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Efficacy of topical tropicamide 1% versus a combination of tropicamide 0.8% and phenylephrine 5% for cycloplegia

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Abstract

Background: In ophthalmic practice, cycloplegia were required on a regular basis for refraction and fundus evaluation. 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.

Objective: To compare 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 deop of Tropicamide 1% in one eye and the combination drop in the other eye. The cyclopleiga 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 cyclopegic effect of tropicamide 1% was marginally better than the combination drop, the difference in the two groups was not statistically significant for cycloplegia (p=0.07) or residual accommodation (p=0.15).

Conclusion: A single drop of a combination of 0.8% Tropicamide and 5% Phenylephrine achieves adequate cycloplegia in patients between 11-40 years of age.

Keywords: Cycloplegia, Troplicamide, Phenylephrine, Eye, Residual accommodation

Introduction

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

In ophthalmic practice, cycloplegics were required on a regular basis for refraction and fundus evaluation. Cycloplegics under inhibits accommodation and allow 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.[1-2]

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 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.[3-4]

The ideal drug should produce:

1. Adequate cycloplegia for refraction
2. Rapid recovery from the cycloplegic 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.

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. 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 in adults, but it is not know if it is an effective cycloplegic agent in children, who have a higher ciliary muscle tone.[5-11]

The aim of our study was to compare 1% tropicamide solution with a combination of 0.8% tropicamide and 5% phenylephrine for cycloplegia.

The objectives of our study were to evaluate, the degree of cycloplegia and the amount of residual accommodation at 20 minutes after instillation of the drop.

Material and Methods

The study was conducted on patients presenting to the outpatient department of Ophthalmology. We include a total of 150 patients presenting for refraction or fundus evaluation, who satisfied the inclusion and exclusion criteria. It was a prospective, randomized study and the study protocol had been cleared by the ethics committee of the institution prior to starting the study.

Inclusion criteria: All patients presenting to the department of Ophthalmology, for refraction or a fundus

examination between 11 to 40 years of age were included in the study.

Exclusion criteria:

1. Patients below 11 years and above 40 years of age; after the age of 40 years, as presbyopia sets in, the accommodation starts naturally declining and this these patients were excluded. In children below 11 years it would have been difficult to get their cooperation for the various tests.
2. Patients with anterior segment disease or abnormality such as uveitis and trauma, patients already using cycloplegics. 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 able to perform the tests. Post ocular surgery. Hypertensive patients. Diabetic patients as they are known to have rigid pupils which are more difficult to dilate.
4. Patients on systemic drugs that could affect the pupil or accommodation e.g. psychotherapeutic drugs.
5. Patients suspected to have ciliary muscle spasm, resulting in artificially increased amount of myopia.
6. Patients with known pseudoexfoliation syndrome, in whom the pupils are expected to be rigid

Data collection: A written informed consent was obtained from all patients. The demographic details of the patients 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.

The visual acuity was recorded using an illuminated Snellen's chart, with the patient seated at a distance of 6 meters. 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 Snellens near vision chart, held at a distance of 33 cms from the patient. Anterior segment examination was done using the Zeiss slit lamp (model no. SL115 Classic) to rule out any anterior segment disease or abnormality.

The resting papillary diameter was measured at the slit lamp using a millimeter rule (baseline measurement) keeping the magnification at 12 and the illumination at $1/8^{th}$ intensity. Non cycloplegic refraction at baseline was estimated using the Automated Refractometer – Zeiss / Humphrey system, model no. 599.

The patients then received the dilating drops. The drops were labeled as A and B by a third person. Each patient received one drop of drop A in 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 labeling 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 papillary dilation to bright light was noted. This was measured by increasing the illumination of the slit lamp to the maximum and noting any papillary reaction. More than 1 mm constriction was taken as a reacting pupil, indicating that the dilatation was not resistant to bright light.

The post cycloplegic refraction was measured on the autorefractometer 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 residual accommodation was measured as follows: the amount of plus add was increased till the target became clear, the plus add was further increased till the target appeared to blur. The difference in the maximum and minimum amount of plus power between which the patient could see the target clearly, gave the amount of residual accommodation remaining after cycloplegia.

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.

To negate the effect of positive and negative values of spherical equivalent recorded at baseline and at 20 minutes, the difference in the two readings of spherical equivalent was taken for statistical analysis, to study the latent error uncovered by the two drugs.

Cycloplegia was calculated as the differences in the amount of near add required to view the near target before and after instillation of drops.

All other parameters evaluated were taken as quantitative data. All data were recorded in a proforma designed specifically for this study.

