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### Comparative studies on mydriatic effect of tropicamide 0.8% and phenylephrin 5.0% in teenagers & geriatric people

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#### ABSTRACT



Prospective study on the comparison of mydriatic effect of Tropicamide 0.8% and Phenylephrine 5% in teenagers and geriatric people was carried out in suthrama Eye Hospital madanapalle, India. The main objective of this study was to compare the mydriatic effect of a combination of drug in teenagers and geriatric people. It also evaluated the ADR's produced and the efficacy of the drug in two age groups. In this study population majority of the subjects were female in group A and male in group B. Among the whole population under study in group A and B no one has reported with any case of congenital anomalies. A number of ADR's are reported but no serious adverse events had occurred. The study was carried out in 100 eyes ie. 50 subjects whom are divided into 2 groups based on age. The comparison of mydriatic effect was done in each group after instilling one drop of a combination of 0.08% Tropicamide and 0.5% Phenynilephrine. The pupillary size where measured before and after administration of drug and the results were compared. The results showed that there is a large difference in the normal pupil size between teenagers and geriatric people. After dilation the difference in pupil size was statistically significant among the two groups. The study concludes that the pupillary dilation produced by administering 0.8% Tropicamide and 5% Phenylephrine produces higher mydriatic effect in teenagers than geriatric people.

**Keywords:** mydriatic effect; teenagers; geriatric;

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#### INTRODUCTION

Mydriasis is the dilation of the pupil, usually defined as when having a non-physiological cause,<sup>[1]</sup> but sometimes defined as potentially being a physiological pupillary response.<sup>[2]</sup> Non-physiological causes of

mydriasis include disease, trauma, or the use of drugs. Normally, as part of the pupillary light reflex, the pupil dilates in the dark and constricts in the light to respectively improve vividity at night and to protect the retina from sunlight damage during the day.

A mydriatic pupil will remain excessively large even in a bright environment. The excitation of the radial fibres of the iris which increases the pupillary aperture is referred to as a mydriasis. More generally, mydriasis also refers to the natural dilation of pupils, for instance in low light conditions or under sympathetic stimulation.

An informal term for mydriasis is blown pupil,<sup>[3]</sup> and is used by medical providers. It is usually used to refer to a fixed, unilateral mydriasis, which could be a symptom of raised intracranial pressure.

The opposite, constriction of the pupil, is referred to as miosis. Both mydriasis and miosis can be physiological. Anisocoria is the condition of one pupil being more dilated than the other.

**Effects:** Natural release of the hormone oxytocin can cause mild to moderate mydriasis. Strong sexual arousal can often lead to very enlarged pupils, rather

than the minor dilation observed during sexual affection.

**Autonomic neuropathy:** The parasympathetic nervous supply, which causes constriction of the pupil, or miosis, is supplied by cranial nerve III, the oculomotor nerve. Damage to this nerve typically manifests itself as mydriasis, because the sympathetic supply to the pupil, which causes mydriasis, remains unaffected, and therefore unopposed.

Multiple central nervous system disorders e.g. epilepsy, stroke, and impending brain herniation are known to lead to temporal mydriasis as well. A brain catastrophe, or a rapidly increasing brain mass, can cause compression of the oculomotor nerve.

### Traumatic pupillary response

In cases of head injury or orbit trauma (eye injury), the iris sphincter (the muscle responsible for closing the pupil) or the nerves controlling it can be damaged, reducing or eliminating consensual reactivity to light.

### Mydriatics

A mydriatic is an agent that induces dilation of the pupil. The commonly used mydriatics comprise two groups of drugs Parasympatholytic and Sympathomimetic drugs. Most mydriatics reach their maximal effect by 30 to 60 minutes, although in children and people with deeply pigmented irises this may take longer.

**Parasympatholytic drugs:** which cause pupillary dilatation and paralysis of accommodation by rendering the sphincter pupillae and ciliary muscles insensitive to acetylcholine.

