"A ONE YEAR RANDOMIZED CLINICAL TRIAL OF TOPICAL VERSUS INTRACAMERAL MYDRIATICS IN SUSTAINING MYDRIASIS DURING PHACOEMULSIFICATION CATARACT SURGERY IN PATIENTS ADMITTED IN KLE'S DR.PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE BELAGAVI"

By

REG. NO.BK0115004

Dissertation

Submitted to the KLE University, Belagavi, Karnataka. In partial fulfilment of the requirements for the degree of

MASTER OF SURGERY

IN

OPHTHALMOLOGY

DEPARTMENT OF OPHTHALMOLOGY,

JAWAHARLAL NEHRU MEDICAL COLLEGE,

BELAGAVI, KARNATAKA.

APRIL - 2018

KLE UNIVERSITY, BELAGAVI,

KARNATAKA.

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This is to certify that the dissertation entitled **"A ONE YEAR RANDOMIZED CLINICAL TRIAL OF TOPICAL VERSUS INTRACAMERAL MYDRIATICS IN SUSTAINING MYDRIASIS DURING PHACOEMULSIFICATION CATARACT SURGERY IN PATIENTS ADMITTED IN KLE'S DR.PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE BELAGAVI"** is a bonafide research work done by **REG. NO.BK0115004.**

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LIST OF ABBREVIATIONS USED

TM	-	Topical Mydriatics
MSICS	-	Manual small incision cataract surgery
NSAID	-	Non steroidal anti-inflammatory drug
ICM	-	Intracameral Mydriatics
CF	-	Counting Fingers
HMCF	-	Hand movements close to face
IOP	-	Intraocular Pressure
IFIS	-	Intraoperative floppy iris syndrome
BSS	-	Balanced salt solution
ECCE	-	Extracapsular cataract extraction
ICCE	-	Intracapsular Cataract Operation
IOL	-	Intra-Ocular Lens
mm	-	Millimeters
nm	-	Nanometers
µm	-	Micrometers
T1	-	Thoracic
α	-	Alpha
β	-	Beta
M3	-	Muscarinic
CNS	-	Central Nervous System

Ml	-	Millilitre
LASIK	-	Laser assisted In Situ Keratomileusis
RCTs	-	Randomized Clinical Trials
OCT	-	Optical Coherence Tomography
M	-	Meters
SBP	-	Systolic blood pressure
DBP	-	Diastolic blood pressure
Pre op	-	Preoperative
Post op	-	Postoperative

ABSTRACT

Background and objectives

Adequate pupillary mydriasis is a must in order to be able to perform cataract surgery either by phacoemulsification or by manual small incision cataract surgery. This is usually attained by frequent topical administration of anticholinergic and sympathomimetic mydriatic agents. In an attempt to find an alternative to this repeated eye drop instillation regimen we studied the use of an intracameral mydriatic regimen of 0.5% lignocaine and 0.001% epinephrine in initiating and maintaining the pupillary mydriasis during phacoemulsification under topical anesthesia, without any topical mydriatic or NSAID use.

The objectives of our study are

1. To evaluate the safety and efficacy of an intracameral mydriatic regimen comprising of preservative free lignocaine 0.5% and epinephrine 0.001% in initiating and maintaining the pupillary mydriasis during phacoemulsification cataract surgery and to compare it with traditional preoperative topical mydriatic eye drops.

2. To evaluate perioperative circulatory side effects of intracameral epinephrine used as a component of the intracameral mydriatic regimen being used.

Methodology

The present study was conducted in the Department of Ophthalmology, KLES Dr.Prabhakar Kore Hospital and Medical Research Centre, Belagavi to study the safety and efficacy of an intracameral mydriatic regimen comprising of preservative free lignocaine 0.5% and epinephrine 0.001% in initiating and maintaining the pupillary mydriasis during phacoemulsification in comparison with traditional preoperative topical mydriatic eye drops. To evaluate the intraoperative circulatory side effects of intracameral epinephrine used as a component of the intracameral mydriatic regimen during the period of 1stJanuary 2016 to 31st December 2016. The study was approved by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belagavi.

Results

The mean age in group 1 was 62.32 years and in group 2 was 60.88 years. In both groups 64% of patients were females and 36% were male.

In our study the mean pupillary diameter in group 1 prior to the use of topical mydriatics was 1.74 mm with a SD of 0.29 and in group 2 prior to the use of intracameral mydriatics was 1.74 mm with a SD of 0.29. ($p=1.000$). After the use of topical mydriatics in group 1 the mean pupil size increased to 7.36 mm with a SD of 0.57 while in group 2 following the use of intracameral mydriatics it increased to mean pupil size of 5.92 mm with a SD of 0.64 ($p<0.001$). However, towards the end of surgery the pupillary diameter in group 1 was 5.82 mm with a SD of 1.05 and in group 2 it was 6.30 mm with a SD of 1.24 ($p=0.147$) indicative of decrease in

pupillary diameter in group 1 and an increase in pupillary diameter in group 2($p<0.001$).

The mean pulse rate prior to the use of topical mydriatics in group 1 was 71.20 beats/min with a SD of 8.60 and prior to the use of intracameral mydriatics in group 2 was 76.24 beats/min with a SD of 13.14 ($p=0.001$). After the use of topical mydriatics in group 1 the mean pulse rate increased to 80.24 beats/min with a SD of 16.75 and after the use of intracameral mydriatics in group 2 was 73.88 beats/min with a SD of 10.90 ($p=0.119$). At the end of surgery the mean pulse rate in group 1 was 74.88 beats/min with a SD of 14.30 and in group 2 was 72.28 beats/min with a SD of 10.34 ($p=0.465$).

The mean systolic blood pressure in group 1 prior to the use of topical mydriatics was 133.44 mmHg with a SD of 14.23 and in group 2 prior to the use of intracameral mydriatics was 146.76 mmHg with a SD of 16.48 ($p=0.004$). After the use of topical mydriatics in group 1 the mean systolic blood pressure was 147.40 mmHg with a SD of 17.5 and after the use of intracameral mydriatics in group 2 was 142.92 mmHg with a SD of 16.14 ($p=0.346$). At the end of surgery in group 1 the mean systolic blood pressure in group 1 was 138.96 mmHg with a SD of 30.78 and in group 2 was 142.00 mmHg with a SD of 13.87 ($p=0.655$).

The mean diastolic blood pressure in group 1 prior to the use of topical mydriatics was 82.20 mmHg with SD of 9.35 and in group 2 prior to the use of intracameral mydriatics was 87 mmHg with a SD of 8.01 ($p=0.095$). Following the use topical mydriatics in group 1 the mean diastolic blood pressure was 85.76 mmHg with a SD of 10.14 and after the use of intracameral mydriatics in group 2 was 85.72 mmHg with a SD of 8.06 ($p=1.000$). At the end of surgery the mean diastolic blood

pressure being 85.72 mmHg in group 1 with a SD of 10.34 and 86.04 mmHg in group 2 with a SD of 7.76 (p=0.962).

Conclusions and interpretation

Thus we conclude that the use of an intracameral mydriatic regimen of preservative free lignocaine 0.5% and epinephrine 0.001% constitutes a safe, rapid and effective alternative compared to the use of topical mydriatics in sustaining pupillary mydriasis in phacoemulsification cataract surgery. It has the ability to simplify the preoperative procedure done routinely, the induced mydriasis being well sustained, without significant alteration in intraoperative pulse rate and blood pressure. It is especially useful in certain subjects with a high risk for adverse outcomes like patients with cardiac disorders, hypertension, IFIS, patients with allergy to the components of a topical mydriatic regimen etc.

Keywords

Pupillary mydriasis, Topical mydriatics, Intracameral mydriatics.

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INTRODUCTION

Cataract is an opacity of the natural crystalline lens, it could be a small localized or a generalized loss of transparency. The natural crystalline lens has a structure of water and protein to create a clear passage for light.

Cataract surgery has undergone significant developments over the past two decades. With constant improvement in the surgical techniques the need for hospitalization has decreased with procedures requiring less extensive anesthesia and having better postoperative outcomes.

Adequate mydriasis is a must in order to perform cataract surgery, whether it is done by phacoemulsification or by manual small incision cataract surgery (MSICS). Pupillary dilatation is usually attained by the use of topical mydriatic eye drops containing parasympatholytic and sympathomimetic mydriatic agents, commonly used being cyclopentolate 1%, tropicamide 0.8%, phenylephrine hydrochloride 2.5% to 10% and nonsteroidal anti-inflammatory drug (NSAID) eye drops[1]. However, this topical mydriatic regimen has certain disadvantages. Delayed onset of mydriasis due to the slow penetration of the drug through the cornea[1], the time required for cyclopentolate to achieve a maximum mydriatic effect being 30 minutes[2,3] and for phenylephrine hydrochloride being 75 minutes[4]. In clinical practice, thus there is need of a preoperative preparation time of approximately 45 minnutes for the pupils to dilate, which is much longer than the surgical procedure itself. Cyclopentolate 1% and phenylephrine hydrochloride 2.5-10% eye drops are administered three times with a 15 minute interval. The other disadvantages seen are due to the frequent instillation of

eye drops leading to local discomfort and epithelial toxicity due to preservatives in the topical formulas.

High risk groups such as patients with hypertension or coronary artery disease and infants have an increased risk for cardiovascular side effects, as topically administered eye drops have a limited local bioavailability with a significant systemic absorption via the nasal mucosa pathway[5,6,7,8,9].

Pupillary mydriasis has to be sustained during surgery as even if good mydriasis is achieved initially, the mydriatic effect tends to wear off during surgery[10], commonly seen in patients with diabetes mellitus having rigid pupils and intraoperative floppy iris syndrome (IFIS) [11,12].

Pupillary constriction during cataract surgery is associated with an increased risk for intraoperative complications such as damage to the iris, incomplete cortex removal, posterior capsule rent with nucleus drop into the vitreous cavity and increased vitreous loss[13]. A well maintained mydriasis is therefore very important for a good postoperative outcome.

Therefore, there is a need to search for alternatives to this repeated eye drop instillation regimen. Hence the study of intracameral injection of mydriatic drugs is necessary. The preoperative waiting time is markedly reduced with the use of an intracameral mydriatic regimen at the start of the procedure. Intracameral mydraitics are an effective and safe option for initiating and maintaining pupillary dilatation during cataract surgery. The risk for systemic adverse events is reduced due to a decrease in the effective dose of the mydriatic agents and less systemic absorption via

the nasal mucosa with the use of the intracameral route of drug administration, thus making it a safe option.

In this study we aimed at evaluating the efficacy and safety of an intracameral irrigating solution of 0.5% lignocaine and 0.001% epinephrine in initiating and maintaining the pupillary mydriasis without the use of any prior topical mydriatic or NSAID eye drops in phacoemulsification cataract surgery[14].

There have been previous studies which have compared the safety, efficacy and pupillary dilatation of intracameral mydriatics with that of topical mydriatics. However, there has not been a randomised clinical trial comparing the following drug combinations in phacoemulsification cataract surgery in each category respectively.

1. In the group receiving topical mydriatics- tropicamide 0.8%, phenylephrine hydrochloride 5% with chlorbutol 0.5% as preservative.

2. In the group receiving intracameral mydriatics- preservative free lignocaine 0.5% with epinephrine 0.001%.

AIMS AND OBJECTIVES

1. To evaluate the safety and efficacy of an intracameral mydriatic regimen comprising of preservative free lignocaine 0.5% and epinephrine 0.001% in initiating and maintaining the pupillary mydriasis during phacoemulsification cataract surgery and to compare it with traditional preoperative topical mydriatic eye drops.

2. To evaluate perioperative circulatory side effects of intracameral epinephrine used as a component of the intracameral mydriatic regimen being used.

REVIEW OF LITERATURE

Definition of cataract

Cataract is any opacity of the lens, resulting in a loss of transparency. The term cataract is a latin word “cataracta”, meaning “waterfall” or “blockage of flow”. Constantinus Africanus (AD 1010-1087) first introduced the cataract procedure. The most frequent indicators of cataract include diminished visual acuity, monocular diplopia, glare and photophobia.

History of cataract surgery

The archive of cataract surgery dates back to 800 BC when Susruta and other surgeons in India performed “couching”. In this method the opaque lens was placed posteriorly and inferiorly into the vitreous cavity with the help of a blunt needle and a lancet. During the 18^{th} and 19^{th} centuries this technique was also popular in a number of the European countries. Serious complications were frequent, and there was no method for optical rehabilitation. Thus, patients suffered from optical aphakia for the rest of their lives[14].

Jacques Daviel in1745 was unsuccessful in executing a couching procedure. This led to the subsequent developments in the techniques of cataract surgery. He introduced the first extracapsular cataract operation (ECCE); with an intact lens capsule wherein he made an incision on the inferior part of the cornea and place a needle posterior to the lens and delivered it with some loss of vitreous. This technique was subsequently refined by others e.g. Albrecht von Graefe (1828-1870)[14].

George de la Faye (1752) and Samuel Sharp (1753) introduced intracapsular cataract operation (ICCE) at around the same time, where the lens together with the capsule was taken out. Following section and iridectomy, and with the pupil dilated, the inferior section of the anterior capsule was held by the forceps and by a number of rocking manoeuvres the zonules were debilitated and disconnected from the ciliary muscle (most frequently without a breach of the capsule). Following this, the lens was inverted by an action known as tumbling. The procedure of ICCE was enhanced during the 19th and 20th centuries with the utilization of other instruments e.g. curette, spoon and strabismus hook. Joaquin Barraquer in 1957, launched Zonulysin (alpha chymotrypsin, a digestive proteolytic enzyme of bovine origin), which could be introduced into the posterior chamber prior to either of the methods resulting in zonulolysis, thereby simplifying removal of the lens. Cryoextraction of the lens was launched by Tadeusz Krwawicz, in 1961. ICCE was the most popular method. However, due to a higher occurrence of cystoid macular edema, retinal detachment, vitreous loss, astigmatism and use of anterior chamber intraocular lens, there was a switch from the technique of ICCE to the newer technique of ECCE. This was in an effort to bring down the complications and to make easier the placement of intraocular lenses.[14]

The introductory attempt to place a lens implant was done by casaamata as reported in Leipzig 1795. However, it immediately slid posteriorly towards the retina. The year 1949 witnessed newer developments in the intraocular lenses (IOLs). During the battle of Britain in World War II many plastic canopies of spitfire air planes were shattered by enemy gun fire. This plastic material (poly methyl methacrylate) occasionally lodged inside the eyes of pilots. It was noted that it resulted in little response to the plastic material, only if it did not move about inside the eye. Thus,

Ridley realized that such a plastic material can be used to substitute the human lens. Subsequently, he began placing the disc form PMMA lenses in a biconvex design posterior to the iris following ECCE[15]. Although this lens design was abandoned due to the numerous undesirable effects, it led to the development of IOLs.

The various advancements in the operative techniques included permitting the lens removal while leaving behind the lens capsule .The unbroken capsule represents a barrier, preventing the lens material from dropping into the vitreous cavity. This permitted less advanced cataracts to be treated, considering that any leftover fragments would be eliminated at the time of surgery with aspiration and would not be kept in the vitreous, where they would provoke inflammation.

Phacoemulsification has now become the method of choice for all surgeons due to a smaller size of the incision. The most meaningful change made in the current times was the launch of phacoemulsification surgery by Dr.Charles Kelman in 1967[16]. This technique is established on the ultrasound waves generated when an intraocular probe is introduced through a corneal incision that breaks the lens into smaller pieces, these minute fragments are then aspirated. Thus a combined ultrasonographic, aspiration and irrigation hand piece allows the expulsion of any lens through a small incision.

History of mydriatics

Around 500 years ago, an anticholinergic drug was extracted from leaves of the fatal nightshade plant and instilled into the eye to induce mydriasis. Since large and dilated pupils were considered beautiful the term “belladonna” was introduced in the 1500s.The main active component of belladonna is atropine. Later anticholinergic drugs with shorter lifespan like tropicamide and cyclopentolate were introduced in

and around 1950s. Later in 1897, a new group of mydriatic drugs was introduced, the adrenergic agonists consisting of epinephrine and phenylephrine[17].

Need for intracameral mydriatics

To perform an uneventful cataract surgery, sufficient mydriasis is a must. It is normally obtained by administration of topical anticholinergic and sympathomimetic mydriatic agents, often cyclopentolate, phenylephrine and tropicamide[1]. However, the main disadvantages associated with these are slow rate of penetration through the cornea, delaying the beginning of mydriasis with a maximum mydriatic effect at 30 minutes for cyclopentolate[3], 75 minutes for phenylephrine[4] and 20-40 minutes for tropicamide. Thus, the time required for the dilatation of the pupils is much longer than the surgical procedure itself[18]. Thus waiting for 45 min preoperatively following administration of the dilatation eye drops is essential[19]. Topically administered substances have a low bioavailability with notable systemic absorption which occurs through the nasal mucosa pathway. Thus, they increase the possibility of cardiovascular side effects, principally in high-risk groups such as subjects with hypertension, cardiovascular diseases and children[4,5,6,7,8] . During phacoemulsification cataract surgery intraoperative pupil constriction is mainly thought to occur due to an inadequate adrenergic stimulation of the dilator pupillae, thus the addition of an adrenergic substance to an intracameral mydriatic is an effective way to overcome this short coming.[20]

Need for sustained intraoperative pupillary mydriasis

A well sustained mydriasis is crucial for an uneventful cataract surgery. Many times although initially good mydriasis is attained, the mydriatic effect tends to

diminish during surgery[9], chiefly in patients with either rigid pupils as in diabetes mellitus or in patients with intraoperative floppy iris syndrome (IFIS)[10,11]. Intraoperative pupillary constriction multiplies the risk for complications, such as incomplete cortex removal, iris damage, and posterior capsule rupture[12] with the nucleus dropping into the vitreous and vitreous loss. Different complementary measures proposed to sustain a good mydriasis intra operatively include; mechanically, e.g. with iris retractors, pharmacologically, e.g. with topical non-steroidal anti-inflammatory drugs (NSAIDs)[1], viscous metaoxedrine 10%, or with intraoperative intracameral irrigation with epinephrine[9].

The amount of mydriasis induced by any pharmacological agent can be classified as; weak (pupil size <4.0 mm), moderate (4.0 to 6.0mm), large (6.0 to 8.0mm), or very large (>8.0mm) [21].

Applied Anatomy and physiology

Cornea

The primary function of the cornea is to refract the incoming light. It forms approximately 2/3 of the total refractive power of the eye (the lens refracts the persisting part).

The cornea is composed of six layers –

1. The anterior corneal epithelium
2. Bowman's membrane
3. Stroma
4. The dua's membrane
5. Descmets membrane
6. Endothelium.

Epithelium-The corneal epithelium is stratified, squamous, non keratinized and lacks goblet cells. At the limbus it is continuous with that of the conjunctiva. The epithelium accounts for about 5-10 % of the overall corneal thickness; 540 microns[22]. It is a multilayered structure. The basal cells are held together by desmosomes and to the underlying basal lamina by hemidesmosomes. Similarly, the epithelial cells at the surface are held together by desmosomes and zonulae occludentes. These tight junctions make the corneal epithelium semipermeable. The epithelial cells possess surface microvilli that helps stabilize the precorneal tear film.

Bowman's layer- It is a narrow, cellular homogeneous zone, 8-14 microns thick, immediately subjacent to the basal lamina of the cornea epithelium with a compact arrangement of collagen. The anterior limit of the bowman’s layer is sharply defined from the overlying epithelium though it is infiltrated by the lamina densa anteriorly and posteriorly it merges with the underlying stroma. Anteriorly the periphery of the Bowman's layer forms the junction between the cornea and the limbus, it is marked clinically by summits of the marginal arcades of the limbal capillaries. Trauma, both mechanical and infective is resisted by the Bowman's layer; once destroyed it cannot regenerate and is substituted by coarse scar tissue. The unmyelinated nerves perforate the bowman’s layer to enter the corneal epithelium.

Stroma (substantia propria) – The stroma is around 500 microns in thickness and collagen fibril lamellae constitute it (approximately 200-300 centrally and 500 in the periphery) organized in layers parallel with one another and with the corneal surfaces. The lamellae lie in a proteoglycan ground substance together with keratocytes. The lamellae in the anterior third run forwards obliquely to be inserted into Bowman's layer. In the deeper stroma the lamellae are arranged approximately at

right-angles to those in the subsequent layers. Each stromal lamella comprises a band of collagen fibrils of uniform diameter arranged in parallel. Fibrils show the typical 64-nm periodicity of the connective tissue collagens with a microperiod of 6 nm. The interfibrillar separation is approximately equal to the fibril diameter. This precise arrangement of collagen fibrils is responsible for the transparency of the corneal stroma. The keratocytes of the corneal stroma occupy 2.5-5% of its volume and are responsible for synthesis of the stromal collagen and proteoglycan. The normal corneal stroma also contains lymphocytes, macrophages and rarely polymorphonuclear leucocytes.

Descemet's membrane- Descemet's membrane forms the basal lamina of the corneal endothelium. It initially appears in the second month of gestation. Its thickness increases with age, it is around 3-4 µm thick at birth, 5 µm thick in childhood and around 10-12 µm in adulthood. An increase in Descemet's membrane thickness is also seen in degenerative conditions of the corneal epithelium such as congenital endothelial dystrophy or posterior polymorphous dystrophy. The descemet’s membrane primarily consists of type IV collagen. In adults the anterior third has an irregular banded pattern in cross-section while the posterior two-thirds of the membrane, consists of a homogeneous fibrillogranular material. Posteriorly, the Descemet's membrane is attached to the underlying endothelium by modified hemidesmosomes.

The descemet's membrane is inelastic, however, when stripped by injury, it coils seen on slit lamp biomicroscopy as a highly refractile cigar-shaped roll curling towards the stroma.

Endothelium – The endothelium comprises of a single layer of cuboidal, hexagonal cells on the posterior section of the Descemet's membrane. During early development the endothelial cells differentiate from cells that migrate from the limbal area. They are avascular in origin. With advancing age there occurs a gradual decrease in density and increase in shape (polymegathism) of the endothelial cells. The endothelial density is about 6000 cells at birth and falls by about 26% in the first year. A further 26% is lost over the subsequent 11 years of life but the rate of loss slows down and becomes constant around middle age and becomes less in adulthood to a total count of 1500-2500 cells/ mm2[23]. A reduction in the endothelial call density may occur due to trauma, intraocular surgery and eye diseases in addition to that seen due to advancing age.

The endothelial cells contribute to maintaining the stroma in a dehydrated state by controlling the ion transport across the endothelium and thus the term “fluid pump” has been used to describe the potential of the endothelium to dehydrate the stroma. A break in the endothelial cell layer that decreases the capability of the fluid pump, can produce corneal oedema or decompensation. The anatomy of the corneal endothelium can be illustrated by a specular microscope and assessed by imaging programs.[24].

