

Effectiveness of Topical Proparacaine 0.5% to Augment the Mydriatic Effect of Tropicamide: Phenylephrine Combination Eye Drops

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Abstract

Introduction: Comprehensive intraocular examination requires pupillary dilation with the help of pharmacological agents to cause mydriasis. Dilation of the pupil is controlled by the sphincter and dilator muscle which are, in turn, innervated by the parasympathetic and sympathetic group of nerves, respectively. Pupillary response to mydriatic agents often depends on factors such as iris pigmentation, diabetes melleitus, and any local pathology.

Materials and Methods: The patients were divided into 2 groups for pupillary dilation. The study group was given a drop of 0.5% Proparacaine before giving a drop of Tropicamide and Phenylephrine while the control group was given the mydriatic combination alone. The pupillary size was measured and recorded before instillation of the mydriatic agent at the baseline (0 min), at 10 min, 20 min, 40 min and 60 min. The end point was taken as 8 mm pupillary size or the pupillary size at the end of 60 min.

Results: There was a statistically significant difference in pupil diameter between study eyes and control eyes at 10 and 20 min ($P < 0.021$ for 10 min, $P < 0.001$ for 20 min). The dilation of the pupil at the end of 60 min in the study eye was 8.00 mm, whereas it was 7.99 in the control eye. In our study, 75 out of 100 patients developed mean dilation of 7.75 ± 0.45 mm in the study eye while 46 of 100 patients developed mean dilation of 7.28 ± 0.75 mm in the control eye. There was no statistically significant difference in the augmentary effect of proparacaine among different age groups of study subjects.

Conclusion: It was found that pre-application of proparacaine followed by a commercially available 0.8% tropicamide - 5% phenylephrine showed a more mydriatic effect compared to commercially available 0.8% tropicamide - 5% phenylephrine alone.

Key words: Mydriasis, Phenylephrine, Proparacaine 0.5%, Tropicamide

INTRODUCTION

Comprehensive intraocular examination requires pupillary dilation with the help of pharmacological agents to cause mydriasis.¹ Dilation of the pupil is controlled by the sphincter and dilator muscle which are, in turn, innervated by the parasympathetic and sympathetic group of nerves, respectively. Pupillary response to mydriatic agents often

depends on factors such as iris pigmentation, diabetes melleitus, and any local pathology.

Tropicamide is non-selective muscarinic agent with no vasopressor effect which produces mydriasis but minimal cycloplegia, due to its parasympatholytic action.²

Phenylephrine^{2,3} is sympathomimetic drug acts on alpha-1 receptors to cause pupillary dilation, by stimulating the dilator pupillae. Because of its effect on alpha-1 receptors, it causes vasoconstriction of systemic, pulmonary and coronary arteries which leads to a reduction in cardiac output. Increase in blood pressure, tachycardia, and reflex bradycardia are the known side effects.^{2,3}

An ideal mydriatic drug should provide quick and adequate dilatation with minimal side effects. The commercially

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available ready mixture of 0.8% tropicamide with 5% Phenylephrine along with preservative is a popular mydriatic agent, often used multiple times to achieve mydriasis.

Proparacaine^{4,5} is a topical anesthetic agent which has membrane stabilizing effect and is used for a variety of tests and outpatient procedures.⁶

The aim of this study is to compare the mydriatic efficacy of preapplication of proparacaine.

Aim

To analyze if preinstillation of topical proparacaine 0.5% can potentiate the mydriatic efficacy of 0.8% tropicamide - 5% phenylephrine combination eye drops.

Objectives

This study aims to compare the mydriatic efficacy of 0.8% tropicamide - 5% phenylephrine combination eye drops with or without preinstillation of 0.5% proparacaine in patients attending ophthalmology outpatient department (OPD) at Sri Siddhartha Medical College and Hospital, Tumkur.