**Atropine (0.5 to 2%):** The most powerful cycloplegic available, producing mydriasis and cycloplegia lasting up to 2 weeks. It can be temporarily reversed by I: 100 intracameral acetylcholine. Indications: (a) Treatment of anterior uveitis. (b) Refracting children under 5 years of age Systemic side-effects: Atropine, hyoscine, and (rarely) homatropine may cause dryness and flushing of the skin, thirst and tachycardia, especially in infants. Delirium and confusion may also occur, particularly in the elderly. These effects are due to systemic absorption and can be prevented by pressing over the lacrimal sac or by tipping the head

**Oxyphenonium (Antrenyl) (1 and 5%):** Produces a powerful mydriasis lasting up to 4 days and cycloplegia lasting up to 12 days. Indications: Useful substitute for atropine in sensitive patients.

**Hyoscine (Scopolamine) (0.25 and 0.5%):** Produces a powerful mydriasis and cycloplegia lasting up to 5 days. Indications: Treatment of anterior uveitis in atropine-sensitive patients.

**Homatropine (1 to 5%):** Mydriasis lasts up to 2 days. It does not cause complete cycloplegia in children. Augmented by cocaine and reversed by eserine. Indications: (a) Ophthalmoscopy. (b) Preoperatively for cataract extraction

**Eucatropine (Euphthalmine) (5 and 10%):** Effective mydriatic lasting only 4 hours, producing little cycloplegia. Indications: (a) Ophthalmoscopy. (b) Provocative test in suspected closed-angle glaucoma.

**Cyclopentolate (Mydrilate, Cyclogyl) (0.5 to 2%):** Short-acting mydriatic and cycloplegic. Indications: (a) Refraction. Maximal cycloplegia occurs within 45 minutes and persists for 30 minutes. Complete recovery occurs within 24 hours but can be reduced to 6 hours by 2% pilocarpine. (b) Ophthalmoscopy. Maximal mydriasis within 30 minutes. Particularly valuable in patients with heavily pigmented irides. (c) Preoperatively for cataract extraction.

**Tropicamide (1 and 2%):** Rapidly-acting mydriatic and cycloplegic reaching its maximal activity in 20 minutes and lasting 6 hours. Indications: (a) Refraction in adults. Maximal cycloplegia persists for only 20 minutes. (b) Ophthalmoscopy. (c) Preoperatively for cataract extraction. Ocular side-effects (i) Blurring of vision and inability to accommodate due to cycloplegia. (2) Precipitation of closed-angle glaucoma in patients with narrow angles. (3) Contact dermatitis in 5 per cent of patients using atropine and less commonly with hyoscine.

**Sympathomimetic drugs:** which imitate or potentiate the action of adrenaline and produce pupillary dilatation but no cycloplegia. These drugs potentiate the action of parasympatholytic drugs

**Phenylephrine (Neo-synephrine) (10%):** Produces mydriasis without cycloplegia within 20 minutes and lasts 3 hours. Particularly effective when combined with a parasympatholytic mydriatic. Indications: (a) Ophthalmoscopy. (b) Breaking posterior synechiae. (c) Preventing iris cysts in patients using long-acting anticholinesterases (use 2-5%) (d) Preoperatively for cataract extraction.

**Ephedrine (5%):** Produces mydriasis within 30 minutes, lasting 3 hours. Indication: Ophthalmoscopy.

**Hydroxyamphetamine (Paredrine) (1%):** Produces mydriasis within 40 minutes. Indication: Ophthalmoscopy.

**Adrenaline:** Very poor mydriatic when instilled into the normal eye, but a 1:1000 solution will dilate the pupil of a patient with Horner's syndrome.

**Indications:** (a) Simple glaucoma. 1 to 2% solutions decrease aqueous production and improve outflow. (b) Conjunctival decongestion. (c) Preventing iris cysts in patients using longacting anticholinesterases

(i to 2%) (d) Diagnosis of Horner's syndrome. (e) Decreasing the absorption of local anaesthetics (1: 50,000 or 1 : 100,000).

**Cocaine (2 to 4%):** Produces mydriasis within 20 minutes lasting 2 hours together with a partial cycloplegia. Augments the action of homatropine.