Iris

The iris is the anterior most part of the uveal tract which is the pigmented middle layer of the eye. It is continuous with the pia-arachnoid coverings of the optic nerve. The iris acts as a diaphragm with an aperture, the pupil. The anterior segment of the eye is divided into the anterior and posterior chamber by the iris that lies between the cornea and the lens. The stroma of the iris is composed of fibroblasts,

melanocytes and loose collagenous material that contain its nerves and blood vessels. The main function of the iris is to control the aperture of the pupil. Larger the pupillary diameter, more is the amount of light entering the eye, while, smaller the diameter the lesser the amount of light entering the eye. The pupil size is controlled by the sphincture pupillae and the dilator pupillae[25]. The sphincter pupillae is formed by circularly arranged smooth muscle fibres at the rim of the pupillary margin. The pupillary aperture decreases upon contraction of these fibers. The dilator pupillae muscle fibers are arranged radially and on contraction increase the pupillary aperture. The anterior surface of the iris has no epithelial covering. The posterior surface of the iris has a bilayered epithelium, its deeper anterior layer is pigmented to absorb light. The more superficial posterior layer is non-pigmented and is in continuity with the pigmented layer of the retina. The muscles of the iris are supplied by autonomic nerves. The constrictor pupillae muscle is innervated by parasympathetic fibers arising from the ciliary ganglia, which also innervate ciliary body and lacrimal glands. Therefore, parasympathetic activation causes not only the contraction of sphincter muscle leading to pupillary constriction but also causes ciliary muscle contraction leading to spasm of accommodation and stimulation of tear secretion.

When stimulated by light, the pupil constricts, reducing its diameter and causing a five-fold decrease in the amount of light entering the eye. The dilator pupillae muscle is innervated by sympathetic autonomic fibers that originate in the T1 segment of the spinal cord. Preganglionic fibers pass to the superior sympathetic cervical ganglion. Postganglionic fibers pass along with the blood vessels such as the internal carotid artery and supplies the dilator pupillae and mullers muscle. When stimulated, the radial fibers of the dilator pupillae constrict and the pupillary diameter increases. The adrenergic receptors in the dilator pupillae are mainly α and a few β

(β2-receptor subtype). Sympathetic control of ciliary muscle action is not well established[26].

Cholinergic receptors in sphincter and ciliary muscle are of muscarinic type with predominance of M3 subtype. Sympathetic input to eye is relatively small as compared to parasympathetic input and maintains a persistent tone in dilator muscle, aiding relaxation of the sphincter and thus causing pupillary dilatation. The sympathetic responses have a slower onset and takes about 30-40 seconds to reach the peak effect. In comparison parasympathetic responses reach the peak effect within 1–2 seconds.

Sympathomimetic drugs have a relatively little effect on accomodation. Sympathomimetics also affect the width of palpebral fissure, diameter of ocular blood vessels and aqueous flow. Parasympatholytic drugs act by blocking of the muscarinic receptors, which are present on both the sphincter pupillae and ciliary muscle, thereby, producing pupillary dilatation and paralysis of accommodation. Sympathomimetics are comparatively weak mydriatic agents and in subjects having an iris difficult to dilate, such as diabetics or blacks, stronger antimuscarinic agents are used[26].

Pharmacology and drug transport

Ideal properties of mydriatics as given by Havener (1975)[26].

- Quick in onset.
- Adequate duration.
- Fast recovery after examination.
- Light reflex abolished.

- No cycloplegia.
- Capable of quick reversal in an emergency.
- Intraocular pressure remains constant.
- No other pharmacological effect.
- No local toxic reaction.
- No systemic toxic reaction.
- No adverse subjective complaints such as 'stinging'.

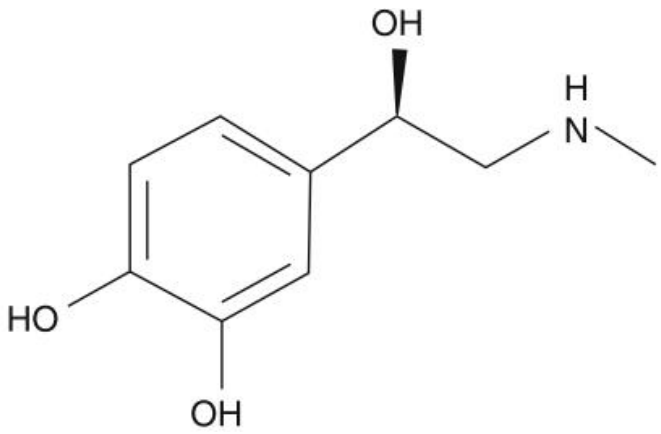
The mydriatics commonly used are:

1. Sympathomimetics: Non selective: epinephrine/adrenaline

   Selective: Phenylephrine, hydroxyamphetamine.

2. Antimuscarinic: Atropine, homatropine, cyclopentolate, tropicamide.

Epinephrine



Epinephrine (adrenaline) is a powerful stimulator of both the α and β (α1, α2, α3, β1, and β2) receptors[5]. Epinephrine is a neurotransmitter which is chiefly

produced by medulla of the adrenal gland and in the synapses of the nerve cells. It predominantly acts on the heart and the vascular smooth muscles.

Epinephrine is a highly potent vasopressor drug known. It causes a significant increase in the blood pressure, the rise of which is significantly proportional to the dose administered. The rise in systolic pressure is more than the rise in diastolic pressure, therefore the pulse pressure rises[27]. The main pathophysiology involved includes the following: a positive inotropic effect due to the direct myocardial stimulation that raises the intensity of ventricular contraction, a positive chronotropic effect with raised heart rate and a rise in the peripheral resistance due to vasoconstriction in the vascular bed, chiefly in the precapillary resistance vessels of the mucosa, the skin, and the kidney accompanied by marked constriction of the veins and thus an increase in the right atrial pressure[5].

There is a notable rise in the pulse rate initially,[27] which later slows down at the peak of the rise of the blood pressure due to a compensatory vagal response. A marked rise in the heart rate, cardiac output, stroke volume, and left ventricular work load is the consequence of the direct cardiac stimulation, the increased venous return and an increase in the peripheral vascular resistance.

Vascular Effects: Epinephrine primarily acts at the level of the smaller arterioles and the precapillary sphincters, however, the large arteries and the veins may also show a response to the drug. The main outcome is a cutaneous vasoconstriction with a notable reduction in blood flow to the extremities such as the feet and hands. However, blood flow to the skeletal muscles is raised at the therapeutic doses via β 2-mediated vasodilator action. In therapeutic doses, epinephrine is known to cause constriction of cerebral arterioles. However, the

cerebral autoregulatory mechanisms limit the increase in cerebral blood flow following an increase in blood pressure. Thus human physiology ensures that the cerebral circulation does not constrict in response to activation of the sympathetic nervous system by stressful stimuli[28].

Cardiac Effects: β1, β2, β3, and α receptors are present in the heart. However, epinephrine which is a potent cardiac stimulant predominantly acts on the β 1 receptor of the myocardium, the pacemaker and the conducting tissues. Thus epinephrine stimulation results in an increase in the contractile force, rise in the isometric tension, reduction in the time to reach the peak tension, an increased excitability, increased spontaneous beating and induction of automaticity in certain sections of the heart[28].

A study was carried out by Salima Bhallil et al to evaluate any perioperative circulatory after effects of intracameral epinephrine in hypertensive patients going in for phacoemulsification. 300 patients who were medically treated for hypertension were included. 2-3 drops of 1ml epinephrine (1mg/ml) was administered to all the patients into the anterior chamber. Pulse rate and blood pressure were recorded prior, during and after the procedure. The mean blood pressure preoperatively was 117±3/75±2 mmHg. The study concluded that the blood pressure intraoperatively and postoperatively after injection of the intracameral epinephrine remained stable:117±2.5/65±1.5 mmHg. Pulse rate changes were not significant[29].

Epinephrine increases the vasoconstriction of the renal vasculature, decreasing the renal blood flow and increasing the renal vascular resistance. Epinephrine results in a persistent increase in the filtration fraction, with a minimally altered glomerular filtration rate. Epinephrine directly acts on the β1 receptors of the glomerular

apparatus resulting in a rise in the renin release. Elimination of of Na+, K+, and Cl– is reduced; urine volume may be decreased, increased, or unchanged[28].

Epinephrine use results in an increase in arterial and venous pulmonary pressures. Coronary blood flow is also enhanced by epinephrine. Epinephrine results in a relative increased duration of diastole with increased heart rate secondary to a decreased blood flow during systole and a rise in the mean aortic pressure. Together these two factors result in an increase in the coronary blood flow. Secondly epinephrine has a direct effect on the cardiac myocytes resulting in an increased strength of contraction and myocardial oxygen demand[28].

Effects on Smooth Muscles: Type of the adrenergic receptors in various organs and systems determine the response to epinephrine.

Effects on the gastrointestinal smooth muscle: Epinephrine acts on both α and β receptors in the gastrointestinal tract to decrease the intestinal tone and decrease the amplitude and frequency of spontaneous contractions. Thus the stomach is usually relaxed with an increase in the contraction of the pyloric and ileocecal shpincters[28].

In the eye, epinephrine primarily results in a decrease in intraocular pressure due to its direct action on the α and β receptors present in ciliary body. It results in the vasoconstriction of the ciliary vessels, therefore a decrease in the production of the aqueous humor. It also decreases the aqueous production by ciliary epithelium and increases the outflow through the trabecular meshwork. It primarily acts on α receptors in the iris, exerting an effect on the dilator pupillae muscle resulting in pupillary mydriasis. Due to this feature and the area of action, epinephrine is

popularly employed in glaucoma and in iritis patients. It is also used prior to ophthalmic surgery to achieve and maintain pupillary mydriasis.

Presently, preservative-free epinephrine in low concentrations is employed in the irrigating solutions to sustain mydriasis during phacoemulsification cataract surgery[7]. Thus, a study was conducted by Lundberg and Behndig in 2007 to evaluate the likelihood of eliminating epinephrine from the irrigating solution in phacoemulsification surgeries when using intracameral mydriatics.140 subjects were randomly distributed into 2 groups both groups received intracameral mydriatics. In group 1, the irrigating balanced salt solution was enhanced with epinephrine. The study revealed that, with the use of intracameral mydriatics, pupil sizes usually increased during the procedure. This increase was significantly greater without epinephrine (13 ± 19% versus 4 ± 14%), concluding that an irrigating solution without the addition of epinephrine can be effectively employed with intracameral mydriatics. The increase in the size of the pupil during the procedure is more without epinephrine[30].

Respiratory Effects: The main effect of epinephrine on respiration is the relaxation of the bronchial muscles. It has a potent bronchodilator effect, especially when the bronchial muscle is contracted due to disease, as in bronchial asthma, or as an effect to drugs or various autacoids. The favorable effects of epinephrine are a result of the inhibition of antigen-induced liberation of inflammatory mediators from mast cells, and to a lesser extent from reduction of the bronchial secretions brought about by the β2 receptors and congestion within the mucosa brought about by the α receptors[28].

Effects on the central nervous system (CNS): Epinephrine is not a potent CNS stimulant in standard therapeutic doses. The common effects seen include restlessness, headache, apprehension, and tremors, these in turn may be a result of the effects of epinephrine on the cardiovascular system.

Metabolic Effects: Epinephrine results in an elevation in the blood levels of glucose and lactate. This effect of epinephrine is mediated via its action on the α 2 receptors, which inhibits the insulin secretion thus decreasing the uptake of glucose by the peripheral tissues. Glucagon secretion is enhanced by its action on the β receptors of the α cells of pancreatic islets. Epinephrine also potentiates glycogenolysis in most of the tissues via β receptors. Epinephrine stimulates β receptors in the adipocytes resulting in an activation of triglyceride lipase, accelerated triglyceride breakdown to free fatty acids and the formation of glycerol[28].

Absorption, Fate, and Excretion: Epinephrine is not effective when administered orally due to its rapid conjugation and oxidization in the gastrointestinal mucosa and the liver. Take up by the subcutaneous tissues occurs relatively slowly as a result of the local vasoconstriction and the uptake may be further reduced by systemic hypotension. Uptake is more rapid after intramuscular injection and peribulbar injections. In emergencies, it is administered intravenously[28].

Epinephrine is obtained in a number of formulations. Epinephrine is not stable in alkaline solutions. It undergoes oxidation to adrenochrome followed by formation of polymers with a change in color from pink to brown respectively[31]. Epinephrine injection is procurable in 1 mg/mL (1:1000), 0.1 mg/mL (1:10,000), and0.5 mg/ml (1:2,000) solutions.

Toxicity, Adverse Effects, and Contraindications: The most frequently encountered unwanted effects include restlessness, tremors, palpitations and throbbing headaches. More severe effects include cardiac arrhythmias and cerebral hemorrhage. The employment of high doses or the accidental, rapid intravenous injection of epinephrine may lead to cerebral hemorrhage from the alarming rise in blood pressure. Ventricular arrhythmias may be induced subsequent to the administration of epinephrine. Epinephrine usage is usually contraindicated in patients receiving non-selective β receptor antagonists, since it does not restrict the actions on vascular α1 receptors which may lead to severe hypertension and cerebral hemorrhage.

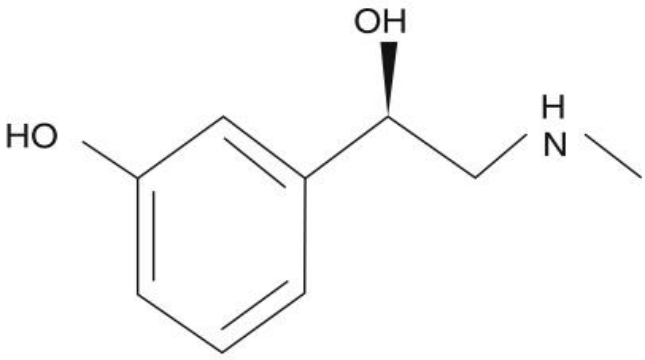
Ocular adverse effects: The most frequent side effects of topically instilled epinephrine include burning, reactive hyperemia, allergy and deposition of black oxidation products in the conjunctiva and cornea. In persons who anatomically possess a narrow iridocorneal angle, angle-closure glaucoma can be induced. A study by Ballin et al. in 1966 reported that the ocular use of topical of epinephrine has a correlation with an increased frequency of cardiac extrasystoles, hence it has to be used carefully in patients having history of heart disease, hyperthyroidism, or abnormal sensitivity to the systemic effects of epinephrine [32]. A study conducted by Thomas et al reported an increased association of topical epinephrine with cystoid macular edema (CME) in aphakic eyes[33].

Intracameral use of epinephrine especially preservative containing intracameral epinephrine may be relayed to the toxic effects on the corneal endothelium. Several studies were done on the use of intracameral mydriatic agents and its effects on the corneal endothelium[18,34,35,36,30,37]. The study conducted by Lundberg and Behndig in 2003 considered corneal oedema/thickness and endothelial

morphology as the main outcome criteria. The results of which revealed a significant morphologic modification of corneal endothelial cells which was reversible compared with the preoperative assessment. However, there was no significant variation in the postoperative endothelial cell loss, inflammatory reaction or corneal swelling if the mydriatics were administered intracamerally or topically[34].

A-YongYu et al in 2015 investigated the mydriatic effect of intracamerally injected epinephrine hydrochloride during phacoemulsification and intraocular lens(IOL) implantation in eighteen cataract patients undergoing phacoemulsification bilaterally and concluded that 1 ml intracameral epinephrine hydrochloride 0.001% appeared to be a substitute to topical mydriatics with easier preoperative preparation, increased rapid pupil dilatation, and comparable surgical performance[5].

Phenylephrine



Phenylephrine is an α 1-adrenergic agonist[37]. It causes contraction of dilator pupillae causing pupillary dilatation, constriction of conjunctival vessels causing blanching and contraction of Muller's muscle causing widening of palpebral aperture. The effect of phenylephrine on accommodation is relatively weak. It is available in single-use units in concentrations of 0.12, 2.5 and 10%[39].

Onset of mydriasis begins in about 10 minutes and reaches peak in 45–60 minutes[10].The pupil returns to pre-instillation size in 6–7 hours. Diabetics dilate slowly and less widely as compared to non-diabetics. Phenylephrine 10% has significantly higher efficacy as compared to 2.5% concentration in diabetics[40]. People with dark iris tend to develop mydriasis slowly but for a longer duration as the drug binds to pigment in iris[41]. It produces less effect on accommodation as compared to muscarinic antagonists.

In addition to its uses as a mydriatic agent, phenylephrine is also used for the following: It causes blanching of superficial conjunctival blood vessels and in very low concentrations (0.125%), it is employed as an ocular decongestant. In a concentration of 10% phenylephrine is applied topically for breaking synechiae. Topical 10% solution is also used for peripheral corneal vasoconstriction during LASIK surgery.

Phenylephrine 2.5% in combination with ecothiophate can be used to prevent the formation of miotic cysts in the treatment of open-angle glaucoma or accommodative esotropia. Phenylephrine also causes widening of the palpebral fissure by stimulation of mueller's muscle therefore ptosis resulting from sympathetic denervation such as in Horner's syndrome may respond favorably. Phenylephrine 1% is also used for the detection of Horner's syndrome. It causes marked pupillary dilatation in the eye with postganglionic sympathetic denervation but minimal or no dilatation in normal eye. If the lesion is central or preganglionic, the pupil behaves in the same way as in the normal eye[28].

Adverse Effects: Ocular adverse effects: Local adverse effects of phenylephrine include stinging, pain, lacrimation and keratitis. It can cause allergic

dermatoconjunctivitis. In elderly patients, phenylephrine causes rebound miosis; long-term repeated use results in slow and less intense mydriasis. Long-term use as an ocular decongestant causes rebound conjunctival congestion. Systemic adverse effects: Phenylephrine 10% is known to cause a rise in mean arterial blood pressure therefore elderly patients especially those with cardiovascular disease, those patients receiving tricyclic antidepressants and monoamine oxidase inhibitors are prone to develop acute rise in blood pressure following topical application of 10% phenylephrine[41,42]. Other systemic adverse effects of 10% phenylephrine include occipital headache, ventricular arrhythmias, tachycardia, reflex bradycardia, subarachnoid hemorrhage, ruptured aneurysm, skin blanching[39,41]. Phenylephrine 2.5% is rarely associated with systemic adverse effects[42,43].

Behndig and Lundberg in 2010 conducted a study to evaluate the mydriatic response to concentrations of phenylephrine injected intracamerally from 0.15 mg/mL to 30.00 mg/mL (0.015% to 3.000%). The results showed that phenylephrine when injected intracamerally does not show a linear mydriatic dose-response relationship in humans. The mydriatic response obtained was almost the same at all the 4 lower phenylephrine concentrations (0.015% to 0.500%),with ultimate sizes of the pupils of approximately 4.3 mm and greater for the two higher concentrations (mean 5.80 mm)[44].

John A. Hovanesian et al conducted a randomized clinical trial in the United States and the Netherlands in twenty centers to study the efficacy and safety of phenylephrine1.0%-ketorolac 0.3% (Omidria) for sustaining mydriasis during the procedure, and for the reduction of ocular pain after, cataract surgery in which they concluded that phenylephrine 1.0%–ketorolac 0.3% given intracamerally with

irrigation solution during cataract surgery was safe and effective for sustaining mydriasis through the procedure and decreasing postoperative ocular pain[1].

Hydroxyamphetamine

Hydroxyamphetamine is an indirect acting sympathomimetic. It stimulates the production of norepinephrine from adrenergic nerve terminals. Topical instillation of 1% solution causes pupillary dilatation and vasoconstriction. It has no significant effect on accommodation and refractive state. The time of onset of mydriasis and the time to reach the peak effect is comparable to phenylephrine 2.5%, it has an onset of action at 10 minutes and reaches its peak action in 45–60 minutes. However, the maximal dilatation may not be adequate hence it is most commonly used in combination with a muscarinic antagonist such as tropicamide 0.25%. The mydriatic effect of this combination is independent of age or color of iris[28].

Hydroxyamphetamine is useful in differentiating preganglionic or central sympathetic lesions from postganglionic lesions in Horner's syndrome. In patients with preganglionic or central lesion hydroxyamphetamine causes pupillary dilatation by stimulating release of norepinephrine from intact postganglionic fibers[45].

Adverse Effects: Topical use of hydroxyamphetamine for routine use causes little ocular irritation. Systemic absorption can elevate the blood pressure, however, tachyphylaxis develops for this effect. It is ineffective in patients with postganglionic denervation. Hydroxyamphetamine is thus safer than phenylephrine in patients with insulin-dependent diabetes, idiopathic orthostatic hypotension and patients receiving reserpine, methyldopa and guanethidine.

Atropine

Atropine is a naturally occurring alkaloid obtained from the plant Atropa belladonna (deadly nightshade). It was the first antimuscarinic used in medicine and is the most potent mydriatic cycloplegic drug[46,47,48]. It is a non-specific muscarinic antagonist and acts by competitively inhibiting the actions of acetylcholine. It acts both centrally and peripherally. It is available commercially as sulfate derivative in 1% solution or 1% ointment formulation. Following application of single drop of 1% solution, mydriasis begins in about 10 minutes and reaches peak in 25–30 minutes. It starts returning to normal size in 2 days and reaches pre-instillation size by the 10th day. Cycloplegia begins in about 15 minutes, reaches peak in about 100 minutes and disappears in 7–12 days[48].

Atropine allows measurement of refractive error without interference by the accommodative power of the eye and is, therefore, used for refraction in young children. However, shorter acting cycloplegics are now preferred. Ocular pain in patients with uveitis and corneal ulcer due to ciliary muscle spasm is relieved by atropine, which causes ciliary muscle relaxation. Some studies have shown that prolonged use of atropine may prevent or delay the progression of myopia. Atropine can also be used to provide pharmacological occlusion in the better eye for the treatment of amblyopia[49].

Adverse Effects: Topical instillation causes transient stinging. Prolonged duration of mydriasis causes photophobia and blurred vision for many days.

Contraindication: In patients with narrow angle, atropine can precipitate an acute attack and is, therefore, contraindicated in patients with angle closure glaucoma.

Topical atropine exacerbates aqueous tear deficiency and is, therefore, contraindicated in patients with dry eyes. It should be avoided in patients with previous history of allergy[28].

The pharmacological response to atropine may be potentiated if administered to patients on drugs with antimuscarinic action such as antihistaminics, tricyclic antidepressants and monoamine oxidase inhibitors.

Atropine, if absorbed systemically in significant amount can cause tachycardia, headache, flushing, dry mouth, heartburn, exacerbation of gut hypomotility, urinary retention in patients with enlarged prostate, CNS toxicity in elderly patients. Atropine should be used carefully in paediatric and elderly patients. It should be used in pregnant and lactating mothers only if clearly indicated. Measures should be taken to avoid excessive systemic absorption such as digital pressure for 2–3 minutes after topical administration. Systemic atropine toxicity presents with dry and flushed skin, fever, blurred vision, rapid and irregular pulse, distended abdomen in infants, mental aberrations and loss of neuromuscular coordination[28].

Atropine poisoning is usually selflimiting and is rarely fatal if further administration is discontinued. Treatment involves supportive measures such as maintaining the patent airways and symptomatic treatment such as for fever and CNS excitation. Physostigmine is used as the antidote[48].

Homatropine

Homatropine hydrobromide is a semi-synthetic derivative of atropine. It is available commercially in a concentration of 2% and 5%. The mydriatic effect appears in 10–20 minutes and reaches peak in 30–40 minutes. Both the light and

accommodative reflexes are lost in 30 minutes. Pupil takes 1–3 days to recover to normal size. It is a less potent antimuscarinic agent in comparison to atropine and thus results in significantly less cycloplegia as compared to similar doses of atropine and cyclopentolate. The duration of cycloplegia generated by homatropine is longer than that produced by cyclopentolate, especially in people with pigmented iris[49].

Homatropine is primarily employed for therapeutic use in the treatment of anterior uveitis as its actions are close to atropine. It is not a preferred drug for fundus examination or cycloplegic refraction because of its prolonged duration of action and relatively weak cycloplegic action.

The adverse effects and contraindications of homatropine are same as those of atropine.

