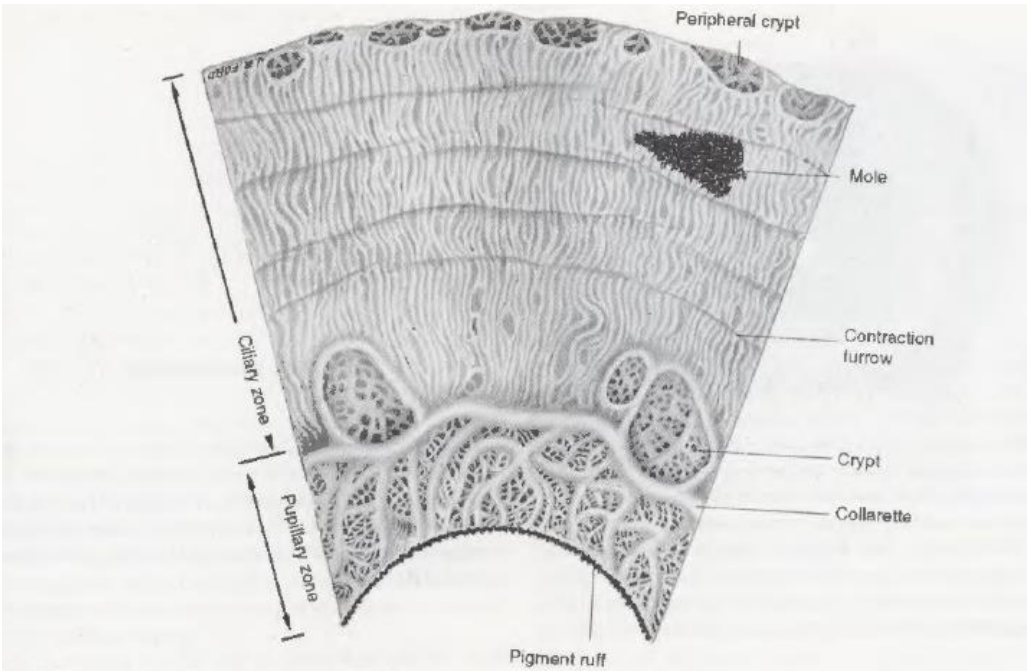

Fig.1Surface anatomy of the front of the iris.

The pupil is an aperture present slightly below and nasal to the centre of the iris

,lying behind the optical zone of cornea in the optical axis.It regulates the entry of light in to eye.

The normal size of the pupil varies from 3mm to 4mm depending on the illumination.The pupil size is relatively small during birth, largest during adolescence and gradually decreases as age increases because of fibrotic changes in the sphincter and atrophy of the dilator muscle.

There are two muscles controlling the pupil.They are the sphincter pupillae and dilator pupillae.The sphincter pupillae is 0.75mm wide and 0.1-0.17 mm thick which surrounds the pupil margin .It originates from the anterior epithelium.It is located in the stroma.It helps in constriction of pupil.

The dilator pupillae is located in the posterior stroma in the ciliary zone of the iris. The muscular processes of its cells are radially oriented, measures up to 60 μm long and 7 μm wide, are filled with myofilaments.It extends from the iris root towards the pupil. The dilator muscle is innervated by the sympathetic supply via the long ciliary nerves.

The dilator muscle receives a sympathetic innervation and the sphincter muscle a parasympathetic innervation, but adrenergic and cholinergic innervation has been shown in both muscles.[4]

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 nonpigmented epithelial cells that are ringed with tight junctions. These tight junctions stamp the secretary nature of this epithelium,and their integrity is essential for the ordinary and normal formation of aqueous humor. The tight junction ensure the preservation of a solute gradient across the bilayer of ciliary epithelia and, in addition, prevent the movement of membrane proteins past junctions, maintaining the symmetry of these transporters to ensure both the direction and content of proper secretion.[5]

FORMATION OF CATARACT

The anterior subcapsular epithelial cells in the pre-equatorial and equatorial regions proliferate and produce new fibres and this results in the increase in thickness of lens throught life.The fibres that are formed migrate below the capsule in an arcuate fashion and squeezes the central fibres in the process.Sclerosis of the central fibres and the colour change of the central fibres to yellowish brown happens over the years.The refractive index of the lens increases and there is myopic shift due to the above changes in the lens.The compactness and the dehydration of the central lens fibres ,along with deposition of pigments results in the formation of nuclear cataract.Advanced nuclear cataracts have been given the names brown cataract(cataract brunescence) and black cataract(cataract nigra).Meanwhile,the formation of water clefts in the lens cortex which increases in size forming wedge like opacities,results in cortical cataract.Hypermature cataract which is pearly white in

appearance is the advanced stage.If there is no intervention done,there is liquefaction of the cortical matter and the nucleus sinks to the bottom of the capsule.Later the lens proteins can leak out due to penetrable nature of the capsule.This leads to the formation of lens induced glaucoma.Membranous cataract is formed due to lens protein leakage without leading to glaucoma.

DEFINITION OF CATARACT

Cataract may be defined, as any type of opacity of the lens. Small congenital or punctate opacities maybe observed in 10 to 20 percent of the individuals without any adverse effect on vision.

Framingham Eye Study, Indo-US Study and American National Studies defined senile cataract as "the presence of lens opacities (excluding early cortical changes), which could not be ascribed to congenital, secondary or other specific causes with visual acuity of 6/9 or worse".

CLASSIFICATION OF CATARACT

Immature cataracts are classified according to Duke –Elder into the following groups:

1. Nuclear

2. Cortical

a. Cuneiform

b. Perinuclear

c. Cupuliform

Cuneiform opacitiesThese are the earliest features of cortical cataract. These are wedged shaped opacities,with their apex towards the center of the lens, extending in a radial direction toward the anterior pole of the lens. These opacities increase in size,

as well as in extent to finally involve most of the lens cortex. Intumescent immature cataract, is an intermediate stage in the development of cortical cataract, in which the lens swells up due to accumulation of fluid.

Perinuclear variety of cortical *cataract* It is characterized by multiple dot like opacities in the deeper cortex,which surrounds the adult nucleus like a ring.

Cupuliform cataract It is the term used to describe localized posterior subcapsular opacity. Such cataracts are usually associated with nuclear sclerosis.

For epidemiology study and follow-up, classification of cataract has been made after taking photographs,and studying the color change and position of the opacity inside the lens

The American Cooperative Cataract Research Group (CCRG) has proposed a classification based on the stereoscopic color photographs of excised human lenses. Six stereoscopic views of the lens are usually taken, and the color transparencies are utilized in a marked manner for classification. Extent of opacities are described semiquantitatively.

Accordingly, the following classification has evolved:

1. ***Hypermature (H)***A totally opaque lens, that has
undergone a marked anteroposterior swelling.
2. ***Mature (M)***A totally opaque lens with no recognizable
anatomical zone swelling.
3. ***Immature cataracts***These possess some amount of normal lens anatomy.

This group may further be subclassified into the following (Fig 2):

a. Anterior subcapsular (SCA)

b. Posterior subcapsular (SCP)

c. Anterior cortex (CXA)

d. Equatorial cortex (CXE)

e. Posterior cortex (CXP)

f. Supranuclear (SN)

g. Nuclear (N).

Extent of subcapsular cataracts is graded by relating the opacity to a series of concentric circles, the outermost representing the equatorial circle of the lens. Each circle indicates a predetermined areaof the lens shown in percentage of total area (Figure. 3). The enface view of the lens is divided into 100 equal segments (Figure. 7). By counting the number of segments involved, the extent of opacities is immediately calculated.

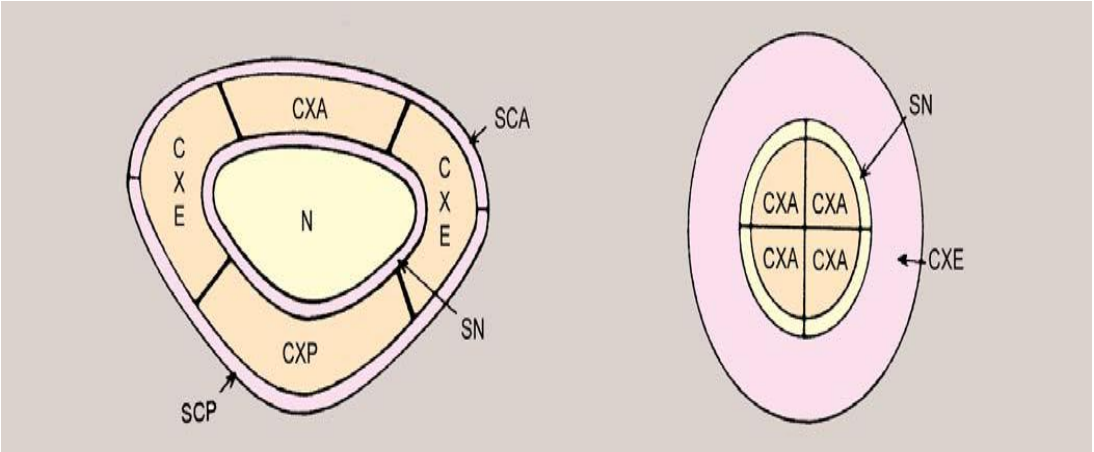

Figure2 Diagram of the scheme used in the CCRG classification system, showing the various anatomical zones of the lens in the sagittal and enface

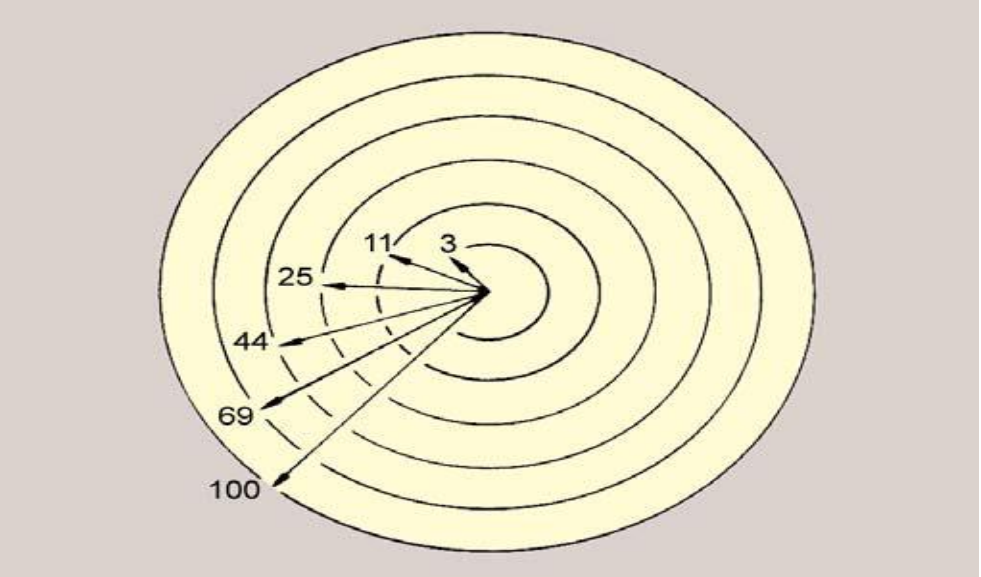

Figure. 3:Estimation of the area involved by a subcapsular cataract (SCA or SCP) in the CCRG system. The smaller circles are designated with a number representing the percentage of the area of the equatorial (outermost) circle occupied by the designated circle

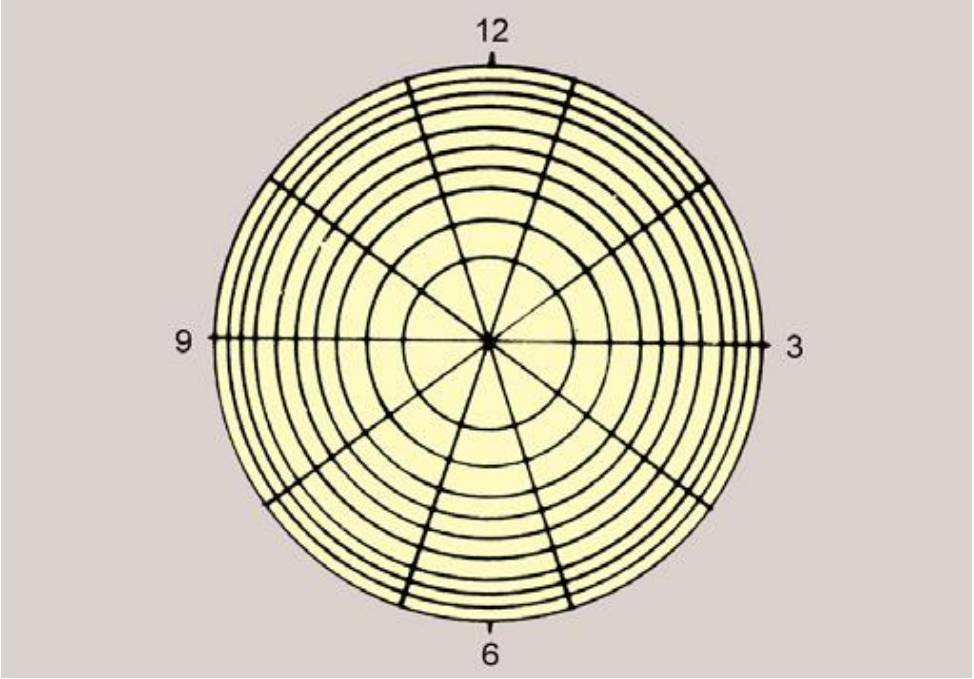

Figure. 4: En face view of the lens dividing it into one hundred equal segments. The largest circle represents equator of the lens

Classification schemes such as the Lens Opacities Classification System II6 and III7 (LOCS II and LOCS III), and the Age Related Eye Diseases study (AREDS Manual of Operations, 1994) use photographic standards to subdivide each major type into grades These grades are based either on density and color (in case of the nucleus or according to the anatomic area of the cataract (in the case of the cortical and posterior subcapsular areas). One may directly compare the patients' lens as seen by the slit lamp with a photographic copy of the various standard grades, as set up in the various classification schemes (clinical grading), or one may take photographs of
the lens being studied, and later grade the photographs according to the classification scheme used (photographic grading).