**Indications:** (a) Ophthalmoscopy. (b) Preoperatively for cataract extraction. (c) Local anesthetic. Ocular side-effects (1) Precipitation of closed-angle glaucoma in patients with narrow angles. (2) Transient corneal oedema may occur with phenylephrine. (3) Melanin deposits in the conjunctiva and cornea with adrenaline. (4) Macular oedema is an uncommon side-effect of adrenaline therapy. (5) Ocular pain and stinging. (6) Desiccation of the corneal epithelium with cocaine.

**Systemic side-effects:** The adrenergic drugs may produce tachycardia and palpitations and should be used with caution in patients with hypertensive cardiovascular disease. Cocaine may produce hyperreflexia, restlessness, delirium, tachycardia, irregular respiration, chills and fever, the result of central nervous system stimulation which may terminate in convulsions. These side-effects may be counteracted by a short-acting barbiturate. Compound MYDRICAIN is a solution of atropine, procaine, and adrenaline, which when injected subconjunctivally produces mydriasis within a minute. Indication: When a very powerful mydriatic is required.

**Mydriatic combinations:** Phenylephrine (5%) and Tropicamide (0.8%) combination is commonly used in ophthalmology today. The major advantage of this combination is that it produces quick mydriasis and mydriatic effect persists to facilitate ocular examination.

**Indications:** Ophthalmoscopic examination, Slit lamp examination, Retinal photography, Prior to ocular surgery and other diagnostic procedures.

It is also used

- As an adjunct in the treatment of anterior uveitis
- In the management of anterior segment burns (to dilate the pupil and prevent iris adhesions to the lense)
- In cycloplegic refraction
- For the management of iridocyclitis associated with stromal keratitis
- For the management of uveal inflammation associated with fungal keratitis

**ADR:** On topical application there may be transient burning or stinging sensation and lacrimation. Blurred vision, photophobia and allergic reactions may occur.

**The aging eye:** The components of human eyes usually last a life time. There may be structural as well as

functional disturbances associated with aging. Systemic diseases such as diabetes mellitus and hypertension may hasten the onset and degree of ocular problems. There are some positive compensations that help the aging of eye. For example, the human macula is particularly vulnerable to damage from ultra violet and blue light. Fortunately, the yellow pigment effectively absorbs or scatters away most of these harmful wavelengths, thus diminishing the potential damage to macula. One of the more remarkable aspects of the aging eye is that the eye lense continually acquires new layers of fibres, becoming both progressively thicker and steeper. These changes would normally lead to an increase in lense focusing power and tendency toward near sightedness in older eyes. Although the population aged above 50 years is known to be about 12-15% in our country, we have no data so far that defines the actual causes of ocular problems in elderly, except for major diseases like cataract and glaucoma.

## METHODOLOGY

**Place of Study:** The study was conducted at the Malabar Eye Hospital, Eranjippalam, Calicut, Kerala India. The study has got institutional ethics committee approval designed to carried out for period of three months. On the population of 50 subjects by following interventional study design.

**Subjects and Recruitment:** Patients are enrolled in the study based on inclusion and exclusion criteria and written consent was obtained from all the subjects.

**Inclusion Criteria:** a. Both Male and Female, b. Age for group A is between 16-20 and for Group B is between 60-75. c. Those who are willing to give informed consent.

**Exclusion Criteria:** Patients with a history of cardiac diseases, High Blood pressure, History of past Ocular surgery, Glaucoma, Eye trauma, Diabetes, Allergic patients, Patients with infection and inflammation of eye, Patients with more than .25 mm of anisocoria before dilation.

**Study Protocol:** 100 eyes in 50 patients requiring pupillary dilation as part of their visit to Malabar Eye Hospital Eranhippalam between November 2015 to January 2016 were recruited to the study.

The subjects were divided into two groups.