Cyclopentolate

Cyclopentolate is a water soluble ester and is available commercially in concentrations of 0.5, 1 and 2% solutions[35]. It is a muscarinic cholinoceptor antagonist[3]. Instillation of two drops of 0.5% solution 5 minutes apart or one drop of 1% solution causes mydriasis in 20–30 minutes and cycloplegia in 30–40 minutes[50]. Pupillary dilatation lags behind the cycloplegia; cycloplegia appears even before the pupil is fully dilated thus facilitating early refraction. It is a less effective mydriatic in blacks and in people with black iris. In people with light iris, acceptable level of cycloplegia may appear within 10 minutes of instillation of 1% solution. In blacks and people with dark iris it may take upto 40 minutes for acceptable level of cycloplegia to appear[51]. The cycloplegic effect lasts longer in blacks and in people with black iris

as compared to people with light iris but in all eyes cycloplegia terminates within 24 hours[2,3].

Cyclopentolate is the cycloplegic agent of choice for routine cycloplegic refraction in all age groups especially in infants and young children. The cycloplegia obtained is superior to homatropine and parallels atropine. The onset of cycloplegia is faster and of shorter duration. Although complete recovery from cycloplegia takes about 24 hours, an acceptable level of recovery occurs in 12 hours[52]. The light reflex is also lost so the pupils do not constrict on exposure to bright light such as during binocular indirect ophthalmoscopic examination or fundus photography. In patients who are sensitive to atropine, cyclopentolate is employed in the treatment of anterior uveitis.

Adverse Effects and Contraindications: The most common adverse effect of cyclopentolate is stinging, burning and lacrimation. This effect is minimum at 0.5% concentration but increases as the concentration increases. In patients allergic to cyclopentolate, ocular irritation, redness, facial rash, lacrimation, white mucus discharge and blurred vision may appear within minutes or hours[53]. Repeated use of high concentration solutions of cyclopentolate over prolonged period causes diffuse epithelial punctuate keratitis with marked conjunctival hyperemia. Cyclopentolate can increase the intraocular pressure in patients having primary open-angle glaucoma and can precipitate an attack of acute glaucoma in patients with narrow angle[50].

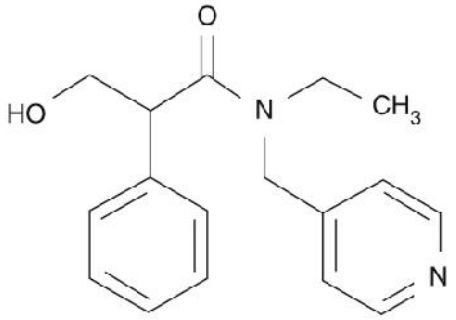
Ocular cyclopentolate was rapidly absorbed systemically, the peak concentrations being reached in 10 ± 5 minutes (mean ± S.D) after instillation of the last drop[53]. It causes adverse effects similar to atropine but the CNS effects are more common with cyclopentolate as compared to atropine[3]. CNS toxicity of

cyclopentolate is manifested as drowsiness, ataxia, disorientation, and slurred speech, and restlessness, tactile and visual hallucinations[53]. The CNS symptoms are particularly common in children when higher concentrations (2% or multiple instillations of 1%) are used[43]. CNS symptoms usually subside within 2 hours in adults and 4–6 hours in children without any permanent damage[53].

Other peripheral adverse effects of antimuscarinic agents due to systemic absorption such as flushed, dry skin and mucus membranes, fever and tachycardia are not observed with cyclopentolate. Treatment of cyclopentolate toxicity is the same as that of atropine toxicity.

In a study conducted by Lundberg and Behndig in 2008 to evaluate the individual mydriatic effects of cyclopentolate, lidocaine hydrochloride, and phenylephrine after intracameral injection and to evaluate whether intracameral lidocaine and phenylephrine can be used without cyclopentolate and still produce adequate dilatation of the pupil cataract surgery. The results showed that lidocaine alone results in significant dilatation of the pupil (mean 4.9 ± 0.6 mm). With cyclopentolate the size of the pupil increased by 1.3 ± 0.6 mm. However, following phenylephrine the size of the pupil increased by 2.1±0.5 mm. Thus, they conclude that cyclopentolate when administrated intracamerally has no instant additive mydriatic effect to intracameral lidocaine combined with phenylephrine[35].

Tropicamide



Tropicamide is a synthetic derivative of tropic acid. It is a non-selective antimuscarinic agent. Its penetration through corneal epithelium is better than atropine, homatropine and cyclopentolate and therefore, it has a quick onset and shorter duration of mydriasis. It is available in two concentrations, 0.5 and 1%. Maximum mydriasis occurs in 20–40 minutes and pupil reaches pre-instillation size in 6 hours[54]. Mydriatic effect of tropicamide is not dependent on concentration and 1% concentration produces only slightly larger pupil. Cycloplegia appears in 30–35 minutes and is dose-related. The pupillary dilatation produced by tropicamide is stronger than its cycloplegic effect. It is not a drug of choice for cycloplegic refraction[55,56,57].

Tropicaimde is free form vasopressor effects and is the safest mydriatic to use in neonates and patients with hypertension or other cardiovascular disease. Tropicamide 1% was also reported to cause greater mydriasis as compared to phenylephrine 2.5% and a combination of tropicamide 1% and phenylephrine 2.5% more effective than either of them used alone[41,43]. The size of the pupil after the use of combination is larger than that produced by hydroxyamphetamine alone or tropicamide 0.5 and 1%. The combination has an equivalent mydriatic efficacy and greater cycloplegic efficacy as compared to phenylephrine 2.5% followed by tropicamide 0.5% instillation. Its effect does not vary with age or iris pigmentation. A

combination of tropicamide 0.5% and phenylephrine 0.5%, injected intracamerally has proved to be effective and safe in dilating pupils in subjects with poor mydriasis following preoperative instillation [58].

Adverse effects and Contraindications: Adverse effects include stinging and burning sensation. In patients with narrow angle, intraocular pressure may rise. It is, therefore, avoided in patients with angle-closure glaucoma. Tropicamide is significantly absorbed in systemic circulation but it has poor affinity for systemic muscarinic receptors and, therefore, its systemic adverse effects are rare[3]. Hypersensitivity to tropicamide has been reported. Patients with hypersensitivity to belladonna also show cross sensitivity to topical tropicamide.

Lignocaine (Lidocaine, Xylocaine)

Lignocaine is currently most common employed anesthetic agent. It is the prototypical amide local anesthetic. As local injection, it is available as 1% to 2% and for topical use it is available as 4% with preservative and 1% as preservative free for intracameral use. Lidocaine at 1% concentration is prepared from 2% solution by diluting in balanced salt solution (BSS) or BSS plus or directly as a 1% unpreserved lidocaine for intracameral irrigation. Lidocaine produces more intense, rapid, longer sustaining, and more extensive anesthesia than does an equal concentration of procaine. Although it is effective when used without any vasoconstrictor, when used with epinephrine, epinephrine reduces the rate of absorption such that the toxicity is reduced and the duration of action usually is prolonged. The various routes of administration include injection, topical, mucosal, and transdermal. At the corneal surface, the onset of anesthesia is slower than with an ester on topical use as an eye drop. Lidocaine crosses rapidly the corneal epithelium and stroma causing sodium

channel blockade thus resulting in local anesthesia. Lidocaine is not degraded within the eye and thus exerts its anaesthetic effect on anterior chamber structures for a long period of nearly 20 minutes[59].

Preservative free lidocaine 1% is injected into anterior chamber immediately after first corneal incision or at hydrodissection. The drug is rapidly absorbed by iris, ciliary body and cornea. Consequently, the drug is removed by anterior chamber irrigation thus limiting tissue exposure. Intracameral lidocaine alone dilates the pupil due to the anesthetic action of the lidocaine on the nerves in the iris stroma[59,19]. Inhibiting the action of both the iris sphincter and the dilator results in the dilatation of the pupil because the sphincter has a more powerful tone than the dilator. Lidocaine has no cycloplegic effect[26,60].

Lincoff et al reported the consequence of the use of lidocaine on iris paralysis and mydriasis. They found that accidental intraocular injection of lidocaine without injection of a mydriatic drug dilated the pupil[61].

Lidocaine is metabolized in the liver by dealkylation carried out by cytochrome P450. It is converted to monoethylglycine xylidide and glycine xylidide, which can further be metabolized to monoethylglycine and xylidide. Both, the products monoethylglycine xylidide and glycine xylidide hold back their local anesthetic activity. In humans, approximately 75% of the xylidide is eliminated in the urine as a metabolite 4-hydroxy-2, 6-dimethylaniline.

Adverse effects: The most severe adverse reactions of lidocaine include seizures, coma, cardiac arrest and respiratory paralysis. The most common side effects seen are tinnitus, dizziness, twitching and drowsiness.

Cionni, Barros et al in 2003 introduced a technique with the use of preservative free lidocaine 1% to cause pupillary mydriasis without the use of any preoperative dilating eye drops. The study showed that lidocaine causes paralysis of the sphincter pupillae, achieving adequate mydriasis in about 90 seconds which was sustained or enhanced at the end of surgery[60].

Nikeghbali, Falavarjani et al conducted a prospective comparative case series in 2007 on 57 patients randomized to be administered with either topical mydriatics or intracameral lidocaine to dilate the pupil. Cyclopentolate 1% and phenylephrine 5% were the topical mydriatics administered. Preservative-free lidocaine 1% intracamerally was given to the intracameral group. The study concluded that preservative-free lidocaine 1% administered intracamerally provided rapid, effective mydriasis comparable to that of topical mydriatics[19].

A study was conducted by Rajesh Subhash Joshi at the Vasantrao Naik Government Medical College, in the Department of Ophthalmology, Yavatmal, India to study the effect of intracameral injection of preservative-free lignocaine to induce pupil dilatation, without using any preoperative dilating eye drops or intraoperative mydriatics, on 32 patients patients with age-related cataract associated with type 2 diabetes mellitus. It was concluded that intracameral lignocaine 1% delivers adequate mydriasis for a secure phacoemulsification of the cataract in patients having type 2 diabetes for a variable duration[62].

The various routes of delivery of the mydriatic drugs

The iris is a porous structure, allowing a rapid access of solutes present in the anterior chamber irrespective of size which in turn control the sphincter and dilator

muscles. Thus a drug in the anterior chamber can reach the biophase of these muscles in a very short time, and their response will correspond to that in the incubation bath of an in vitro system[25].

Topical route

Primary routes of drug delivery following topical administration of ocular drugs include cornea and conjunctiva.

Transcorneal drug Absorption- Cornea is the major site of drug absorption into the intraocular tissue following topical administration. The tight junctions in the superficial layer of corneal epithelium serve as selective barrier for the small molecules and completely prevent the diffusion of macromolecules. The corneal epithelium is hydrophobic but lipophilic in nature. High extracellular and low intracellular calcium levels are required for maintaining the normal permeability of tight junctions. Hypertonic solutions showed an increase in the leakiness of tight junctions. The corneal stoma is a rate limiting barrier to minute highly lipophilic molecules owing to its hydrophilic nature, but it permits easy passage to the hydrophilic molecules. The endothelium, which forms the innermost layer of the cornea offers little resistance to the movement of drug molecules attributable to the presence of gap junctions. Due to its biphasic solubility characteristics, cornea functions as a barrier as well as depot for the topically applied drugs. Most of the drugs diffuse through corneal epithelium the intracellular pathways but some through the intercellular pathway. Passive diffusion along the concentration gradient is the main permeation mechanism for most topically applied drugs by both inter and intracellular routes. The anatomical structure of the cornea thus delays the onset of dilatation due to the slow penetration of active ingredients through the cornea, the

time to achieve effective dilatation is longer than the cataract surgery procedure itself[2,3,4].

Transconjunctival drug Absorption - The conjunctiva consists of stratified columnar epithelium and lamina propria. The cells of which have tight junctions forming the main barrier for drug penetration. Lipophilic drugs diffuse through the intracellular pathway but hydrophilic drugs require passage through intercellular pathway. However, the intercellular spaces in conjunctival epithelium are larger than those in corneal epithelium. Thus, the conjunctiva is more permeable to hydrophilic drugs, than the cornea and molecules up to the molecular weight of 20000–40000 kilo Dalton can move through the conjunctiva. It has been proposed that Presence of carrier-mediated systems in the conjunctival epithelium plays a role in transferring drug molecules to the interior of the eye. Therefore, due to a significantly larger surface area than that of the cornea and it being highly vascular in nature the conjunctiva is a major route for the entry of topically applied drugs into the systemic circulation.

Mydriatic agents in eye drops are depot preparations; a wick soaked in standard mydriatic agents is applied on to the ocular surface[63], but the desired site of action is at the iris. The capacity of conjunctival sac is approximately 15–30 μL and the natural tear film volume is 7–8 μL. At the normal blink rate of 15–20 blinks/min, the tear turnover rate is approximately 16 % per minute. Therefore, as a result of the overspill, a significant portion of the solution is lost. The remainder approximately 80% is drained through the nasolacrimal duct until the normal tear volume is restored[8].Approximtely, around 20% of a drop is preserved in the cul-de-sac because there is only a minimal increase in the volume of the lacrimal fluid [25]. Thus, the main

disadvantages of topical mydriatic eyedrops are related to the delayed effect and low bioavailability[18].

Systemic absorption of topically delivered drugs is mainly through the open punctum into the nasolacrimal duct, followed by absorption through the lining mucosa. Absorption via the conjunctival vasculature is also an important route for systemic absorption of topical drugs[8,64]. Instillation of multiple drops at a time increases the risk of adverse effects due to enhanced systemic absorption rather than increasing the ocular bioavailability[45,20].

Standard mydriatic eyedrop regimens in cataract surgery generally combine sympathomimetic and anticholinergic agents because of their additive results. The most commonly used combinations include phenylephrine 2.5% to 10.0% with tropicamide 0.5% to 1.0% or cyclopentolate.

The integration of phenylephrine and tropicamide cumulatively has a stronger mydriatic effect than either agent used alone. When added with tropicamide 1.0%, increasing concentrations of phenylephrine causes significantly increased pupillary mydriasis however it also accelerates the heart rate. Combination of tropicamide and phenylephrine in decreased concentration (0.25% and 1.25%, respectively) can achieve sustained pupil dilatation[38,58].

In the succeeding part of a study conducted by Lundberg and Behnding in 2007, to evaluate the possibility of removing epinephrine from the irrigating solution in phacoemulsification surgery, 50 patients were randomly distributed into 2 groups, all of whom were administered with topical mydriatics. However, only in group 1, epinephrine was added to the irrigating balanced salt solution. The results of the study

showed that size of the pupils decreased intraoperatively in both groups, and significantly more in the group without epinephrine (12 ± 7%)[30].

Intracameral route

Intracameral route of drug administration is mainly used for procedures such as for pupillary dilatation**,** anesthesia for surgical procedures, prevention of intraocular infection and inflammation. This method provides immediate and easy delivery of required concentration of drug into the aqueous humor and, therefore, provides high efficacy. In the intracameral route of drug delivery the concentration of drugs used are less in comparison with those used topically, the permanence time in the anterior chamber is less than 1 minute, and no nasal mucosa absorption occurs thus decreasing the systemic absorption[18,36]. The intracameral injection of epinephrine causes little or no adverse cardiovascular effects[11,27]. The need for repeated administration, as is necessary with the use of topical route, is avoided, which is the main concern in non-compliant patients. The corneal surface toxicity associated with topical application is also avoided. Intracameral administration of medications, however, predisposes to toxic anterior segment syndrome (TASS) which is a sterile postoperative inflammation due to non-infectious causes. Presence of free radicals in the intracameral solution may contribute to endothelial toxicity leading to corneal edema[11, 65, 9]. Solutions for intraocular injections should be preservative free therefore reducing ocular toxicity.

In a study conducted by Behndig and Eriksson in 2004, no significant difference in corneal swelling and postoperative inflammation between intracameral mydriatic injection and mydriatic eye drops in high-volume cataract surgery was seen[18].

A 6 year follow-up of the randomised clinical trial conducted by Lundberg and Behndig in 2003 found that the endothelial cell loss was comparable in the intracameral mydriatic injection (15.0 ± 15.4%) and mydriatic eyedrops (16.5 ± 14.6%) treatment groups[66].

In a study conducted by Hasan Basri Cakmak et al to evaluate the effects of an injection of 1:1,00,000 dilution adrenalin with sodium bisulfite preservative on the corneal endothelium in phacoemulsification cataract surgery, 70 patients were retrospectively assessed, 36 subjects in the adrenalin group and 34 in the control group. The results showed that, in the adrenalin group, the postoperative mean corneal endothelial cell density was 2,191±268 cells/mm2 in essence lower than the preoperative mean cell density (2,270±286 cells/mm2). However, the difference between the 2 groups was not statistically significant. Thus, in this study it was concluded that an intracameral injection of 1:1,00,000 adrenaline with sodium bisulfite preservative is not harmful to the corneal endothelium[9].

The retinal effects of mydriatic eyedrops and intracameral mydriatic injections was compared in 2 randomized clinical trials (RCTs) using optical coherence tomography (OCT).The first RCT, by Johansson et al in 2007compared a binary intracameral solution (phenylephrine 1.5%–lidocaine 1.0%) and mydriatic eyedrops (cyclopentolate 1.0%–phenylephrine 10.0%) associated with intracameral lidocaine. It found a significant increase from preoperative values in mean retinal thickness and macular volume in both treatment groups at 1 week, with no significant between-group difference[67].

The second RCT by Bozkurt et al in 2010 compared retinal changes in patients dilated with the usual mydriatic eyedrops and with or without intracameral

epinephrine. The follow-up extended to 6 months. The study found significantly increased macular thickness from the baseline at 1, 3 and 6 months in both groups, with no significant difference between the groups at any time[68].

The intracameral injection of epinephrine causes little or no adverse cardiovascular effects. Several studies conducted to assess the changes in cardiovascular variables like blood pressure, heart rate, oxygen saturation associated with intracameral mydriatic injections showed that the changes are minimal and do not differ from those expected with conventional mydriatic eyedrops[18,34,36].

A study conducted by Morgado G et al in 2010 to compare the cardiovascular safety of the mydriatic options included three groups; Group A topical mydriatics, group B Mydriasert, and group C intracameral mydriatics with 30 eyes in each group found that the incidence of intraoperative high systolic blood pressure was 30% in the mydriatic eyedrops group, 10% in the mydriatic ophthalmic Insert group and 6.6% in the intracameral mydriatic injections group. Thus concluding that in view of the cardiovascular safety profile intracameral mydriasis was the most safe and topical mydriasis the least safe option[23].

Comparative Studies of Intracameral Combined Solutions and Mydriatic Eyedrops

The intracameral procedure is based on, injecting a mydriatic agent into the anterior chamber at the start of the surgery. In 2003, Lundberg and Behndig published a prospective, randomized, double-masked study in which the patients were randomly given either of the two treatments: traditional topical mydriatics with cyclopentolate 1% and phenylephrine10% plus preservative-free lignocaine 1% intracamerally at the

start of the procedure, or intracameral mydriatics with cyclopentolate 1%, phenylephrine 1.5% and lignocaine 1% intracamerally. The size of the pupils was noted during surgery, at one day and one month postoperatively. Also, the corneal endothelial cell morphology, visual acuity, intraocular pressure (IOP), intraoperative blood pressure and pulse was assessed. They observed that size of the pupils following viscoelastic injection was 6.7±1.0mm in the intracameral group which was smaller than that obtained with topical mydriatics initially. However, the pupils continued to increase in size throughout the procedure as opposed to when topical mydriatics were employed. The corneal endothelial morphology showed no difference between intracameral and topical mydriatics. A significant pulse deceleration was observed with the topical, but not with the intracameral mydriatics. Thus, concluding that the intracameral mydriatic regimen is a safe, rapid and effective substitute to topical mydriatics in phacoemulsification cataract surgery[34].

Myers and Shugar in 2009 conducted a prospective study to compare the efficacy of epi-shuggarcaine (epinephrine 0.025% and lidocaine 0.75% in fortified balanced salt solution) with that of lundberg behndig intracameral dilatation solution (cyclopentolate 0.1%, phenyephrine1.5% and lidocaine1%) for intracameral dilatation during cataract surgery. 42 patients were randomly distributed into the 2 groups both groups received 1 drop of tropicamide 1% at least 20 min prior to surgery. At the end of the study it was found that the pupil was significantly larger with the epi-shuggarcaine solution than with lundberg behndig solution averaging 0.528mm larger 1 min after instillation to 0.34mm larger at the end[31].

In a study conducted by Morgado et al in 2010 to study the mydriatic efficacy and cardiovascular safety of the mydriatic agents.90 eyes were randomly distributed

into 3 groups with topical mydriatics, Mydriasert, and intracameral mydriatics for pupillary mydriasis. The study concluded that the most fruitful mydriasis was obtained within the Mydriasert group, the topical mydriasis group followed. However, intracameral mydriasis was safer in comparison to topical mydriasis from the cardiovascular objective.[6].

Soong et al pilot study of 10 patients having routine phacoemulsification cataract surgery. For intracameral mydriasis, 0.15 mL solution consisting of cyclopentolate hydrochloride 0.1%, phenylephrine hydrochloride 1.5%, and preservative-free lignocaine 1% was used with balanced salt solution. The parameters monitored were blood pressure and pulse of all cases preoperatively and perioperatively. Results showed that the mean alteration in systolic blood pressure was 8.95 mm Hg, diastolic blood pressure was 6.675 mm Hg, and pulse was 10.11beats/min. They thus concluded that the intracameral route of administering mydriatics delivers minute doses of the drugs to the target organ to achieve the desired effect, minimizing potential cardiovascular side effects[69].

Yosai Mori MD et al in 2011 conducted a clinical trial to scrutinize the effectiveness and safety of intracameral injection of commercially available eye drops composed of 0.5% tropicamide and 0.5% phenylephrine hydrochloride (mydrin-P). The results showed that human corneal endothelial cell morphology was constant after Mydrin-P injection and the mean ratio of the pupillary diameter to corneal diameter grew in the intraocular mydriasis group (before: 54.2±4.8%, after: 58.4±6.6%; $P<0.001$) as compared to the control group. Thus, they concluded that the intracameral injection of Mydrin-P appeared to be an efficacious and safe substitute to preoperative instillation of mydriatics[70].

In a study conducted in the year 2014 by Gupta SK et al, 30 patients underwent phacoemulsification under topical anaesthesia with intracameral irrigation solution of 0.5% lignocaine and 0.001% epinephrine to initiate and maintain pupillary mydriasis. At the end of the study it was found that pupil size increased on average from 2.1mm to 6.9mm at the termination of the surgery. Thus, concluding that the intracameral mydriatic solution of lignocaine (0.5%) and epinephrine (0.001%) provides rapid and sustained mydriasis for phacoemulsification[13].

In a study conducted by A-Yong Yu et al in 2016 to investigate mydriatic effect of intracamerally injected epinephrine hydrochloride during phacoemulsification and intraocular lens (IOL) implantation, 18 subjects for bilateral phacoemulsification were randomly chosen to receive intracamerally 1mL epinephrine hydrochloride 0.001% in one eye and tropicamide 0.5% and phenylephrine 0.5% in the contralateral eye. Results showed the mean diameter of the pupil in the intracameral group was 2.20 ± 0.08, 5.09 ± 0.20, 6.76 ± 0.19, 6.48 ± 0.18,and 5.97 ± 0.24mm, respectively, in the topical group it was 7.98 ± 0.15, 7.98 ± 0.15, 8.53 ± 0.14, 8.27 ± 0.16,and7.93 ±0.20mm, respectively. Thus, they concluded that Intracameral epinephrine hydrochloride appeared to be a substitute to the mydriatic modalities for phacoemulsification and IOL implantation. In contrast to topical mydriatics, intracameral epinephrine hydrochloride offers easier preoperative preparation, more rapid pupil dilatation, and comparable surgical performance[5].