ETIOPATHOGENESIS OF CATARACT

Though exact etiopathogenesis of senile cataract is not known, age-related cataract may have multifactorial and synergistic causes. Nuclear sclerosis and nuclear cataract seem to be an age related phenomenon. Epidemiological studies have shown that incidence and type of cataract vary in different parts of the world. For example, in India visual disability from cataracts tends to occur on an average, 14 years earlier than in the West, and cortical or soft cataract is the predominant type as compared to the posterior subcapsular and nuclear varieties. Following aetiopathogenic factors to be considered:

A. Personal factors

B. Environmental factors

C. Other related factors.

Personal Factors

Personal factors are (a) Dietary factors, and (b)Medical factors.

Dietary Factors

Protein and amino acids Since the earliest reports of cataract in tryptophan deficiency, numerous accounts confirming this observation, have been published and the effect is ascribed to the resultant protein deficiency. Epidemiological studies showed an association of cataract and less intake of protein food.

VitaminsRiboflavin, vitamin E, and vitamin C areinvolved in lens metabolism. Riboflavin modifies action of the enzyme glutathione reductase. Vitamins E and C probably act as deoxidant.

Essential elements Calcium deficiency due to any cause leading to hypocalcemia has long been known to cause zonular cataract. Lower plasma levels of calcium has been found in patients with senile cataract as compared to controls.

The role of deficiency of other essential elements such as copper, zinc, and selenium in the development of cataract has also been postulated.Though, the recently conducted Age Related Eye Disease Study (AREDS) sponsored by the National Eye Institute (NEI of USA), in which nutritional supplements were given in the dose of Vitamin C 500 mg, Vitamin E 400 IU, Beta-Carotene 15 mg, Zinc Oxide 80 mg, Cupric Oxide 2mg showedthat nutritional supplements do not seem to prevent cataracts or to keep them from getting worse overtime.

Medical Factors

Diabetes

When blood sugar levels are elevated beyond 200 mg per ml, the enzyme hexokinase is saturated and remaining glucose is converted by aldose reductase to sorbitol, which accumulates in the lens fibers and causes cataract by causing osmotic stress. Thus, diabetics have a greater risk of cataract formation at an early age.

Dehydration An association between prior episodes of dehydration crises resulting from severe diarrhea, cholera or heat stroke and senile cataract has been suggested. During dehydration episodes, the osmotic imbalance secondary to malnutrition and the rise of blood urea and ammonium cyanide levels are responsible for cataract formation; ammonium cyanide is believed to denature crystalline proteins of the lens by carbamylation.

Environmental Factors

Role of Sunlight, UV Radiation, and Thermal Effect

Exposure to radiation from almost the entire range of the electromagnetic spectrum has a cataractogenic potential. Single dose of 200 rads radiation has been shown to be cataractogenic. Clinical, experimental, and epidemiological studies have emphasized cataractogenic influence of sunlight, but the exact mechanism is yet unknown. The photo-perioxidation of lens constituents including amino acid residues,lipid moieties, and other membrane components brought about by near UV light, infrared, and microwaves via generation of free radicals, may play an important role.In addition to its UV component, sunlight can initiate cataractogenesis by a thermal mechanism. Infrared and microwave components of the solar radiation are absorbed by the iris

stroma, raising the temperature of the posterior chamber and lens.Experimental animals exposed to high ambient temperatures, are seen to develop cortical opacities; on the other hand, increase in the temperature of the posterior chamber, and lens in animals exposed to bright sunlight in the tropical climate has been demonstrated. Glassblowers exposed to high infrared radiation have shown increased prevalenceof cortical opacities in their 5th and 6th decades. This shows that the damage caused by the infrared radiation might be cumulative.Studies also show that bright sunlight and high environmental temperature, and total amount of annual exposure to sunlight have a direct relation to high incidence of senile cataract in the hot and dry areas of the world. Epidemiological studies reveal that cortical opacities were seldom seen in the 10 to 12 o'clock segment of the lens. This may be attributed to the protective effect of the upper lid against light induced thermal damage to the lens.

Other Factors

Epidemiological studies indicate that:

a. Dark colored people have higher risk of developing cataract

b. Prevalence of cataract is more in short persons

c. Cataract is common in people of rural origin with poor socioeconomic status.

BIOCHEMICAL CHANGES IN CATARACT

The following biochemical alterations take place in

cataractous lens:

1. Reduced level of soluble proteins (crystallins).

2. Increased level of insoluble proteins (albuminoids).

3. Increase in protein aggregates.

4. Retention of sodium with loss of potassium and inositol.

5. Decrease in the concentration of reduced glutathione.

6. Increase in protein disulfide bonds and oxidized cystein residues.

7. Formation of high molecular weight (HMW) proteins resulting from abnormal products of protein glycosylation/ketolysation.

8. Malonaldehyde formation resulting from lipid peroxidation.

9. Formation of lipid-protein aggregates.

10. Formation of disulfide cross links, leading to aggregation of proteins resulting in opacity.[7]

History of cataract surgery

Ancient and medieval treatment of cataract included *couching*, a technique with a colorful history dating to approximately the 5th century BC. This procedure, which was used throughout the Roman Empire, Europe, India, and sub-Saharan Africa, was performed on mature cataracts. With the patient in a seated position, the surgeon inserted a needle or knife posterior to the corneoscleral junction and then pushed the lens inferiorly.[8](Fig 5)

Figure 5:Couching

By the 17th century, a better understanding of anatomy led to a fundamental improvement in technique. Jacques Daviel (1696–1762) is credited with propelling cataract surgery toward the modern era by introducing a method to extract the cataract rather than simply displace it. His method involved creating an incision through the inferior cornea, enlarging the wound with scissors, incising the lens capsule, expressing the nucleus, and removing the cortex by curettage . This ***extracapsular cataract extraction,*** or*ECCE,* became the new standard of care.[9]

Subsequently, Albrecht von Graefe (1828– 1870) advanced this technique by developing a corneal knife that created a cleaner incision and led to improved wound healing. The development of fine suture material, the invention of the binocular operating microscope, and the introduction of modern sterilization techniques reduced the incidence of surgical complications, and variations on manual ECCE continue to be employed to this day.

The invention of phacoemulsification by Charles Kelman in 1967 marked the beginning of the modern era of cataract surgery. Though initially met with strong resistance, phacoemulsification gained popularity by the 1990s. In this procedure, an ultrasonically driven tip is used to emulsify the lens nucleus and remove the fragments with an automated aspiration system. This paradigm shift allowed

cataract surgery to be performed via relatively small corneal incisions, resulting in a lower incidence of wound-related and vitreous-related complications and more rapid rehabilitation of vision. This advance also coincided with the invention of ophthalmic viscosurgical devices, the evolution of intraocular lens design, and a change to performance of cataract surgery on an outpatient basis.[10]

MANUAL SMALL INCISION CATARACT SURGERY: Due to the further development and refinement in surgical technique and updates in the surgical instrumentation, newer techniques in cataract surgery in the form of suture less cataract surgery was developed. It was Michael Blumenthal who first described manual small incision cataract surgery with such rapid visual recovery and reduced astigmatism.[11]

Construction of a small self sealing wound for delivering the cataractous lens forms the basic principle of manual small incision cataract surgery.

Basic steps in manual small incision cataract surgery :

1. Rectus muscle bridle suture
2. Conjunctival dissection
3. Sclerocorneal tunneling
4. Paracentesis formation
5. Anterior chamber entry

6. Anterior capsulotomy

7. Hydrodissection and hydrodilineation

8. Nucleus prolapse into anterior chamber and delivery

9. Epinucleus and cortex aspiration

10.IOL implantation into capsular bag

11.Closure of the wound

Rectus muscle bridle suture: For a superior approach, the superior rectus muscle is bridled and for temporal approach, the lateral rectus is bridled. Some of the surgeons also bridle the inferior rectus muscle. This is mainly done to position the globe in the centre and maneuver it during surgery. The procedure of manual small incision cataract surgery can be done either in a superior based or a temporal based approach , whichever is convenient for the surgeon. The temporal approach is more convenient for eyes with deep sockets wherein maneuvering through a superior tunnel would be difficult.

Conjunctival dissection: The conjunctiva along with the tenon's capsule is cut depending upon the size and the site of the tunnel. The bleeding vessels are then cauterized.

Sclerocorneal tunnel incision: In manual small incision cataract surgery, the construction of the wound is of utmost importance. The final result of the surgery depends upon the wound architecture. The tunnel is constructed in such a way that it has a self sealing nature and also causes minimal amount of astigmatism. The principle of 'square incisional geometry ' should be adopted in order to construct a

self sealing wound.[12]

This concept behind it is that the length of the tunnel is equal to its width. There are thus two incisions in the sclera tunnel – the external sclera incision and the inner corneal incision. The external incision can be either in the form of a frown or a linear incision. The instruments that are required for sclerocorneal tunnel construction are Bard-Parker knife with no. 15 blade and a crescent blade.

Paracentesis formation: A side port is made at the 9'o clock position using a 24-guage, 15º lancet tip blade or a 20 gauge micro vitreoretinal blade. Some surgeons prefer to make 2 ports at the 3'o clock and 9'o clock positions according to the Mini - nuc technique. An anterior chamber maintainer is usually inserted through another paracentesis made between 4'o clock and 8'o clock position. Thus the anterior chamber is formed. Surgeons who do not prefer using an anterior chamber maintainer use viscoelastic to make eye coats taut and thus help in utmost controlled dissection.

Anterior chamber entry: The internal corneal incision is made using 45º angled 3.2 mm microkeratome is advanced through the tunnel properly and then dipped downward to create a dimple and the anterior chamber is entered. The internal incision is then extended through the whole length of the tunnel parallel to the limbus. This is 20 % longer than the outer sclera incision.

Anterior capsulotomy: The opening of the capsule is then made after the tunnel has been perfectly constructed. This could be done either through the main wound or the side port. Three kinds of anterior capsulotomy are used commonly– can opener technique, envelope technique or a continuous curvilinear capsulorrhexis.[13]

Whatever be the technique , it is done using a sharp cystitome or a bent 26 G needle .An average sized capsulotomy measures about 5.5-6.5 mm. This usually allows the nucleus to prolapse into the anterior chamber. Use of dye like tryphan blue allows safe completion of the capsulorrhexis in cases where the red glow is inadequate. Can opener capsulorrhexis is done by making 10 to 20 punctures in each quadrant circumferential to the equator to avoid damage to the zonules. Envelope technique is used in morgagnian cataract. However , continuous curvilinear capsulorhexis has various advantages over the other two. They are :

1. Secure fixation of " in the bag " IOL implantation
2. Absence of anterior capsular tags ensures safe cortical aspiration
3. Minimal trauma to the zonules
4. In case of posterior capsular rent, it still helps in sulcus implantation of IOL

Hydroprocedures:

It was not until Michael Blumenthal, the founder of mini-nuc technique who first described the ways to perform hydroprocedures. This step is carried out in order to help in reducing the size of the nucleus and thus prolapsing it into the anterior chamber. Faust was the person to coin the term hydrodissection. The main aim of these hydroprocedures in manual small incision cataract surgery were to separate the various layers of the lens into cortex, epinucleus and nucleus from the capsular bag. A properly done hydrodissection would cause the nucleus to freely rotate in the capsular bag which could be easily prolapsed into the anterior chamber. It is done by injecting balanced salt solution or Ringer lactate solution using a 1-2 ml syringe in between the cortex and the anterior capsule in case of hydrodissection and between the epinucleus and nucleus in case of hydrodilineation.

Hydrodissection: Various surgeons proposed various techniques in performing the hydrodissection.

1. Initially, conventional hydrodissection which was followed by almost all the Ophthalmologists involved injecting fluid to separate the superficial cortex and the epinucleus.
2. It was largely replaced by Dr.Howard Fine who first described the cortical cleavage hydrodissection which requires tenting up of the margin of the anterior capsule lightly and then injecting a small amount of the irrigating fluid.
3. Gimbel then introduced a method wherein a cannula was used to sweep between the cortex and the capsule before injecting the irrigating fluid.

Hydrodilineation : It is also known as hydrodelamination or hydrodemarcation. It is done with the same cannula. A golden ring formation as the fluid goes under the nucleus indicates a properly done hydrodilineation. If the ring appears only partially or does not appear, it is now necessary to use the cannula at almost all the clock hour positions and repeat the same procedure at all the sites.

Delivery of the nucleus: The nucleus, once it has been relieved from the capsular attachments, it is carefully rotated up into the anterior chamber by various maneuvers.

1. Using viscoelastic to deliver out the nucleus
2. Using one or two sinskey hooks to deliver the nucleus Once the equator of the nucleus is seen, then the whole nucleus can be cartwheeled in the clockwise or anticlockwise direction and prolapsed into the anterior chamber. Once the nucleus is brought to the anterior chamber, then it can be delivered out by many methods.

- Hydroexpression
- Viscoexpression
- Vectis assisted delivery

- Phacosandwich technique
- Phacofracture technique
- Fish hook technique
- Blumenthal technique
- **Irrigating vectis**: The instrument was founded by Steinert. It works on the combination of both hydrostatic and mechanical forces. The vectis is a wired snare which has an anterior, slightly concave surface and a posterior end which is attached to a syringe containing ringer lactate or balanced salt solution.[14]

. The anterior end has three irrigating ports. The nucleus is now engaged within the body of the vectis and as the superior rectus muscle is pulled tight, the nucleus is slowly delivered under control.

- **Viscoexpression**: It utilizes the pressure that is exerted by the ophthalmic viscoelastic devices that can be injected through the paracentesis wound to expel the nucleus. Viscoeleastic can also be injected through the main section by simultaneously pressing over the posterior lip which would engage the nucleus in the wound and expel it consequently.[15]
- **Phacosandwich technique**: This technique is very useful in delivering harder cataracts with ease. The instruments used are an irrigating vectis and sinskey hook. In this method, the nucleus is sandwiched between the vectis and the sinskey hook. The nucleus is safely pulled out without causing much traction on the iris.
- **Fish hook technique:** A 30 G needle is used which is bent into a hook is used to extract the nucleus. This hook is taken into the anterior chamber, maneuvered behind the nucleus and its undersurface is hooked. The nucleus is now slid out with a little downward pressure on the posterior part of the section of the tunnel.