**Group A:** includes subjects in an age group between 18 to 20 years and

**Group B:** include subjects with age between 60 to 75

The pupil diameter of both the eyes were measured with a transparent measuring scale in all the subjects in both the groups. After measuring the normal pupil size one drop of Tropicamide plus (Tropicamide

0.8% and Phenylephrine 5%) was administered to both eyes of all subjects. The eye drops were placed between the conjunctival sac of the lower eye lid and patients were directed to close their eyes approximately one minute after drop delivery to prevent loss of medication through punctum in the conjunctival sac.

Diameter of pupil of all subjects were measured after 15 minutes, 30 minutes and 45 minutes after drug administration. The adverse effects produced and return of ocular function was assessed by interview method.

**RESULTS AND DISCUSSION**

The pupil is a aperture present in the centre of the iris. It limits the amount of light reaching the retina. The pupil is under the control of autonomic nervous system. Parasympatholytics as well as Sympathomimetic drugs have been used to dilate the pupil. The parasympathetic regulation dominates over the sympathetic effect in the control of the pupil. But Parasympatholytics alone may not provide sufficient pupil dilation. Combination of both drugs offers greater pupil dilation.

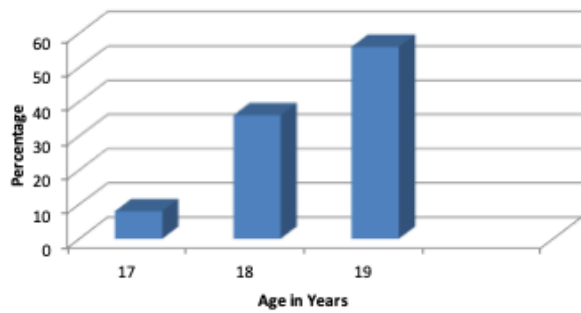
In the hospital where the study was conducted, Tropicamide plus (Tropicamide 0.8% and Phenylephrine 5%) eye drops was frequently used for the purpose of pupil dilation and for cycloplegic refraction for fundus examination and photocoagulation and for preventing the formation of posterior iris synechiae in uveitis. Dilation is also essential in preparation for several intra ocular procedures such as cataract extraction.

This study was undertaken to compare the difference in pupillary response to a same drug in teenagers and geriatric people. The patients who have satisfied the inclusion criteria where enrolled for the study and are assigned in two groups. Such as Group A and Group B. A total of 50 patients where included (ie. 100 eyes) in the study.

**Age:** In Group A majority of the subjects (56%) were of 19 years old. 36% of the subjects belonged to the age 18 and remaining 8 percent of the subjects are of 17 years old (Table 1).

**Table 1: Age distribution of subjects in group A**

Age (Years)	Frequency	Percentage
17	2	8
18	9	36
19	14	56
<b>TOTAL</b>	<b>25</b>	<b>100</b>



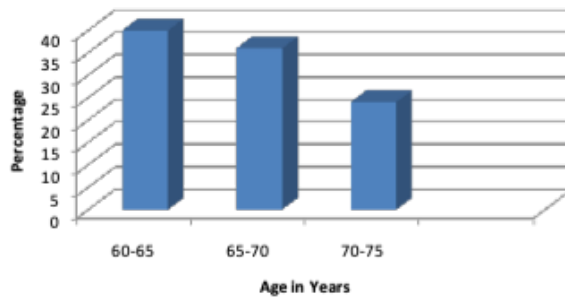
**Figure 1: Distribution of subjects based on age in group A**

In the study population of Group A, majority of subjects fell under the age of 19 (56%). 36% of the subjects belonged to the age of 18 & remaining 8% of the subjects are of 17 years old.

In Group B majority of the subjects fell under the age group of 60 to 65 years (40%). 36% of the subjects belonged to the age group 65-70 years and the remaining 24% of subjects were in the age group of 70 to 75 years (Table 2).