Ajay, et al in 2017 carried out a randomized clinical trial on 127 patients who were randomly distributed into 2 groups one of which received topical mydriatics (tropicamide 0.8% plus phenylephrine 5% drops) and the other intracameral mydriatics (0.5% lignocaine plus 0.001% epinephrine). Both groups were subjected to

MSICS under peribulbar block. Mean pupil size prior to the peribulbar block was 7.3 mm in topical group and 3.3 mm in intracameral group. Mean pupil size in intracameral group increased to 7.3 mm 30 seconds after injecting the intracameral dilating solution. However, the mean pupil size in both groups progressively reduced, reaching 5.1 mm and 5.5 mm, respectively, at the end of surgery. Thus, they concluded that the intracameral mydriatic solution could be a safe and effective alternative to topical mydriatics[71].

METHODOLOGY

The present study was conducted in the Department of Ophthalmology, KLES Dr.Prabhakar Kore Hospital and Medical Research Centre, Belagavi to study safety and efficacy of an intracameral mydriatic regimen comprising of preservative free lignocaine 0.5% and epinephrine 0.001% in initiating and maintaining the pupillary mydriasis during phacoemulsification in comparison with traditional preoperative topical mydriatic eye drops. To evaluate perioperative circulatory side effects of intracameral epinephrine used as a component of the intracameral mydriatic regimen during the period of 1stJanuary 2016 to 31st December 2016. The study was approved by the Ethical and Research Committee of Jawaharlal Nehru Medical College, Belagavi

Source of data:

All patients diagnosed with cataract and admitted for the purpose of phacoemulsification cataract surgery at Dr.Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

Method of collection of data

Study Design: A randomized clinical trial

Study Period: One year – 1st January 2016 to 31st December 2016.

Sample Size:

Sample size of 50 cases.

50 patients were randomly distributed into 2 groups 25 each group. Randomization was done with the help of random number table.

Sample size was calculated by the following formula

X_1- mean pupil size with intracameral mydriatics

X_2-mean pupil size with topical mydriatics

$$N=\frac{2(Z_\alpha+Z_\beta)^2(S_1^2+S_2^2)}{(X_1-X_2)^2}$$

$$=\frac{2(1.96+0.84)^2\,(0.9^2+0.9^2)}{(7-8)^2}$$

25.088 Approximately 25 for each group

Selection Criteria:

Inclusion criteria

Patients with-

1. Age related cataract planned for phacoemulsification cataract surgery.
2. Minimum pupillary dilatation 6mm checked 1 day prior to surgery with tropicamide 0.8%, phenylephrine hydrochloride 5% and chlorbutol as preservative.

Exclusion criteria

Patients with-

1. Uncooperative attitude; unable to understand and follow verbal commands (children, mentally challenged, involuntary movements)
2. Previous same eye ocular surgery
3. Pupillary deformity
4. Allergy to components of medicine; sensitivity to lignocaine, epinephrine

5. Use of topical or systemic NSAID /prostaglandins / parasympathomimetics.
6. Maximum pupillary dilatation of <6mm
7. Ocular diseases other than cataract

Methodology proper

1. All the patients who satisfy the inclusion criteria were included in the study. The patients were enrolled into the study and written informed consent was taken after explaining the procedure and associated risk.
2. Data regarding demographic parameters such as age, sex, occupation and address were noted on a predesigned proforma at the time of first visit.
3. Detailed history of following symptoms was noted:

- H/O Diminution of vision RE/LE
    A. Duration
    B. Gradual/Sudden
    C. Progression/static
    D. Distant/Near vision
    E. Visual improvement with bright light or dim light
    F. Painful/ Painless
- Diplopia/Polyopia
- Photophobia
- Flashes of light
- Coloured halos
- Floaters
- Watering
- Redness

- Discharge
- Black spots in front of the eye
- H/O Curtain falling in front of the eyes
- H/O wearing glasses
- H/O Diabetes Mellitus, Hypertension.

4. History was followed by ocular examination on the day prior to surgery.

- Visual acuity testing for distance and near using Snellen's distant chart and Jaeger's near vision chart respectively, both unaided and aided.
- External ocular examination
- Slit lamp biomicroscopic examination for evidence of the following findings.

    A. Pseudoexfoliation material at the pupillary margins.

    B. Pseudoexfoliation material on the cornea

    C. Anterior chamber depth

    D. Presence of posterior synechiae.

    E. Pseudoexfoliation on the anterior surface of the lens capsule.

    F. Pupillary reaction

    G. Measurement of pupil size

- IOP was measured with Non Contact Tonometer
- The pupil was dilated with topical mydriatic eye drops containing tropicamide 0.8%, phenylephrine hydrochloride5%, with chlorbutol as a preservative to measure the maximum pupillary diameter.
- Detailed Slit lamp examination was done for the following
    - ✓ Measuring pupil dilatation. 6 mm or more was considered sufficient dilatation - the inclusion criteria
    - ✓ Examination of lens capsule for pseudoexfoliation material deposition.

- ✓ Evaluation of lens for the type of cataract and grading of the cataract

- A thorough posterior segment evaluation was done using direct and indirect ophthalmoscopy.
- Keratometry
- A scan was done for calculation of the power of the intraocular lens to be used.
- Patency of the lacrimal drainage pathway was checked by lacrimal sac syringing.
- Basal parameters such as pulse rate, blood pressure, random blood sugar levels were assessed.
- Xylocaine sensitivity test.
- On the night prior to surgery patients were given alprazolam 0.5mg.
- On the day of surgery patients in each group were given acetazolamide 250mg stat.

Surgical technique

- ✓ The first group received:
    a. For Topical mydriatics: tropicamide 0.8% and phenylephrine hydrochloride 5% with chlorbutol as a preservative eye drops at 15 minutes intervals, 1 hour prior to surgery.
    b. For topical anaesthesia: proparacaine hydrochloride 0.5% with chlorbutol as a preservative eye drops every 15 minutes, 45 minutes prior to surgery
- ✓ The second group received:

a. For topical anaesthesia: proparacaine 0.5% with chlorbutol as a preservative every 15 minutes, 45 minutes prior to surgery

- ✓ Prior to surgery the intracameral mydriatic regimen was prepared -2ml 1:1000 epinephrine is added to 50 ml 2% preservative free lignocaine, 0.5 ml of this was combined with 1.5 ml of Balanced Salt Solution giving a concentration of lignocaine 0.5%, and epinephrine 0.001%.

The steps of the surgery

- ✓ Under all aseptic precautions eye painted with povidone iodine and draped, universal eye speculum put and copious amounts of lignocaine jelly 2% poured on the exposed ocular surface to cover it.
- ✓ After waiting for 90 seconds superior rectus bridle suture was taken.
- ✓ Fornix based conjunctival flap raised, hemostasis achieved with wet field cautery.
- ✓ Scleral incision taken 6.5 mm, made 1.5 mm posterior to surgical limbus with 11 number blade at the 12 o'clock position.
- ✓ Selfsealing sclerocorneal tunnel was made using a crescent knife and dissection continued 1 mm into clear cornea
- ✓ Side port entry was made at 10 o'clock and 2 o'clock position.
- ✓ Anterior chamber was entered from the anterior limit of sclerocorneal tunnel using a 2.8 mm keratome

a. In the first group for supplementing the topical anaesthesia anterior chamber was irrigated with intracameral preservative free lignocaine 1%.

b. In the second group anterior chamber was irrigated with the intracameral mydriatic regimen comprising of a 2ml solution of 1.5 ml balanced salt solution (BSS) with 0.5 ml combination of preservative free lignocaine 0.5% and adrenaline 0.001%.

- ✓ Formation of a capsulorrhexis with a cystitome
- ✓ Hydrodelineation
- ✓ Lens removal through phacoemulsification and aspiration of the lens substance
- ✓ Aspiration of the remaining lens cortex either with simcoe irrigation/aspiration cannula or bimanual irrigation aspiration hand pieces
- ✓ Injection of viscoelastic material into the anterior chamber followed by insertion of a rigid IOL (PMMA) into the capsular bag
- ✓ Removal of the viscoelastic material
- ✓ Anterior chamber was maintained
- ✓ Topical antibiotic eye drops were put
- ✓ Eye padded and patched

During the above procedure the following parameters were noted in both groups-

A. <u>Pupil size measurement with Castroviejo Caliper</u>

In Group 1 who received topical mydriatics pupil size was measured

- ✓ Before the use of topical mydriatics.
- ✓ Just before the incision.
- ✓ At the end of surgery.

In Group 2 who received intracameral mydriatics pupil size was measured

- ✓ Just before the incision.

- ✓ 30 seconds after instilling the mydriatic agent in the anterior chamber.
- ✓ At the end of surgery.

B. Pulse rate and blood pressure

In Group 1 who received topical mydriatics blood pressure and pulse rate was measured

- ✓ Before the use of topical mydriatics.
- ✓ Just before the incision.
- ✓ At the end of surgery

In Group 2 who received intracameral mydriatics blood pressure and pulse rate was measured

- ✓ Just before the incision
- ✓ 30 seconds after instilling the mydriatic agent in the anterior chamber
- ✓ At the end of surgery

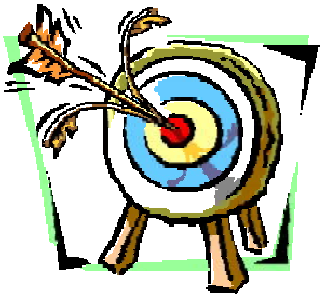
On the day following surgery the following was assessed

1. Uncorrected and pinhole visual acuity was noted.
2. Detailed slit lamp examination was done
3. IOP was noted using noncontact tonometer

Statistical analysis

The data was tabulated on Microsoft excel spread sheet. The data was analyzed using SPSS version 20.0 Categorical data was expressed as rates, ratios and percentages and continuous data was expressed as mean ± SD. Categorical data was compared using Chi-square test or Fisher's exact test and continuous data was compared using independent sample 't' test. Within group comparison was done using Wilcoxon Signed Rank test. A probability value of ≤ 0.050 at 95% confidence interval was considered as statistically significant

Introduction



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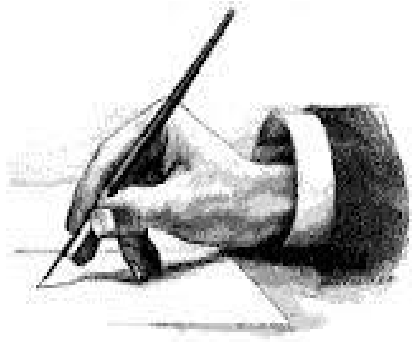


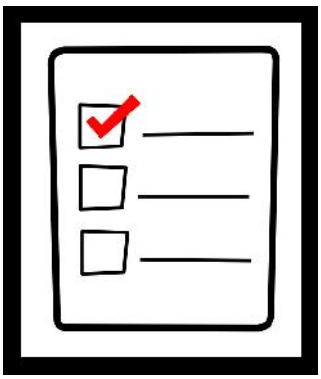
Annexure-I

Annexure-II

Annexure-III

Annexure-IV

Annexure-V



Annexure-IV

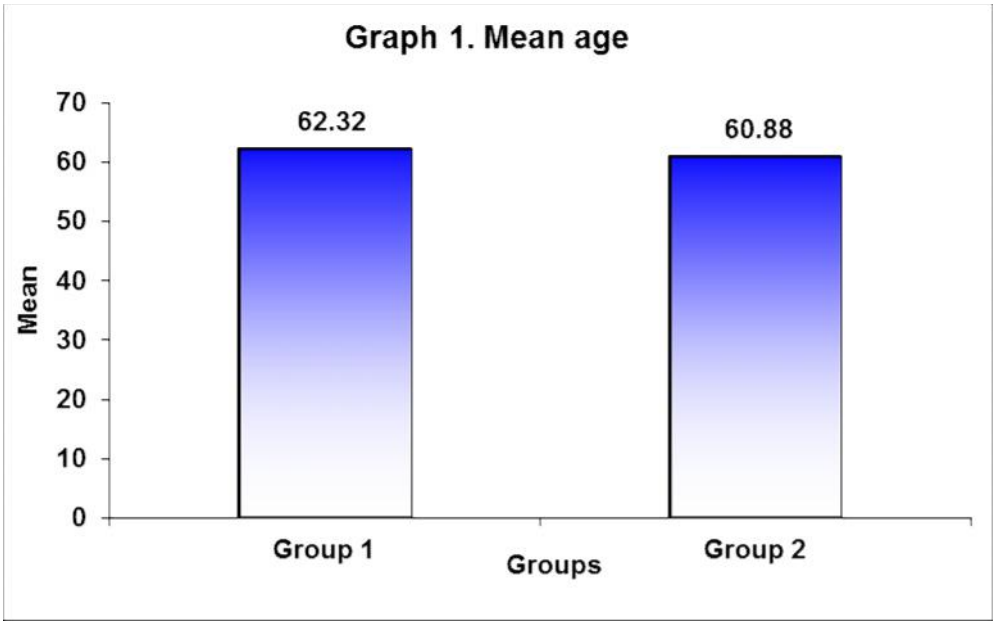
RESULTS

The present study was conducted in the department of Ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi on subjects with cataract undergoing phacoemulsification cataract surgery.The patients were divided into two groups that is Group 1 (Topical mydriatics containing tropicamide 0.8% and phenylephrine hydrochloride 5% with chlorbutol as a preservative was used for pupillary mydriasis) and Group 2 (Intracameral mydriatic regimen of preservative free epinephrine 0.001 % with lignocaine 0.5% was used for pupillary mydriasis) The data obtained was tabulated as below.

The data was tabulated on Microsoft excel spread sheet. The data was analyzed using SPSS version 20.0 Categorical data was expressed as rates, ratios and percentages and continuous data was expressed as mean ± SD. Categorical data was compared using Chi-square test or Fisher's exact test and continuous data was compared using independent sample 't' test. Within group comparison was done using Wilcoxon Signed Rank test. A probability value of ≤ 0.050 at 95% confidence interval was considered as statistically significant.

Table 1. Mean age

Variables	Group 1 (n=25)		Group 2 (n=25)		p value
	Mean	SD	Mean	SD	
Age (Years)	62.32	7.66	60.88	9.19	0.550

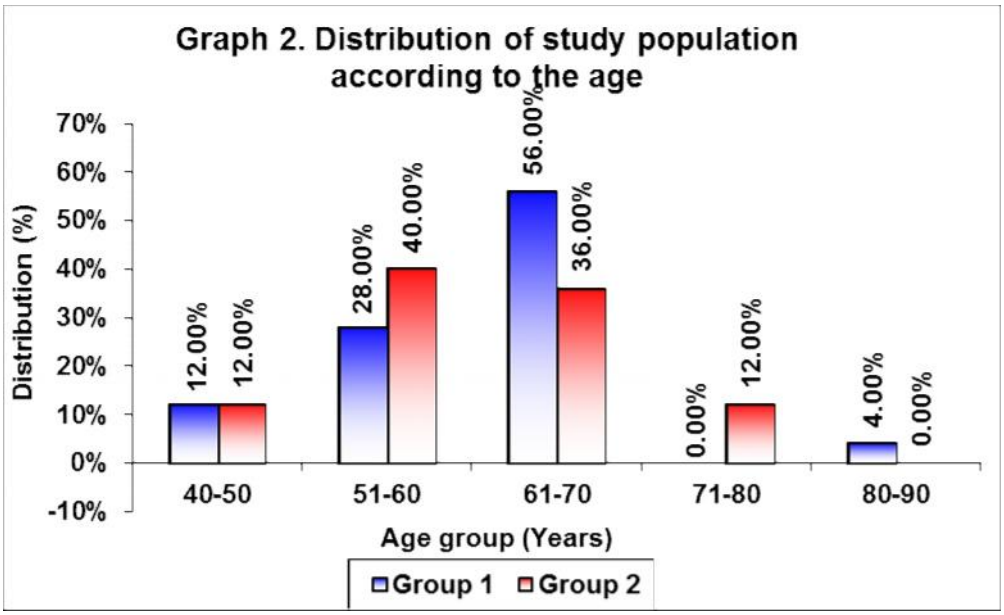


In our study the mean age in group 1 was 62.32 years and in group 2 it was 60.88 years (P=0.550).

Table 2. Distribution of study population according to the age

Age group (Years)	Group 1 (n=25)		Group 2 (n=25)	
	Number	Percentage	Number	Percentage
40-50	3	12.00	3	12.00
51-60	7	28.00	10	40.00
61-70	14	56.00	9	36.00
71-80	0	0.00	3	12.00
80-90	1	4.00	0	0.00
Total	**25**	**100.00**	**25**	**100.00**

p = 0.223

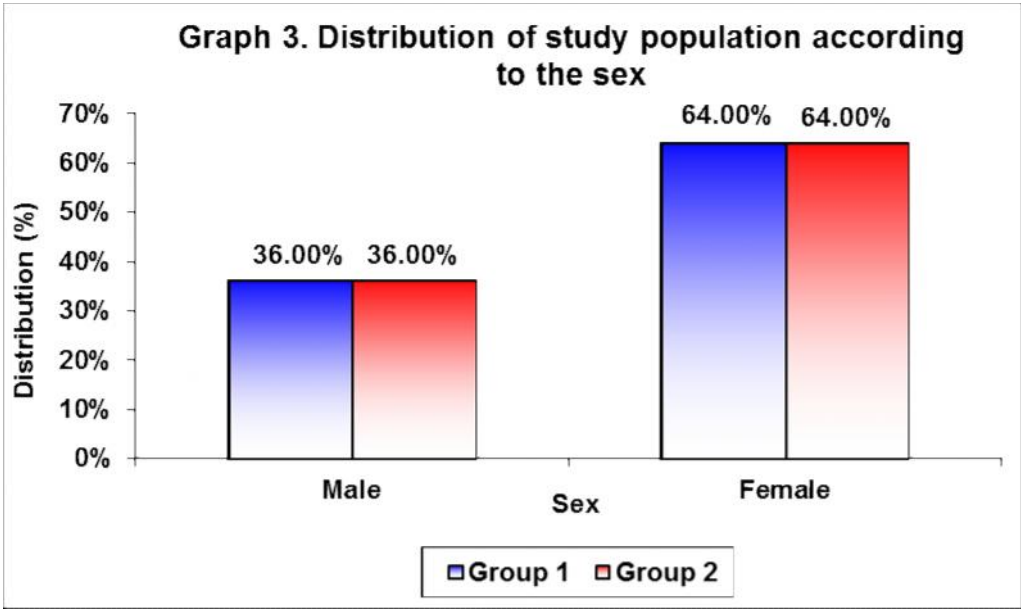


In both groups the majority of the patients were in the age group of 51 to 70 years.

Table 3. Distribution of study population according to the sex

Sex	Group 1 (n=25)		Group 2 (n=25)	
	Number	**Percentage**	**Number**	**Percentage**
Male	9	36.00	9	36.00
Female	16	64.00	16	64.00
Total	**25**	**100.00**	**25**	**100.00**

x^2< 0.001 **p = 1.000**

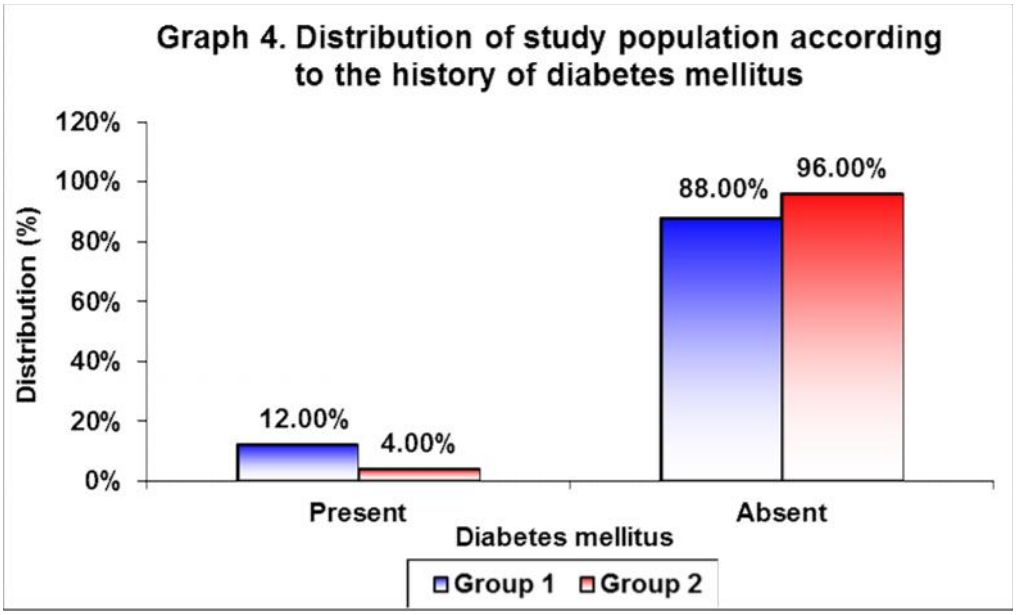


In group 1, 64% of patients were females and 36% were male with a male to female ratio of 0.56 In group 2, 36% were males and 64% were females with a male to female ratio of 0.56 (P=1.000).

Table 4. Distribution of study population according to the history of diabetes mellitus

Diabetes mellitus	Group 1 (n=25)		Group 2 (n=25)	
	Number	**Percentage**	**Number**	**Percentage**
Present	3	12.00	1	4.00
Absent	22	88.00	24	96.00
Total	**25**	**100.00**	**25**	**100.00**

p = 0.305

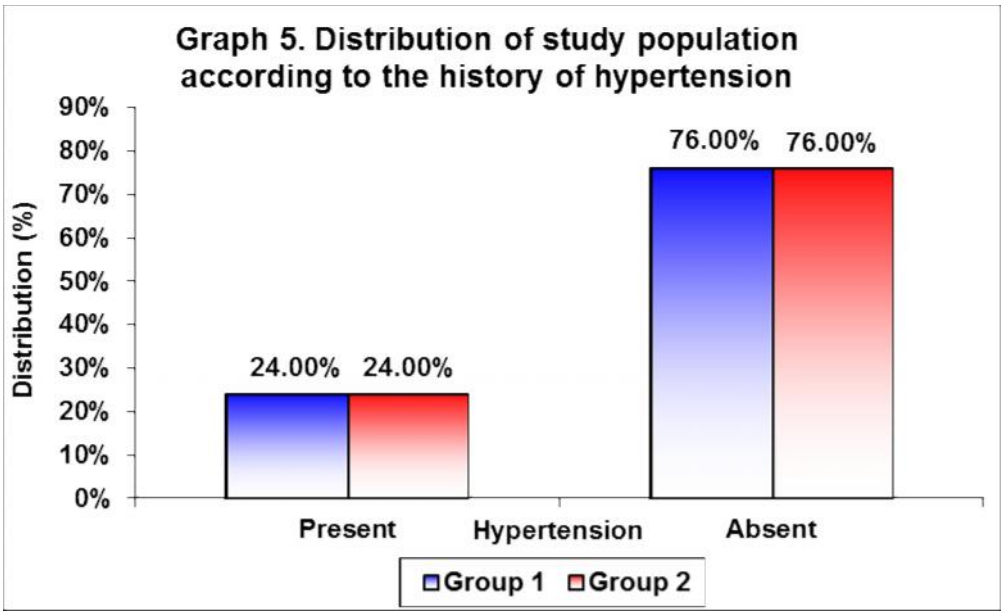


The distribution of patients with diabetes mellitus in both groups was as follows; patients with diabetes and cataract were 12% in group 1 and 4% in group 2 (p=0.305).