- **Classical Blumenthal technique**: In this technique, once the nucleus is in the anterior chamber, a glide is taken through the main wound half to 1/3rd of the nucleus diameter. The nucleus is then made to sit in the inner lip of the main entry and slight manipulations are made in the glide and also by continuous inflow of irrigating fluid, the nucleus would pass out of the wound.
- **Phacofracture technique**: This technique is very helpful in moderately hard to soft cataracts. The nucleus is broken into fragments by a number of methods like bisector technique, trisector technique, phacosalute and fracture and wireloop techniques

Aspiration of the epinucleus and the cortical matter : Epinucleus remaining after nucleus removal can also be delivered out in the same way as nucleus delivery. It can also be removed by manual or automated aspiration. Similarly cortex removal is done either by manual or automated aspiration. Even though automated aspiration requires a learning curve, it has a lot of advantages over manual technique. Aspiration of cortex done manually is done using a simcoe cannula through the main wound or the side port.[16]

. Other techniques are the iris massage maneuver, ice-cream scoop maneuver and post intraocular lens implantation maneuver.

IOL implantation: After ensuring that all the residual cortex has been removed, viscoelastic is injected to form the anterior chamber and the intraocular lens is implanted. The most commonly used intraocular lens following a small incision cataract surgery is a rigid 6-6.5 mm optic sized single piece lens made of polymethylmethacrylate(PMMA). The IOL is implanted using an IOL holding forceps. It is curved forceps – Shepard's or Kratz forceps. The correct position of the intraocular lens being implanted is an 'inverted S ' shape. A lens manipulator or even

sinskey hook may also be used to place the intraocular lens into the capsular bag. Some surgeons prefer to do it using viscoelastics.

Wound closure: After the IOL implantation is done, a thorough wash should be done in order to remove viscoelastics used. In the event of leaving the viscoelastics behind, it may lead to severe post operative inflammation. Usually no sutures are required to close the wound if it has been constructed well. Its integrity can however be checked by gently pressing the eye and noticing the egress of fluid. It can also be done by hydrating the stroma using balanced salt solution through the paracentesis wound and observing the deepening of the anterior chamber.The reflected conjunctiva is now approximated over the main wound by diathermy. Some surgeons however do not prefer cautery and simply draw it over the wound.

PHACOEMULSIFICATION:

It was not until 1967 when Charles Kelman found the role of dental deplaque instrument in cataract surgery. He adapted those ultrasonic devices to phacoemulsify the cataractous lens nucleus in the anterior chamber. After this invention, several years of development and refinement were required to bring to the present day phacoemulsification.

In the present day modern world, phacoemulsification is the common method of cataract extraction. Even though phacoemulsification is the surgery of choice, it requires a learning curve. A thorough understanding of the working of the phacoemulsification machine, the fluidics and the manipulations is necessary before proceeding with the surgery in order to prevent complications. The main advantage of phacoemulsification over other surgeries is the smaller incision which prevents a great deal of postoperative astigmatism. The two types of incision used are two planar

scleral incision and a clear corneal incision. Clear corneal incisions are more commonly used nowadays because it does not require sutures and also due to the availability of foldable intraocular lenses. All the steps in phacoemulsification are as described above except for the nucleus removal. Here, after hydrodissection , the nucleus is broken into smaller fragments. The broken fragments are then aspirated. This is effectively done by a phaco handpiece which houses an electronic transducer. This converts electrical energy into mechanical vibrator energy that is used to break the nuclear fragments. After the aspiration of the lens matter, a foldable intraocular lens is implanted in the bag with an injector.[17,18]

Principles of MICS

Generally, the principles of the MICS surgery are the same as the standard coaxial cataract surgery. Bimanuality is the main advantage. This gives us chance to extend the limits of surgery. We have easy access to the all parts of the anterior chamber from practically 360°. The MICS technique reduces manipulation in normal and complicated cases in the anterior chamber.

MICS concept is as follows:

- 1.5 mm trapezoidal incision: trapezoidal shape of the incision protect wound from deformation during manipulation at an incision size larger than 1 mm. If incision size is lower than 1 mm incision does not require this profile;
- Closed and stable anterior chamber: using separate fluid infusion in one incision we can maintain anterior chamber stable during whole surgery time while second incision can be used to do phacoemulsification, removal of the masses or IOL injection;

- Increased use of vacuum: bimanual surgery can diminish use of ultrasound (US) power to break the masses. Instead of the US, we can use high vacuum in the phaco tip with proper use of hydrochopper;
- Use of pressurized infusion to balance fluidics: MICS hydrochopper is prepared to deliver fluid to anterior chamber with 60–70 ml/min. This amount of the fluid is sufficient to fill the AC when we use vacuum 500 mm Hg to break the cataract masses. Gas forced infusion is used in MICS to provide more security in surgery. High infusion stabilizes the anterior chamber;
- Decrease use of US power settings: high vacuum and high volume of the fluid infusion can be very helpful in breaking the nucleus. For this reason, we do not need US power to break the masses in many situations;
- Bimanual use of specific MICS instruments: using two independent tools in both hands we can increase the range of surgery. Two opposite incisions give us opportunity to get free access to iris adhesion or difficult capsulorhexis from each side.
    - Use of MICS IOLs: small incision allows to implant only MICS IOLs, without enlargement of the incision.[19]

Postoperative Uveitis

Following cataract extraction, nearly all eyes exhibit some degree of intraocular inflammation. With uncomplicated cataract surgery and the use of postoperative topical corticosteroids and/or NSAIDs, most eyes should be free of inflammation by 3–4 weeks postoperatively. Complicated cases requiring manipulation of intraocular tissues (eg, iris sphincterotomy, iridectomy, or repair), involving vitreous loss or prolapse, or requiring sulcus fixation of an IOL may have a more prolonged recovery. Increased inflammation may also be seen in children; in patients with diabetes

mellitus; in patients who have had previous surgery, pseudoexfoliation syndrome, or pigment dispersion syndrome; and with long-term miotic use.

Low-grade inflammation lasting more than 4 weeks raises the possibility of chronic infection, retained lens fragments, or other causes of chronic inflammation. IOL malposition is an important cause of chronic inflammation if the lens comes in contact with the iris, ciliary body, or angle structures. An IOL designed for capsular bag placement may cause inflammation if placed in the ciliary sulcus. Retained lens material may be an insidious cause of chronic low-grade inflammation or corneal edema (see the following section). The presence of hypopyon or vitritis should prompt intervention to determine the source of the inflammation and to rule out an infectious etiology.

The surgeon should also investigate the possibility of microbial endophthalmitis in patients who have persistent uveitis without a previous history of inflammation. Chronic uveitis following cataractsurgery has been reported in association with low-grade infections with bacterial pathogens, including *Propionibacterium acnes* and *Staphylococcus epidermidis.* Such patients may have an unremarkable early postoperative course and lack the classic findings of acute endophthalmitis. Weeks or months after surgery, however, they develop chronic uveitis that is variably responsive to topical corticosteroids.This condition is usually associated with granulomatous keratic precipitates and, less commonly, with hypopyon. A localized focus of infection sequestered within the capsular bag may occasionally be observed. Diagnosis requires a high level of clinical suspicion, coupled with examination and cultures of appropriate specimens of aqueous, vitreous, and (where applicable) retained lens material that may harbor a nidus of infection. Appropriate intravitreal antibiotic therapy is indicated. If this treatment fails, the clinician may need to search

for and remove any visible focus of infection in order to sterilize the eye. In some cases, total removal of the residual capsule and IOL is necessary.

Patients with preexisting uveitis may have excessive postoperative inflammation but generally do well with small-incision cataract surgery with IOL implantation in the capsular bag. Some surgeons prefer acrylic IOL material over silicone in patients with preexisting uveitis or a risk of chronic inflammation.

Management of chronic uveitis is directed toward the cause. Surgery is used for correction of mechanical issues with IOL malposition, vitreous incarceration, or retained lens fragments. If no obvious etiology can be found, prolonged use of topical or subconjunctival corticosteroids is indicated, with continued efforts to identify a cause.[20]

Small pupil is a well-known risk factor associated with numerous complications during and after cataract surgery. Inadequate preoperative mydriasis and/or intraoperative miosis might result in iris trauma and photophobia.[21,22,23]

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One of the most significant cataract surgery complications – vitreous loss in patients whose pupils failed to dilate increases by a factor of two.[24,25]

Anterior capsular tear, increased inflammation, irregular pupil shape, posterior capsular rupture, and retained lens material are the other complications. Small pupils are not a purely geometrical issue limiting the access to the surgical field. Keeping in mind that, there are numerous factors leading to poor pupil dilation including but not limited to the systemic diseases, intake of some pharmacological agents, local comorbidities (glaucoma, ocular trauma, previous ocular surgery, uveitis, etc.), these eyes are generally more prone to increased permeability of the blood-aqueous barrier,

leading to postoperative inflammation.[26]

Furthermore, the pathology of the lens zonular apparatus, loss of lens capsule elasticity, and increase of nucleus hardness should be considered as the factors aggravating cataract surgery through the small pupil. Intraoperative floppy iris syndrome (IFIS) was described by Chang and Campbell in 2005 and proved to be associated with systemic administration of alpha-1a receptor antagonist Tamsulosin (Flomax). The main reason of that is atrophy of iris dilator muscle and decrease of iris tissue rigidity.[27]

Complication rates in patients having that syndrome can be up to 12.5%.[28]

Advances in Pharmacological Pupil Expansion: Various pharmacological agents are used to dilate the pupil. The usual topical protocol consists of the combination of cycloplegic (tropicamide 1%) and adrenergic receptor agonist (phenylephrine 2.5%).[29]

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) preoperatively has also been shown to support mydriasis and/or prevent miosis.[30,31,32] Various drugs of that class can be administered preoperatively in multiple daily doses with the aim to inhibit prostaglandin release during and after cataract procedure.

OCULAR INFLAMATION:

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 reestablishment of the blood aqueous barrier in patients undergoing cataract surgery .[33,34]

Surgical trauma and manipulations.

Due to acute injury, there is vasodilatation of blood vessels in the iris and ciliary body. The increase in hydrostatic pressure by vasodilatation causes disruption of the blood aqueous barrier; vascular leakage, forcing the plasmoid aqueous into the posterior chamber. Anterior chamber cells are predominantly lymphocytes, but a significant number of neutrophils may also be present early in the course of the disease. Increased protein content in the anterior chamber is a manifestation of the breakdown of the blood-ocular barrier.

There is approximately 7 gms of protein per 100 ml of blood, but only 11 mg of protein per 100 ml of aqueous. At the molecular level, these events are dictated by a host of plasma and cell derived vasoactive mediators including histamine,serotonin,neuropeptides, prostaglandins, kinins, complement fragments and coagulation cleavage products. These mediators promote fibrin deposition, clotting and fibroblast proliferation; that are the probable causes of fibrinous uveitis and posterior synechiae .[35]

MEASUREMENT OF ANTERIOR CHAMBER CELLS AND FLARE

The anterior chamber is easily examined with a slit lamp for signs of ocular inflammation because normally the anterior chamber is optically empty. The presence of cells or increased flare is the evidence of spill over from the inflammed iris or ciliary body. The inflammation begins in the iris and ciliary body and only when sufficient inflammatory cells accumulate within the tissues do the cells begin to enter the aqueous and become visible to the clinician. Therefore anterior chamber inflammation is a convenient but some what 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 disease. It is seen that the size of the individual cells in the anterior chamber will decrease as the inflammation begins to resolve. This may occur before the number actually decreases, inflammatory anterior chamber cells are white and should be differentiated from brown pigmented cells which may not indicate inflammation. Pigmented cells may be uveal cells, melanin containing macrophages, red blood cells, macrophages with blood pigment or even

free pigment.

Anterior chamber cells are best seen by directing the slit beam obliquely across the eye and focusing posterior to the cornea. Neusenblatt suggests a 1 X 1mm slit beam. The cells between the lens and cornea in the slit beam should actually be counted and not estimated to make the grading more reliable and reproducible. It can be then graded according to Satndard Uveitis Nomenclature(SUN) Classification

ANTERIOR CHAMBER FLARE

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

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.[35,36]

Table 1:STANDARD UVEITIS NOMENCLATURE[37]

Grading of Anterior chamber cells		**Grading of anterior chamber flare**	
Grade	**Cells**	**Grade**	**Description**
0.5+	1-5	0	None
1+	6-15	1+	Faint
2+	16-25	2+	Moderate
3+	26-50	3+	Marked
		4+	Intense

Ocular inflammation can be either due to endogenous causes like autoimmune diseases or it can be due to ocular surgeries and injuries.In our study the inflammation due to ocular surgery ,particularly cataract surgery is studied upon.[38]

Ocular tissue is traumatised during surgery leading to the activation of phospholipase A23, and the liberation of two groups of lipid molecules: arachidonic acid (AA) metabolites, and platelet-activating factors (PAFs). Arachidonic acid forms the substrate for further reactions mainly by the cyclo-oxygenase and the lipoxygenase pathways. The main products of the cyclooxygenase pathway are prostaglandins (PGs), and of lipoxygenase pathway are leukotrienes (LTs). Endogenous PGs produce many effects such as: miosis during surgery, postoperative inflammation, increased permeability of the blood-ocular barriers, conjunctival hyperaemia and changes in intraocular pressure. The decrease in pupil diameter can make cataract removal more difficult and increases the risk of surgical trauma, postoperative ocular inflammation,

and posterior capsule rupture. It was reported that, when mydriasis is greater than 6mm, the incidence of posterior capsule rupture was reduced by half. Thus, maintaining adequate pupil dilatation is considered an important part of ensuring smooth cataract removal. Topical adrenergic agonists, such as phenylephrine in combination with a cholinergic antagonist such as tropicamide or cyclopentolate are used to dilate pupil preoperatively. Nevertheless, in many eyes subsequent onset of miosis begins soon after the surgeon makes entry to the anterior chamber.[39]

Recent studies have reported incidence rates of Cystoid Macular Edema(CME) after uncomplicated modern small-incision cataract surgery in healthy individuals (without diabetes or uveitis) as high as 9% to 19% using fluorescein angiography.Although CME can be treated, its development increases the cost of cataract surgery by approximately 50% and chronic CME can result in permanent visual impairment. Although the exact pathogenesis of CME remains to be elucidated, disruption of the blood-retinal barrier resulting from inflammation after cataract surgery may play a causative role. It has been hypothesized that release of prostaglandins and other inflammatory mediators increases permeability of perifoveal capillaries, resulting in accumulation of fluid and cystoid changes in the retinal layer.[40]

The response of the host tissue to injury manifests as inflammation. It is a cascade of events which starts with the release of arachidonic acid by the action of phospholipase A2 on the phospholipid of the cell membrane. The arachidonic acid so produced can further go into two pathways.They are the cyclooxygenase pathway and lipooxygenease pathway.The cyclooxygenase pathway gives rise to prostaglandins

and thromboxanes while eicosanoids are the end products of the lipooxygenase pathway.