Statistical analysis: Descriptive statistics such as range, mean and standard deviation for quantitative variables, category frequency counts and percentage for qualitative variables was used. Univariate analysis to evaluate correlation between two 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

ANOV (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 was < 0.05. All statistical analysis was done using SPSS v16.0.

Results

Two groups were studied – Group T being the eyes with received Tropicamide 1% and Group TP being the eyes which received the combination drop – Tropicamide 0.8% with Phenyleprine 5%. Comparisons were made to study papillary dilatation and resistance to bright light during the specified time period of 15 mins, 30 mins, and 45 mins over the baseline. The two groups werealso compared for the cycloplegic effect, measured at 20 mins from baseline.

Baseline characteristics of study groups:

The study included 62 males (41.3%) and 88 females (58.7%). The age of the patients in the study ranged from 11 years – 39 years, with a mean of 23.87 years ± 7.62.

The patients were divided into 3 age groups for the purpose of statistical analysis;

Group -1 (11-20 years): 60 patients (40%)
Group-2 (21-30 years): 56 patients (37%)
Group-3 (31-40 years): 34 patients (23%)

Visual acuity: 143 patients had a best corrected visual acuity (BCVA) 0f 6/6. One patient had a BCVA of 6/9 in both 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 dark irises.

Table 1: Changes in near add over time (cycloplegia)

Near Add	Mean (SD)	Statistical test
Baseline-Group T	0.25 (0.33)	F=3.08 P=0.08
Baseline- Group TP	0.28 (0.35)	
20 mins – Group T	1.37 (0.44)	
20 mins – Group TP	1.32 (0.43)	

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 deducing 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=0.07).

Table 2: Residual accommodation

Group	Mean	SD	t-value	df	p-value
T	1.20	0.36	1.45	298	0.15
TP	1.26	0.36			

The measured residual accommodation in Group T was marginally lower than that in Group TP, however the difference was not statistically significant (p=0.15).

Table 3: Correlation between latent error and amount of cycloplegia and residual accommodation

Parameter	Beta coefficient	t-value	p-value
Latent error vs residual accommodation	0.06	1.04	0.3
Latent error vscycloplegia	0.32	0.55	0.57

There was no statistically significant co-relation between the latent error with either residual accommodation (p=0.3) or cycloplegia (p=0.57).

Table 4: Effect of age on residual accommodation and cycloplegia

Parameter	Age group	Mean (SD)	F	df	p-value
Cycloplegia	11-20	0.95 (0.32)	18.25	2	P<0.001
	21-30	1.19 (0.29)			
	31-40	1.14 (0.36)			
Residual accommodation	11-20	1.39 (0.38)	30.94	2	P<0.001
	21-30	1.19 (0.23)			
	31-40	1.0 (0.4)			

The near add at baseline and at 20 minutes increased with increasing age, the difference between the groups was statistically significant (p<0.001). The amount of cycloplegia increased with increasing age, the difference between the age groups was statistically significant (p<0.001). The residual accommodation decreased with increasing age, the difference was statistically significant (p<0.001).

Discussion

Cycloplegics were routinely required in ophthalmic practice for the diagnosis of refractive errors, cataracts and retinal pathologies. A pupil diameter of atleast 6 mm is required for performing indirect ophthalmoscopy and for the accurate diagnosis of cataracts.[12-13]

Most of the hospitals, use frequent instillation of the mydriatics drop for papillary dilation, 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 single instillation and evaluate their efficacy in producing adequate mydriasis and cycloplegia.

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 iris colour, which may have a bearing on the papillary diameter and residual accommodation. Our method was similar to studies done by Kergoat et al[14] and Leonard et al[15] who used either eye of the patients as controls.

With a reduction in the strength of tropicamide in the fixed drug combination, the efficacy of the combination as a good cycloplegic was in doubt. This study has shown that the combination drug produced adequate cycloplegia after instillation of a single drop which was comparable to that induced by tropicamide alone.

The adequacy of drug as a cycloplegic is evaluated by measuring the amount of residual accommodation remaining after its use. Our literature search did not reveal any method which would directly measure the amount of induced cycloplegia. The reports vary slightly on the acceptable amount of residual accommodation for adequate cycloplegia; most authors agree that less than 2 D[16,17] of residual accommodation is acceptable.

The earlier methods using the various near point rules (RAF rule, Prince rule etc.) obtained a subjective assessment of the residual accommodation. Now with the availability auto-refractometers, this can be calculated objectively as the difference between the distance and near autorefraction.[18,19] In our study we attempted to calculate not only the residual accommodation but also the amount of cycloplegia caused. The calculations were made on the autorefractometer, using a combination of the subjective and objective method as per our machine parameters. After the distance autorefraction, the near target on the machine 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 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 was0.25 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 autorefractometers. 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 two 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 cycloplegia together or in isolation.

