

Efficacy of Topical Tropicamide 1% versus Combination of Tropicamide 0.8% and Phenylephrine 5% for Mydriasis.

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ABSTRACT

Background: In ophthalmic practice, mydriasis is required on regular basis for refraction & Fundus examination. The study is done to compare effect of 1% tropicamide solution with a combination of 0.8% tropicamide and 5% phenylephrine, the rate of mydriasis and maximal mydriasis caused by a single drop of each solution, and to assess whether this mydriasis is resistant to bright light. **Methods:** In this prospective, randomized study, 150 patients who presented to the Department of Ophthalmology were evaluated for mydriasis. They received 1 drop of Tropicamide 1% in one eye and the combination drop in the other eye. The mydriasis was assessed at 15,30 and 45 minutes after instillation of the drops. **Results:** The fixed drug combination of 0.8% tropicamide with 5% phenylephrine was found to be a better mydriatic than 1% tropicamide alone, with a statistically significant difference between the two groups at 30 mins and 45 mins ($p<0.001$). **Conclusion:** A single drop of a combination of 0.8% tropicamide and 5% phenylephrine achieves adequate mydriasis, in patient 11- 40 years of age.

Keywords: Mydriasis; Tropicamide; Phenylephrine.

INTRODUCTION

Most patients visiting the ophthalmology clinic present with complaints of decreased vision, common causes of which include uncorrected refractive errors, lens opacities and retinal and optic nerve pathology. The evaluation of these conditions requires correct estimate of the refractive error be made, and a detailed fundus examination be carried out.^[1]

Mydriasis is the dilation of the pupil, usually having a non-physiological cause, or sometimes a physiological pupillary response. Non-physiological causes of mydriasis include disease, trauma, or the use of drugs.^[2] 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.^[3-5]

There are two types of muscle that control the size of the iris: the iris sphincter, composed of circularly arranged muscle fibres, and the iris dilator, composed of radially arranged muscle fibres. The sphincter is innervated by (signalled by nerves of) the parasympathetic nervous system; the dilator by the sympathetic nervous system. Sympathetic stimulation of the adrenergic receptors causes the contraction of the radial muscle and subsequent dilation of the pupil. Conversely, parasympathetic stimulation causes contraction of the circular muscle and constriction of the pupil.^[6-10]

The mechanism of mydriasis depends on the agent being used. It usually involves either a disruption of the parasympathetic nerve supply to the eye (which normally constricts the pupil) or over-activity of the sympathetic nervous system (SNS).^[11]

Mydriatics belong to two classes of drugs, parasympatholytics and sympathomimetics. Of these parasympatholytic drugs also have a cycloplegic action. Hence the drug used can either be a combination drop containing both types of drugs, which would produce adequate mydriasis and cycloplegia, or a parasympatholytic drug alone

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which would be as effective as the combination. The combination medication too can be different drops put one after another or formulated as a single drop.^[12-14]

The ideal drug should produce: 1. Prompt, maximal and transient mydriasis after instillation of a single drop. 2. Rapid recovery from the mydriatic action - as most patients would like to resume their daily activities soon after the examination. 3. Consistency in its effectiveness. 4. Minimal ocular and systemic side effects.^[15,16]

The commonly used drugs these days for mydriasis are tropicamide, which is a parasympatholytic and phenylephrine, a sympathomimetic. A combination of both these drugs is known to produce maximal mydriasis due to synergistic action of both classes of drugs.^[17]

The aim of our study was to compare 1% tropicamide solution with a combination of 0.8% tropicamide and 5% phenylephrine for mydriasis. The objective of our study was to evaluate the rate of mydriasis and maximal mydriasis caused by a single drop of each solution, and also to assess whether this mydriasis was resistant to the intense illumination of the indirect ophthalmoscope, that allowing a dilated fundus evaluation.