The right eye is the test eye/study eye - to receive 0.5% proparacaine followed by commercially available 0.8% tropicamide - 5% phenylephrine and left eye is the control eye - to receive only the combination eye drops - 0.8% tropicamide - 5% phenylephrine. Serial measurements of pupillary size are done to (i) compare the time taken for onset of action - mydriasis, and (ii) compare the time taken to achieve peak mydriasis.

MATERIALS AND METHODS

The study was conducted in the Department of Ophthalmology Sri Siddhartha Medical College, Tumkur, from October 2015 to February 2016. 200 consecutive eyes of 100 patients attending ophthalmic outpatient department were taken for the study. All patients who required pupillary dilation (mydriasis) as a part of their routine ophthalmic evaluation were included in the study. The study was approved by the Institutional Ethics Committee and a waiver of consent was given as the procedure is a routine ophthalmic outpatient procedure.

The subjects underwent routine ophthalmic evaluation - history, visual acuity testing, slit lamp examination, and retinoscopy. The patients were explained about the need for mydriasis and the expected side effects like transient stinging and lacrimation.

The patients were seated comfortably with their head resting. Baseline pupillary diameter was measured in both

eyes with the patient looking at distance, it was measured in the ambient light along the vertical meridian using a transparent scale, by resting the scale on the supraorbital margin and holding the scale in the mid pupillary line. All the measurements were made by the same observer, seated opposite to the patient and recorded in millimeters.

The study/test eye -RE ($n = 100$) received 1 drop of 0.5% of proparacaine eye drops in the inferior fornix. After 2 min, both the test eye and the control eye received 1 drop of the mydriatic eye drop - commercially available 0.8% tropicamide - 5% phenylephrine. The control eye - LE ($n = 100$) was the control eye wherein tropicamide and phenylephrine eye drops were given. All patients had preliminary anterior segment examination including slit lamp examination after visual acuity recording. A drop of topical proparacaine 0.5% eye drops was instilled in the lower fornix of the right eye of all the patients after explaining the procedure. The subjects were told to expect transient stinging and lacrimation immediately following the instillation. After a gap of 2 min mydriatic eye drops were instilled in the control eye and the test eyes, successively. The same was repeated at 10 min and 20 min. After any drop instillation, punctual occlusion was done for 1 min, patients were instructed to keep their eyes gently closed and avoid any globe movement. All these manoeuvres were intended to maximize the available time of the drug in the cul-de-sac.

The pupillary size was recorded before instillation of the mydriatic agent, 5 times in all -at the baseline (0 min), at 10 min, 20 min, 40 min and 60 min. The end point was taken as 8 mm pupillary size or the pupillary size at the end of 60 min.

Inclusion Criteria

A total of 200 eyes of 100 consecutive patients attending ophthalmology OPD, above the age of 18 years, who were able to understand and assent to the pupillary dilation procedure were included in the study.

Exclusion Criteria

History of diabetes,⁷ hypertension, use of any topical medication, presence of pupillary abnormalities, history of or signs of intraocular inflammation, any intraocular procedure/surgery like cataract surgery,⁸ formed the exclusion criteria.

OBSERVATION AND RESULTS

A total of 200 eyes were studied, belonging to 100 consecutive patients, of which 52 were men and 48 were women (Table 1, Figure 1). Their age ranged from 20 to 80 years, (Table 2, Figure 2) with a mean of

41.59 ± 14.41 years (men) and 43.85 ± 14.67 years (women) (Table 3).

There was a statistically significant difference in pupil diameter between study eyes and control eyes at 10 and 20 min ($P < 0.021$ for 10 min, $P < 0.001$ for 20 min)

Table 1: Frequency distribution of patients according to gender

Gender	Female	Male	Total
Observations (%)	48 (48.00)	52 (52.00)	100 (100.00)

Table 2: Distribution of patients according to Age group

Age group	Female	Male	Total (%)
20-39	21	29	50 (50)
40-59	19	12	31 (31)
60-79	8	11	19 (19)
Total	48 (48)	52 (52)	100 (100)

Table 3: Mean age of patients under study

Gender	Observations	Mean age±SD
Female	48	43.85±14.67
Male	52	41.59±14.41

SD: Standard deviation

(Table 4, Figure 3). The dilation of the pupil at the end of 60 min in the study eye was 8.00 mm whereas it was 7.99 in the control eye.

