THE EFFECT OF PROPARACAINE INSTILLATION BEFORE AND AFTER TROPICAMIDE TO INITIATE EARLY MYDRIASIS

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ABSTRACT

PURPOSE
To analyze the effect of Proparacaine 0.5% in potentiating a better mydriasis prior to and after application of Tropicamide 1%.

METHODS
This was a randomized single blind clinical trial enrolling 60 eyes of 30 healthy subjects aged 10-50 years. Right eye received one drop of 0.5% Proparacaine first and then one drop of Tropicamide 1% after 3 minutes. Left eye received one drop of Tropicamide 1% first and then one drop of Proparacaine 0.5% 3 minutes later. A ruled pupilometer recorded pupil diameters every 10 minutes for 30 minutes.

RESULTS
The mean maximum diameter achieved in right eye 7.00 (6.00-7.50) mm was much larger than the left eye 6.50 (6.00-7.00) mm, P=<0.001. The total mydriatic effect in right eye was also significantly higher than left eye (P=<0.001).

CONCLUSION
Prior application of Proparacaine is better than applying it after instilling tropicamide to achieve better mydriasis.

KEYWORDS
Mydriasis, Tropicamidc, Proparacaine, Pupil.


INTRODUCTION
Dilatation of pupils is a routine practice in standard ophthalmologic examination to view the lens, vitreous, retina and for refraction. Adequate dilatation has always remained a problem, especially in dark-coloured eyes. [1-4] These darker eyes may require much more mydriatic drops and time to achieve adequate dilatation, thus also increasing chances of local and systemic side effects. The use of Proparacaine as a potentiating agent for mydriasis induced by both Phenylephrine. [5,6] and Tropicamide. [7] is well documented. In these studies Proparacaine was applied prior to the mydriatic.

On the contrary, Siderov et al. [8] reported that there was no statistical significance in pupillary dilatation in dark coloured irides.

In another study conducted by Rajanandh et al. [9] reported that proparacaine does not produce or potentiate any significant mydriasis as compared to tropicamide. Despite its local anaesthetic effect it had no significant role in mydriasis and that Tropicamide alone was superior in producing mydriasis.

In this study we compare the effect of Proparacaine on potentiating Tropicamide induced mydriasis both prior to and after the instillation of the afore mentioned mydriatic eye drop.

MATERIALS AND METHODS
60 eyes of 30 healthy subjects aged between 10-50 years were included in the study. The study followed the tenets of the Declaration of Helsinki, with due approval from the institutional ethics committee. After informed consent, each subject during enrolment underwent a complete ophthalmic workup including history, general physical examination, corrected visual acuity, slit lamp biomicroscopy for corneal and pupil examination and determining anterior chamber depth by the Van Herick method, direct ophthalmoscopy with undilated pupil, and digital tension.

Subjects with any abnormality of pupils and irides, glaucoma, uveitis, trauma, past history of ocular surgeries, dry eyes, corneal changes, epiphora, contact lens wear, pseudoxfolliation in the anterior segment, known allergies to the drugs used, concurrent usage of other eye drops and systemic diseases such as diabetes mellitus, hypertension and arthritis were excluded from the study.

The baseline measurements of both the pupils were then recorded with a simple ruled pupilmeter at ambient room light conditions. This pupilmeter is accurate up to 0.5 mm with a wide range of 1.5 to 8.0 mm, without requiring undue instrumentation or the patient's cooperation. It was placed transversely at the midlevel of the pupil, as close to the eye as possible without touching it or the lashes. Pupil size was compared with the painted black semicircles of different sizes.
on the edge of the scale, while the subject fixated on a distant object. A pupil size of 6mm was considered adequate for ophthalmoscopy.

The right eye of every subject received a drop of Proparacaine 0.5% followed by Tropicamide 1% after 3 minutes. The left eye first received a drop of Tropicamide 1% followed by Proparacaine 0.5% after 3 minutes. The drops were placed carefully in the conjunctival cul-de-sac taking care as to not touch the ocular surface to avoid contamination.

The subject was then asked to close the eyes gently and not to blink or squeeze the eyelids for 1 minute. The subjects were blinded to the drops being used. The drops were applied and at 10, 20 and 30 minute intervals pupillary diameters were measured and recorded.

**STATISTICAL ANALYSIS**

Data was analysed using the statistical software SPSS version 18.0. The data on change in pupil diameter was skewed (By Kolmogorov-Smirnova test) at all the stages. The right eye and left eye of the same subject were used for comparison of pupillary diameter between the two methods. The changes in pupil diameter were summarized in terms of median and IQR (Inter quartile range). Wilcoxon signed rank test was used to compare the change in pupil diameter between the two methods at different stages. P<0.05 was considered for statistical significance.