MATERIALS AND METHODS

A prospective & randomized study was done in department of ophthalmology on 150 patients who were evaluated for mydriasis in OPD. A written informed consent was obtained from all patients. The demographic details of the patient were recorded. A detailed history including presenting symptoms, history of use of glasses, any previous or coexistent ocular or systemic disease and use of medications, both systemic and topical, was obtained.

Examination: The visual acuity was recorded using an illuminated Snellen's chart, with the patient seated at a distance of 6 metres. The vision was checked with and without correction and with pin hole, and the best corrected visual acuity was noted. The near vision was checked using the Steffens near vision chart, held at a distance of 33 cms from the patient. Anterior segment examination was done using the Binocular slit lamp to rule out any anterior segment disease or abnormality. The resting pupillary diameter was measured at the slit lamp using a millimeter rule (baseline measurement) keeping the magnification at 12 and the illumination at 1/8th intensity.

The patients then received the dilating drops. The drops were labelled as A and B by a third person. Each patient received one drop of drop A one eye and drop B in the other eye. Block randomization was used to decide which drop was put in the right eye; accordingly the left eye received the other drop. Hence the process of administering the dilating

drops was randomized and blinded. The details of the randomization table and the labelling of the drops were revealed only after the study was over, at the time of analysis. The horizontal pupillary diameter was measured at 15 mins, 30 mins and 45 mins after putting the drops, by the same procedure described earlier. At each measurement, the resistance of pupillary dilatation to bright light was noted. This was measured by increasing the illumination of the slit lamp to the maximum and noting any pupillary reaction. More than 1 mm constriction was taken as a reacting pupil, indicating that the dilatation was not resistant to bright light.

For the purpose of analysis, the 300 eyes of 150 patients were divided into two groups of 150 each; Group T included eyes which received Tropicamide 1% and Group TP included eyes which received the fixed combination of 0.8% Tropicamide with 5% Phenylephrine.

Further, to study the effect of age on the various parameters, the patients were divided into 3 groups; Group 1 included patients between 11 — 20 years of age, Group 2: 21 — 30 years and Group 3: 31 — 40 years. The data was analysed as follows: first the descriptive statistics were computed. These included the range, mean and standard deviation for quantitative variables, and category frequency counts and percentages for qualitative variables. Univariate analysis to evaluate correlation between 2 parameters was done using Student's t test and analysis of variance (ANOVA) was performed when there were more than two categories. To study the difference in the effect of the two drugs over the period of evaluation, Repeated Measures ANOVA (RMANOVA) was done. Statistical significance was considered when $p < 0.05$. All statistical analysis was done using SPSS Version 10.0 Statistical package.

RESULTS

In our study titled "Efficacy of topical Tropicamide 1% versus a combination of Tropicamide 0.8% and Phenylephrine 5% for mydriasis, a total of 150 Indian patients presenting for refraction or fundus evaluation were included. Two groups were studied — Group T being the eyes which received Tropicamide 1% and Group TP being the eyes which received the combination drop - Tropicamide 0.8% with Phenylephrine 5%. Comparisons were made to study pupillary dilatation and resistance to bright light during the specified time period of 15mins, 30mins and 45mins over the baseline.

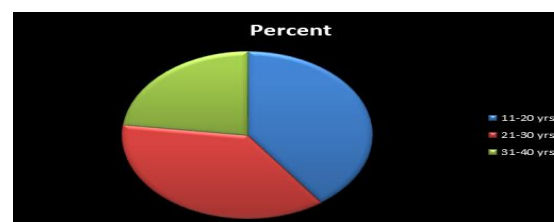


Figure 1: Baseline characteristics of study group.

The age of the patients in the study ranged from 11 years - 39 years, with a mean of 23.87 ± 7.62 years [Figure 1].

Visual Acuity: 143 patients had a best corrected visual acuity (BCVA) of 6/6. 1 patient had BCVA of 6/9 in both the eyes and 6 patients had BCVA of 6/9 in one eye. All patients had a near vision of N6 as tested by the Snellens near vision chart.

