Effect on Ciliary Muscles and Accommodation: Comparative Study Between Topical Tropicamide 1% versus Combination of Tropicamide 0.8% and Phenylephrine 5%

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ABSTRACT

Background: Cycloplegia is the paralysis of the ciliary muscles achieved by blocking the muscarinic receptors normally stimulated by the release of acetylcholine from the nerve endings of the parasympathetic system. The study is done to compare effect of 1% tropicamide solution with a combination of 0.8% tropicamide and 5% phenylephrine, for the degree of cycloplegia and the amount of residual accommodation at 20 minutes after instillation of the drop.

Methods: In this prospective, randomized study, 150 patients who presented to the Department of Ophthalmology were evaluated for cycloplegia. They received 1 drop of Tropicamide 1% in one eye and the combination drop in the other eye. The cycloplegia and residual accommodation were assessed at 20 minutes using the autorefractometer.

Results: In the eyes that received Tropicamide 1%, the mean cycloplegia measured at 20 minutes was 1.12 D and the mean residual accommodation was 1.20 D. In the eyes that received the combination drop, the mean cycloplegia was 1.05 D and the mean residual accommodation was 1.26 D. Though the cycloplegic effect of tropicamide 1% was marginally better than the combination drop, the difference in the two groups was not statistically significant for cycloplegia (p=0.007) or residual accommodation (p=0.15).

Conclusion: A single drop of a combination of 0.8% tropicamide and 5% phenylephrine achieves adequate cycloplegia, in patient 11-40 years of age.

Keywords: Cycloplegia; Tropicamide; Phenylephrine.

INTRODUCTION

Cycloplegia is the paralysis of the ciliary muscles achieved by blocking the muscarinic receptors normally stimulated by the release of acetylcholine from the nerve endings of the parasympathetic system. Since the parasympathetic nervous system also enervates the pupil sphincter pupillae muscle, cycloplegia is always accompanied by mydriasis (although mydriasis is not always accompanied by cycloplegia). Cycloplegic drugs are used to produce the above effects and can thus prevent or reduce accommodation during refraction, thus making latent refractive errors to become manifest, thus enabling an accurate estimation of the error. A well dilated pupil helps the refraction to be carried out more easily and accurately, and also allows a thorough examination of the lens and fundus.³⁷

The cycloplegic agents used are atropine, cyclopentolate and tropicamide. Whereas atropine and cyclopentolate are effective in children, they have a much longer duration of action than tropicamide, and are less effective for rapid mydriasis. Tropicamide produces rapid mydriasis and adequate cycloplegia in adults, but it is not known if it is an effective cycloplegic agent in children, who have a higher ciliary muscle tone. Cycloplegic agents are drugs that act by antagonizing the muscarinic action of acetylcholine. They do so by blocking its action at structures innervated by postganglionic parasympathetic nerve fibres. These agents paralyse the constrictor pupillae as well as the ciliary muscle, causing mydriasis as well as cycloplegia. For many years, atropine was the only cycloplegic agent available. To bring about full cycloplegia in children, it had to be instilled two or three times...
daily for three days prior to cycloplegic refraction. The resulting cycloplegia persisted for seven to ten days and the accompanying mydriasis lasted as long as two weeks.8-12 The sphincter pupillae and ciliary muscles, which belong to the adrenergic system, are innervated by the postganglionic parasympathetic efferent fibres of the short ciliary nerve branches of the oculomotor nerve (CN III) that have synapsed in ciliary ganglion. The dilator pupillae muscle is innervated by long ciliary nerves carrying postganglionic fibres of the sympathetic nervous system that have synapsed in the superior cervical ganglion. Cholinergic stimulation of the sphincter pupillae muscle causes papillary constriction (miosis), and cholinergic stimulation of the ciliary muscle brings about increased accommodation. Blockade of the cholinergic system dilates the pupil (mydriasis) and relaxes the ciliary muscle, causing a decrease in accommodation (cycloplegia).13-17 The aim of our study was to compare 1% tropicamide solution with a combination of 0.8% tropicamide and 5% phenylephrine, for cycloplegia. The objective of our study was to evaluate the degree of cycloplegia and the amount of residual accommodation at 20 minutes after instillation of the drop.

MATERIALS AND METHODS

A prospective & randomized study was done in Department of Ophthalmology on 150 patients who were evaluated for cycloplegia in OPD.

Exclusion Criteria

1. Patients already using mydriatics or cycloplegics.
2. All cases of glaucoma.
3. Patients with Best Corrected Visual Acuity < 6/60 or near vision <N12, to exclude patients with poor vision who would not be able to perform the tests.
4. Post ocular surgery.
5. Hypertensive patients.
6. Diabetic patients as they are known to have rigid pupils which are more difficult to dilate.
7. Patients on systemic drugs that could affect the pupil or accommodation, e.g. psychotherapeutic drugs.
8. Patients suspected to have ciliary muscle spasm, resulting in artificially increased amount of myopia.
9. Patients with known pseudoexfoliation syndrome, in whom the pupils are expected to be rigid.