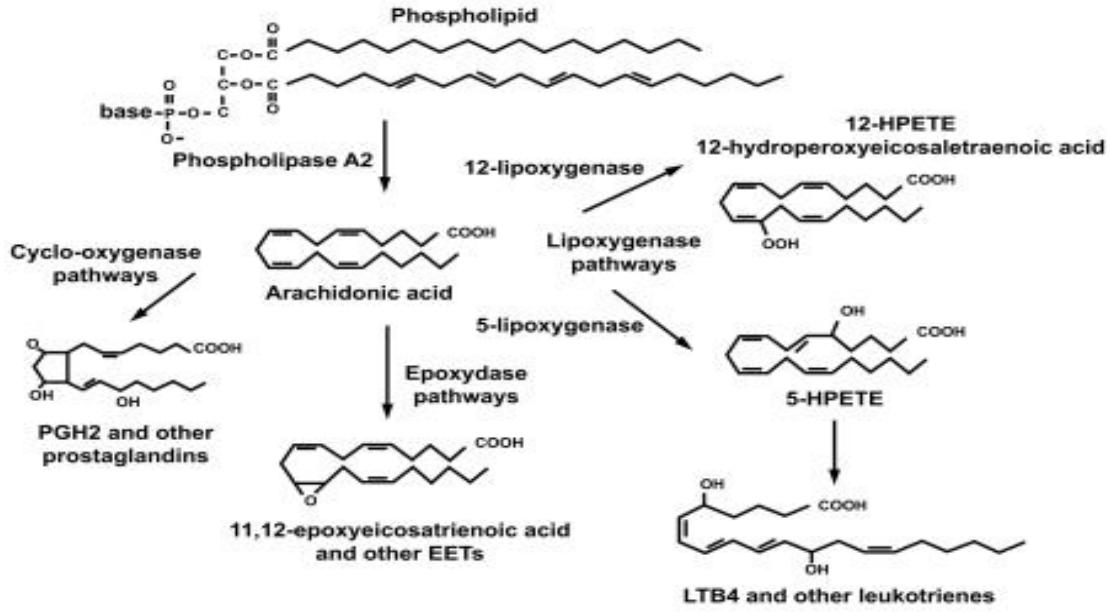

Figure 6:The cyclooxygenase and lipoxygenase pathway

The prostaglandins that are produced acts in three different ways on the ocular tissue.Their first action is on the IOP. Increase in permeability of the blood aqueous barrier and local vasodilatation by PGE1& 2 causes IOP hike, whereas PGF2reduces the IOP by increasing the uveoscleral outflow.The second action is on the iris smooth muscle causing miosis.This is followed by elevated aqueous humor protein concentration due to vasodilatation and increased vascular permeability. [41]

When PG release is inhibited with topical nonsteroidal anti-inflammatory drugs (NSAIDs) applied preoperatively, mydriasis is adequately maintained during surgery, thereby decreasing trans-operative complications such as posterior capsule rupture.

Topical ophthalmic NSAIDs have been shown to be effective in treating a variety of conditions in which prostaglandins are believed to play a causative role,

including surgically induced miosis, postoperative inflammation, treatment and prevention of cystoid macular oedema (CME).The anti-inflammatory action of the NSAIDs is primarily due to the inhibition of the cyclooxygenase enzyme (COX1 and COX-2) and due to a decrease in the biosynthesis and the release of the proinflammatory PGs- PGE2, PGF2α PGD2 and PGI2. Additional mechanisms like suppressing the leukocyte motility and chemotaxis, inhibiting the inflammatory cytokines and the free radical scavenging activity, may also contribute to their antiinflammatory action.[39]

Nonsteroidal anti-inflammatory drugs specifically inhibit cyclooxygenase enzyme, and thereby the synthesis of all downstream proinflammatory prostaglandins. The antiinflammatory properties of NSAIDs largely result from this mechanism. Corticosteroids, however, inhibit prostaglandins and leukotrienes, and they downregulate several other inflammatory-mediated events (e.g., epithelial adhesion, emigration, chemotaxis, phagocytosis). Consequently, corticosteroids possess far broader anti-inflammatory properties than NSAIDs.[40]

Inflammation can be managed by anti-inflammatory drugs.Higher ocular drug concentrations can be achieved and systemic side effects can be avoided by topical administration of drugs.Only a small number of anti-inflammatory drugs which has few established properties can be prepared in to a fitting dosage form for the management of ocular inflammation.Corticosteroids which were the initially used in the treatement of ocular inflammation, but due to serious side effects like elevation of IOP and advancement of cataract NSAIDs are preferred over corticosteroids.Recently NSAIDs are used in the prevention of intraoperative miosis and treatement of postoperative inflammation.

NSAIDS have various chemically diverse class of drugs which have the ability to inhibit cyclooxygenease.Nevertheless, comparatively water soluble salicylic acid, indole acetic acid, aryl acetic acid, aryl propionic acid and enolic acid derivatives are used predominantly for topical use in ophthalmology.NSAIDS which are mostly weakly acidic and ionize at the pH of tears and hence have poor permeability at the isoelectric point(pI) of 3.2 of anionic cornea. The unionized fraction of the drug can be increased by decreasing the pH of the drug formulation.The reduction in the ph will enhance the inherent irritant property of the NSAID and also make them less soluble.

CLASSIFICATION OF NSAIDS:

SALICYLIC ACID DERIVATIVE

Aspirin

INDOLE ACETIC ACID DERIVATIVES

Indomethacin

Bendazac

ARYL ACETIC ACID DERIVATIVES

Diclofenac

Ketorolac

Nepafenac

Tolmetin

ARYL PROPIONIC ACID DERIVATIVES

Ibuprofen

Flurbiprofen

Ketoprofen

Naproxen

Oxaprozin

Pranoprofen

Suprofen S

ENOLIC ACID DERIVATIVE

Piroxicam[41]

NEPAFENAC

Nepafenac which is a 2-amino-3-benzoylbenzeneacetamide is a prodrug and is produces as a 0.1% suspension. NSAIDS like flurbiprofen,bromfenac,ketorolac are water soluble phenylalkonic acid or phenylacetic acid.Owing to their water solubility,they have less ability to penetrate the corneal epithelium.Amfenac is the active form of the amide prodrug ,Nepafenac.The amount of drug absorbed by the cornea is directly related to the lipid solubility and indirectly to the degree of ionization.Ophthalmic nepafenac which has a pH of 7.4 remains in the unionized form and hence is easily absorbed by the cornea.Once in the aqueous humor , Nepafenac which is an amide gets metabolized into amfenac by amide hydrolysis.[38]

Flurbiprofen

Flurbiprofen, 2-(2-fluorobiphenyl-4-yl) propionic acid, is practically insoluble in water. Aqueous solutions of flurbiprofen sodium (0.03% wt/vol) are employed to inhibit intraoperative miosis during cataract surgery and to control postoperative inflammation of the anterior segment of the eye.[42]

Flurbiprofen sodium eye drops have also been used in the topical treatment of cystoid macular edema. Flurbiprofen ophthalmic solution USP has a recommended pH of 6–7.

Studies on in vitro corneal permeation of flurbiprofen have revealed that increase in

the concentration of drug in aqueous decreased the % permeation or in vitro ocular availability.Permeation of flurbiprofen was higher at pH 6.4 and decreased on increase of pH to physiological range. Permeation of flurbiprofen was enhanced by benzalkonium chloride due to formation of more lipid soluble ion-pair between anionic flurbiprofen and cationic benzalkonium chloride which develops opalescence. Phenylmercuric nitrate also enhanced corneal permeation of flurbiprofen .[43]

An in vivo study, which reported 30% greater ocular availability of flurbiprofen (0.15%, wt/vol) topical aqueous solution compared with flurbiprofen (0.30%, wt/vol) topical solution, supports the in vitro data on the effect of drug concentration on corneal permeation.[44]

Flurbiprofen solutions of concentration greater than 0.2% (wt/vol) are quite irritating.[41]

Literature review:

NSAIDs were found to be effective in maintaining intraoperative mydriasis and controlling postoperative inflammation as evidenced by many studies.

Several studies compared the effects of topical NSAIDs with placebo in inhibiting miosis during cataract surgery.[42,43,44]

Flach et al in 1988 studied the effect of Ketorolac in controlling postoperative inflammation after cataract surgery.They found that it was better than placebo in controlling postoperative inflammation.[45]

Following this multiple studies were carried out to compare the effect of other NSAIDs on intraoperative mydriasis and postoperative inflammation .

A study done by **Roberts et al**, comparing the efficacy of diclofenac 0.01% and flurbiprofen 0.03% to inhibit surgically induced miosis in cataract surgery, found

both the drugs are equally effective.[46]

Gimbel et al compared flurbiprofen 0.03% and indomethacin 1% and found no difference in their efficacy in maintaining mydriasis during cataract surgery .[47]

Topical ketorolac tromethamine 0.5% was found to be more effective inhibitor of miosis during phacoemulsification surgery and gives stable mydriatic effect throughout surgical procedure than topical flurbiprofen 0.03% in a study done by **Solomon et al**.[48]

A study was done by **Atanis et al**, in which they found topical nepafenac 0.1% was more effective than topical ketorolac 0.5% in maintenance of mydriasis.[49]

Saumya et al analyzed the effect of topical nepafenac 0.1% and topical flurbiprofen 0.03% in preventing miosis during small incision cataract surgery and concluded that nepafenac provides more stable mydriatic effect than flurbiprofen.[50]

However, in another study by **Sanjana et al** there was no statistically significant difference in the efficacy between nepafenac and flurbiprofen.[51]

Lane.S.S et al found that nepafenac 0.1% was better than placebo in controlling post operative inflammation[52]

In a study by **Hebbar et al** both topical bromfenac 0.09% and flurbiprofen 0.03% were found to be efficacious in reducing postoperative pain and anterior chamber inflammation but bromfenac was found to have an earlier effect.[53]

There was no difference in postoperative inflammation between the two groups receiving diclofenac and flurbiprofen in a study by **Kocak et al.**[54]

Patil et al found that nepafenac was superior than ketorolac in controlling postoperative inflammation.Their study concluded that the significant difference observed between nepafenac and ketorolac for their effect on postoperative inflammation was found in the immediate postoperative period but at the end of the

study ,there was no significant difference appreciated between both the groups.[55]

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MATERIALS AND METHODS

MATERIALS AND METHODS:

SOURCE OF DATA

This Prospective comparative study was conducted on 110 eyes of patients with senile cataract attending the department of Ophthalmology, R. L. Jalappa Hospital& Research centre, Kolar from January 2019 to June 2020. The study was conducted after obtaining ethical clearance from Institutional Ethical Committee of Sri Devaraj Urs Medical College and written informed consent from the subjects.

Study Design:

Inclusion criteria: Males and females aged 50 years and above with senile cataract undergoing Small incision cataract surgery with intraocular lens implantation.

Exclusion criteria:

1. Patients with systemic comorbidities like .Hypertension,diabetes.
2. Patients with pupil diameter less than 6 mm with mydriatic.
3. Pseudoexfoliation
4. Primary or secondary glaucomas,uveitis
5. History of ocular trauma or ocular surgery to the operating eye
6. Patients on topical or systemic steroids and NSAIDs within 30 days prior to inclusion in the study
7. History of hypersensitivity to nepafenac or flubiprofen
8. Patient not consenting for the procedure

METHOD OF COLLECTION OF DATA:

A total of 110 eyes of patients with senile cataract were included in this prospective comparative study.All patients fulfilling inclusion criteria underwent similar protocol

for standard cataract evaluation, including detailed history, recording of visual acuity by Snellen's chart, intraocular pressure measurement by applanation tonometry slit lamp examination, fundus evaluation with indirect ophthalmoscopy, B Scan if needed and ultrasound biometry with IOL power calculation by SRK 2 formula.

RANDOMIZATION:

The selected patients were randomized into two groups based on random number table prepared using random number generator in to two groups A and B .

GROUP A: 55 EYES- Nepafenac 0.1%

GROUP B: 55 EYES- Flurbiprofen 0.03%

Group A was administered Nepafenac 0.1% eye drops and patients in group B were administered with Flurbiprofen 0.03% eye drops.

SAMPLE SIZE CALCULATION:

Sarkar et al in his study found that the mean(SD) change in mydriasis from baseline to 3.81 mm(0.89) in Flubiprofen group and 3.23 mm (0.98) in the Nepafenac group ,with 95% confidence interval,90% power and 1:1 allocation ratio.[50]According to this,the minimum required sample size in each group was calculated to be 55,i.e; a total of 110(calculated by OpenEpi Version 3.01)

$$n1=\frac{(\sigma_1^2+\sigma_2^2/\kappa)(z_{1-\alpha/2}+Z_{1-\beta})^2}{\text{ɤ}^2}$$

$$n2=\frac{(\kappa * \sigma_1^2+\sigma_2^2)(z_{1-\alpha/2}+Z_{1-\beta})^2}{\text{ɤ}^2}$$

n1 = sample size of Gp1

n2=sample size of Gp2

$\sigma_{1=}$SD of group 1

$\sigma_{2=}$ SD of Gp2

$\bar{x}$ = Difference in group mean

K=Ratio n2/n1

$z_{1-\alpha/2}$=Two sided Z value (Eg Z=1.95 for 95% confidence interval)

$Z_{1-\beta}$=Power

TECHNIQUE

Preoperative: All patients received oral tab Ciprofloxacin 500mg twice daily and Ciprofloxacin 0.3%eye drops hourly one day before the surgery. Group A received nepafenac 0.1% three times one day before surgery.One drop every 30 minutes was instilled just before the planned time of surgery.Group B received 0.03% of Flurbiprofen eye drops 3 times one day before surgery.One drop every 30 minutes was instilled just before the planned time of surgery .Both Group A and Group B received Tropicamide 0.8% with Phenylephrine 5% ophthalmic solution 2 times at an interval of 10 minutes,half an hour before surgery.The diameter of the pupil was measured in both horizontal and vertical meridian using Castroviejo's calipers before peribulbar anesthesia.