Iris Colour: All patients studied had grade 5 dark irides.

Table 1: Comparison of the pupillary site over the period of evaluation between Group T and Group TP.

Time	Group	Mean (mm)	SD+/-	Statistical Test
Baseline	T	3.99	0.39	F = 147.34 P<0.00.1
	TP	3.98	0.39	
15 mins	T	5.46	0.51	
	TP	5.51	0.49	
30 mins	T	6.61	0.56	
	TP	6.97	0.52	
45 mins	T	7.59	0.57	
	TP	8.21	0.51	

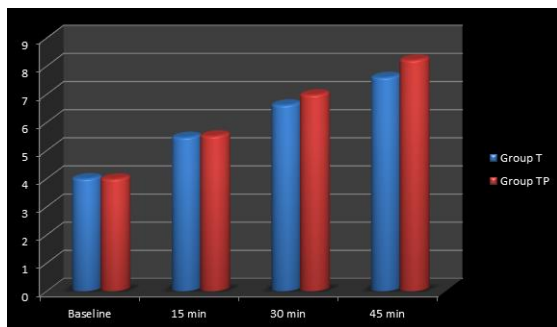


Figure 2: Graphic representation of comparison of the pupillary site over the period of evaluation between Group T and Group TP.

There was a statistically significant difference ($p < 0.001$) between the 2 groups over the period of evaluation [Table 1, Figure 2]. Further pair wise analysis was done to evaluate the time at which there was a significant difference between the groups.

Table 2: Group-wise differences in pupillary diameter at 15 mins, 30 mins and 45 mins.

Time	Grouping pairs	Df	t value	p value
Baseline	GrpT vs GrpTP	149	0.82	0.42
15 mins	GrpT vs GrpTP	149	1.35	0.18
30 mins	GrpT vs GrpTP	149	10.14	<0.001
45 mins	GrpT vs GrpTP	149	19.04	<0.001

The pupillary diameter in both groups was similar at baseline and 15 minutes, whereas at 30 and 45 minutes the difference was statistically significant, with a greater pupillary diameter observed in group 2. The average pupillary diameter measured at 45 minutes was 7.59mm (± 0.57) in Group T, with 3

patients reaching a maximal size of 9mm. In Group TP, the average diameter at 45 mins was 8.21mm (± 0.51) with 13 patients reaching a maximal size of 9mm [Table 2].

Table 3: Resistance of pupillary dilatation to bright light at 15, 30 and 45mins.

Time	Group	Mean	SD+/-	Statistical Test
15 mins	T	0	0	F = 0.249 P = 0.697
	TP	0	0	
30 mins	T	0.13	0.33	
	TP	0.14	0.33	
45 mins	T	0.98	0.12	
	TP	0.99	0.08	

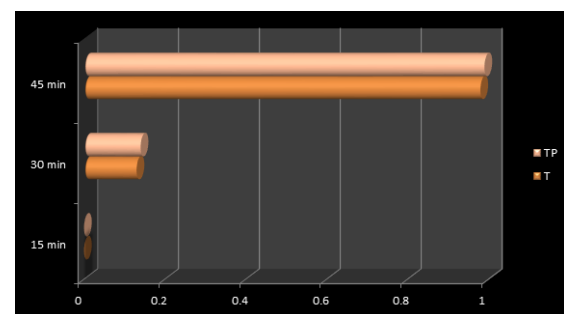


Figure 3: Graphical representation of comparison of resistance of pupillary dilatation to bright light at 15, 30 and 45mins.

At baseline and at 15 minutes, all the pupils were briskly reacting to light. There were 19 patients each in group T and TP whose pupils were resistant to bright light at 30 minutes, with no difference between the two groups. In the others, the pupils still showed at least a 1 mm constriction. At 45 minutes, there were 2 patients in group T and 1 patient in group TP in whom the pupils were still reacting to light; the rest were resistant to the bright light. As there was no statistically significant difference between the two groups at all times, no further analysis was done [Table 3, Figure 3].