Proper history was taken and detailed examination was done. Patients were informed about the study and written consent was taken. Non cycloplegic refraction at baseline was estimated using the Automated Refractometer as follows: a) Patients were first presented with the distant target at 6m and the spherical equivalent for distance was noted. b) Then the near target at 33cm was present. The patients were asked to view the target and report it as seen clearly, if not, a near add was presented on the machine, which was within the target.

The post cycloplegic refraction was measured on the automated refractometer at 20 minutes. The measurement was done in a similar manner to that described earlier, with the patients first being presented with the distant target and then the near target. The near add was increased till the patients were able to see the target clearly. Compared to the non cycloplegic refraction, post cycloplegia all the patients required an increased amount of near add to view the same target clearly.

The results were analyzed 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 differences in the effect of the two drugs over the period of evaluation. Repeated Measures ANOVA (RMANOVA) was done. To evaluate any correlation between latent error, residual accommodation and cycloplegia, linear regression analysis 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 “Effect on Ciliary Muscles & Accommodation: Comparative Study between Topical Tropicamide 1% versus Combination of Tropicamide 0.8% and Phenylephrine 5%”, 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%. The 2 groups were compared for the cycloplegic effect, measured at 20 mins from baseline.

There was no statistically significant difference in the change in refraction readings (latent error) over time between the two groups (p=0.23) [Table 1]. There was a marginal difference in the near add between the two groups over time, with a higher near add required for group T, which was not statistically significant (p = 0.08). Cycloplegia induced by each group was further calculated by deducting the baseline near add from the 20 mins near add. The mean (± SD) cycloplegia for Group 1 was 1.12 (± 0.33) and for Group 2 was 1.05 (± 0.34); the difference was not statistically significant (p = 0.08) [Table 2].
Table 1: Changes in spherical equivalent over time.

<table>
<thead>
<tr>
<th>Spherical equivalent</th>
<th>Mean (SD)</th>
<th>Statistical test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline – Group 1</td>
<td>-0.64 (1.39)</td>
<td>F = 1.143</td>
</tr>
<tr>
<td>Baseline – Group 2</td>
<td>-0.66 (1.43)</td>
<td>P = 0.23</td>
</tr>
<tr>
<td>20 mins – Group 1</td>
<td>-0.44 (1.44)</td>
<td></td>
</tr>
<tr>
<td>20 mins – Group 2</td>
<td>-0.40 (1.43)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Changes in near add over time (cycloplegia).

<table>
<thead>
<tr>
<th>Near Add</th>
<th>Mean (SD)</th>
<th>Statistical test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline – Group 1</td>
<td>0.25 (0.33)</td>
<td>F = 3.081</td>
</tr>
<tr>
<td>Baseline – Group 2</td>
<td>0.28 (0.35)</td>
<td>P = 0.08</td>
</tr>
<tr>
<td>20 mins – Group 1</td>
<td>1.37 (0.44)</td>
<td></td>
</tr>
<tr>
<td>20 mins – Group 2</td>
<td>1.32 (0.43)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Residual accommodation.

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean</th>
<th>SD</th>
<th>t</th>
<th>df</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>1.20</td>
<td>0.36</td>
<td>1.45</td>
<td>298</td>
<td>0.15</td>
</tr>
<tr>
<td>TP</td>
<td>1.26</td>
<td>0.36</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: Comparison of residual accommodation in two groups.

Table 4: Correlation b/w latent error and amount of cycloplegia and residual accommodation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Beta coefficient</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latent error vs Residual accommodation</td>
<td>0.06</td>
<td>1.04</td>
<td>0.30</td>
</tr>
<tr>
<td>Latent error vs Cycloplegia</td>
<td>0.32</td>
<td>0.55</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Table 5: Effect of age on residual accommodation and cycloplegia.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age group</th>
<th>Mean (± SD)</th>
<th>F</th>
<th>df</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycloplegia</td>
<td>1</td>
<td>0.95 (0.32)</td>
<td>18.25</td>
<td>2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1.19 (0.29)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1.14 (0.36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residual</td>
<td>1</td>
<td>1.39 (0.38)</td>
<td>30.94</td>
<td>2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Accommodation</td>
<td>2</td>
<td>1.19 (0.23)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1.0 (0.40)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The measured residual accommodation in Group T was presented, which stimulates accommodation. The difference in the amount of near add required to view the near target before and after using the drops, is suggested as a method of directly calculating the amount of cycloplegia caused by the drug. This method of calculating induced cycloplegia has not been reported by any other study to the best of our knowledge.