Intraoperative: All patients underwent Small incision cataract surgery with posterior chamber IOL implantation under peribulbar anesthesia. During the procedure , the horizontal and vertical pupillary diameters were measured using Castroviejo's calipers during the following two steps of the surgery

1)After initial entry in to the anterior chamber

2)After IOL implantation, upon completing the intervening surgical steps

Postoperative: Combination of ciprofloxacin and dexamethasone eye drops were given 6 times a days for the first week.It was then tapered over 5 weeks.On day 1 visual acquity was recorded and slit lamp examination was done for detailed assessment and documentation of post operative inflammation and graded according to Standard Uveitis Nomenclature (SUN Classification) The same was done on day 7.

ASSESSMENT OF AQUEOUS CELLS

The light intensity and magnification of the slit lamp was maximal and a beam 3mm long and 1mm wide was taken. The number of cells was assessed and graded according to Standard Uveitis Nomenclature(SUN)

ASSESSMENT OF AQUEOUS FLARE

The light intensity and magnification of the slit lamp was maximal and a beam 3mm long and 1mm wide was taken. The beam was passed obliquely to the plane of the iris to evaluate the degree of obscuration of iris details and was graded according to SUN classification.

STATISTICAL METHODS USED FOR THIS STUDY

Collected data were coded and entered in MSExcel and analysed using SPSS22 version software.Categorical variable like gender, eye(R/L) will be expressed using proportion(%).Continuous variables like age,mydriasis were expressed using mean±SD or median(IQR) depending on normal distribution.The difference in flare and cells grading across groups were tested using two tailed test.P value of < 0.05 was considered statistically significant.

OBSERVATIONS

OBSERVATIONS

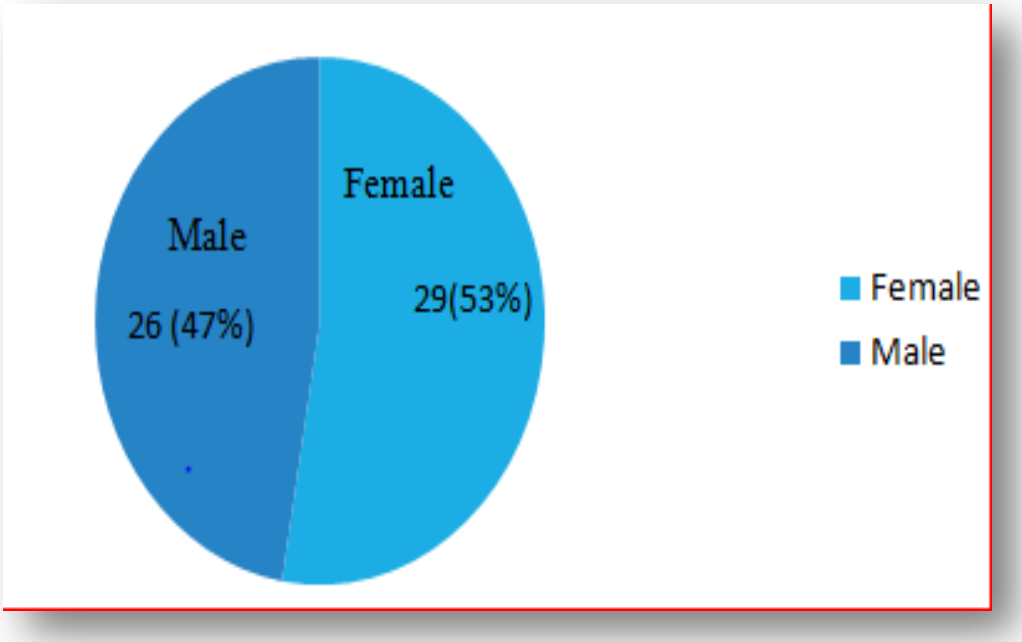
The Average age of patients treated under Group A is 63.27, the average age of Group B is 62.87.

Table 2: Comparison of age distribution between both groups

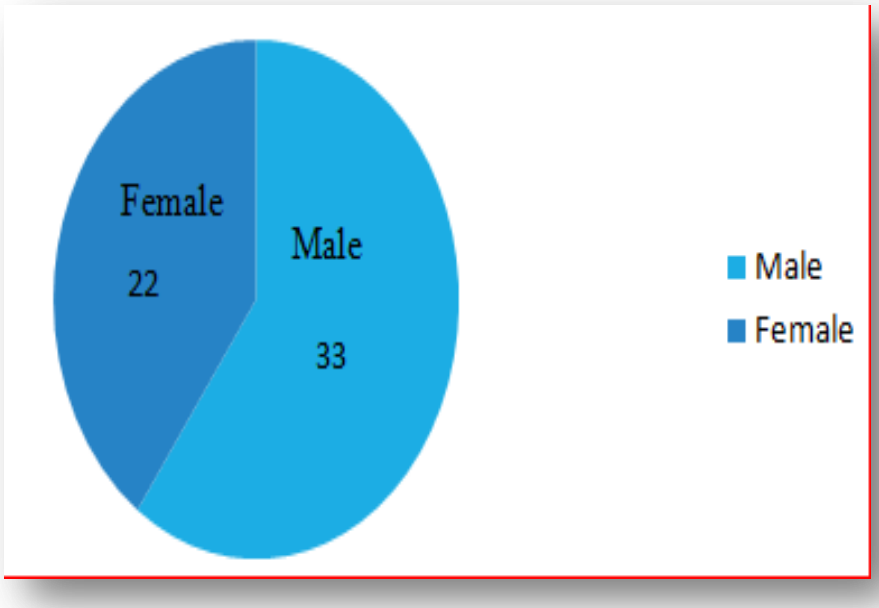
Parameter	**Nepfenac (n=55)**	**Flubiprofen (n=55)**
Age (years) (Mean±SD)	63.27±7.86	62.87±8.38

47% of the participants in group A were males and 53% were females.In group B 60% of the participants were males and 40% were females.

Graph 1:Genderdistribution in group A



Graph 2: Gender distributuion in Group B



The laterality distribution was equal in nepafenac group and in flurbiprofen group about 64% of the included participants were left eyed.

Graph2:Distribution of laterality in both the groups

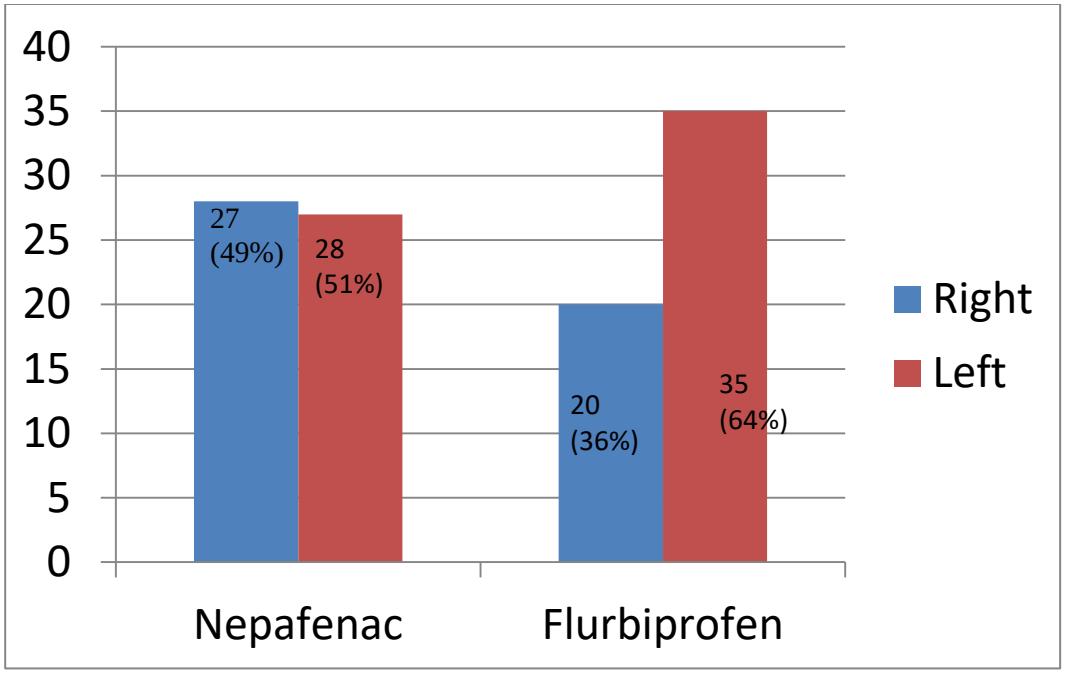


Table 3:Comparison of laterality distribution between both the groups

Parameter	Nepfenac (n=55)	Flubiprofen (n=56)
LE	27 (49%)	35 (64%)
RE	28 (51%)	20 (36%)

Table 4:Comparison of vertical pupillary diameter (mean ± SD in mm) between both groupsat different stages of cataract surgery

Parameter	Group A (Nepafenac)	Group B (Flurbiprofen)	P value
PREOPERATIVELY	7.59±0.57	7.67±0.51	0.45
END OF SURGERY	6.98±0.79	6.34±1.07	0.001
TOTAL CHANGE	0.59±0.63	1.33±1.05	0.001
% LOSS*	7.46	16.67	0.002

The above table shows that the average preoperative vertical pupillary diameter was comparable for both groups (7.59±0.57 mm in group A and 7.67±0.51 mm in group B) and there was no significant difference found statistically (P = 0.45) ($p > 0.05$). The difference in vertical pupillary diameters between both the groups was statistically significant (P = 0.001) ($p<0.05$) at the end of surgery . The total loss of mydriasis was significantly less in group A (mean: 0.59 mm) when compared to group B (mean: 1.33 mm). At the end of surgery, the percentage loss of mydriasis is less in group A (mean: 7.46%) group compared to group B (mean: 16.67 %).

Table 5:Comparison of horizontal pupillary diameters (mean ± SD in mm) between both groups at different stages of cataract surgery

Parameter	Group A (Nepafenac)	Group B (Flurbiprofen)	P value
PREOPERATIVELY	7.52±0.61	7.65±0.51	0.22
END OF SURGERY	6.80±1.25	6.34±1.07	0.04
TOTAL CHANGE	0.57±0.63	1.31±1.05	0.001
% LOSS*	7.53	16.25	0.002

The above table shows that the average preoperative horizontal pupillary diameter was comparable for both groups (7.52±0.61 mm in group A and 7.65±0.51 mm in group B) and there was no significant difference found statistically (P = 0.22) ($p > 0.05$). The difference in horizontal pupillary diametres between both the groups was statistically significant (P = 0.04) ($p<0.05$at the end of surgery.The total loss of mydriasis was significantly less in group A (mean: 0.57 mm) when compared to group B (mean: 1.31 mm). At the end of surgery, the percentage loss of mydriasis is less in group A(mean: 7.53 %) compared to group B(mean: 16.25%).

Postoperative inflammation

Tables 6 shows the comparison of grades of flare(graded according to SUN classification) between both the groups on day 1 ,

Table 6:Comparison of grade of flare between both the groups on Day 1

Grade of Flare on Day 1	Group A (Nepafenac)	Group B (Flubirprofen)
0	35 (65%)	24 (43%)
1	19 (35%)	31 (55%)
2	-	1 (2%)

2	-	1 (2%)

Tables 7 shows the comparison of grades of flare(graded according to SUN classification) between both the groups on day 7 ,

Table 7:Comparison of grade of flare between both the groups on Day 7

Grade of flare on Day 7	Group A (Nepafenac)	Group B (Flubirprofen)
0	55(100%)	55 (100%)

Table 8 gives the comparison of grades of cells(graded according to SUN classification) between both the groups on day 1 and day 7

Table 8: Comparison of grade of cells between both the groups on Day 1 and Day 7

Grade of Cells on Day 1	**GROUP A(NEPAFENAC)**	**GROUP B (FLURBIPROFEN)**
0	**37 (65%)**	**11 (21%)**
1	**18 (35%)**	**44 (79%)**
Grade of Cells on Day 7		
0	**55 (100%)**	**55(100%)**

Table 9 shows the comparison of average postoperative flare on day 1 between both groups (0.35±0.48 in Nepafenac group and 0.59±0.53 in Flurbiprofen group) and it was found to be statistically significant ($P = 0.02$) ($p < 0.05$). The postoperative cells on day 1 was compared between both groups (0.35±0.48 in Nepafenac group and 0.79±0.41 in Flurbiprofen group) and there was significant difference found statistically ($P = 0.00$) ($p < 0.05$).

Table 9: Comparison of flare and cells between both the groups on day 1

Parameter	**Group A (Nepafenac)**	**Group B (Flurbiprofen)**	**P value**
POST OP D1 FLARE	**0.35±0.48**	**0.59±0.53**	**0.02**
POST OP D1 CELLS	**0.35±0.48**	**0.79±0.41**	**0.002**

The Postoperative Best Corrected Visual Acquity(in logMAR) was compared between both the groups on day 1 and day 7 and it showed no significant difference P>0.05.

Table 10:Comparison of BCVA between both the groups on day 1 and day 7

BCVA(logMAR)	Nepafenac	Flubirprofen
BCVA POD 1		
0	49 (89%)	48 (87%)
0.3	6(10%)	7(13%)
BCVA POD 7		
0	54(98%)	53(96%)
0.3	1(2%)	2(4%)

RESULTS

Results:

The baseline characters of the patients in both the groups were assessed.

There was equitable distribuition in age between both groups and male preponderance was found among the participants included in the study.

Left Eye laterality was observed more in the patients taking Flubirprofen, whereas patients taking Nepafenac had equal distribution of laterality.

The change observed in vertical and horizontal pupil diameters in both groups at the end of the surgery was assessed.

It was found that the percentage loss in both vertical and horizontal diameters were more in group B when compared to group A.