Table5. Distribution of study population according to the history of hypertension

Hypertension	Group 1 (n=25)		Group 2 (n=25)	
	Number	Percentage	Number	Percentage
Present	6	24.00	6	24.00
Absent	19	76.00	19	76.00
Total	**25**	**100.00**	**25**	**100.00**

x^2< 0.001 **p = 1.000**

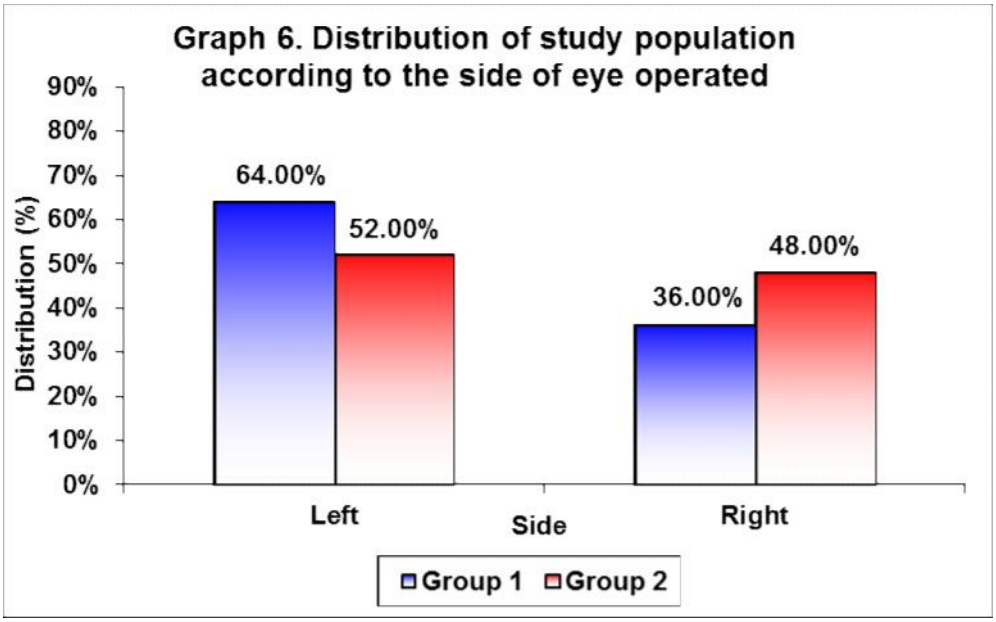


The distribution of patients with hypertension in group in both the groups was as follows; patients with cataract and hypertension were 24% in group 1 and 24% in group 2 (p = 1.000).

Table 6. Distribution of study population according to the side of eye operated

Side	Group 1 (n=25)		Group 2 (n=25)	
	Number	**Percentage**	**Number**	**Percentage**
Left	16	64.00	13	52.00
Right	9	36.00	12	48.00
Total	**25**	**100.00**	**25**	**100.00**

x^2=0.739 **p = 0.390**



In 52% patients left eye was operated while 48% underwent right eye cataract surgery.

Table 7. Distribution of study population according to the pre operative vision

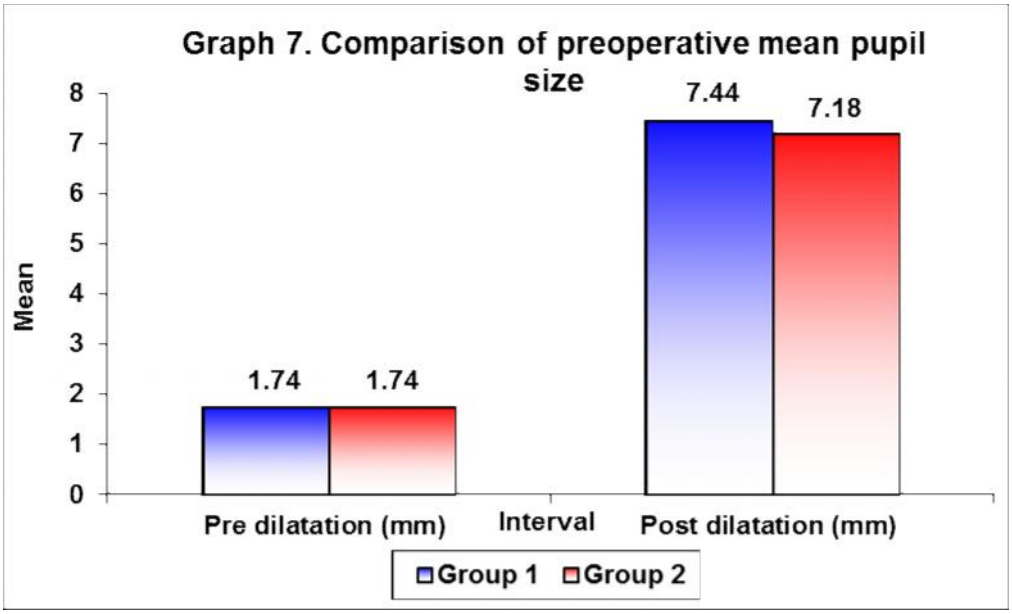
Vision	Group 1 (n=25)		Group 2 (n=25)	
	Number	**Percentage**	**Number**	**Percentage**
6/18	1	4.00	0	0.00
6/18(P)	0	0.00	1	4.00
6/24	2	8.00	1	4.00
6/24(P)	0	0.00	1	4.00
6/36	3	12.00	1	4.00
6/60	3	12.00	5	20.00
CF0.5MT	3	12.00	0	0.00
CF1.5MT	0	0.00	2	8.00
CF1MT	4	16.00	2	8.00
CF2.5MT	0	0.00	1	4.00
CF2MT	3	12.00	7	28.00
CF3MT	4	16.00	2	8.00
CF4MT	1	4.00	1	4.00
CF5MT	0	0.00	1	4.00
HMCF	1	4.00	0	0.00
Total	**25**	**100.00**	**25**	**100.00**

x^2=15.767 **p = 0.328**

In group 1, 36% of the patients had vision ranging from 6/18 to 6/60 while 64% of the patients had vision ranging from hand movements close to face to counting fingers at 5 meters. Similarly in group 2, 36% of patient had vision ranging from 6/18 to 6/60 while majority of the patients i.e 64% had vision ranging from hand movements close to face to counting fingers at 5 meters($p = 0.328$).

Table 8. Comparison of pre operative mean pupil size

Interval	Group 1 (n=25)		Group 2 (n=25)		p value
	Mean	SD	Mean	SD	
Pre dilatation (mm)	1.74	0.29	1.74	0.29	1.000
Post dilatation (mm)	7.44	0.49	7.18	0.38	**0.040**

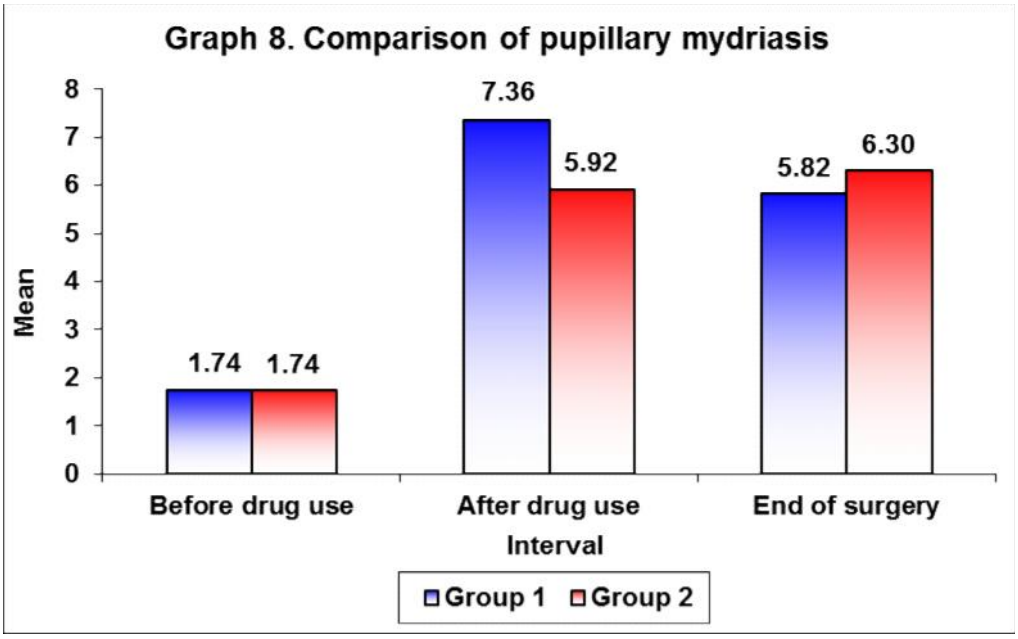


Mean pupillary diameter prior to pupil dilatation in group 1 was 1.74 mm with a SD of 0.29, in group 2 was 1.74 mm with a SD of 0.29 (p=1.000). Post dilatation the mean pupillary diameter in group 1 was 7.44 mm with SD of 0.49 and in group 2 was 7.18 mm with a SD of 0.38 (p= 0.040).

Table 9. Comparison of Intraoperative pupillary mydriasis

Interval	Group 1 (n=25)		Group 2 (n=25)		p value
	Mean	SD	Mean	SD	
Before drug use	1.74	0.29	1.74	0.29	1.000
After drug use	7.36	0.57	5.92	0.64	**<0.001**
End of surgery	5.82	1.05	6.30	1.24	0.147
t value	-4.450		-4.442		
*p value	< 0.001		<0.001		

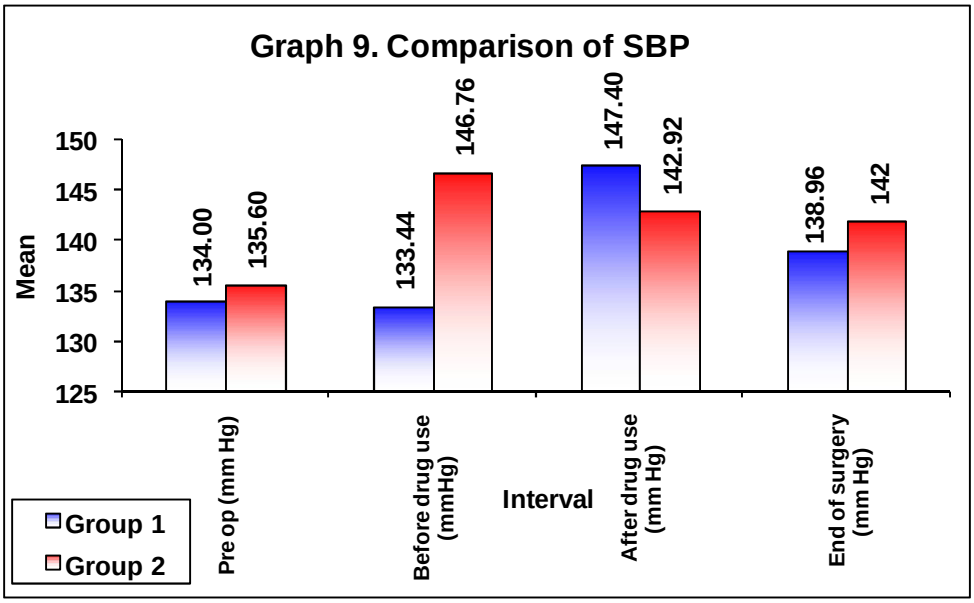
*** within group comparison**



In group 1 prior to the use of topical mydriatics pupil diameter was 1.74 mm with a SD of 0.29 and in group 2 prior to the use of intracameral mydriatics was 1.74 mm with a SD of 0.29. ($p=1.000$). After the use of topical mydriatics in group 1 the mean pupil size increased to 7.36 mm with a SD of 0.57 while in group 2 following the use of intracameral mydriatics it increased to mean pupil size of 5.92 mm with a SD of 0.64 ($p<0.001$). At the end of surgery pupil diameter in group 1 was 5.82 mm with a SD of 1.05 and in group 2 it was 6.30 mm with a SD of 1.24 ($p=0.147$).

Table 10. Comparison of systolic blood pressure (SBP)

Interval	Group 1 (n=25)		Group 2 (n=25)		p value
	Mean	SD	Mean	SD	
Pre op (mm Hg)	134.00	13.54	135.60	10.03	0.637
Intraoperative					
Before drug use (mm Hg)	133.44	14.23	146.76	16.48	**0.004**
After drug use (mm Hg)	147.40	17.15	142.92	16.14	0.346
End of surgery (mm Hg)	138.96	30.78	142.00	13.87	0.655

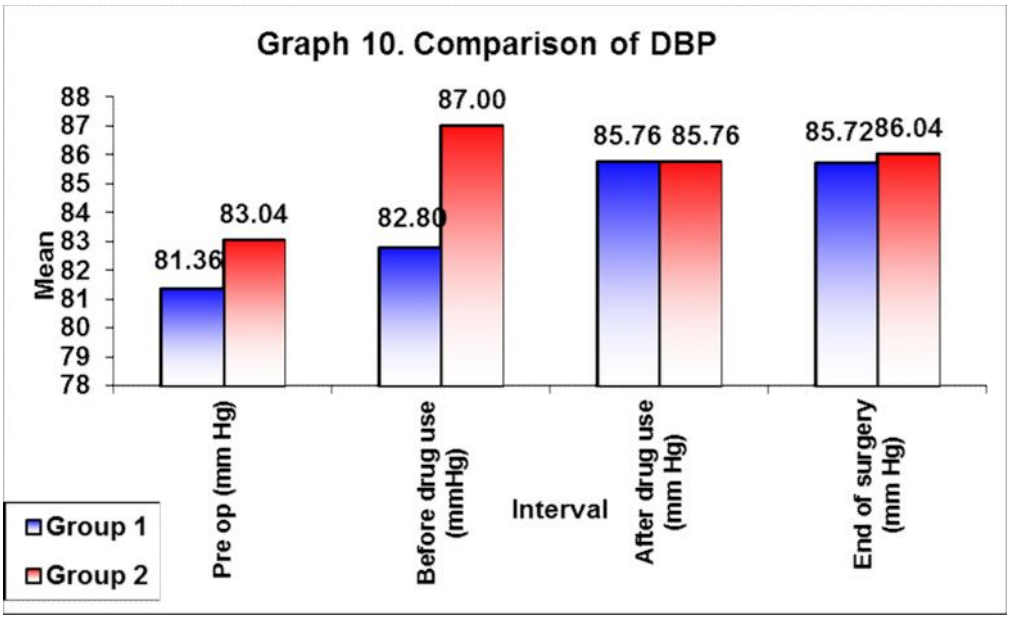


The mean systolic blood pressure on the day prior to surgery in group 1 was 134 mmHg with a SD of 13.54 and in group 2 was 135.60 mmHg with a SD of 10.03. (p=0.637). The mean systolic blood pressure on the day of surgery in group 1 prior to the use of topical mydriatics was 133.44 mmHg with a SD of 14.23 and in group 2

prior to the use of intracameral mydriatics was 146.76 mmHg with a SD of 16.42 (p=0.004). After the use of topical mydriatics in group 1 the mean systolic blood pressure was 147.40 mmHg with a SD of 17.5 and after the use of intracameral mydriatics in group 2 was 142.92 mmHg with a SD of 16.14 (p=0.346). At the end of surgery in group 1 the mean systolic blood pressure was 138.96 mmHg with a SD of 30.78 and in group 2 was 142.00 mmHg with a SD of 13.87 (p=0.655).

Table 11. Comparison of diastolic blood pressure (DBP)

Interval	Group 1 (n=25)		Group 2 (n=25)		p value
	Mean	SD	Mean	SD	
Pre op (mm Hg)	81.36	9.01	83.04	8.13	0.492
Intraoperative					
Before drug use (mm Hg)	82.80	9.35	87.00	8.01	0.095
After drug use (mm Hg)	85.76	10.14	85.76	8.06	1.000
End of surgery (mm Hg)	85.72	10.34	86.04	7.67	0.902

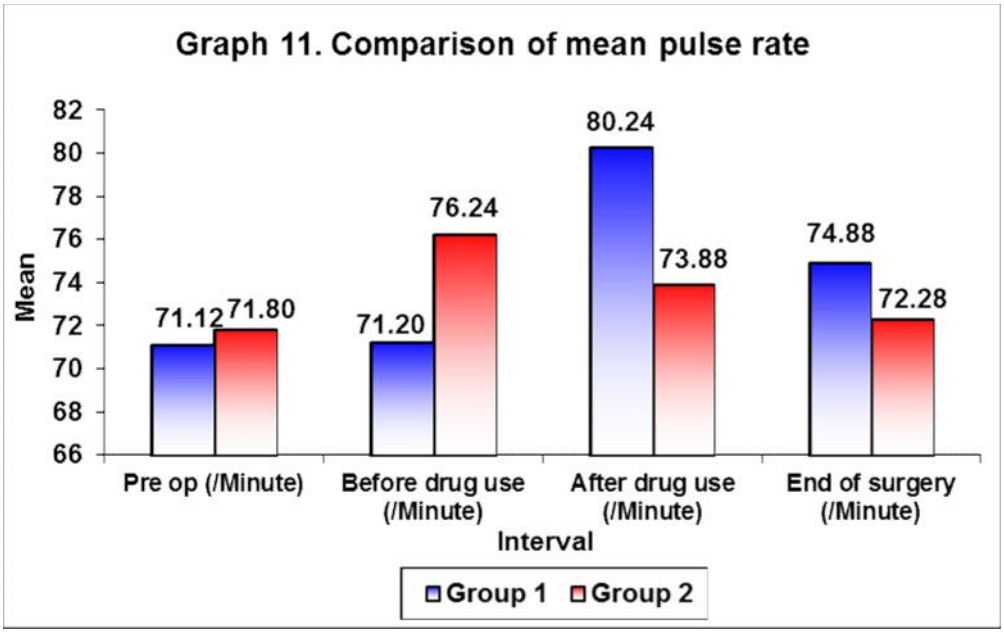


The mean diastolic blood pressure on the day prior to surgery in group 1 was 81.36 mmHg with a SD of 9.01 and in group 2 was 83.04 mmHg with a SD of 8.13. (p=0.492).The mean diastolic blood pressure on the day of surgery in group 1 prior to the use of topical mydriatics was 82.80 mmHg with SD of 9.35 and in group 2 prior

to the use of intracameral mydriatics was 87 mmHg with a SD of 8.01 (p=0.095). Following the use topical mydriatics in group 1 the mean diastolic blood pressure was 85.76 mmHg with a SD of 10.14 and after the use of intracameral mydriatics in group 2 was 85.76 mmHg with a SD of 8.06 (p=1.000). At the end of surgery the mean diastolic blood pressure being 85.72 mmHg in group 1 with a SD of 10.34 and 86.04 mmHg in group 2 with a SD of 7.67 (p=0.962).

Table 12. Comparison of mean pulse rate

Interval	Group 1 (n=25)		Group 2 (n=25)		p value
	Mean	SD	Mean	SD	
Pre op (/Minute)	71.12	8.02	71.80	7.62	0.760
Intraoperative					
Before drug use (/Minute)	71.20	8.60	76.24	13.14	0.116
After drug use (/Minute)	80.24	16.75	73.88	10.90	0.119
End of surgery (/Minute)	74.88	14.30	72.28	10.34	0.465

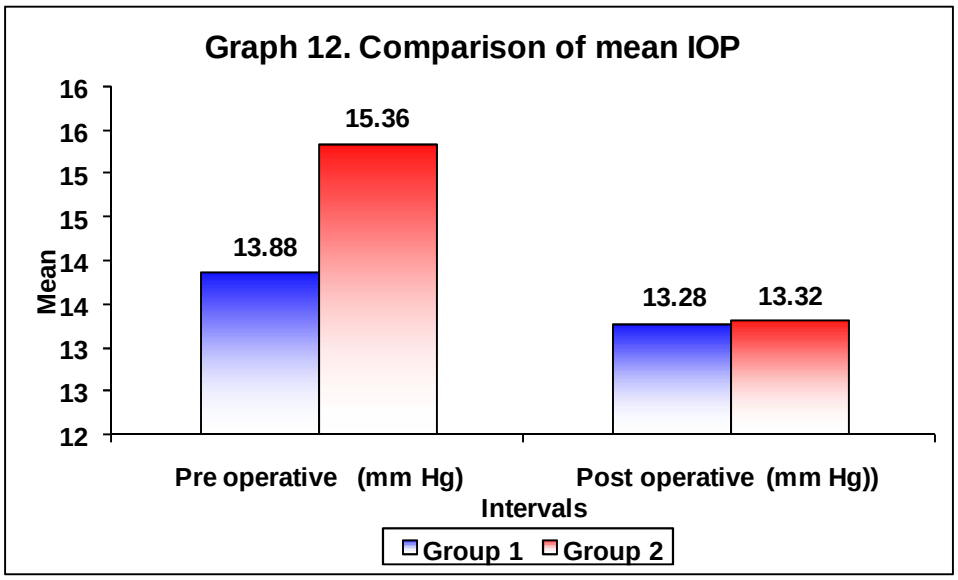


The mean pulse rate assessed on the day prior to surgery in group 1 was 71.12 beats/min with a SD of 8.02 and in group 2 was 71.80 beats/min with a SD of 7.62. (p=0.760). The mean pulse rate on the day of surgery prior to the use of topical mydriatics in group 1 was 71.20 beats/min with a SD of 8.60 and prior to the use of

intracameral mydriatics in group 2 was 76.24 beats/min with a SD of 13.14 (p=0.001). After the use of topical mydriatics in group 1 the mean pulse rate increased to 80.24 beats/min with a SD of 16.75 and after the use of intracameral mydriatics in group 2 was 73.88 beats/min with a SD of 10.90 (p=0.119). At the end of surgery the mean pulse rate in group 1 was 74.88 beats/min with a SD of 14.30 and in group 2 was 72.28 beats/min with a SD of 10.34 (p=0.465).

Table 13. Comparison of mean IOP

Intervals	Group 1 (n=25)		Group 2 (n=25)		p value
	Mean	SD	Mean	SD	
Pre operative (mm Hg)	13.88	3.47	15.36	2.66	0.096
Post operative (mm Hg)	13.28	2.94	13.32	2.25	0.953



In group 1 preoperative mean intraocular pressure (IOP) was 13.88 mmHg with SD of 3.47 and in group 2 preoperative mean IOP was 15.36 mmHg with SD of 2.66. (P= 0.096). In group 1 the postoperative mean intraocular pressure (IOP) on day 1 was 13.28 mmHg with SD of 3.47 and in group 2 postoperative mean IOP was 13.32 mmHg with SD of 2.25(P= 0.953).