In our study, 75 out of 100 patients developed mean dilation of 7.75 ± 0.45 mm in the study eye while 46 of 100 patients developed mean dilation of 7.28 ± 0.75 mm in the control eye.

There was no statistically significant difference in the augmentary effect of proparacaine among different age groups of study subjects (Table 5).

DICUSSION

An adequate mydriasis allows for a complete intraocular examination which is achieved with the help of a suitable pharmacological mydriatic with little or no side effects.

In current ophthalmic practice, commercially available drops containing a combination of drugs are used to achieve pupillary dilation.^{9,10} Tropicamide acts by relaxing the iris sphincter muscle. It acts by non-selectively inhibiting the muscarinic action of acetylcholine, thereby blocking the cholinergic nerves supplying the smooth muscles of iris. The end effect is mydriasis and paralysis of ciliary muscle with the loss of accommodation for near objects.

Table 4: Mydriatic effect of proparacaine+tropicamide and phenylphrine - study eye (RE) and tropicamide and phenylephrine control eye (LE)

Mydriatic effect at different min	Right eye test/study	Left eye control	P	Association
	0.5% paracaine+0.8% tropicamide and 5% phenyl ephrine (mean±SD)	0.8% tropicamide and 5% phenyl ephrine (mean±SD)		
0 min	2.61±0.49	2.61±0.49	0.417	Not significant
10 min	4.23±0.73	3.67±0.88	0.021	Significant
20 min	6.19±0.61	5.52±0.89	0.001	Highly significant
40 min	7.75±0.45	7.28±0.76	0.381	Not significant
60 min	8.00±0.00	7.99±0.01	0.533	Not significant

SD: Standard deviation

Table 5: Mydriatic effect of tropicamide and phenyl ephrine + paracaine in right eye and tropicamide and phenyl ephrine alone among young and old age group

Mydriatic effect of right eye at different min	(mean±SD)		P	Association
	Age group<40	Age group>40		
	Study eye	Control eye		
	Tropicamide and phenyl ephrine+ paracaine	Tropicamide and phenyl ephrine		
0 min	2.58±0.49	2.64±0.48	0.236	Not significant
10 min	4.20±0.60	4.26±0.85	0.432	Not significant
20 min	6.22±0.61	6.16±0.61	0.317	Not significant
40 min	7.80±0.45	7.70±0.46	0.173	Not significant
60 min	8.00±0.00	8.00±0.00	0	Not significant