The post operative inflammation was compared between both the groups on Day 1 and Day 7.It was found that there was a significant difference in flare and cells between both the groups on day 1.Group A had less inflammation on day 1 when compared to group B.On day 7 the postoperative inflammation in both the groups were comparable.There was no significant difference found.There was no significant difference found in BCVA between both the groups.

DISCUSSION

DISCUSSION

Topical ophthalmic NSAIDs have been shown to be effective in treating a variety of conditions in which prostaglandins are believed to play a causative role, including surgically induced miosis, postoperative inflammation, treatment and prevention of cystoid macular edema (CME).[56]

This Prospective comparative study tested the hypothesis that nepafenac is better than flurbiprofen in maintaining intraoperative mydriasis and reducing postoperative inflammation.

The baseline characteristics of the patients in both the groups were analyzed. There was no difference in age observed between the groups.

Gender wise , male preponderance was found in the study.This was comparable to a meta-analysis done by **Ye Q et al** in South Asia where the ratio of females undergoing cataract surgery was significantly less compared to the males.This can be attributed to the higher illiteracy rate and financial instability.[57]Ours being medical college catering to rural population the gender bias comes into light more

In our study both vertical and horizontal pupil diameters were considered separately as difference in the diameters in different the meridians were expected ,as put forward by Rachel L Rushforth et al.[58]

Assessment of mydriasis:

The **vertical pupil diameters** were comparable between both the groups preoperatively.There was a mean loss of 0.59 mm in nepafenac group and 1.33 mm in flubiprofengroup At the end of surgery, the percentage loss of mydriasis was

significantly lower, 7.46% in Nepafenac group when compared to 16.67 % of Flurbiprofen group

This was comparable to a study by **Sarkar et al** where the total reduction in vertical pupillary diameter from the beginning to the end of surgery was significantly less in nepafenac group.[50]

Rodríguez-García A*et al* compared the effectiveness of 0.1% nepafenac, 0.03% flurbiprofen, 0.4% ketorolac and control group in inhibiting surgically induced miosis during uncomplicated cataract surgery. The percentage of pupillary area loss at the end of surgery was 7.50% with nepafenac, 9.84% with flurbiprofen, 10.09% with ketorolac, and 13.83% with control. A trend to larger pupillary area and diameters was found in the nepafenac, flurbiprofen, and ketorolac groups compared with the control group, with better performance in maintaining larger pupil diameters and area in the nepafenac group at all surgical stages.[59]

The **horizontal pupil diameters** between both the groups were compared.There was no significant difference found between the preoperative horizontal pupil diameters. The pupillary size at the end of surgery was significantly ($P = 0.04$) ($p<0.05$) different in two groups. The mean total loss of mydriasis was 0.57mm in Nepafenac group when compared to 1.33mm of Flurbiprofen group. At the end of surgery, the percentage loss of mydriasis was 7.53% in Nepafenac group compared to 16.25% of Flurbiprofen group.

This was consistent with the findings of **Sarkar et al and Rodríguez-García A *et al.*[50,59]**

In this study Nepafenac was found to be a better at maintaining mydriasis when compared to flubiprofen.

Nepafenac is the only ophthalmic suspension which is a prodrug.This might explain the superiority of nepafenac over flurbiprofen in maintaining mydriasis. This peculiar design helps to be specific to the target.After penetration of drug , nepafenac is converted into amfenac which is a potent COX inhibitor(COI). The powerful anti-inflammatory property of this drug is due to the active form of the drug. [60]

The activity and the concentrations of the conventional NSAIDs reduce as the active form of the drug tend to accumulate on the ocular surface. Nepafenac is formulated specially to increase the intraocular efficacy. The even distribution of the drug intraocularly due to its prodrug nature helps achieve better suppression of inflammation. In addition to that the toxicity encountered with conventional NSAIDs is also reduced. Nepafenac which is a neutral molecule, is thought to have considerably better corneal permeability and thus doesn't accumulate on the corneal surface.

The anti-inflammatory nature of the drug is determined by its intraocular concentrations. The sustained activity of nepafenac is attributed to the near maximum concentration of amfenac which is maintained longer..[61]

The results of our study was not consistent with the findings of **Prakash et al** who concluded that both nepafenac and flurbiprofen were efficient in maintaining intraoperative mydriais. In this study diabetic patients were included. In Diabetic patients, cytokines and TNFα- levels are increased in the diabetic retina due to leukocyte adhesion and breakdown of blood retinal barrier. Flurbiprofen can suppress TNFα production thus inhibiting leukocyte adhesion and breakdown of blood retinal

barrier.[51] **VMG Ferguson et al** in his study showed that the presence of diabetes mellitus was related to excessive damage to the blood aqueous barrier immediately after surgery.[62]

Assessment of Postoperative inflammation:

Postoperative inflammation was assessed in both the groups in terms of flare and cells.In this study it was found that nepafenac is better than flurbiprofen in controlling inflammation on postoperative day 1.However on day 7, postoperative inflammation was comparable between both the groups.

In a study by **Lane.S.S ET AL** it was found that nepafenac 0.1% was better than placebo in controlling post operative inflammation[52]

A study by **Hebbar et al showed** that both the medications, topical bromfenac 0.09% and topical flurbiprofen 0.03% effective and safe in reducing pain and anterior chamber inflammation after cataract surgery but the response was earlier with bromfenac 0.09%.[53]

In a study by **Kocak et al** both diclofenac and flurbiprofen were eqaually effective in controlling postoperative inflammation after cataract surgery. There was no statistical difference between the two groups in flare values at all the study visits.[54]

The superiority of nepafenac over ketorolac in controlling postoperative inflammation was established in a study by **Patil et al.**Their study concluded that there was significant difference observed between nepafenac and ketorolac for

their effect on anterior chamber cells and flare in immediate postoperative period, i.e., 1st week (day 7), but ultimately at the end of the observation period, there was no significant difference observed between two drugs.[55]

Walters *et al*.found that nepafenac has better bioavailability and Cmax achievement. This may be the cause of slight early better results observed with nepafenac over the anterior chamber cells and flare with respect to flurbiprofen in our study.[63]

Cyclooxygenase inhibitors work best when they are given before the onset of inflammation.[64,65,66] **Sawa** in his study states that COIs prevent synthesis of prostaglandin but do little to antagonize their effect once present.[67]
Hence in this study NSAIDs were started one day prior to the surgery to achieve maximum potential.

Postoperatively topical steroids were used and NSAIDS were not used to minimize the risk of potential corneal complications including corneal infiltrate and erosion, though reported infrequently.[68] Therefore the postoperative inflammation on day 1 showcases the true effect of preoperative NSAIDS.In our study steroids were added postoperatively.Hence the postoperative inflammation assessed on Day 7 exhibits predominantly the effect of corticosteroids and not NSAIDs.Multicentric randomized studies are required to assess the exclusive safety and efficacy of NSAIDs on postoperative inflammation which if proven can substitute the steroids . This study has taken into consideration only uncomplicated cataract surgery.Hence more studies have to be done to compare the efficacy of the these drugs in diabetics and other ocular morbidities predisposed to ocular inflammation for better scientific

proof.

In this study slit lamp biomicroscope was used to assess and grade the cells and flare using SUN classification.Although a standard system assists in translating the findings, its disadvantage is its subjective nature.[69]Laser Flare Photometry(LFP) was shown to be superior to slit-lamp cell evaluation in monitoring intra-ocular inflammation and flare becomes a quantitative and an objective parameter when measured by FLP.[70]

CONCLUSION

CONCLUSION

This study concludes that topical nepafenac is better in maintaining intraoperative mydriasis and controlling postoperative inflammation when compared to flurbiprofen.

Though many studies have been conducted to study the effect of nepafenac and flurbiprofen on mydriasis intraoperativey ,this might be the first study comparing the effect of nepafenac and flurbiprofen on postoperative inflammation.

Hence multicentric randomized studies need to be conducted to compare the effect of these two drugs. Continuation of preoperative NSAIDs through the post operative period will be cost effective and also will improve compliance.

SUMMARY

SUMMARY

One of the most important factors for a successful cataract surgery is adequate preoperative dilation of pupil .Intraoperative reduction in size of the pupil can pose as a challenge for the operating surgeon and can lead to many complications. .In order to counter that, NSAIDs can be used preoperatively in addition to the routine tropicamide phenylephrine combination. NSAIDs have been proved to maintain intraoperative mydriasis and also help control postoperative inflammation.This prospective comparative study was taken up to compare the efficacy of flurbiprofen and Nepafenac

This study was performed on 110 patients, 55 were allocated in each group and were given either of the topical NSAID's Nepafenac or Flurbiprofen prior to cataract surgery. Pupillary diameter was measured at the beginning and at the end of the surgery and the values were compared between the groups. Postoperative inflammation was also compared between both the groups. The mean pupillary diameter of the two groups were comparable at the beginning of surgery .The mean change in the pupillary diameter was more in flurbiprofen group when compared to nepafenac group at the end of the surgery.There was statistically significant difference among both the groups in maintenance of intraoperative mydriasis .The comparison of postoperative inflammation was also statistically different between both the groups. Hence this study concluded that Nepafenac is better than flurbiprofen in maintaining intraoperative mydriasis and controlling postoperative inflammation.

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ANNEXURES

Annexure 1

CASE PROFORMA

Group:	Case no:
Name:	Date:
Age:	IP no:
Sex:	DOA:
Occupation:	DOS:
Address:	

Chief complaints:

History of Presenting illness:

Past history:

DM/HTN/BA/Epilepsy

Family history:

Personal history:

Appetite – Sleep – Bowel –

Diet – Habits – Bladder –

GPE:

Pallor / Edema /Icterus / Cyanosis / Clubbing / Lymphadenopathy

Vital signs:

a. Pulse – c) RR –

b. BP – d) Temp –

Systemic examination:

a. CVS – c. RS –

b. PA – d. CNS –

OCULAR EXAMINATION		
	RE	**LE**
1. HEAD POSTURE 2. OCULAR POSTURE 3. FACIAL SYMMETRY		
4. OCULAR MOVEMENTS		
5. VISUAL ACUITY: a) Distant b) Near		
6. ANTERIOR SEGMENT		
7. FUNDUS (IDO & Slit Lamp +90D)		

ASSESSMENT OF PUPIL SIZE

Parameter	**Vertical diameter**	**Horizontal diameter**
Before surgery		
After anterior chamber entry		
After IOL implantation		
Change from baseline		
Percentage total loss		

ASSESSMENT OF POSTOPERATIVE INFLAMMATION

Postoperative inflammation	**Postoperative day 1**	**Postoperative day 7**
Grade of Anterior chamber flare		
Grade of Anterior chamber cells		

ASSESSMENT OF POSTOPERATIVE BCVA

BCVA(in LogMAR)	**Postoperative day 1**	**Postoperative day 7**

Annexure II

INFORMED CONSENT FORM

Group:

Case no:

IP no:

TITLE:"COMPARISON BETWEEN TOPICAL NEPEFENAC AND FLURBIPROFEN IN MAINTAINING INTRAOPERATIVE MYDRIASIS AND CONTROLLING POSTOPERATIVE INFLAMMATION IN CATARACT SURGERY"

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 technique 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 had the opportunity to ask questions regarding the 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 research project does not involve any financial burden to me.

Name	Signature	Date	Time
Patient:			
Witness1:			
Witness 2:			
Primary Investigator/ Doctor:			

ತಿಳಿವಳಿಕೆಸಮ್ಮತಿನಮೂನೆ

ಈಸಂಶೋಧನೆಗೆರೋಗಿಯಗುರುತಿನಸಂಖ್ಯೆ:

ಐಪಿಸಂಖ್ಯೆ:

ಶೀರ್ಷಿಕೆ:

"ಟೋಪಿಕಲ್ನಪೇನ್ಪೆನಾಕ್ಮತ್ತುಫ್ಲರಿಬಿಪ್ರೊನ್ನಸ್ತ್ರಚಿಕಿತ್ಸಾಸಮಯದಲ್ಲಿಉಂಟಾಗಬಹುದಾದವಿಡ್ರಿಯಾಸಿಸ್ಮತ್ತುಪೊರೆಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯನಂತರದನಂಜಿನನಡುವಿನಸಂಬಂಧವು"

ಅಂಗೀಕರಿಸಿದನಾನು,

ಈಅಧ್ಯಯನದಲ್ಲಿಪಾಲ್ಗೊಳ್ಳಲುಒಪ್ಪುತ್ತೇನೆಮತ್ತುಈಸಮ್ಮತಿಯರೂಪದಲ್ಲಿವಿವರಿಸಿರುವಂತೆನನ್ನವೈಯಕ್ತಿಕಮಾಹಿತಿಯಸಂಗ್ರಹಣೆಮತ್ತುಬಹಿರಂಗಪಡಿಸುವಿಕೆಯನ್ನು ದೃಢೀಕರಿಸುತ್ತೇನೆ.

ನಾನುಈಅಧ್ಯಯನದಉದ್ದೇಶ,

ತಂತ್ರಗಳಅಪಾಯಗಳುಮತ್ತುಪ್ರಯೋಜನಗಳನ್ನುಮತ್ತುಅಧ್ಯಯನದಲ್ಲಿಸಂಗ್ರಹಿಸಿದಮತ್ತುಬಹಿರಂಗಪಡಿಸುವಮಾಹಿತಿಯಗೌಪ್ಯತೆಗೆನಾನುಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಸಂಗ್ರಹಿಸಿದಮಾಹಿತಿಯನ್ನುಸಂಶೋಧನೆಗೆಮಾತ್ರಬಳಸಲಾಗುತ್ತದೆ.

ಈಅಧ್ಯಯನದವಿವಿಧಅಂಶಗಳನ್ನುಕುರಿತುಪ್ರಶ್ನೆಗಳನ್ನುಕೇಳಲುನನಗೆಅವಕಾಶವಿದೆಮತ್ತುನನ್ನತೃಪ್ತಿಗೆನನ್ನಪ್ರಶ್ನೆಗಳಿಗೆಉತ್ತರನೀಡಲಾಗಿದೆ.

ಈಸಂಶೋಧನಾಉದ್ದೇಶಕ್ಕಾಗಿಕ್ಯಾಟರಾಕ್ಟ್‌ಸ್ಸ್ರ್ಜಚಿಕಿತ್ಸೆಯನಂತರಶೀಘ್ರದಲ್ಲೇಅಧ್ಯಯನದಲ್ಲಿ 4 ಮಿಲಿರಕ್ತವನ್ನುದಾನಮಾಡಲುನಾನುಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದಒಪ್ಪುತ್ತೇನೆ.