Table 14. Distribution of study population according to the post operative vision

Post operative vision	Group 1 (n=25)		Group 2 (n=25)	
	Number	Percentage	Number	Percentage
6/12	11	44.00	8	32.00
6/12(P)	1	4.00	0	0.00
6/18	2	8.00	8	32.00
6/18(P)	0	0.00	1	4.00
6/24	3	12.00	1	4.00
6/36	3	12.00	1	4.00
6/6	1	4.00	1	4.00
6/9	2	8.00	4	16.00
6/9(P)	1	4.00	1	4.00
CFCF	1	4.00	0	0.00
Total	**25**	**100.00**	**25**	**100.00**

x^2=9.740 **p = 0.372**

On the postoperative day one 64% patients in group 1 with topical mydriatics had vision ranging from 6/12 to 6/6 while 32% had vision ranging from 6/36 to 6/18. However, 1 patient had a vision of counting fingers close to face due to corneal oedema. In group 2 with intracameral mydriatics 56% of the patients had vision ranging from 6/12 to 6/6 and 44% has vision ranging from 6/36 to 6/18.

DISCUSSION

The present study was conducted in the department of ophthalmology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi during study period of 1 year from 1st January 2016 – 31st December 2016 on subjects undergoing phacoemulsification cataract surgery. The patients were divided into two groups, group 1 received topical mydriatics (tropicamide 0.8% and phenylephrine hydrochloride 5%) and group 2 intracameral mydriatic regimen (0.5% lignocaine and 0.001% epinephrine) for pupillary dilatation.

A well sustained pupillary mydriasis is a must for proper visualization of the lens capsule for a successful cataract surgery by MSICS or phacoemulsification. However, poor mydriasis during cataract surgery increases the risk of intraoperative complications such as posterior capsule rent and dropped nucleus into the vitreous cavity[12]. There is a significant risk of damaging the iris resulting in sphincter tears, intraoperative bleeding and an atonic pupil.

The current preoperative routine to achieve pupillary dilatation involves the repeated topical administration of a combination of mydriatic agents comprising of anticholinergics such as cyclopentolate 1%, tropicamide 1%, homatropine 5% or scopolamine 0.25% and sympathomimetic mydriatic agents such as phenylephrine 2.5% to 10%. This preoperative use of the eye drops is usually started 45 minutes to 1 hour before the surgical procedure.

The topical mode of drug use has certain disadvantages such as the slow penetration of mydriatic substances through the cornea thus delaying the onset of pupillary dilatation with the time required for cyclopentolate to achieve maximum

mydriasis being 30 minutes[3] and with phenylephrine being as much as 75 minutes[4]. Thus, resulting in a preoperative waiting period of approximately 45 minutes to one hour. The increased risk for cardiovascular adverse effects[6] is seen in people on antihypertensive medication, with known cardiac diseases and in young children[8] with the use of topical eye drops due to enhanced systemic absorption secondary to a limited local bioavailability.

The mydriatic effect is known to wear off during the surgery. Thus, to increase the sustainability of pupillary mydriasis, the preoperative use of topical flurbiprofen 0.003%, indomethacin 1% or suprofen 1% known nonsteroidal anti-inflammatory drops has been suggested.

Lundberg and Behnding were the first to introduce the idea of injecting mydriatic agents intracamerally along with that of intracameral lidocaine in the year 2003. The intracameral mydriatic agent was administered following anterior chamber entry in phacoemulsification cataract surgery[34].

In the present study a randomised clinical trial patients were randomly distributed into 2 groups to assess the above findings as stated by Lundberg and Behndig. Group 1 received topical mydriatics containing tropicamide 0.8% and phenylephrine hydrochloride 5% with chlorbutol as a preservative while group 2 received intracameral mydriatic solution of preservative free epinephrine 0.001 % with lignocaine 0.5%.

In our study we assessed the ability of the intracameral mydriatic regimen comprising of preservative free lignocaine 0.5% and epinephrine 0.001% in initiating and maintaining the pupillary mydriasis during phacoemulsification and compared it

with traditional preoperative topical mydriatic eye drops. We also studied the perioperative circulatory side effects of intracameral epinephrine used as a component of the intracameral mydriatic regimen.

All calculations were performed using SPSS statistical software version 20.0. A probability ('p' value) of less than or equal to 0.05 at 95% confidence interval was considered as statistically significant.

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

In the present study, in both the groups majority of the patients were in the age group of 51 to 70 years. The mean age in group 1 was 62.32 years and in group 2 it was 60.88 years (P=0.550).

In group 1, 64% of patients were females and 36% were male with male:female ratio of 0.56 In group 2, 36% were males and 64% were females with male:female ratio of 0.56 (P=1.000).

The distribution of patients with diabetes mellitus in both groups was as follows; patients with diabetes and cataract were 12% in group 1 and 4% in group 2 (p=0.305).

The distribution of patients with hypertension in group in both the groups was as follows; patients with cataract and hypertension were 24% in group 1 and 24% in group 2 (p = 1.000).

In group 1, 36% of the patients had vision ranging from 6/18 to 6/60 while 64% of the patients had vision ranging from hand movements close to face to

counting fingers at 5 meters. Similarly in group 2, 36% of patient had vision ranging from 6/18 to 6/60 while majority of the patients nearly 64% had vision ranging from hand movements close to face to counting fingers at 5 meters(p = 0.328).

On the day prior to surgery the mean pupillary diameter prior to pupil dilatation in group 1 was 1.74 mm with a SD of 0.29, the same as that observed in group 2; 1.74 mm with a SD of 0.29 (p=1.000). Post dilatation the mean pupillary diameter in group 1 was 7.44 mm with SD of 0.49 and in group 2 was 7.18 mm with a SD of 0.38 (p= 0.040).

The mean pulse rate assessed prior to surgery in group 1 was 71.22 beats/min with a SD of 8.02 and in group 2 was 71.8 beats/min with a SD of 7.62. (p=0.760).

The mean systolic blood pressure prior to surgery in group 1 was 134 mmHg with a SD of 13.54 and in group 2 was 135.60 mmHg with a SD of 10.03. (p=0.637). While the mean diastolic blood pressure prior to surgery in group 1 was 81.36 mmHg with a SD of 9.01 and in group 2 was 83.04 mmHg with a SD of 8.13. (p=0.492).

In group 1 preoperative mean intraocular pressure (IOP) was 13.88 mmHg with SD of 3.47 and in group 2 preoperative mean IOP was 15.36 mmHg with SD of 2.66. (P= 0.096).

The two groups were similar in terms of the following parameters such as age, sex variation, distribution of cases, preoperative vision, pupillary diameter prior to and post dilatation, pulse rate, blood pressure and intraocular pressure. Thus, both the groups were comparable in all aspects and any statistically significant difference in the intraoperative and postoperative parameters assessed including pupillary

mydriasis, pulse rate and blood pressure were due to the use of topical mydriatics and the intracameral mydriatics in the two groups respectively.

Intraoperative pupillary mydriasis

In our study the mean pupillary diameter in group 1 prior to the use of topical mydriatics was 1.74 mm with a SD of 0.29 and in group 2 prior to the use of intracameral mydriatics was 1.74 mm with a SD of 0.29. ($p=1.000$). After the use of topical mydriatics in group 1 the mean pupil size increased to 7.36 mm with a SD of 0.57 while in group 2 following the use of intracameral mydriatics it increased to mean pupil size of 5.92 mm with a SD of 0.64 ($p<0.001$). The above results show that the initial pupil dilatation was significantly more following the use of topical mydriatics in comparison to following the use of intracameral mydriatics.

Our results are consistent with the findings of Lundberg and Behndig who in their study of topical mydriatics (cyclopentolate 1% and phenylephrine10%) versus intracameral mydriatics (cyclopentolate1%, phenylephrine 1.5% and lignocaine1%) for pupillary dilatation observed that the pupil size after viscoelastic injection was 6.7±1.0 mm in the intracameral group which was smaller than with topical mydriatics (7.7±1.0 mm) at the start of surgery[34].

In a similar study conducted by Morgado et al to compare the mydriatic efficacy and cardiovascular safety of topical mydriatics, Mydriasert, and intracameral mydriatics for pupillary mydriasis the results showed that the initial mydriasis was 8.1mm in the Mydriasert group, followed by the topical mydriasis group with a pupillary diameter 8.2mm and intracameral mydriatics with a pupillary diameter of 6.3mm thus indicating that initial mydriais is significantly more in the topical mydriasis group in comparison to the intracameral mydriasis group[36].

Gupta SK et al conducted a prospective interventional case series on 30 patients with the same intracameral mydriatic regimen as used in our study; 0.5% lignocaine and 0.001% epinephrine. In the study it was noted that the pupil size increased from 2.1mm (Range 2-3.5mm SD ± 0.32) to 6.9mm (Range 5-9mm SD ± 1.02) in 30 seconds time after intracameral mydriatic solution administration. It thus correlates with the results as obtained in our study[13].

Similarly A-Yong Yu et al in 2016 showed that the mean pupil diameter in the intracameral group was on an average 2.20 ± 0.08 mm at the start of surgery which later increased to 5.09 ± 0.20 mm 30 seconds after the intracameral mydriatic regimen in comparison with the topical group it was 7.98 ± 0.15mm at the start of surgery. Thus, concluding that the mydriasis at the start of surgery was much more in the topical mydriatic group in comparison with that of the intracameral epinephrine hydrochloride group[5].

However, towards the end of surgery pupillary diameter in our study in group 1 was 5.82 mm with a SD of 1.05 and in group 2 it was 6.30 mm with a SD of 1.24 (p=0.147) indicative of decrease in pupillary diameter in group 1 and an increase in pupillary diameter in group 2. Thus, showing a better well sustained pupillary mydriasis in the intracameral mydriatic group. A Within group comparison using Wilcoxon Signed Rank test showed a t value in group 1 of -4.450 and in group 2 of -4.442 while it showed a p value in group 1 of <0.001 and in group 2 of <0.001 thus indicating a significant decrease in pupillary mydriasis in group 1 and a significant increase and well sustained pupillary mydriasis in group 2 with intracameral mydriatics.

Our results are consistent with the results of Gupta SK et al where the pupil diameter following the use of intracameral mydriatic regimen of lignocaine 0.5% and epinephrine 0.001% increased from an average of 2.1mm (2-3.5 mm SD ±0.32) to 7.0 mm (3.5-9mm SD ± 0.20) at the end of surgery[13].

The study conducted by Lundberg and Behndig also showed that the pupil size after viscoelastic injection was 6.7 ± 1.0 mm in the intracameral group which was smaller than with topical mydriatics initially however, the pupils continued to enlarge throughout the procedure (+4.5% ± 8.1%) in the intracameral group whereas the pupils in the topical group continued to contract (-2.1% ± 7.8%)[34].

In a study conducted by Ajay, et al in 2017 on 127 patients who were randomly distributed into 2 groups one of which received topical mydriatics (tropicamide 0.8% plus phenylephrine 5% drops) and the other intracameral mydriatics (0.5% lignocaine plus 0.001% epinephrine). The same combination of drugs used as in our study. The difference between our study and this study being both the groups in this study underwent MSICS under peribulbar block while in our study phacoemuslfication cataract surgery was done under topical anesthetic eye drops[71]. The use of a peribulbar block instead of topical anesthesia is a confounding factor as seen in a study by Lincoff et al where it was found that the pupil dilated after accidental intraocular injection of lidocaine without administration of a mydriatic drug[61].

The results showed that the average pupil size just before peribulbar block was 7.3 mm in topical group and 3.3 mm in intracameral group. Mean pupil size in intracameral group increased to 7.3 mm 30 seconds after injecting the intracameral dilating solution. However, the mean pupil size in both groups progressively reduced,

reaching 5.1 mm and 5.5 mm, respectively, at the end of surgery[71]. In contrast to the results in this study, in our study the pupillary mydriasis increased and was better sustained in the intracameral mydriatic group (mean 6.30mm) with a p value of 0.001 at the end of surgery compared to that in the topical mydriatic group.

Intraoperative cardiovascular outcome

1. **Intraoperative pulse rate assessment**

In our study the mean pulse rate prior to the use of topical mydriatics in group 1 was 71.20 beats/min with a SD of 8.60 and prior to the use of intracameral mydriatics in group 2 was 76.24 beats/min with a SD of 13.14 (p=0.001). After the use of topical mydriatics in group 1 the mean pulse rate increased to 80.24 beats/min with a SD of 16.75 and after the use of intracameral mydriatics in group 2 was 73.88 beats/min with a SD of 10.90 (p=0.119). At the end of surgery the mean pulse rate in group 1 was 74.88 beats/min with a SD of 14.30 and in group 2 was 72.28 beats/min with a SD of 10.34 (p=0.465). The results showed no significant change in the pulse rate on using the intracameral mydriatic regimen of epinephrine 0.001% and lignocaine 0.5%.

The findings of our study are consistent with the findings of Salima Bhallil et al to evaluate any perioperative circulatory side effects of intracameral epinephrine in hypertensive patients undergoing phacoemulsification where in no significant pulse rate changes were noted (p=0.007)[29].

Around 60% or more of the topically applied substances are absorbed systemically. However, the systemic absorption of intracamerally administered substances is much less due to the aqueous humor turnover rate, the risk of systemic

adverse events is much less after intracameral than after topical use of a given amount of a drug. Behndig and Eriksson in 2004 assessed the variations in the pulse rate and oxygen saturation following the use of intracameral mydriatics. They found that the mean pulse rate was 72 ± 12min at the beginning of surgery, 71 ± 12min immediately after the intracameral mydriatic injection and 71±13min at the end of surgery thus indicating no significant alteration in the pulse rate following the use of the intracameral mydriatic regimen.(p=0.57)[18].

2. Intraoperative blood pressure assessment

In our study the mean systolic blood pressure in group 1 prior to the use of topical mydriatics was 133.44 mmHg with a SD of 14.23 and in group 2 prior to the use of intracameral mydriatics was 146.76 mmHg with a SD of 16.48 (p=0.004). After the use of topical mydriatics in group 1 the mean systolic blood pressure was 147.40 mmHg with a SD of 17.15 and after the use of intracameral mydriatics in group 2 was 142.92 mmHg with a SD of 16.14 (p=0.346). At the end of surgery in group 1 the mean systolic blood pressure in group 1 was 138.96 mmHg with a SD of 30.78 and in group 2 was 142.00 mmHg with a SD of 13.87 (p=0.655).

The increase in systolic blood pressure observed in the intracameral mydriatic group before the start of surgery is not attributable to the drugs, since at this time, the patient was not in contact with the mydriatic agent. This increase was probably due to surgery related stress or anxiety[36].

The mean diastolic blood pressure in group 1 prior to the use of topical mydriatics was 82.20 mmHg with SD of 9.35 and in group 2 prior to the use of intracameral mydriatics was 87 mmHg with a SD of 8.01 (p=0.095). Following the

use topical mydriatics in group 1 the mean diastolic blood pressure was 85.76 mmHg with a SD of 10.14 and after the use of intracameral mydriatics in group 2 was 85.76 mmHg with a SD of 8.06 mmHg (p=1.000). At the end of surgery the mean diastolic blood pressure being 85.72 mmHg in group 1 with a SD of 10.34 and 86.04 mmHg in group 2 with a SD of 7.67 (p=0.962). There was no significant intraoperative alteration in the systolic and diastolic blood pressure before and after the use of an intracameral mydriatic agent.

The results of our study are consistent with the findings of Morgado et al where in 90 eyes were randomly distributed into 3 groups with topical mydriatics (group A), Mydriasert (group B), and intracameral mydriatics (group C) for pupillary mydriasis. The systolic blood pressure was greater than 180 mmHg in 9 (30%) patients in group A, 3 (10%) in group B, and 2 (6.6%) in group C. Thus, concluding that intracameral mydriatics are safer when compared to topical mydriatics from the cardiovascular point of view[36].

A study conducted by Soong et al showed that the mean changes in systolic blood pressure was 8.95 mm Hg, diastolic blood pressure was 6.675 mm Hg, and pulse was 10.1 beats/min on use of cyclopentolate hydrochloride 0.1%, phenylephrine hydrochloride 1.5%, and preservative-free lignocaine 1% as an intracameral mydriatic agent. Thus, concluding that the intracameral route of administering mydriatics delivers minute doses of the drugs to the target organ to achieve the desired effect, minimizing potential cardiovascular side effects[69].

Postoperative outcomes

On the postoperative day one 64% patients in group 1 with topical mydriatics had vision ranging from 6/12 to 6/6 while 32% had vision ranging from 6/36 to 6/18. However, 1 patient had a vision of counting fingers close to face due to corneal oedema. In group 2 with intracameral mydriatics 56% of the patients had vision ranging from 6/12 to 6/6 and 44% has vision ranging from 6/36 to 6/18. Though the postoperative day one visions were better in the intracameral group relative to the topical group the results were not statistically significant (p=0.372).

Behndig and Eriksson in 2004 reported that the best corrected visual acuity was significantly better on day 1 in the intracameral mydriatic group in comparison with the topical mydriatic group[18].

In our study in group 1 the postoperative mean intraocular pressure (IOP) on day 1 was 13.28 mmHg with SD of 3.47 and in group 2 postoperative mean IOP was 13.32 mmHg with SD of 2.25(P= 0.953). Thus no significant difference in the postoperative intraocular pressure was noted.

The results of our study are similar to those observed by Lundberg and Behndig in a 6 year follow up to their study conducted in 2003 where they observed that there was no statistically significant difference in the postoperative best corrected visual acuity or the intraocular pressure following the use of intacameral mydriatics in phacoemulsification cataract surgery[66].

CONCLUSION

Thus we conclude that the use of an intracameral mydriatic regimen of preservative free lignocaine 0.5% and epinephrine 0.001% constitutes a safe, rapid and effective alternative compared to the use of topical mydriatics in sustaining pupillary mydriasis in phacoemulsification cataract surgery. It has the ability to simplify the preoperative procedure done routinely, the induced mydriasis being well sustained, without significant alteration in intraoperative pulse rate and blood pressure. It is especially useful in certain subjects with a high risk for adverse outcomes like patients with cardiac disorders, hypertension, IFIS, patients with allergy to the components of a topical mydriatic regimen etc.

However a larger sample size is required for conclusive evidence.

SUMMARY

Adequate pupillary mydriasis is a must in order to perform an uneventful cataract surgery either by phacoemulsification or by manual small incision cataract surgery. This is usually achieved by the preoperative frequent instillation of topical anticholinergic and sympathomimetic mydriatic agents. In order to find an alternative to this repeated eye drop instillation regimen we studied the use of an intracameral mydriatic regimen of 0.5% lignocaine and 0.001% epinephrine in initiating and sustaining the pupillary dilatation during phacoemulsification cataract surgery under topical anesthesia, without any topical mydriatic or NSAID use.

50 patients were randomly distributed into 2 groups, 25 each group. The first group received topical mydriatics for pupillary dilatation i.e tropicamide 0.8% and phenylephrine hydrochloride 5% with chlorbutol as a preservative eye drops at 15 minutes intervals, 1 hour prior to surgery. The second group received an intracameral mydriatic regimen for pupillary dilatation i.e a 2ml solution of 1.5 ml balanced salt solution (BSS) with 0.5 ml combination of preservative free lignocaine 0.5% and adrenaline 0.001%.

The Pupil size was measured intraoperatively in each of the groups before the drug use, after the drug use and at the end of surgery in group 1 with the use of topical mydriatics and in group 2 with the use of the intracameral mydriatic regimen. Similarly, in order to study the intraoperative circulatory side effects of intracameral epinephrine used as a component of the intracameral mydriatic regimen the pulse rate, systolic and diastolic blood pressure was assessed.

In our study we found that the onset of pupillary mydriasis was faster with the use of an intracameral mydriatic regimen than that with the use of topical mydriatics but the induced dilatation lasted longer. The initial pupillary diameter, however, being significantly larger with topical mydriatics ($p<0.001$) than that with intracameral mydriatics. However, the pupil constricted intraoperatively in the topical mydriatic group but the pupillary diameter increased or remained the same in the intracameral mydriatic group ($p<0.001$).

There was no significant alteration in the pulse rate and intraoperative blood pressure on using intracameral mydriatics in comparison with use of topical mydriatics ($p>0.05$).

Thus we conclude that the use of an intracameral mydriatic regimen of preservative free lignocaine 0.5% and epinephrine 0.001% constitutes a safe, rapid and effective alternative compared to the use of topical mydriatics in sustaining pupillary mydriasis in phacoemulsification cataract surgery. It has the ability to simplify the preoperative procedure done routinely, the induced mydriasis being well sustained, without significant alteration in intraoperative pulse rate and blood pressure. It is especially useful in certain subjects with a high risk for adverse outcomes like patients with cardiac disorders, hypertension, IFIS, patients with allergy to the components of a topical mydriatic regimen etc.

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CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

ID NO. | | | |

Mr/Mrs/Ms_____

You are invited to participate in our research study titled **"A ONE YEAR RANDOMIZED CLINICAL TRIAL OF TOPICAL VERSUS INTRACAMERAL MYDRIATICS IN SUSTAINING MYDRIASIS DURING PHACOEMULSIFICATION CATARACT SURGERY"** at KLES Hospital and medical reaearch centre, Belagavi.

Respected Sir/Madam we request you to enroll yourself to participate in our study as you are eligible for doing so. Your participation in the study is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N. Medical College. If you decide to participate you are free to withdraw at any time.

Purpose of the study :-The purpose of the research is to evaluate topical versus intra cameral mydriatics in sustaining mydriasis during phacoemulsification surgery.

Procedure Involved :-If you agree to enroll yourself in this study, you will be randomly distributed into 2 groups with the use of random number table for the purpose of randomization, group 1 receiving topical mydriatics and group 2 receiving intracameral mydriatics for pupillary dilatation. You will asked to give a detailed history. Then you will be clinically examined in detail by slit-lamp examination, fundoscopy, tonometry for measurement of intraocular pressure. Syringing for patency of the lacrimal sac and investigations like Blood Pressure measurement, Random Blood

sugar, pulse rate will be done. Then you will be undergoing phacoemulsification cataract surgery under topical anaesthesia with use of either topical or intracameral mydriaitics in attaining pupillary dilatation.

Risks and Benefits :- Rare complications of phacoemulsification surgery includes rupture of posterior lens capsule, posterior loss of lens fragments, posterior dislocation of intraocular lens,acute postoperative endophthalmitis, posterior capsular opacification, anterior capsule fibrosis and contraction, cystoid macular edema, corneal decompensation, malposition of the intraocular lens, retinal detachment for which all necessary precautions will be taken. The above mentioned complications of the procedure involved can be seen in both groups i.e group 1 receiving topical mydriatics and group 2 receiving intracameral mydriatics.

Your participation may benefit you and others in establishing an alternative modality to attain and sustain pupillary mydriasis in phacoemulsification cataract surgery.

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

Costs for participating in this research:-There will not be any extra cost incurred by the participant. There is no commitment for any reimbursement or any other compensation for the participant.

Privacy and Confidentiality:-The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to others without your written permission.