**RESULTS**

60 eyes of 30 subjects were evaluated in this study (Male: Female=16:14). 50% of subjects were in the age group of 10-30 and 50% were in 31-50 age group. The baseline values of both pupils were naturally identical 3.00 (3.00-4.00) mm. The mean maximum diameter achieved in right eye 7.00 (6.00-7.50) mm was much larger than the left eye 6.50 (6.00-7.00) mm. The total mydriatic effect of Tropicamide (Maximal pupil diameter minus the baseline value) in right eye was 4.00 mm compared with 3.50 mm in the left eye (P<0.001).

<table>
<thead>
<tr>
<th>FEATURE</th>
<th>RIGHT EYE Median (IQR) (in mm)</th>
<th>LEFT EYE Median (IQR) (in mm)</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>baseline</td>
<td>3.0 (3.0 - 4.0)</td>
<td>3.0 (3.0 - 4.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>at 10 min</td>
<td>4.0 (3.5 - 5.0)</td>
<td>4.0 (3.5 - 4.0)</td>
<td>0.028</td>
</tr>
<tr>
<td>at 20 min</td>
<td>5.25 (5.0 - 6.0)</td>
<td>5.0 (4.8 - 6.0)</td>
<td>0.009</td>
</tr>
<tr>
<td>at 30 min</td>
<td>7.0 (6.0 - 7.5)</td>
<td>6.5 (6.0 - 7.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The maximal dilatation achieved was resistant to the bright light of the indirect ophthalmoscope permitting a good view of the fundus up to periphery. None of the subjects complained about local or systemic side effects of the drugs used.

**DISCUSSION**

Dilated pupil examination of the fundus is now a standard routine ophthalmic procedure performed on patients with the help of mydriatic agents. Often patients who undergo mydriasis are made to wait for a long time in order for their pupils to be maximally dilated and in busy clinical practice this can be troublesome for both the patient and the doctor as more frequent instillation is required.

The current study was undertaken in order to find out a way of achieving mydriasis with the help of Proparacaine 0.5% by reducing the frequency of instillation of Tropicamide. Tropicamide 1% eye drop is the drug of choice for use in ophthalmic practice to achieve mydriasis as it has a relatively faster onset and shorter duration of action when compared with other commercially available mydriatic preparations.

Tropicamide blocks the acetylcholine action on the muscarinic receptors leading to the paralysis of sphincter iris muscles. This effect is followed by the unopposed actions of the adrenergic innervations to the radial dilator muscle ultimately leading to dilatation. The maximal dilatation is usually achieved within 40 minutes and the effects last up to 6 hours.\[^{10}\]

Proparacaine is widely used as a general-purpose topical anaesthetic. It produces little or no discomfort or irritation on instillation and is therefore readily accepted by most patients. 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. Blockade of sodium transport is thought to occur through binding of the local anaesthetic to a specific binding site located within a voltage-gated sodium channel present in the cell membrane.\[^{10}\]

Proparacaine is known to cause changes in corneal thickness for about 5 minutes after instillation.\[^{10,11}\] Earlier studies on rabbit and rat corneal epithelia, using proparacaine,\[^{12,14}\] demonstrated altered electrical resistance, as well as surface micromodification,\[^{12,13}\] and other cytoskeletal changes,\[^{14,15}\] leading to loosening of tight junctions with disruption of intercellular spaces. This may be one of the reasons for the changes in corneal thickness noted after proparacaine instillation.

Proparacaine is also known to cause significant decrease in tear film quantity and tear film stability after instillation when compared with 0.5% Tetracaine.\[^{16}\]

The above 2 reasons maybe the cause for the better mydriasis achieved in this study. The proper time interval between the topical anaesthetic and the mydriatic could be very crucial. Instilling the mydriatic too soon after the anaesthetic may not be desirable, because it would lead to dilution of the mydriatic by the anaesthetic drop itself, which may still be present in the conjunctival sac.

Moreover, it may also not allow enough time for the anaesthetic to produce whatever effect, either inducing corneal microepithelial changes, or by altering the tear film quantity and quality, required for this potentiation. In fact, keeping too long a time interval might lead to the waning of these effects of the anaesthetic and thus to a relative decrease in the potentiation. Keeping these factors in mind, a time interval of 3 minutes was decided on for this study.

This study is not without its limitations. Controls were not used to determine the rate of dilatation as previous studies had already proven Proparacaine as a potentiator to mydriasis.\[^{5,7}\] Instead we wanted to compare the amount of dilatation achieved, by instilling prior to and after Tropicamide. Also, the study was not double-blinded as the earlier studies. Only the subjects were blinded to the drops being used.

This study shows that pre-instillation of Proparacaine prior to Tropicamide helps in achieving a better mydriasis rather than instilling Proparacaine after Tropicamide has
already been instilled. Therefore it would be prudent to practice instilling of Proparacaine before performing mydriasis on a patient in order to achieve maximal dilatation of the pupils.

**CONCLUSION**

This study concludes that pre-instillation of Proparacaine 0.5% helps to induce a better mydriasis achieved by Tropicamide rather than instilling after. Also single instillation of Tropicamide will reduce the incidence of side effects and increases the patient's comfort level.

**REFERENCES**