ನಾನುಈಅಧ್ಯಯನದಿಂದಯಾವುದೇಸಮಯದಲ್ಲಿಹಿಂತೆಗೆದುಕೊಳ್ಳಲುಮುಕ್ತವಾಗಿರುತ್ತೇನೆಮತ್ತುಇದುನನ್ನಮುಂದಿನಕಾಳಜಿಯನ್ನುಬದಲಿಸುವುದಿಲ್ಲಎಂದುನಾನುಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಈಸಂಶೋಧನಾಯೋಜನೆಯಭಾಗವಹಿಸುವಿಕೆನನಗೆಯಾವುದೇಹಣಕಾಸಿನಹೊರೆಒಳಗೊಂಡಿರುವುದಿಲ್ಲ.

ಹೆಸರು	ಸಹಿ	ದಿನಾಂಕ	ಸಮಯ
ರೋಗಿಯ:			
ಸಾಕ್ಷಿ 1:			
ಸಾಕ್ಷಿ 2:			
ಪ್ರಾಥಮಿಕತನಿಖೆದಾರ / ಡಾಕ್ಟರ್:			

Annexure III

PATIENT INFORMATION SHEET

This information is to help you understand the purpose of the study **"Comparison between topical nepafenac and flurbiprofen in maintaining intraoperative mydriasis and controlling postoperative inflammation in cataract surgery"**You are invited to take part voluntarily in this research study, it is important that you read and understand the purpose, procedure, benefits and discomforts of the study.

1. What is the purpose of this study ?

   To compare the efficacy of topical nepefenac and flurbiprofen in maintaining intraoperative mydriasis and controlling postoperatveinflammation incataract surgery

2. What are the various investigations being used? Are there any associated risks?

   Absolutely no risks are associated with various investigations involved in this study such as B scan, A scan, manual keratometer and routine ocular examination.

3. What is the benefit for me as a participant?

   Comparing the efficacy of topical nepefenac and flurbiprofen in maintaining pupillary dilatation during surgery and controlling inflammation after cataract surgery would be of importance in reducing the complications during and after surgery, and also postoperative inflammation.

   Participation in this research study may not change the final outcome of your eye condition. However, patients in the future may benefit as a result of knowledge gained from this study. You will not be charged extra for any of the procedures

performed during the research study. Your taking part in this study is entirely voluntary. You may refuse to take part in the study or you may stop your participation in the study at any time, without a penalty or loss of any benefits to which you were otherwise entitled before taking part in this study.

CONFIDENTIALITY

Your medical information will be kept confidential by the study doctor and staff and will not be made publicly available. Your original records may be reviewed by your doctor or ethics review board. For further information,/clarification please contact Dr. K. KANTHAMANI, SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR – 563101

DOCTOR'S DETAILS:

DR. SANDHYA .R, MBBS, MS.

PROFESSOR& HOD

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SDUMC, KOLAR – 563101

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ಶ್ರೀದೇವರಾಜ್ಅರಸ್ಉನ್ನತಶಿಕ್ಷಣಮತ್ತುಸಂಶೋಧನಾಸಂಸ್ಥೆ,

ಟಮಕ, ಕೋಲಾರ - 563101.

ರೋಗಿಯಮಾಹಿತಿನಮೂನೆ:-

"ಈಅಧ್ಯಯನವುಉದ್ದೇಶಪೂರ್ವಕ"ಟೋಪಿಕಲ್ನಿಪೇನ್ಪೆನಾಕ್ಮತ್ತುಫ್ಲರಿಬಿಪ್ರೊನ್ನ್ಯಸ್ತ್ರಚಿಕಿತ್ಸಾಸಮಯದಲ್ಲಿಉಂಟಾಗಬಹುದಾದಮಿಡ್ರಿಯಾಸಿಸ್ಮತ್ತುಪೊರೆಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯನಂತರದನಂಜಿನನಡುವಿನಸಂಬಂಧವು"ಎಂಬಅಧ್ಯಯನವನ್ನುಅರ್ಥಮಾಡಿಕೊಳ್ಳಲುಸಹಾಯಮಾಡುವುದು

"ಈಸಂಶೋಧನಾಅಧ್ಯಯನದಲ್ಲಿನಿಮ್ಮನ್ನುಸ್ವಯಂಪ್ರೇರಿತವಾಗಿಪಾಲ್ಗೊಳ್ಳುವಂತೆಆಹ್ವಾನಿಸಲಾಗಿದೆ, ಉದ್ದೇಶ, ವಿಧಾನ,

ಪ್ರಯೋಜನಗಳುಮತ್ತುಅಧ್ಯಯನದಅಸಮಂಜಸತೆಗಳನ್ನುನೀವುಓದುವುದುಮತ್ತುಅರ್ಥಮಾಡಿಕೊಳ್ಳುವುದುಮುಖ್ಯ.

1. ಈಅಧ್ಯಯನದಉದ್ದೇಶವೇನು?

ಜಟಿಲವಾದಮಿಡಿಯಾಸ್ಸಿಸ್ಅನ್ನುಕಾಪಾಡಿಕೊಳ್ಳಲುಮತ್ತುಜಟಿಲಗೊಂಡಿರದಕಣ್ಣಿನಪೊರೆಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯನಂತರದಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯತೊಡಕುಗಳನ್ನುನಿಯಂತ್ರಿಸುವಲ್ಲಿಸಾಮಯಿಕನೆಪೀಫೆನಾಕ್ಮತ್ತುಫ್ಲ್ಬರಿಪ್ರೊಫೆನ್ಸಳಪರಿಣಾಮಕಾರಿತ್ವವನ್ನುಹೋಲಿಸಲು.

2.ವಿವಿಧತನಿಖೆಗಳನ್ನುಬಳಸಲಾಗುತ್ತಿದೆ? ಯಾವುದೇಸಂಬಂಧಿತಅಪಾಯಗಳಿವೆಯೇ? ಬಿಸ್ಕ್ಯಾನ್,ಎಸ್ಕ್ಯಾನ್,ಮ್ಯಾನ್ಯುವಲ್ಕೆರಾಟೋಮೀಟರ್ಮತ್ತುವಾಡಿಕೆಯಕಣ್ಣಿನಪರೀಕ್ಷೆಯಂತಹಈಅಧ್ಯಯನದಲ್ಲಿಒಳಗೊಂಡಿರುವವಿವಿಧತನಿಖೆಗಳೊಂದಿಗೆಯಾವುದೇಅಪಾಯಗಳುಸಂಪೂರ್ಣವಾಗಿಸಂಬಂಧಿಸಿಲ್ಲ.

3. ಭಾಗವಹಿಸುವವನಾಗಿನನಗೆಏನುಪ್ರಯೋಜನ?

ಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯಸಮಯದಲ್ಲಿಶಿಶುವಿಹಾರದದುರ್ಬಲತೆಯನ್ನುಕಾಪಾಡುವುದರಲ್ಲಿಮತ್ತುಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯಸಮಯದಲ್ಲಿಮತ್ತುನಂತರದತೊಡಕುಗಳನ್ನುಕಡಿಮೆಮಾಡಲುಕಣ್ಣಿನಪೊರೆಶಸ್ತ್ರಚಿಕಿತ್ಸೆಮಹತ್ವದ್ದಾಗಿರುತ್ತದೆಮತ್ತುಶಸ್ತ್ರಚಿಕಿತ್ಸೆಯನಂತರತೊಡಕುಗಳನ್ನುಉಂಟುಮಾಡುವಲ್ಲಿಸಾಮಯಿಕನೆಪಿಫೆನಾಕ್ಕತ್ತುಫ್ಲಿ್ಬರಿಪ್ರೊಫೆನ್ನಳಪರಿಣಾಮಕಾರಿತ್ವವನ್ನುಹೋಲಿಸುತ್ತದೆ.ಈಸಂಶೋಧನಾಅಧ್ಯಯನದಲ್ಲಿಭಾಗವಹಿಸುವಿಕೆಯು, ನಿಮ್ಮಕಣ್ಣಿನಸ್ಥಿತಿಯಅಂತಿಮಫಲಿತಾಂಶವನ್ನುಬದಲಿಸಬಾರದು.ಆದಾಗ್ಯೂ,ಭವಿಷ್ಯದಲ್ಲಿರೋಗಿಗಳುಈಅಧ್ಯಯನದಿಂದಪಡೆದಜ್ಞಾನದಫಲಿತಾಂಶವಾಗಿಪ್ರಯೋಜನಪಡೆಯಬಹುದು.ಸಂಶೋಧನಾಅಧ್ಯಯನದಸಮಯದಲ್ಲಿನಡೆಸಿದಯಾವುದೇಪ್ರಕ್ರಿಯೆಗಳಿಗೆನಿಮಗೆಹೆಚ್ಚುವರಿಶುಲ್ಕವಿಧಿಸಲಾಗುವುದಿಲ್ಲ.ಈಅಧ್ಯಯನದಲ್ಲಿನಿಮ್ಮಪಾಲ್ಗೊಳ್ಳುವಿಕೆಯುಸಂಪೂರ್ಣವಾಗಿಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ.ಅಧ್ಯಯನದಲ್ಲಿಪಾಲ್ಗೊಳ್ಳಲುನೀವುನಿರಾಕರಿಸಬಹುದುಅಥವಾಈಅಧ್ಯಯನದಲ್ಲಿಪಾಲ್ಗೊಳ್ಳುವುದಕ್ಕೆಮುಂಚಿತವಾಗಿನೀವುಯಾವುದೇಅರ್ಹತೆಯಿಂದಯಾವುದೇದಂಡಅಥವಾನಷ್ಟವಿಲ್ಲದೆಯೇಯಾವುದೇಸಮಯದಲ್ಲಿನೀವುಭಾಗವಹಿಸುವಿಕೆಯನ್ನುನಿಲ್ಲಿಸಬಹುದು.

<u>ಗೌಪ್ಯತೆ</u>

ನಿಮ್ಮವೈದ್ಯಕೀಯಮಾಹಿತಿಯನ್ನುಅಧ್ಯಯನದವೈದ್ಯರುಮತ್ತುಸಿಬ್ಬಂದಿಗೌಪ್ಯವಾಗಿಡಲಾಗುವುದುಮತ್ತುಸಾರ್ವಜನಿಕವಾಗಿಲಭ್ಯವಿರುವುದಿಲ್ಲ. ನಿಮ್ಮಮೂಲದಾಖಲೆಗಳನ್ನುನಿಮ್ಮವೈದ್ಯರುಅಥವಾನೈತಿಕವಿಮರ್ಶೆಮಂಡಳಿಪರಿಶೀಲಿಸಬಹುದು.

ಹೆಚ್ಚಿನಮಾಹಿತಿಗಾಗಿಸಂಪರ್ಕಿಸಿ

ಡಾ.ಸಂಧ್ಯಾಆರ್

ವರ್ಷ

ಎಸ್ಜಿಯುಎಮ್ಸ್.

ಟಮಕ, ಕೋಲಾರ

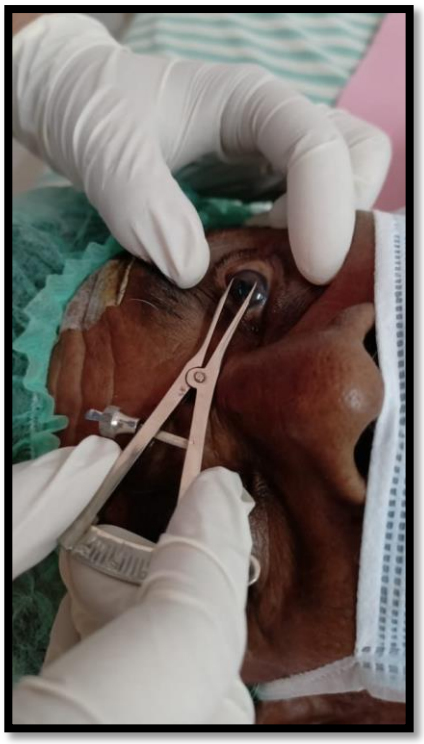
ಸಂಪರ್ಕಸಂಖ್ಯೆ: 944833038 ಅಥವಾ7373705325

ANNEXURE IV

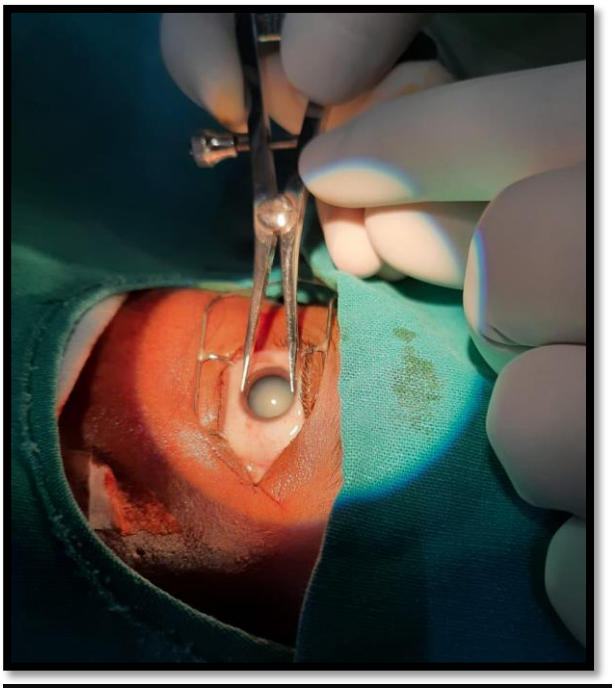
PHOTOGRAPHS

Photgraph1:Flurbiprofen eye drops

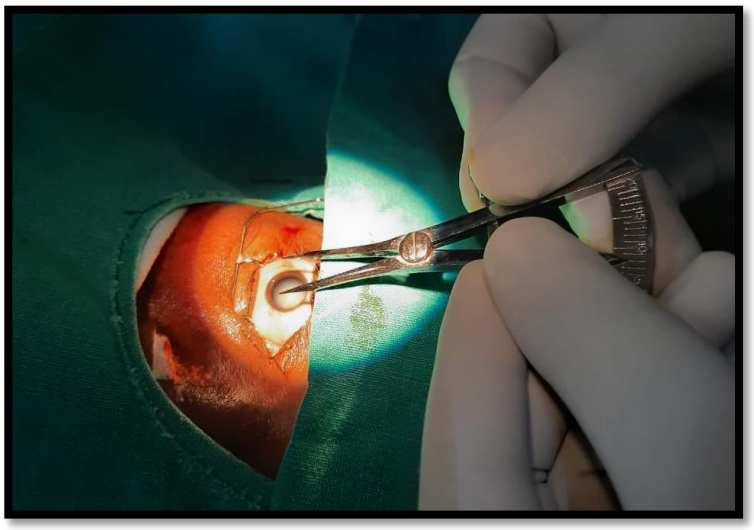
Photograph2:Nepafenac eye drops



Photograph 3 :Preoperative pupil diameter measurement using castroviejo's caliper