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

identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

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

Questions:-

If you need any further information regarding your rights as a study participant contact

1. **Dr. GANGA S. PILLI** **MD.DCP.DPM**

   CHAIRPERSON ETHICAL COMMITTEE FOR HUMAN SUBJECT RESEARCH

   PROFESSOR DEPARTMENT OF PATHOLOGY

   JNMC, BELAGAVI. Contact No. 08312471350/09480275601

CONSENT FOR PARTICIPATION IN RESEARCH TRIAL

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

Subject Name: _____

Signature or the Left Thumb Print of Subject: _____

Witness Name: _____

Signature of Witness: _____

Investigators Name: _____

Signature of Investigator: _____

Date: _____

ANNEXURE-II

PROFORMA

PATIENTS ID NO: | | | |

NAME: | | | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | | | |

AGE: | | | Years

SEX: | | (1-Male; 2-Female)

ADDRESS: | | | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | | | |

CONTACT NUMBER:- | | | | | | | | | | |

OP NUMBER: | | | | | | | | |

IP NUMBER: | | | | | | | | |

DATE OF ADMISSION: | | / | | | / | | | | |

DATE OF DISCHARGE: | | / | | | / | | | | |

IS THE PATIENT ELIGIBLE FOR STUDY? (1-YES; 2-NO) | |

HAS INFORMED CONSENT BEEN GIVEN? (1-YES; 2-NO) | |

FINAL RESULT INFORMATION | |

1- INELIGIBLE
2- ELIGIBLE- REFUSAL
3- ELIGIBLE- PARTICIPATING

SURGEON'S NAME: | | | | | | | | | | | | | |

SURGEON'S SIGNATURE: _____

DATE OF SURGERY : | | / | | | / | | | | |

CHIEF COMPLAINTS:

DIMINUTION OF VISION ☐

RE

Duration:_____ days/ months/years

LE ☐

Duration: _____ days/ months/years

HISTORY OF PRESENT ILLNESS:

1. DIMINUTION OF VISION 1- Gradual; 2- Sudden ☐

1- Progressive; 2- Static ☐

1- Painless; 2- Painful ☐

1- For distance; 2- For near ☐

2. DIPLOPIA/POLYOPIA 1- Present; 2- Absent ☐

3. COLOURED HALOS 1- Present; 2- Absent ☐

4. BLACK SPOTS BEFORE THE EYES 1- Present; 2- Absent ☐

5. WATERING 1- Present; 2- Absent ☐

6. REDNESS 1- Present; 2- Absent ☐

7. DISCHARGE 1- Present; 2 - Absent ☐

8. H/O WEARING GLASSES (1-Distance; 2-Near; 3-Both) ☐

Duration: ☐☐ months/years

PAST HISTORY:

OCULAR SURGERY: 1- Present; 2- Absent ☐

Type of surgery: _____

Duration: ☐☐ months/years

DIABETES: 1- Present 2- Absent ☐

Duration: ☐☐ months/years

HYPERTENSION: 1- Present 2- Absent ☐

Duration: ☐☐ months/years

CORONARY HEART DISEASE: 1-Present 2- Absent ☐

☐☐ Duration:

ANY OTHER MEDICAL DISORDERS: _____

PERSONAL HISTORY:

SMOKING: 1- Present; 2- Absent ☐

Duration: ☐☐ months/years

ALCOHOLISM: 1- Present; 2- Absent ☐

Duration: ☐☐ months/years

ANY OTHER ADDICTIONS: _____ ☐

Duration: ☐☐ months/years

GENERAL PHYSICAL EXAMINATION:

General Appearance:

1- Well built, 2- Moderately built, 3- Poorly built, 4- emaciated ☐

Pallor: 1- Present 2- Absent ☐

If present 1- Mild 2- Moderate 3- Severe ☐

Pulse: ☐☐☐ /minute

BP: ☐☐☐/☐☐ mm of hg

Temperature: ☐☐☐ degree Fahrenheit

Respiratory rate: ☐☐ / minute

SYSTEMIC EXAMINATION:

CVS: 1- Normal 2- Abnormal ☐
if 2, specify:_____

RS: 1- Normal 2- Abnormal ☐
if 2, specify:_____

CNS: 1- Normal 2- Abnormal ☐
if 2, specify: _____

Per Abdomen: 1- Normal 2- Abnormal ☐
if 2, specify: _____

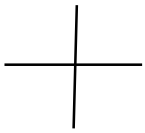
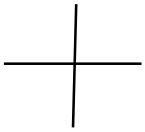
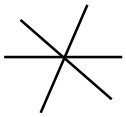
OCULAR EXAMINATION:

Head posture: 1- Erect, 2- Tilted ☐

Visual Axis: 1- Parallel, 2- Deviated ☐

Facial Symmetry: 1- Symmetrical, 2-Asymmetrical ☐

Extraocular movements:

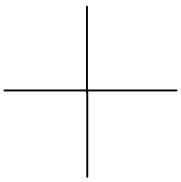
RE-  LE-  Binocular :- 

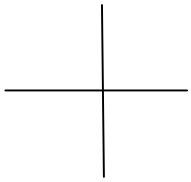
(N- Normal, R- Restricted)

1) Visual Acuity:

	RE	LE
DISTANT		
PINHOLE		
NEAR		
AIDED		

REFRACTION/RETINOSCOPY:

OD 

OS 

	RE				LE			
	SPH	CYL	AXIS	VISION	SPH	CYL	AXIS	VISION
DISTANCE								
NEAR								

	OD	OS
1. Adnexa (1- Normal; 2-Abnormal)	☐	☐
2. Sclera (1- Normal; 2- Congested)	☐	☐
3. Conjunctiva (1-normal; 2-conjunctival congestion; 3-ciliary congestion; 4-chemosis)	☐	☐
4. Cornea (1- normal; 2-opacity; 3-vascularisation)	☐	☐
5. Anterior chamber (1- normal depth; 2-shallow; 3-deep)	☐	☐
6. Iris (1-normal colour& pattern; 2-Abnormal)	☐	☐
7. **Pupil**: **SIZE**- ____ in mm measured 1day prior to surgery Shape- 1- Round & Regular; 2-Abnormal Reaction: Direct (1. Present, 2. Absent) Indirect (1. Present, 2. Absent) Near reflex (1. Present, 2. Absent) Pseudoexfolition:(1.Present,2.Absent)	☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐
8. Lens Clarity- 1. Clear, 2. Opaque Cataract - (1) , PCIOL - (2) Cataract if present- 1.immature 2.mature 3. hyper mature A) CORTICAL- (1.Present, 2. Absent)	☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐

B) NUCLEAR SCLEROSIS- 1. PRESENT, 2- ABSENT If present- A. Grade-1 B. Grade-2 C.Grade-3 D. Grade-4	☐ ☐	☐ ☐
(C) POSTERIOR SUBCAPSULAR CATARACT PRESENT, 2. ABSENT	☐	☐

FUNDUS	**OD**	**OS**
GLOW		
MEDIA		
DISC		
C :D		
BACKGROUND		
BLOOD VESSEL		
MACULA		

DIAGNOSIS:-

IMPRESSION:-

INVESTIGATIONS:

1. Ocular

A) Lacrimal patency

(1-PATENT; 2- regurgitation: 2A- Clear fluid, 2B- Mucopurulent; 3-BLOCKED)

RE ☐

LE ☐

B) IOP: (with Non contact tonometer)

RE: ☐ mm of hg

LE : ☐ mm of hg

C) Blood sugar: _____mg%

D) Blood Pressure: _____mm of hg

E) Pulse rate:_____ beats/min

OPERATIVE PROCEDURE: 1.PHACOEMULSIFICATION CATARACT SURGERY UNDER TOPICAL ANAESTHESIA WITH TOPICAL MYDRIATICS (PHENYLEPHRINE HYDROCHLORIDE 5%, TROPICAMIDE 0.8%, CHLORBUTOL) SUPPLEMENTED WITH INTRACAMERAL PRESERVATIVE FREE LIGNOCAINE 1%.

2. PHACOEMULSIFICATION CATARACT SURGERY UNDER TOPICAL ANAESTHESIA WITH INTRACAMERAL MYDRIATICS (PRSERVATIVE FREE LIGNOCAINE 0.5% WITH EPINEPHRINE 0.001%)

DATE:_____/_____/_____

OPERATING EYE : _____

Anaesthesia:Topical anaesthesia with proparacaine hydrochloride 0.5%with chlorbutol as a preservative eye drops and lignocaine jelly 2%

PUPILLARY DIAMETER :

1. Just before the use of topical mydriatics:
2. Just before the incision:
3. 30 Seconds after instilling the intracameral mydriatic:
4. At the end of surgery:

BLOOD PRESSURE:

1. Just before the use of topical mydriatics:
2. Just before the incision:
3. 30 Seconds after instilling the intracameral mydriatic:
4. At the end of surgery:

PULSE RATE:

1. Just before the use of topical mydriatics:
2. Just before the incision:
3. 30 Seconds after instilling the intracameral mydriatic:
4. At the end of surgery:

Operative Complications: 1. Present, 2. Absent ☐

If present- specify

Post- operative complications: 1. Present, 2. Absent ☐

If present- specify

FOLLOW UP PLAN: 1 DAY post-operatively

1. Conjunctiva (1-normal; 2-conjunctival congestion; 3-ciliary congestion; 4-chemosis)	☐
2.Section/suture site (1-edges opposed; 2- edges gaping)	☐
3.Cornea (1-clear; 2-hazy/descemets fold)	☐
4. Anterior chamber:A -Depth (1- normal depth; 2-shallow; 3-deep) B –cells (1-grade 1,2-grade 2,3-grade3, 4-grade 4) C-flare (1-grade 1,2-grade 2,3-grade3, 4-grade 4)	☐ ☐ ☐
5.iris (1-normal color & pattern;2-abnormal)	☐
6. Pupil: Size- ____ in mm Shape- 1- Round & Regular; 2-Abnormal IF 2 (Specify) :	☐
7.Intraocular Lens (1-in situ, 2-decentred)	☐

VISUAL ACUITY	RE	LE
DISTANT		
PINHOLE		

IOP: (non contact tonometer)

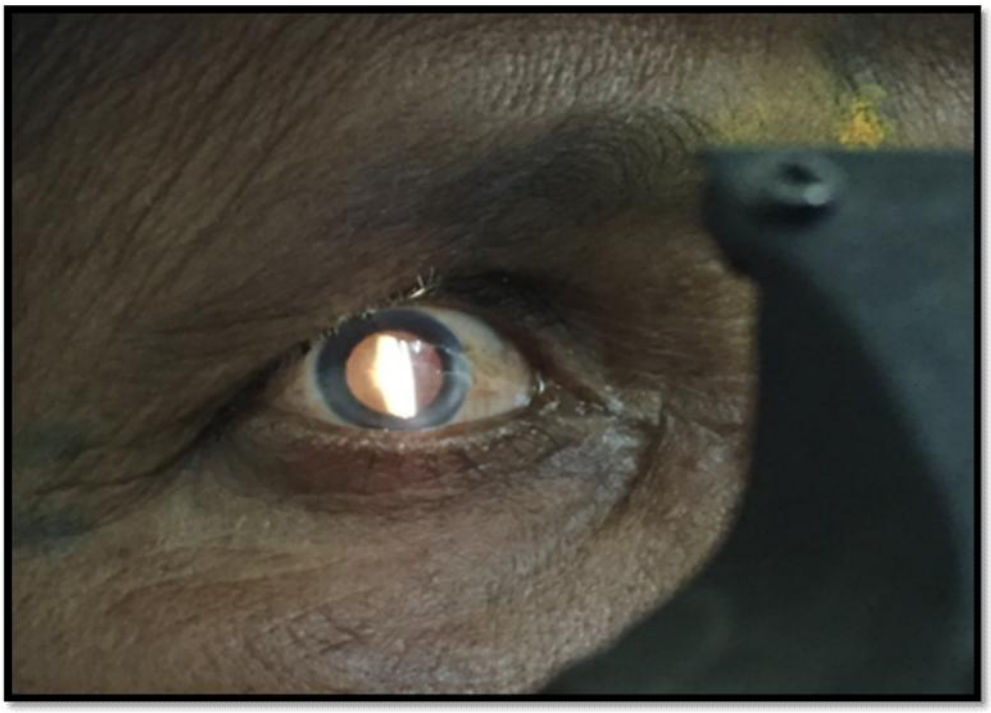
RE: ☐ mm of hg

LE : ☐ mm of hg

COMPLICATIONS (IF ANY OTHER):

ANNEXURE III – PHOTOGRAPHS

Photograph 1-Slit Lamp Examination



Photograph 2-Pupil Assessment A Day Prior To Surgery

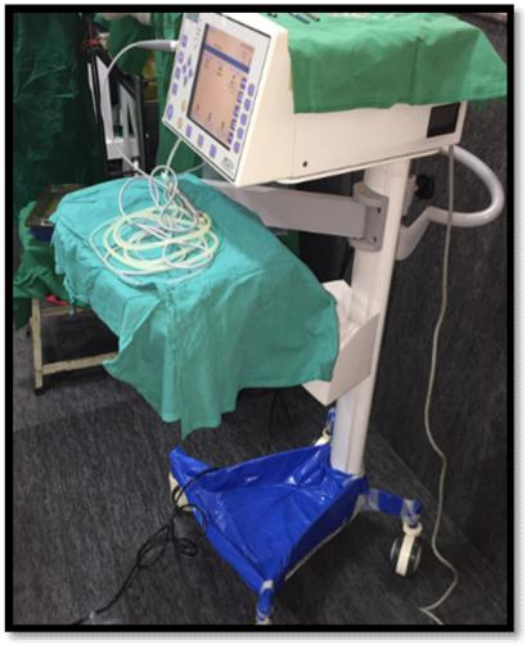
Photograph 3 - Castroviejo Caliper

Photograph 4-Topical Mydriatic Containing Tropicamide 0.8% And Phenylephrine Hydrochloride 5% With Chlorbutol As A Preservative.

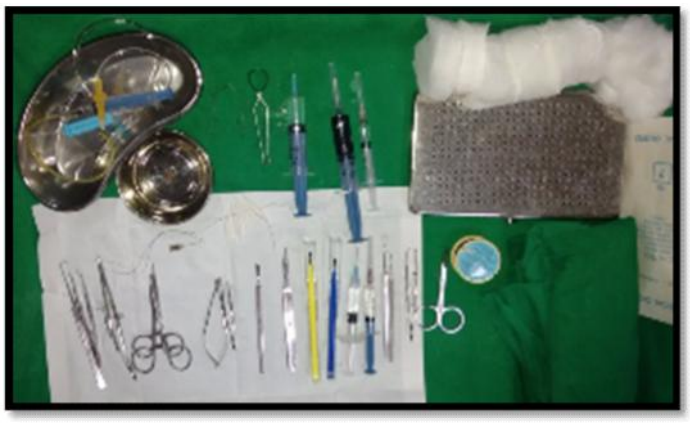
Photograph 5- Components Of The Intracameral Mydriatic Regimen i.e; Preservative Free Lignocaine Hydrochloride 2 %, Epinephrine 1:0000, Balanced Salt Solution, Preservative Free Lignocaine 1%.

Photograph 6- Topical Anaesthetic Agents i.e; Proparacaine 0.5% With Chlorbutol, Lignocaine Jelly 2%

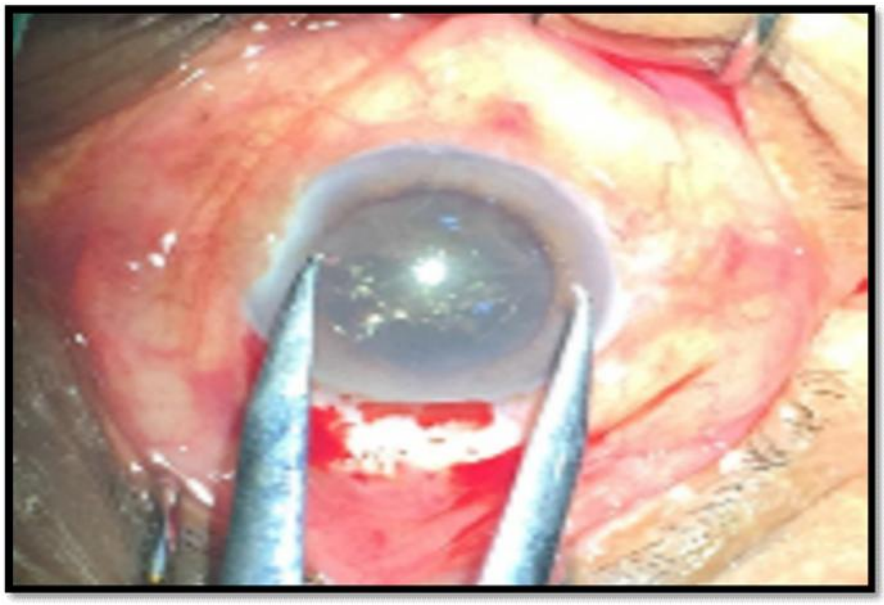
Photograph 7-Operation Theatre



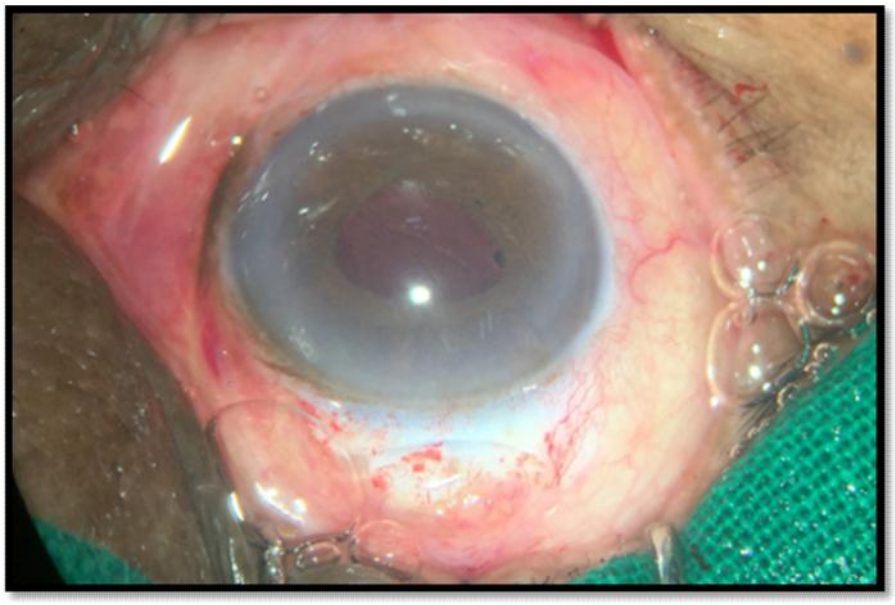
Photograph 8 – Phacoemulsification Machine



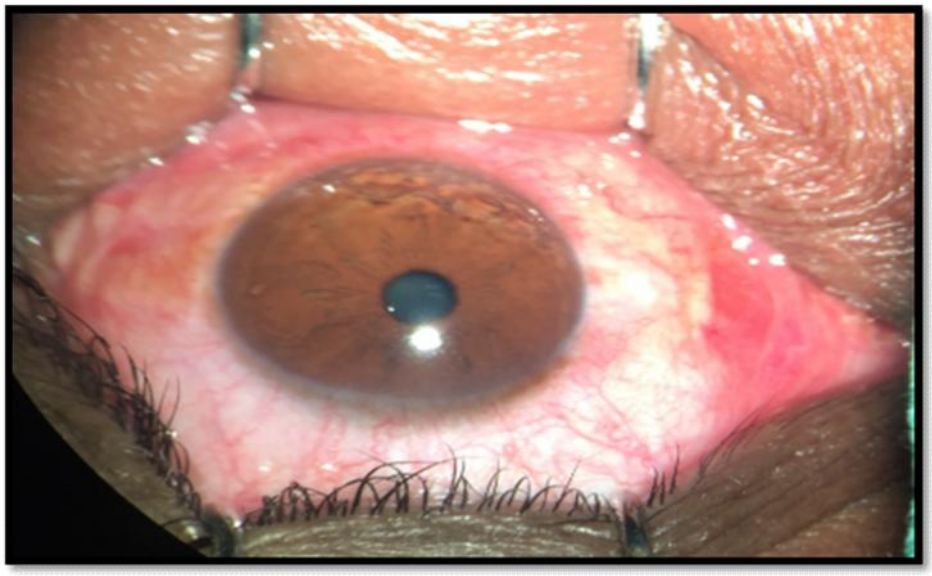
Photograph 9 – Cataract Set



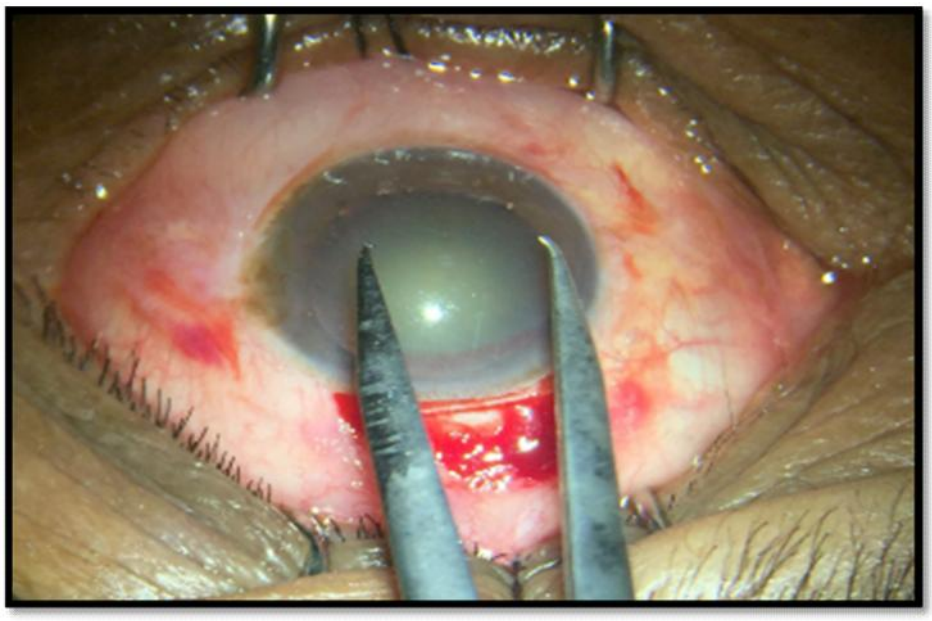
Photograph 10 – Pupil Assessment At The Start Of Surgery In Group 1 With Topical Mydriatics



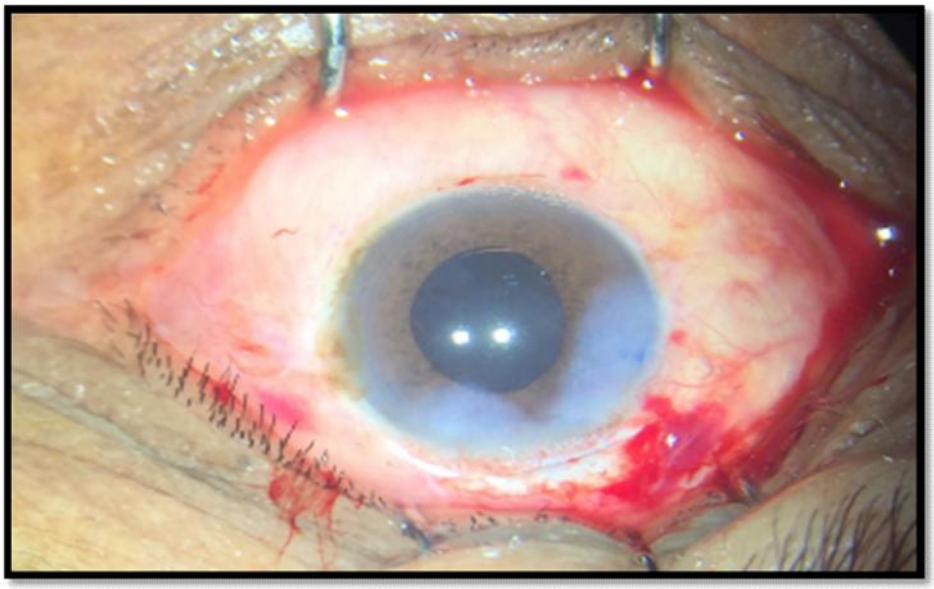
Photograph 11- Pupil Assessment At The End Of Surgery In Group 1 With Topical Mydriatics



Photograph 12 - Pupil Assessment At The Start Of Surgery In Group 2 With Intracameral Mydriatics



Photograph 13 - Pupil Assessment In Group 2, 30 Seconds After Irrigation With Intracameral Mydriatics.