SD: Standard deviation

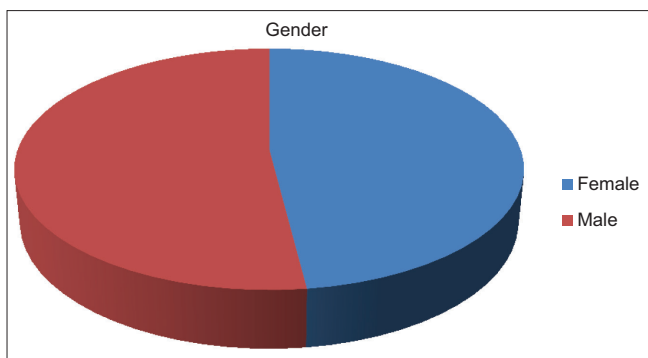


Figure 1: Frequency distribution of patients according to gender

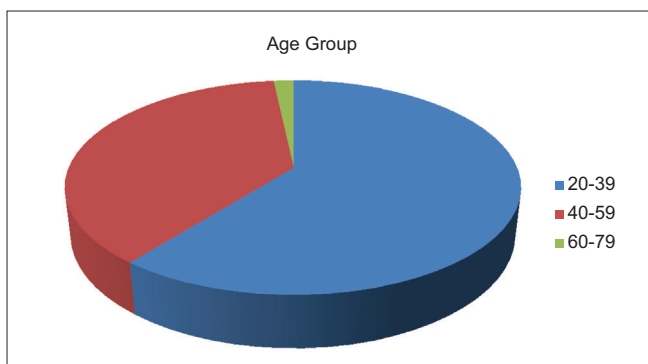


Figure 2: Distribution of patients according to age group

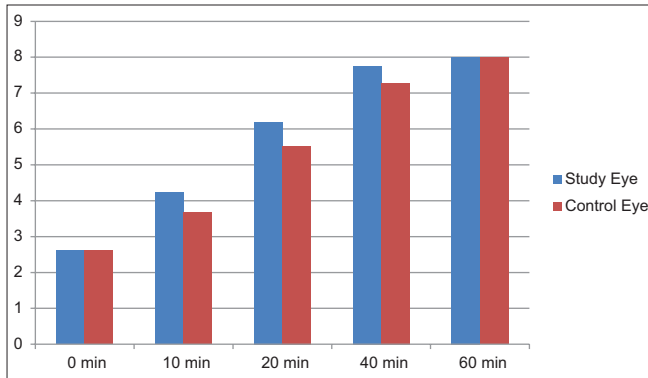


Figure 3: Mydriatic effect of proparacaine + tropicamide and phenylephrine - study eye (RE) and tropicamide and phenylephrine control eye (LE)

Phenylephrine^{11,12} acts on alpha-1 adrenergic receptors of sympathetic nerves supplying the dilator muscle. However, it has the potential to cause undesirable systemic effects like tachycardia and elevated blood pressure.

Proparacaine^{13,14} is a general purpose topical anesthetic in ophthalmological clinics. It is accepted by most patients as it causes minimal, transient discomfort, or irritation on instillation. It acts on the cell membrane and blocks the transient increase in membrane permeability to sodium ions that normally occurs with depolarization of the membrane.

In addition, local anesthetics causes lowering of the tear break-up-time, along with increase of corneal thickness, both point to subclinical micro epithelial changes, and this minimal damage to the corneal epithelial barrier facilitates increased transcorneal permeability of the drug thereby reducing dilation time, increasing the amplitude of maximum dilation and increasing the duration of dilation.^{14,15}

Our study mainly focused on the effectiveness of proparacaine to augment mydriatic effectiveness using tropicamide and phenylephrine eye drops. Baseline pupillary size was recorded in millimeters using a transparent scale. The end point was taken as 8 mm or the pupillary size at 60 min.

In our study, it was found that mydriasis was achieved comparatively quicker with the use of proparacaine in the study eye compared to the control eye with a *P* value of 0.001

A study by Ghose *et al.* found that pupillary diameters in the study eyes increased by 3.62 ± 0.75 mm, significantly more than in the placebo (control) group (*P* = 0.000). 90% of study eyes attained the clinically significant 6-mm size with preinstillation of lignocaine-many more than the 67% of control eyes (*P* = 0.016). The median time to achieve this critical 6 mm size was significantly faster in the study group (*P* = 0.005).¹⁶

In our study, we also compared the mydriatic effectiveness of proparacaine among different age groups as pupillary dilation in older age groups is generally more tedious and found that there was no statistical significance.

The limitations of this study included the lack of randomization and the method of pupillary size measurement.

CONCLUSION

It was found that preapplication proparacaine followed by a commercially available 0.8% tropicamide - 5% phenylephrine showed a more mydriatic effect compared to commercially available 0.8% tropicamide - 5% phenylephrine alone. Furthermore, the quicker onset of action increased patient comfort level by reducing stinging effect of commercially available 0.8% tropicamide - 5% phenylephrine, were an added advantage. This, in turn, helps in reducing patient waiting time and allowing quicker examination of patient, apart from increasing the compliance.

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