**Table 2: Age distribution of subjects in group B**

Age (Years)	Frequency	Percentage
60-65	10	40
65-70	9	36
70-75	6	24
<b>TOTAL</b>	<b>25</b>	<b>100</b>



**Figure 2: Distribution of subjects based on age in group B**

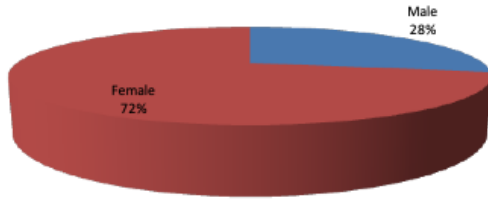
In this study population of group B, majority of the subjects fell under the age group of 60 to 65 years (40%), 36% of the subjects belonged to the age group 65 – 70 and the remaining 24% of the subjects were in the age group of 70 – 75 years

Generally, pupils are relatively small at birth, larger during adolescence and tends to slowly grow smaller with increasing age.

**Gender:** In group A out of the total subject’s 28 percent were male and 72 percent were female (Table 3) whereas majority of the subjects in Group B were male (56%) and 44% were female (Table 4)

**Table 3: Distribution of subjects based on gender in group A and B**

Gender	Group A		Group B	
	Frequency	%	Frequency	%
Male	7	28	14	56
Female	18	72	11	44
Total	25	100	25	100



**Figure 3: Distribution of subjects based on gender in group A and B**

The Study group A consisted of 7 males (28%) and 18 females (72%) and B consisted of 14 males (56%) and 11 females (44%). The study shows that there is no significant difference in pupillary size between male and female.

**Table 4: Distribution of subjects based Congenital Anomalies**

Group	Congenital Anomalies	Frequency	Percentage
Group A	No	25	100
Group B	No	25	100

Among the whole population under study in group A and B no one has reported with any case of congenital anomalies.

**ADR:** As per the study the adverse effects produced by Tropicamide and Phenylephrine varies depending upon the subjects. (Table 5).

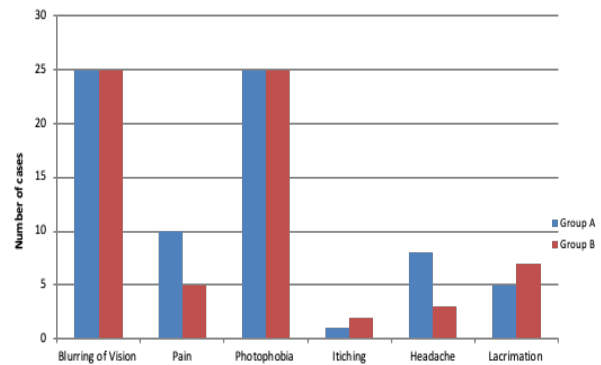
In both groups A and B, blurring of vision was produced as a major side effect in all the subjects (100%). Transient pain after the administration of drug was reported in 40% of subjects of group A and 20% of subjects in group B.

Photophobia was reported in all the subjects of group A and group B (100%) during the period of dilation. Itching was uncommon, which was reported in only 4% subjects of group A and 8% of subjects in group B. Headache was reported in 32% of subjects in group A but only 12% subjects were reported having headache in group B.

**Table 5: Distribution of subjects based on ADR**

ADR	Group A		Group B	
	Frequency	Percentage	Frequency	Percentage
Blurring of vision	25	100	25	100
Pain	10	40	5	20
Photophobia	25	100	25	100

Itching	1	4	2	8
Headache	8	32	3	12
Lacrima-tion	5	20	7	28



**Figure 4: Distribution of subjects based on ADR**

During the study period, after administration of the mydriatic drug various adverse reactions were reported. Such as blurring of vision, pain, photophobia, itching, headache and lacrimation.

Lacrimation was shown by 22% of the subjects of group A and 28% of subjects in group B.

### Pupil size

**Before Administration of Drug:** The normal pupil size in adults varies from 2mm to 4 mm in diameter in bright light. As per the study the mean of normal pupil size of group A was found to be 3.52 mm and of group B it was 2.84 mm (Table 6 & 7). This shows that the group A in which the subjects are teenagers have larger pupil size than geriatric people in group B. As we age the muscles that control our pupil size and reaction to light loss some strength this causes pupil to become smaller and less responsible to changes in ambient lighting.