Photograph 14 - Pupil Assessment At The End Of Surgery In Group 2 With Intracameral Mydriatics

Sl. No	IP No	Age	preop SBP	preop DBP	pre operative pulse	Pre operative pupil size (mm)		Pre operative IOP	INTRAOPERATIVE PUPILLARY MYDRIASIS			INTRAOPERATIVE BP ANALYSIS(MM Hg)						INTRAOPERATIVE PULSE ANALYSIS(BEATS/MIN)			Post operative IOP (mm hg)
						Pre dilatation	Post dilatation		Before	After	end of Surgery	SBP Before drug u	DBP Before drug	SBP After drug us	DBP After drug us	SBP End of surger	DBP End of surger	Before drug use	After drug use	end of surgery	
5	714881	50	150	90	72	2.0	8.0	17.3	2	8	8	150	90	159	89	126	80	80	88	80	14.6
7	716424	65	130	90	78	1.5	7.5	11.3	1.5	7.5	6.5	120	80	131	84	24	80	80	88	78	11
9	725219	50	150	90	70	1.5	6.5	14.6	1.5	6	4	140	80	142	80	157	100	70	70	72	14.6
12	731795	65	120	70	78	2.0	8.0	14.6	2	8	6.5	110	90	168	94	166	90	78	98	73	14.6
14	734450	60	120	70	72	2.0	7.5	17.3	2	7	4.5	120	90	166	82	151	80	72	99	95	14.6
15	737823	65	150	90	66	2.0	7.5	17.3	2	7	6	140	60	142	60	140	66	66	66	67	13.2
17	741505	68	120	70	78	1.5	7.5	8.5	1.5	7.5	7	150	90	160	99	140	91	72	92	81	10.2
20	744819	66	130	80	70	1.5	7.5	14.6	1.5	7.5	7.5	130	80	141	80	120	86	70	72	68	13.4
21	756999	63	130	70	64	2.0	7.0	14.6	2	7	6	110	70	140	87	150	90	62	66	66	15.6
22	758363	62	140	90	72	1.0	6.0	17.3	1	6	5.5	140	90	139	80	139	80	78	91	91	14.6
23	761117	57	130	90	76	1.5	7.5	14.6	1.5	7.5	5.5	150	90	156	90	162	100	76	91	92	13.9
25	762620	70	160	94	62	2.0	7.5	12.2	2	7.5	5.5	160	90	164	96	168	96	58	59	62	12.2
26	764359	45	120	80	66	1.5	7.5	15.9	1.5	7.5	6.5	140	90	140	90	138	90	66	69	64	14.4
27	764382	60	120	80	80	2.0	8.0	12.2	2	8	6.5	130	80	143	77	122	69	70	72	64	12.2
30	771654	65	130	80	70	2.0	7.5	10.5	2	7.5	7	110	74	106	74	110	78	74	76	76	10.5
33	774120	65	150	90	82	1.5	7.0	10.2	1.5	6.5	5	146	96	150	96	146	95	74	123	104	10.4
37	782788	60	140	90	70	1.5	7.0	20.9	1.5	7	4	140	90	135	84	116	74	70	89	71	22.1
38	783988	60	140	80	80	1.5	7.5	11.2	1.5	7.5	6	130	80	140	80	137	80	80	87	72	11.2
39	784012	52	150	90	70	2.0	8.0	12	2	8	6.5	140	90	156	97	152	97	78	83	72	11.4
40	786492	82	130	70	62	2.0	8.0	14.1	2	8	4.5	140	90	191	102	194	101	62	63	63	11.4
41	786515	69	140	70	60	1.5	7.5	14.1	1.5	7.5	5	140	70	138	70	136	70	60	62	62	13.4
42	786474	64	110	80	58	2.0	7.5	8.1	2	7.5	5.5	110	80	118	80	116	80	58	57	53	8.1
43	786466	60	120	70	56	1.5	8.0	9.9	1.5	8	6.5	120	70	162	96	163	97	56	57	55	12.1
46	787784	70	120	70	80	2.0	7.0	12.2	2	7	5	140	70	150	80	152	80	80	82	82	12.6
50	789130	65	150	90	86	2.0	7.5	21.4	2	7.5	5	130	90	148	97	149	93	90	106	109	19.7

Sl. No	IP No	Age	preop SBP	preop DBP	pre operative pulse	Pre operative pupil size (mm)		Pre operative IOP	INTRAOPERATIVE PUPILLARY MYDRIASIS			INTRAOPERATIVE BP ANALYSIS(MM Hg)						INTRAOPERATIVE PULSE ANALYSIS(BEATS/MIN)			Post operative IOP (mm hg)
						Pre dilatation	Post dilatation		Before	After	end of Surgery	SBP Before drug u	DBP Before drug	SBP After drug us	DBP After drug us	SBP End of surge	DBP End of surge	Before drug use	After drug use	end of surgery	
1	689927	60	140	90	60	2.0	8.0	15.2	2	6.5	7	140	90	138	90	140	90	60	60	58	12.6
2	689928	70	130	90	72	1.5	7.0	21.2	1.5	6.5	6.5	130	90	124	86	124	86	72	70	70	18.2
3	712610	61	130	80	80	1.5	7.0	14.6	1.5	5	6	162	80	156	81	156	81	72	72	62	12.2
4	712599	78	150	90	80	1.5	7.5	17.3	1.5	5	6	183	86	177	83	162	83	80	80	78	14.6
6	714877	68	140	70	80	2.0	7.0	18.9	2	7	7	151	100	142	94	142	94	84	78	70	12.2
8	724784	60	110	70	78	1.5	7.0	17.3	1.5	6	3	128	67	115	63	117	61	77	75	72	14.6
10	725228	40	120	70	70	1.5	6.5	14.6	1.5	5	5	137	78	136	83	129	87	114	98	94	14.2
11	731834	60	130	90	74	2.0	6.5	17.3	2	5.5	5.5	130	90	134	88	130	92	80	72	78	15.6
13	733223	60	140	70	64	1.5	7.0	18.9	1.5	5	2.5	170	80	177	85	169	88	64	64	60	14.6
16	740045	52	120	70	72	1.5	7.0	17.3	1.5	5.5	6	163	99	163	100	163	100	89	88	88	14.6
18	743905	55	140	80	72	1.5	7.5	17.3	1.5	6	7	145	90	138	90	138	90	76	71	71	15.2
19	744851	66	140	90	72	1.5	7.5	14.6	1.5	6	7	145	90	138	88	138	88	76	71	72	14.6
24	762537	64	140	90	78	2.0	7.0	17.3	2	6.5	7	140	90	142	90	148	90	81	84	80	14.6
28	767005	70	130	90	60	2.5	7.0	17.3	2.5	7	7	116	77	116	76	120	80	59	59	56	16.5
29	767001	73	130	90	80	1.5	7.0	12.2	1.5	6	7	151	92	152	93	151	92	78	79	78	10.2
31	772045	61	130	90	70	2.0	7.0	12.2	2	6	7	152	90	150	90	144	89	84	80	78	12.2
32	774107	64	130	80	59	1.5	7.0	13.7	1.5	5.5	6	124	87	126	87	136	90	59	58	61	8.8
34	775349	41	140	80	60	2.0	7.0	14.4	2	6	7	142	81	130	78	131	81	61	65	66	12.7
35	777066	60	140	80	58	2.0	7.5	10.1	2	7	7.5	130	76	128	76	125	75	54	52	52	10.8
36	783077	55	140	80	72	1.5	7.0	11.1	1.5	6	7	140	92	140	88	140	88	72	69	69	8.9
44	787825	60	140	76	82	2.0	7.5	14.6	2	5.5	7	147	78	138	76	138	76	98	92	87	14.2
45	787811	55	130	90	78	1.5	7.0	14.6	1.5	5	6	178	92	153	80	155	82	76	77	77	11.2
47	789176	74	150	90	76	1.5	7.5	12.2	1.5	6	7	157	99	157	99	157	90	78	78	79	12.2
48	789131	50	150	90	70	2.0	8.0	14.1	2	6.5	7.5	153	90	153	90	149	90	75	71	72	13.4
49	789149	65	150	90	78	2.0	7.5	15.7	2	6	6	155	91	150	90	148	88	87	84	79	14.2

Sl. No	IP No	Age	Sex	K/C/O DM	K/C/O HTN	Eye	preoperative Vn	preoperative BP	preoperative pulse	pupil size 1 day prior		pxf	lens	Preoperative IOP	INTRAOPERATIVE PUPILLARY MYDRIASIS				INTRAOPERATIVE BP ANALYSIS(MM Hg)			INTRAOPERATIVE PULSE ANALYSIS(BEATS/MIN)			AFTER SURGERY VISION DAY 1		AFTER SURGERY IOP Day 1
										pre D	postD	pxf	cataract		before TM	before incision	30 sec after ICM	end of Surgery	Before drug use	After drug use	end of surgery	Before drug use	After drug use	end of surgery	UCVA	PH	(mm hg)
1	689927	60	F	_	_	LE	CF1.5MT	140/90	60	2MM	8MM	_	11NS+PSC	15.2	_	2MM	6.5MM	7MM	140/90	138/90	140/90	60	60	58	6/12	6/9	12.6
2	689928	70	M			LE	CF2MT	130/90	72	1.5MM	7MM		11NS+PSC	21.2		1.5MM	6.5MM	6.5MM	130/90	124/86	124/86	72	70	70	6/9	NI	18.2
3	712610	61	F	_	_	RE	CF2MT	130/80	80	1.5MM	7MM	_	11NS+PSC	14.6	_	1.5MM	5MM	6MM	162/80	156/81	156/81	72	72	62	6/12	6/9	12.2
4	712599	78	F	_	_	LE	CF1.5MT	150/90	80	1.5MM	7.5M	_	11NS+PSC	17.3	_	1.5MM	5MM	6MM	183/86	177/83	162/83	80	80	78	6/12	6/9	14.6
5	714881	50	F			RE	CF1MT	150/90	72	2MM	8MM		11NS+PSC	17.3	2MM	8MM		8MM	150/90	159/89	126/80	80	88	80	6/12	6/9	14.6
6	714877	68	M	_	_	RE	CF2MT	140/70	80	2MM	7MM	_	11NS+PSC	18.9	_	2MM	7MM	7MM	151/100	142/94	142/94	84	78	70	6/36	6/18	12.2
7	716424	65	M			RE	CF1MT	130/90	78	1.5MM	7.5MM		11NS+PSC	11.3	1.5MM	7.5MM		6.5MM	120/80	131/84	124/80	80	88	78	6/24	6/12	11
8	724784	60	M			LE	CF2MT	110/70	78	1.5MM	7MM		1NS+PSC	17.3		1.5MM	6MM	3MM	128/67	115/63	117/61	77	75	72	6/18	6/12	14.6
9	725219	50	M	_	_	LE	6/36	150/90	70	1.5MM	6.5MM	_	111NS+PSC	14.6	1.5MM	6MM	_	4MM	140/80	142/80	157/100	70	70	72	6/36	NI	14.6
10	725228	40	F			RE	6/24(P)	120/70	70	1.5MM	6.5MM		1NS+PSC	14.6		1.5MM	5MM	5MM	137/78	136/83	129/87	114	98	94	6/9	6/6	14.2
11	731834	60	F			RE	6/60	130/90	74	2MM	6.5MM		11NS+PSC	17.3		2MM	5.5MM	5.5MM	130/90	134/88	130/92	80	72	78	6/12	6/9	15.6
12	731795	65	M	_	+	RE	6/60	120/70	78	2MM	8MM	_	11NS+PSC	14.6	2MM	8MM	_	6.5MM	110/90	168/94	166/90	78	98	73	6/12	6/9	14.6
13	733223	60	F	_	+	LE	CF2MT	140/70	64	1.5MM	7MM	_	11NS+PSC	18.9	_	1.5MM	5MM	2.5MM	170/80	177/85	169/88	64	64	60	6/9(P)	6/9	14.6
14	734450	60	F		+	LE	6/24	120/70	72	2MM	7.5MM		11NS+PSC	17.3	2MM	7MM		4.5 MM	120/90	166/82	151/80	72	99	95	6/24	6/18	14.6
15	737823	65	F	_	_	LE	CF2MT	150/90	66	2MM	7.5MM	_	11NS+PSC	17.3	2MM	7MM	_	6MM	140/60	142/60	140/66	66	66	67	6/9	6/6	13.2
16	740045	52	M			LE	CF1MT	120/70	72	1.5MM	7MM		11NS+PSC	17.3		1.5MM	5.5MM	6MM	163/99	163/100	163/100	89	88	88	6/18	NI	14.6
17	741505	68	F	_	_	RE	6/60	120/70	78	1.5MM	7.5MM	_	11NS+PSC	8.5	1.5MM	7.5MM	_	7MM	150/90	160/99	140/91	72	92	81	6/12	6/9	10.2
18	743905	55	M	_	_	RE	CF2MT	140/80	72	1.5MM	7.5MM	_	11NS+PSC	17.3	_	1.5MM	6MM	7MM	145/90	138/90	138/90	76	71	71	6/18	6/12	15.2
19	744851	66	F			LE	6/60	140/90	72	1.5MM	7.5MM		11NS+PSC	14.6		1.5MM	6MM	7MM	145/90	138/88	138/88	76	71	72	6/18(P)	6/18	14.6
20	744819	66	F	_	_	LE	6/36	130/80	70	1.5MM	7.5MM	_	11NS+PSC	14.6	1.5MM	7.5MM	_	7.5MM	130/80	141/80	120/86	70	72	68	6/36	6/12	13.4
21	756999	63	F			LE	CF3MT	130/70	64	2MM	7MM		11NS+PSC	14.6	2MM	7MM		6MM	110/70	140/87	150/90	62	66	66	6/12	NI	15.6
22	758363	62	F		+	RE	CF3MT	140/90	72	1MM	6MM		11NS+PSC	17.3	1MM	6MM		5.5MM	140/90	139/80	139/80	78	91	91	6/9(P)	6/9	14.6

Sl. No	IP No	Age	Sex	K/C/O DM	K/C/O HTN	Eye	preoperative Vn	preoperative BP	preoperative pulse	pupil size 1 day prior		pxf	lens	Preoperative IOP	INTRAOPERATIVE PUPILLARY MYDRIASIS				INTRAOPERATIVE BP ANALYSIS(MM Hg)			INTRAOPERATIVE PULSE ANALYSIS(BEATS/MIN)			AFTER SURGERY VISION DAY 1		AFTER SURGERY IOP Day 1
										pre D	postD	pxf	cataract		before TM	before incision	30 sec after ICM	end of Surgery	Before drug use	After drug use	end of surgery	Before drug use	After drug use	end of surgery	UCVA	PH	(mm hg)
23	761117	57	M	+	_	LE	6/18	130/90	76	1.5MM	7.5MM	_	11NS+PSC	14.6	1.5MM	7.5MM	_	5.5MM	150/90	156/90	162/100	76	91	92	CFCF	NI	13.9
24	762537	64	M			LE	CF2MT	140/90	78	2MM	7MM		11NS+PSC	17.3		2MM	6.5MM	7MM	140/90	142/90	148/90	81	84	80	6/18	NI	14.6
25	762620	70	M	_	_	LE	CF1MT	160/94	62	2MM	7.5MM	_	11NS+PSC	12.2	2MM	7.5MM	_	5.5MM	160/90	164/96	168/96	58	59	62	6/18	NI	12.2
26	764359	45	M	_	_	RE	CF0.5MT	120/80	66	1.5MM	7.5MM	_	11NS+PSC	15.9	1.5MM	7.5MM	_	6.5MM	140/90	140/90	138/90	66	69	64	6/36	NI	14.4
27	764382	60	F			LE	CF3MT	120/80	80	2MM	8MM		1NS+PSC	12.2	2MM	8MM		6.5MM	130/80	143/77	122/69	70	72	64	6/12	6/9	12.2
28	767005	70	M	_	+	RE	CF4MT	130/90	60	2.5MM	7MM	_	11NS+PSC	17.3	_	2.5MM	7MM	7MM	116/77	116/76	120/80	59	59	56	6/18	6/9	16.5
29	767001	73	M		+	LE	6/36	130/90	80	1.5MM	7MM		11NS+PSC	12.2		1.5MM	6MM	7MM	151/92	152/93	151/92	78	79	78	6/18	NI	10.2
30	771654	65	F			LE	CF2MT	130/80	70	2MM	7.5MM		11NS+PSC	10.5	2MM	7.5MM		7MM	110/74	106/74	110/78	74	76	76	6/12	6/9	10.5
31	772045	61	F	+	+	RE	6/60	130/90	70	2MM	7MM	_	11NS+PSC	12.2	_	2MM	6MM	7MM	152/90	150/90	144/89	84	80	78	6/12	6/9	12.2
32	774107	64	F			RE	CF3MT	130/80	59	1.5MM	7MM		11NS+PSC	13.7		1.5MM	5.5MM	6MM	124/87	126/87	136/90	59	58	61	6/6		8.8
33	774120	65	F		+	LE	CF4MT	150/90	82	1.5MM	7MM		11NS+PSC	10.2	1.5MM	6.5MM		5MM	146/96	150/96	146/95	74	123	104	6/6		10.4
34	775349	41	F	_	_	LE	6/24	140/80	60	2MM	7MM	_	1NS+PSC	14.4	_	2MM	6MM	7MM	142/81	130/78	131/81	61	65	66	6/18	6/12	12.7
35	777066	60	F			LE	CF3MT	140/80	58	2MM	7.5MM		11NS+PSC	10.1	_	2MM	7MM	7.5MM	130/76	128/76	125/75	54	52	52	6/12	6/9	10.8
36	783077	55	F			RE	CF2.5MT	140/80	72	1.5MM	7MM		11NS+PSC	11.1		1.5MM	6MM	7MM	140/92	140/88	140/88	72	69	69	6/9	NI	8.9
37	782788	60	F	_	_	LE	CF1MT	140/90	70	1.5MM	7MM	_	11NS+PSC	20.9	1.5MM	7MM	_	4MM	140/90	135/84	116/74	70	89	71	6/12	6/9	22.1
38	783988	60	M			RE	6/60	140/80	80	1.5MM	7.5MM		11NS+PSC	11.2	1.5MM	7.5MM		6MM	130/80	140/80	137/80	80	87	72	6/12	6/9	11.2
39	784012	52	F	_	_	RE	6/24	150/90	70	2MM	8MM	_	1NS+PSC	12	2MM	8MM	_	6.5MM	140/90	156/97	152/97	78	83	72	6/9	NI	11.4
40	786492	82	F	_	_	LE	6/36	130/70	62	2MM	8MM	_	11NS+PSC	14.1	2MM	8MM	_	4.5MM	140/90	191/102	194/101	62	63	63	6/12	6/9	11.4
41	786515	69	M		+	LE	CF2MT	140/70	60	1.5MM	7.5MM		11NS+PSC	14.1	1.5MM	7.5MM		5MM	140/70	138/70	136/70	60	62	62	6/18	6/9	13.4
42	786474	64	M	_	_	LE	CF0.5MT	110/80	58	2MM	7.5MM	_	11NS+PSC	8.1	2MM	7.5MM	_	5.5MM	110/80	118/80	116/80	58	57	53	6/12	6/9	8.1
43	786466	60	F			LE	HMCF	120/70	56	1.5MM	8MM		1NS+PSC	9.9	1.5MM	8MM		6.5MM	120/70	162/96	163/97	56	57	55	6/12(P)	6/12	12.1
44	787825	60	F		+	LE	CF1MT	140/76	82	2MM	7.5MM		11NS+PSC	14.6		2MM	5.5MM	7MM	147/78	138/76	138/76	98	92	87	6/18	6/12	14.2

Sl. No	IP No	Age	Sex	K/C/O DM	K/C/O HTN	Eye	preoperative Vn	preoperative BP	preoperative pulse	pupil size 1 day prior		pxf	lens	Preoperative IOP	INTRAOPERATIVE PUPILLARY MYDRIASIS				INTRAOPERATIVE BP ANALYSIS(MM Hg)			INTRAOPERATIVE PULSE ANALYSIS(BEATS/MIN)			AFTER SURGERY VISION DAY 1		AFTER SURGERY IOP Day 1
										pre D	postD	pxf	cataract		before TM	before incision	30 sec after ICM	end of Surgery	Before drug use	After drug use	end of surgery	Before drug use	After drug use	end of surgery	UCVA	PH	(mm hg)
45	787811	55	F	_	_	RE	6/18(P)	130/90	78	1.5MM	7MM	_	11NS+PSC	14.6	_	1.5MM	5MM	6MM	178/92	153/80	155/82	76	77	77	6/9	NI	11.2
46	787784	70	F	+		LE	CF0.5MT	120/70	80	2MM	7MM	_	11NS+PSC	12.2	2MM	7MM		5MM	140/70	150/80	152/80	80	82	82	6/12	NI	12.6
47	789176	74	M	_	+	RE	6/60	150/90	76	1.5MM	7.5MM	_	11NS+PSC	12.2	_	1.5MM	6MM	7MM	157/99	157/99	157/90	78	78	79	6/12	6/6	12.2
48	789131	50	F	_	_	RE	CF5MT	150/90	70	2MM	8MM	_	11NS+PSC	14.1	_	2MM	6.5MM	7.5MM	153/90	153/90	149/90	75	71	72	6/24	6/18	13.4
49	789149	65	F		_	LE	6/60	150/90	78	2MM	7.5MM	_	11NS+PSC	15.7		2MM	6MM	6MM	155/91	150/90	148/88	87	84	79	6/12	6/9	14.2
50	789130	65	F	+	+	RE	CF3MT	150/90	86	2MM	7.5MM	_	11NS+PSC	21.4	2MM	7.5MM	_	5MM	130/90	148/97	149/93	90	106	109	6/24	NI	19.7

ANNEXURE V – KEY TO MASTER CHART

DM	–	Diabetes mellitus
HTN	–	Hypertension
CF	–	Counting fingers
CFCF	–	Counting fingers close to face
HMCF	–	Hand movements close to face
IOP	–	Intraocular pressure
IP No	–	Inpatient number
Sr No	–	Serial number
LE	–	Left eye
RE	–	Right eye
M / F	–	Male / Female patient
Op	–	Operated eye
V_n	–	Vision
PH	–	Pinhole vision
Pre D / Post D	–	Pre dilatation / Post dilatation
NS	–	Nuclear sclerosis

PSC	–	Posterior subcapsular cataract
PxF	–	Pseudoexfoliation
SBP/DBP	–	Systolic/ Diastolic blood Pressure
UCVA	–	Uncorrected visual acuity
TM	–	Topical Mydriatics
ICM	–	Intracameral Mydriatics
MM	–	millimeters
Hg	–	mercury
Min	–	minutes

ANNEXURE – VI – ETHICAL CLEARANCE LETTER

K.L.E.UNIVERSITY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
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Ref: MDC/DOME/ 390 **Date: 16/11/2015**

To,

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"A ONE YEAR RANDOMIZED CLINICAL TRIAL OF TOPICAL VERSUS INTRACAMERAL MYDRIATICS IN SUSTAINING MYDRIASIS DURING PHACOEMULSIFICATION SURGERY IN PATIENTS ADMITTED IN KLE'S DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELAGAVI "**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Ganga Pilli)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

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