Photograph 4:Intraoperative vertical pupil diameter measurement using castroviejo's calipers



Photograph 5: Intraoperative horizontal pupil diameter measurement using castroviejo's calipers

ANNEXURE V

KEY TO MASTER CHART

1. SI No: Serial number
2. IP No: In patient number
3. M: Male
4. F: Female
5. VA: Visual Acuity
6. PRE-OP:Preoperative
7. V:Vertical pupil diameter
8. H:Horizontal pupil diamter
9. IOL:Intraocular lens
10. POD:Post operative Day

11. AC:Anterior Chamber

12. Group A:Nepafenac Group

13. Group B:Flurbiprofen Group

14. BCVA: Best corrected visualacuity

15. % Loss: % Loss of Mydriasis

MASTERCHART

S.NO	IP NO	Age	Sex	PREOPBC VA(Log	EYE	PRE-OP		AFTER AC ENTRY		After IOL		TOTAL CHANGE		% LOSS		POST OP DAY 1		POST OP DAY 7		BCVA POD 1	BCVA POD7	GROUP
						v	h	v	h	v	h	V	H	V	H	flare	cells	flare	cells			
1	660775	65	M	1.30	RE	8	8	7	7	7	7	1	1	12.5	12.5	0	0	0	0	0	0	A
2	660762	65	M	1	RE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	A
3	662423	76	F	1.3	LE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	A
4	668681	72	M	1.4	LE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	A
5	667659	65	M	1.4	RE	8	8	8	8	6	6	2	2	25	25	1	1	0	0	0	0	A
6	668624	65	F	1	RE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	A
7	671085	55	F	1.4	RE	8	8	7	7	7	7	1	1	12.5	12.5	1	1+	0	0	0	0	A
8	673041	51	F	1.3	RE	7	7	7	7	6	6	1	1	14.2	14.2	0	0	0	0	0	0	A
9	679006	75	M	1.3	LE	8	8	7	7	7	7	1	1	12.5	12.5	0	0	0	0	0	0	A
10	679014	65	M	1	RE	7	7	6	6	6	6	1	1	14.2	14.2	1	1	0	0	0.3	0	A
11	678009	68	F	1.4	LE	8	8	7	7	7	7	1	1	12.5	12.5	1	1	0	0	0	0	A
12	677254	63	F	1	LE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	A
13	675054	55	F	1.4	RE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	A
14	682430	50	F	0.9	RE	7	7	7	7	6	6	1	1	14.2	14.2	0	0	0	0	0	0	A
15	687950	60	F	0.9	LE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	A
16	687924	60	M	1.3	RE	7	7	6	6	6	6	1	1	14.2	14.2	1	1	0	0	0	0	A
17	687933	68	M	1.3	LE	8	8	7	7	7	7	1	1	12.5	12.5	0	0	0	0	0.3	0	A
18	689951	60	M	1	LE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	A
19	695178	65	F	1.4	LE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	A
20	692968	66	M	1	RE	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	0	A
21	695986	52	M	1.3	RE	8	8	8	8	7	7	0	0	12.5	12.5	1	1	0	0	0.3	0	A
22	703119	75	M	1	RE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	A
23	703113	57	M	1	LE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	A
24	701898	60	F	0.9	RE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	A
25	831462	70	F	1.4	RE	8	7	8	7	8	7	0	0	0	0	0	0	0	0	0	0	A
26	660760	60	M	0.9	RE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	A
27	661301	70	F	1.3	RE	7	7	7	7	6	6	1	1	14.2	14.2	0	0	0	0	0	0	A
28	666078	55	F	1.3	LE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	A
29	671091	58	M	1	LE	7	6	7	6	6	5	1	1	14.2	16.6	1	1	0	0	0	0	A
30	679003	65	M	1.4	LE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	A
31	618099	67	F	1.4	LE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	A
32	675288	76	M	1.3	LE	7	7	7	7	6	6	1	1	0	0	0	0	0	0	0	0	A
33	681642	50	F	1	LE	8	7	8	7	7	6	1	1	12.5	14.2	1	1	0	0	0	0	A
34	684297	65	M	0.9	LE	7	7	6	6	6	6	1	1	0	0	0	0	0	0	0	0	A
35	689930	60	M	0.6	LE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	A
36	690734	60	F	1.3	LE	8	8	8	8	7	7	1	1	12.5	12.5	1	1	0	0	0.3	0	A
37	689931	60	F	1	LE	7	8	7	8	7	8	0	0	0	0	0	0	0	0	0	0	A
38	533868	62	F	1.4	LE	9	9	9	9	9	9	0	0	0	0	0	0	0	0	0	0	A
39	699336	59	F	1	LE	8	8	6	6	6	6	2	2	25	25	1	1	0	0	0.3	0	A
40	693368	59	F	1.4	LE	7	7	7	7	6	6	1	1	14.2	14.2	1	1	0	0	0	0	A
41	693374	50	F	1.3	LE	8	7	8	7	8	7	0	0	0	0	1	1	0	0	0	0	A
42	683396	72	M	1	RE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	A
43	695931	58	F	1.4	RE	8	8	7	7	7	7	1	1	12.5	12.5	1	1	0	0	0	0	A
44	701024	76	F	1.3	RE	8	8	6	6	6	6	2	2	25	25	1	1	0	0	0	0	A
45	701095	65	M	1	RE	9	9	8	8	8	8	1	1	11	11	0	0	0	0	0	0	A
46	703108	60	F	0.9	RE	7	7	5	5	5	5	2	2	28	28	1	1	0	0	0	0	A
47	703111	65	F	1.4	RE	8	8	7	7	7	7	1	1	12.5	12.5	1	1	0	0	0	0	A
48	702992	55	M	1.3	RE	8	7	7	7	7	7	1	0	12.5	12.5	0	0	0	0	0	0	A
49	702706	60	F	1.4	RE	8	8	7	7	7	7	1	1	12.5	12.5	0	0	0	0	0	0	A
50	833753	70	M	1	LE	7	7	7	7	7	7	0	0	0	0	1	1	0	0	0	0	A

51	831473	82	M	1.4	RE	7	7	7	7	7	7	0	0	0	0	1	1	0	0	0	0	A
52	831479	76	F	1	RE	7	7	6	6	6	6	1	1	14.2	14.2	1	1	0	0	0	0.3	A
53	833281	65	M	0.9	LE	8	8	8	8	7	7	1	1	12.5	12.5	0	0	0	0	0	0	A
54	833279	65	F	0.9	LE	8	8	8	8	7	7	1	1	12.5	12.5	0	0	0	0	0.3	0	A
55	833283	70	F	1.3	LE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	B
56	831484	65	M	1	LE	7	8	7	7	7	7	0	1	0	0	0	0	0	0	0	0	B
57	828047	68	F	1.3	LE	8	8	8	8	7	7	1	1	12.5	12.5	1	1	0	0	0	0	B
58	831491	70	M	1	LE	7	7	5	5	5	5	2	2	28.5	28.5	1	1	0	0	0	0	B
59	853285	50	M	1.4	LE	7	7	6	6	6	6	1	1	14.2	14.2	0	0	0	0	0	0	B
60	833346	80	F	1	LE	8	8	7	7	7	7	1	1	12.5	12.5	1	1	0	0	0	0	B
61	834209	60	M	1.4	LE	8	8	6	5	6	5	2	3	25	37.5	1	1	0	0	0.3	0	B
62	836788	70	F	0.9	RE	7	7	6	6	6	6	1	1	14.2	14.2	0	0	0	0	0	0	B
63	834569	55	M	0.9	RE	7	7	7	7	5	5	2	2	28.5	28.5	1	1	0	0	0	0	B
64	838457	75	M	1.3	LE	8	8	7	7	7	7	1	1	12.5	12.5	0	0	0	0	0	0	B
65	838472	50	M	1.3	LE	8	8	7	7	6	6	2	2	25	25	1	1	0	0	0	0	B
66	838459	65	F	1	LE	7	7	5	5	5	5	2	2	28.5	28.5	1	1	0	0	0.3	0.3	B
67	838462	70	F	1.4	LE	8	8	7	7	7	7	1	1	12.5	12.5	0	0	0	0	0	0	B
68	838465	75	F	1	LE	7	7	6	6	6	6	1	1	14.2	14.2	1	1	0	0	0	0	B
69	838471	70	M	1.3	LE	8	8	6	6	6	6	2	2	25	25	1	1	0	0	0	0	B
70	836784	80	M	1	LE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	B
71	836791	63	M	1	RE	8	8	6	6	6	6	2	2	25	25	1	1	0	0	0	0	B
72	835918	55	M	0.9	LE	8	8	8	8	7	7	1	1	12.5	12.5	0	0	0	0	0	0	B
73	833284	65	M	1.4	RE	8	8	8	8	8	8	0	0	0	0	1	1	0	0	0	0	B
74	828040	65	M	0.9	LE	7.5	7.5	7	7	7	7	o.5	o.5	0.06	0.06	0	0	0	0	0	0	B
75	831495	65	M	1.3	LE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	B
76	831497	65	M	1.3	LE	7	7	7	7	7	7	0	0	0	0	0	0	0	0	0	0	B
77	831496	65	M	1	LE	8	8	8	8	8	8	0	0	0	0	0	0	0	0	0	0	B
78	828094	70	F	1.4	RE	8	8	7	7	7	7	1	1	12.5	12.5	1	1	0	0	0.3	0.3	B
79	828037	52	M	1.4	LE	8	8	8	8	5	5	3	3	37.5	37.5	1	1	0	0	0	0	B
80	828032	55	F	1.3	RE	8	8	7	7	7	7	1	1	12.5	12.5	1	1	0	0	0	0	B
81	828042	60	F	1	RE	7	7	7	7	6	6	1	1	14.2	14.2	0	1	0	0	0	0	B
82	831459	60	F	0.9	LE	8	8	7	7	7	7	1	1	12.5	12.5	0	1	0	0	0	0	B
83	828030	70	F	0.6	LE	7	7	6	6	6	6	1	1	14.2	14.2	0	1	0	0	0	0	B
84	831488	75	F	1.3	RE	7	7	6	6	6	6	1	1	14.2	14.2	1	1	0	0	0	0	B
85	828025	71	F	1	LE	7	7	5	5	5	5	2	2	28.5	28.5	1	1	0	0	0.3	0	B
86	820836	80	M	1.4	RE	8	7	6	6	6	6	2	1	25	14.2	0	1	0	0	0	0	B
87	834203	70	M	1	RE	8	8	7	7	7	7	1	1	14.2	14.2	0	1	0	0	0	0	B
88	831487	65	M	1.4	RE	8	8	7	7	4	4	4	4	50	50	1	1	0	0	0	0	B
89	831456	70	M	1.3	RE	8	7	6	6	5	5	3	2	37.5	28.5	1	1	0	0	0	0	B
90	831263	65	F	1	LE	7	7	6	6	6	6	1	1	14.2	14.2	1	1	0	0	0	0	B
91	831288	75	M	1.4	LE	8	8	6	6	4	4	4	4	50	50	2	1	0	0	0	0	B
92	824389	70	M	1.3	LE	8	8	8	7	6	5	2	3	25	37.5	1	1	0	0	0	0	B
93	824567	70	F	1	LE	8	8	7	7	6	6	2	2	25	25	1	1	0	0	0	0	B
94	716004	65	F	0.9	LE	7	7	6	6	5	6	2	1	28.5	14.2	1	1	0	0	0	0	B
95	830651	70	M	1.4	RE	8	8	7	7	7	7	1	1	12.5	12.5	0	1	0	0	0.3	0	B
96	835914	65	F	1.3	RE	7	7	7	7	5	6	2	1	28.5	14.2	1	1	0	0	0	0	B
97	835011	70	M	1.4	LE	8	8	8	8	5	5	3	3	37.5	37.5	1	1	0	0	0	0	B

98	837262	63	M	1	LE	8	8	7	7	7	7	1	1	12.5	12.5	0	1	0	0	0.3	0	B
99	838464	70	F	1.4	LE	8	8	8	8	6	6	2	2	25	25	1	1	0	0	0	0	B
100	838467	50	M	1	LE	8	8	8	8	5	5	3	3	37.5	37.5	1	1	0	0	0	0	B
101	836790	50	M	0.9	LE	8	8	6	6	6	6	2	2	12.5	12.5	1	1	0	0	0.3	0	B
102	833464	75	M	0.9	LE	7	7	7	7	7	7	0	0	0	0	0	1	0	0	0	0	B
103	838458	70	M	1.3	RE	8	8	8	8	8	8	0	0	0	0	0	1	0	0	0	0	B
104	845763	65	F	1	RE	7	7	7	7	7	7	0	0	0	0	0	1	0	0	0	0	B
105	851889	55	F	1.3	RE	9	9	9	9	8	8	1	1	11.1	11.1	1	1	0	0	0	0	B
106	851051	55	M	0.9	RE	8	8	8	8	8	8	0	0	0	0	1	1	0	0	0	0	B
107	829039	73	M	0.9	LE	8	8	8	8	5	5	3	3	37.5	37.5	1	1	0	0	0	0	B
108	829038	71	M	1.3	LE	8	8	6	6	6	6	2	2	12.5	12.5	1	1	0	0	0	0	B
109	829023	73	F	1	RE	7	7	7	7	7	7	0	0	0	0	0	1	0	0	0	0	B
110	829044	70	F	1.3	RE	8	8	8	8	8	8	0	0	0	0	0	1	0	0	0	0	B