At baseline, the average near add required to view the target was 0.25 for the group receiving tropicamide and 0.28 the group receiving the combination drop, with no statistically significant difference in the two groups. Twenty minutes after instillation of the drops, the near add required to view the same target increased to a mean of 1.37 (±0.44) in group T and 1.32 (±0.43) in group TP, indicating a marginally higher add required by the group who received tropicamide 1% alone. However, this difference was not found to be statistically significant (p = 0.08).

The mean cycloplegia measured at 20 minutes for Group T was 1.12 (± 0.33) and for Group TP was 1.05 (± 0.34) which was not statistically significant (p = 0.07).

The residual accommodation was calculated after the near add was given. The near add was increased till the subject reported blurring of the target. The difference between this value and the previous value gave the amount of residual accommodation. This is similar to the earlier subjective methods used, the difference being that we did it on the autorefractometer. By this method, the mean residual accommodation for the eyes receiving tropicamide 1% was 1.20 (± 0.36) D, and that for the eyes receiving the combination drop was 1.26 (± 0.36) D. The values were marginally lower in the 1st group, however this difference was not statistically significant (p = 0.15) with both groups well within the limits of 2 D of residual accommodation agreed upon by different authors. The lack of statistically significant difference in residual accommodation and induced cycloplegia between the 2 groups indicates that the combination drop which contains reduced amounts of tropicamide is as effective a cycloplegic as 1% tropicamide alone. 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.

After instillation of drops, there was a mean hypennetropic shift (latent error) in the refraction from baseline because of the induced cycloplegia. The latent error uncovered by the cycloplegia was 0.21 D in group T and 0.26 D in group TP. The amount of cycloplegia and residual accommodation should influence the estimation of refractive error. However, we did not find any correlation between latent error and cycloplegia or residual accommodation. Our result is similar to the study done by Manny et al (46). The significance of the above finding is not understood at the present time. On analysis by age groups, it was found that the residual accommodation was higher in the younger age groups compared to the older age groups: 1.39 (± 0.38) in group 1, 1.19 (±0.23) in Group 2 and 1.0 (± 0.40) in Group 3. The difference between the groups was statistically significant (p < 0.01) indicating that the drugs produces less cycloplegia in younger persons who are known to have a higher accommodative tone. However, in each group, the mean value for residual accommodation was less than 2 D, indicating that the cycloplegia was adequate for refraction. The amount of near add required at baseline was analyzed according to age groups, and it was found that Group 3 required a much higher add compared to groups 1 and 2, the difference being statistically significant (p < 0.001). This
was in spite of all patients reading N6 on the Snellen near vision type. This difference could be due to different accommodative amplitudes and reserves in different persons, which decreases as the person grows older. This decrease was not apparent while testing using the standard near vision charts, but became evident as an increasing amount of plus add required to view the near target at baseline, indicating that probably subtle changes are poked up by the machine earlier than other methods.

The only complication we noted was mild stinging immediately following the application of the drops which lasted for less than 2 minutes. Mild lid retraction occurred in 10 eyes which received the combination drop. Phenylephrine is known to cause systemic toxicity like elevated blood pressure, arrhythmias and myocardial infarction. However, we did not check blood pressure or any other systemic parameters before and after drop instillation and hence cannot comment upon the occurrence of any systemic complications induced by the combination drug. This study did not establish the efficacy of tropicamide or the combination drop as a mydriatic or cycloplegic in the presence of systemic and local pathology. The cycloplegia and residual accommodation caused by the two drops were comparable, with no statistically significant difference between the two drops. We noted a mean hyperopic shift (latent error) occurring in the refractive error in both groups, due to the induced cycloplegia. The cycloplegia and residual accommodation were adequate in all the three age groups studied, indicating that the combination drop is effective even in younger patients who are known to have a higher accommodative tone. In this study we also suggest a method to directly measure the amount of cycloplegia caused by a drug, using the autorefractometer, calculated as the difference in the near before and after instillation of drops. Earlier reports suggest the use of residual accommodation as an indicator of the amount of cycloplegia; this method of directly calculating the amount of induced cycloplegia has not been reported earlier, to the best of our knowledge.

CONCLUSION
In the eyes that received Tropicamide 1%, the mean cycloplegia measured at 20 minutes was 1.12 D and the mean residual accommodation was 1.20 D. In the eyes that received the combination drop, the mean cycloplegia was 1.05 D and the mean residual accommodation was 1.26 D. Though the cycloplegic effect of tropicamide 1% was marginally better than the combination drop, the difference in the two groups was not statistically significant for cycloplegia (p=0.007) or residual accommodation (p=0.15). A single drop of a combination of 0.8% tropicamide and 5% phenylephrine achieves adequate cycloplegia, in patient 11-40 years of age.

REFERENCES
10. J. Mordi et al. Effects of 0.1% cyclopentolate or 10% phenylephrine on pupil diameter and accommodation, Ophthalmic and Physiological Optics, 1986; 6(2):221–227.

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