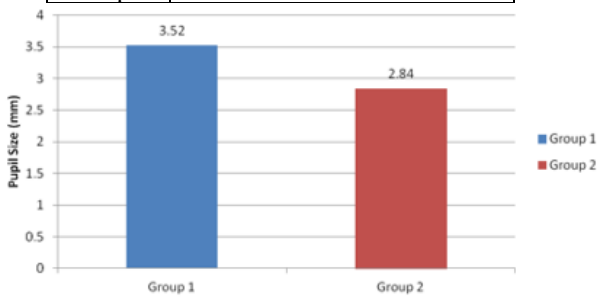
**After Administration of Drug (Table 8):** After administering one drop of the drug (Tropicamide 0.8% and Phenylephrine 5%) The pupil size was measured at 15 minutes, 30 minutes and 45 minutes in both the groups. There was a gradual increase in pupil diameter in both groups but the pupil response was more rapid and of greater magnitude in group A. After 15 minutes the mean pupil diameter was found larger in group A ie. 6.2 mm and 5.28 mm in group B. The observed difference was statistically significant ( $p < 0.05$ ). The mean pupil size was larger in group A ie. 7.4 mm than group B ie. 6.5 mm after 30 minutes. The observed difference was statistically significant ( $p < 0.05$ ). All pupils reached their maximum diameter at 45 minutes in Group A the mean pupil diameter was 8.2 mm and for group B was 7.48 mm. The observed difference was statistically significant ( $p < 0.05$ ).

The mean pupil size with Tropicamide and Phenylephrine was significantly larger in Group A (6.2

mm) than Group B (5.28 mm) after 15 minutes (P=0.49). The mean pupil size with Tropicamide and Phenylephrine was significantly larger in Group A(7.4 mm) than Group B (6.56 mm) after 30 minutes (P=0.03). The mean pupil size with Tropicamide and Phenylephrine was significantly larger in Group A(8.2 mm) than Group B (7.48 mm) after 45 minutes (P=0.12)

**Table 6: Comparison of mean pupil size of group A and B before dilation**

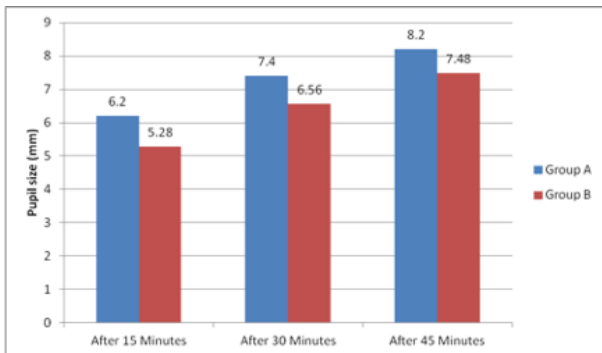
Group	Mean Of Normal Pupil Size (mm)
Group A	3.52
Group B	2.84



**Figure 5: Comparison of mean pupil size of group A and B before dilation**

**Table 7: Comparison of pupillary diameter after 15 minutes, 30 minutes and 45 minutes of drug administration**

Group	Mean of Normal Pupil Size(mm)	Pupil Size After 15 Minutes	Pupil Size After 30 Minutes	Pupil Size After 45 Minutes
A	3.52	6.2 mm	7.4 mm	8.2 mm
B	2.84	5.28 mm	6.56 mm	7.48 mm

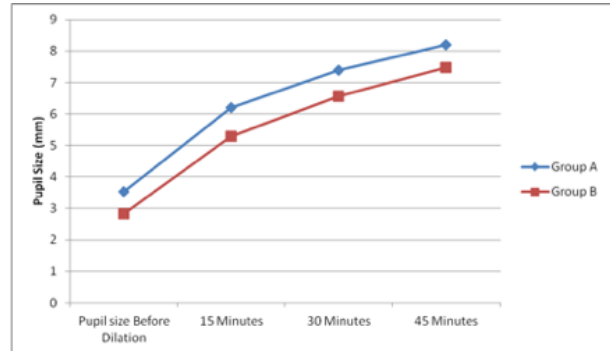


**Figure 6: Comparison of pupillary diameter after 15 minutes, 30 minutes and 45 minutes of drug administration**

**Rate of increase in Pupil size after dilation (table 10)**

In group A, the normal pupil size was 3.52. It was increased 2.68mm after 15 minutes and then the pupil size became 6.2mm. In group B, the normal pupil size was 2.84. It was increased 2.44 mm after 15 minutes and reached 5.28 mm. After 30 minutes the pupil size