DISCUSSION

Mydriatics are routinely required in ophthalmic practice for the diagnosis of refractive errors, cataracts and retinal pathologies. A pupil diameter of at-least 6mm is required for performing indirect ophthalmoscopy and for the accurate diagnosis of cataracts.^[18]

Most hospitals including ours, use frequent instillations of the mydriatic drop for pupillary dilatation; 1 drop every 5 minutes for 3— 6 times. We attempted to study two drops; a combination of 0.8% tropicamide and 5% phenylephrine, and 1% tropicamide alone, as a single instillation, and evaluate their efficacy in producing adequate mydriasis.

Each patient received one drop in the right eye and the other drop in the left eye. This method was

chosen to make sure that the eyes receiving the two drops are comparable in all aspects and to avoid the other confounding factors such as ethnicity, race, gender, age and his colour, which may have a bearing on the pupillary diameter. Our method was similar to studies done by many researchers who used either eye of the patients as controls.^[3,9,15]

This study has established that the fixed drug combination of 0.8% tropicamide with 5% phenylephrine is a better mydriatic than 1% tropicamide alone, with a statistically significant difference between the two groups. A further pairwise analysis showed the difference to be significant at 30 and 45 minutes after instillation of the drops. In both groups at 30 minutes, the average pupillary diameter was more than 6 mm, however the dilatation was not sustained, with only 19 patients in each group whose pupils were resistant to bright light. At 45 minutes, the mean diameter was 7.59mm (± 0.57 mm) in Group T and 8.21mm (± 0.51 mm) in Group TP, with only 3 patients in Group T who reached a maximal size of 9 mm at 45 minutes compared to 13 patients in Group TP. However, nearly all the pupils were resistant to the bright light, with the exception of 2 patients in group T and 1 patient in group TP in whom the pupils were still reacting.

This study has also established that a single drop of the fixed drug combination is sufficient to produce a well sustained pupillary dilatation, eliminating the need for multiple instillations and thus minimizing systemic toxicity. Our findings confirm with previous studies on the adequacy of a single dose regimen for pupillary dilatation.^[1,8,11,12] Blansett DK,^[5] compared single instillation of 1% tropicamide and 10% phenylephrine versus multiple instillations of the same drop and found the former to be as effective as the latter. In our study even a lower strength medication on single instillation was found to be effective. Our findings were similar to that of Leopold IH and Pop M et al who have described that the single instillation of 0.8% tropicamide and 5% phenylephrine produces well sustained pupillary dilatation.^[8,10] Kenawy NB et al studied even further reduced concentrations of the drugs;^[18] 0.5% tropicamide with 2.5% phenylephrine and 1% tropicamide with 2.5% phenylephrine. They found that at 60 minutes all pupils were dilated to minimum 7mm and the dilatation was well sustained. However, the measured diameters at 45 minutes were less compared to those in our study, indicating that increasing the concentration of tropicamide and phenylephrine helps achieve faster dilatation.

In conclusion, a single drop of a combination of 0.8% tropicamide with 5% phenylephrine causes adequate mydriasis and cycloplegia in patients between 11 - 40 years of age. The mydriatic effect of this combination drop has been evaluated by other studies; our findings concur with these studies. As

compared to 1% tropicamide, the combination drop showed better mydriasis, the difference between the two being statistically significant at 30 and 45 minutes.

This study has proven the adequacy of a single drop, hence avoiding the need for multiple instillations and minimizing systemic complications. Hence in clinical practice, the combination drug may be used as a single drop in situations requiring adequate mydriasis and cycloplegia together or in isolation. The results of our study are applicable to the Indian population with dark coloured irides.

CONCLUSION

The fixed drug combination of 0.8% tropicamide with 5% phenylephrine was found to be a better mydriatic than 1% tropicamide alone, with a statistically significant difference between the two groups at 30 mins and 45 mins ($p < 0.001$).

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