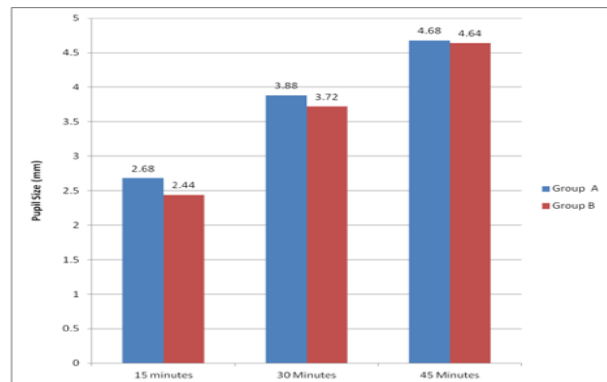
was increased 3.88 mm and reached 7.4 mm in group A. In group B the pupil size was increased by 3.72 mm and reached 6.56 mm. After 45 minutes the pupil size of group A was increased 4.68 mm to reach the pupil size 8.2 mm. in group B pupil size increased by 4.64 mm to reach 7.48 mm. As per the study it was found that there is a gradual increase in pupil size according to time after the administration of one drop of Tropicamide 0.8 5 and phenylephrine 5%.



**Figure 7: Comparison of pupil size of group A and B**

**Table 8: Comparison of rate of increase in pupil size after dilation**

Group	Mean of normal pupil size (mm)	After 15 min (mm)	After 30 min (mm)	After 45 min (mm)
A	3.52	2.68	3.88	4.68
B	2.84	2.44	3.72	4.64
Difference	0.68	0.18	0.16	0.04



**Figure 8: Comparison of rate of increase in pupil size after dilation**

The comparison between these values of pupil size in teenagers and geriatric people shows that there was only a small difference in the size of the pupil after dilation. But the drug produces satisfactory dilation after 45 minutes in geriatric people, which is less as compared to teenagers.

The current study showed that the difference of the pupil size between teenagers and geriatric people after dilation was statistically significant. The decrease in pupil size of geriatric subjects in group B may be



due to the factors which influence the structure and function of eye of the old age. It may be the reduced normal pupil size of aged persons. The size of the pupil varies with age. They become smaller with increasing age. As we age the muscles that control our pupil size and reaction to lights lose some strength. This causes pupil to become smaller and less responsible to changes in ambient lighting. There is another important factor which is responsible for tis findings may be decreased drug permeability across cornea and the functional loss of corneal endothelium due to old age. Even though all these factors may influence the geriatric subjects' eye, the drug produced satisfactory dilation in them. But as compared to teenagers it was less. The difference between pupil size in both groups was statistically significant ( $p < 0.05$ ). All the subjects in group B achieved pupil size larger than 6 mm. This is an acceptable size for conducting general fundus examination therefore the study showed that the drug produced satisfactory pupillary dilation in geriatric subjects also.

### LIMITATIONS

The study population was small. If the study was conducted with larger group of subjects for a long duration more significant results would have been obtained.

The current study followed the pupil size for 45 minutes after eye drops administration. Thus, the effects beyond 45 minutes could not be analysed.

### CONCLUSION

The current study concludes that the mydriatic effect produced by the combination of 0.8% Tropicamide and 5% Phenylephrine in teenagers was higher than geriatric people. There was a significant increase in pupil size after administering the drug, which was higher in teenagers. The observed difference was found to be statistically significant. The decreased mydriatic effect in geriatric people may be due to the structural and functional changes of eye in old age.

**CONFLICTS OF INTEREST:** None

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### DISCLOSURES

**Name:** B. Syed salman

**Contribution:** This author helped write the manuscript. B. Syed salman has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.

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