After instillation of drops, there was mean hypermetropic 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.[18] The significance of the above finding is not understood at the present time.

On analysis by age groups, it was found that the residual accommodations 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 (±0.4) in group 3. The difference between the groups was statistically significant ($p<0.01$) indicating that the drugs produce 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 Snellens 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 picked up by the machine earlier than other methods.

The only complications we noted were 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, arrthythmias and myocardial infarction. However, we did not check blood pressure or any other systematic parameters before and after drop instillation and hence cannot comment upon the occurrence of any systemic complications induced by the combination drug. This study does not establish the efficacy of tropicamide or the combination drop as a cycloplegic in the presence of systematic and local pathology.

Conclusion

In conclusion, a single drop of a combination of 0.8% tropicamide with 5% phenylephrine causes adequate cycloplegia in patients between 11-40 years of age. However, we have not come across studies evaluating the cyclopegic effect of this drop, especially in the Indian population, who are known to have dark coloured iris.

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.

This study has proven the adequacy of a single drop, hence avoiding the need for multipleinstillations and minimizing systemic complications.

Hence in clinical practice, the combination drug may be used as a single drop in situations requiring adequate cycloplegia together or in isolation. The results of our study are applicable to the Indian population with dark colourediris.

In this study, we also suggest a method to directly measure the amount of cycloplegia caused by a drug, using the autorefractometers, calculated as the difference in the near add 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.

Summary

A total of 150 patients were evaluated for cycloplegia caused by 2 drops; 1% tropicamide and a fixed drug combination of 0.8% tropicamide with 5% phenylephrine. The cycloplegia and residual accommodation were assessed at 20 minutes using the autorefractometers.

In the eyes that received Tropicamide 1%, the mean cycloplegia measured at 20 minute 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=0.07) or residual accommodation (p=0.15).

In conclusion, a single drop of a combination of 0.8% Tropicamide and 5% Phenyleprine achieves adequate cycloplegia, in patients between 11-40 years of age.

Reference

1. KD Tripathi. Essentials of medical pharmacology. 5thed: p 106-114.
2. Geyer O, Neudorfer M, Lazar M et al: Cellular sensitivity in allergic blepharoconjuntivitis due to phenylephrine eye drops. Graefes Arch ClinExpOphthalmol, 1993: p 231-748.
3. Bron A, Tripathi R, Tripathi B. Wolff's anatomy of the eye and orbit. 8th ed. Chapman and Hall, 1997: p 308-334.
4. Duke-Elders System of Ophthalmology Vol 12: 605.
5. Wilhem J, Wilhelm H, Moro S, Barbur J L. Pupil response components: studies in patients with Parinaud's syndrome. Brain 125(10):2296, 2002.
6. Bron A, Tripathi R, Tripathi B. Wolff's anatomy of t he eye and orbit. 8th ed. Chapman and Hall, 1997: p 336-366.
7. Bron A, Tripathi R, Tripathi B. Wolff's anatomy of t he eye and orbit. 8th ed. Chapman and Hall, 1997: p 411-423.
8. Duke –Elders system of Ophthalmology Vol 12: 613.
9. Lowenfeld IE. Simple central anisocoria: a common condition, seldom recognized. Trans Am AcadOphthalmolOtolaryngol. 1997;83:832-39.
10. Duke – Elder S: System of ophthalmology. St. Louis, CV Mosby Co, 1964 vol12, 616-635.
11. Duke – Elder S: System of ophthalmology. St. Louis, CV Mosby Co, 1964 vol12, 601-604.
12. Margo L, Lawrence W, Battistutta D et.al. Comparative pupil dilation using phenylephrine alone or in combination with tropicamide. Ophthalmology 1998;105(4):726-732.
13. Ratanapakorn T, Yospaiboon Y, Chaisrisawadsuk N. Single dose 0f 1% Tropicamide and 10% Phenylephrine for pupil dilatation. J. Med Assoc Thai, 2006;89(11):1934-39.
14. Kergoat H, Lovasik JV, Doughty MJ. A pupillographic evaluation of a phenylephrine HCI 5% - Tropicamide 0.8% combination mydriatics. J OculPharmacol, 1989;5(3):199-216.
15. Apt L, Henrick A. Pupillary dilatation with single eyedropmydriatics combination. Am J Ophthalmol, 1980;89:553-59.
16. Milder B. Tropicamide as a cycloplegic agent. Arch Ophthalmol, 1961;66:70-72.
17. Stine GT. Clinical investigation of a new mydriatics and cycloplegic drug EENT Digest 1960;22:11-15.
18. Manny RE, Hussein M, Scheiman M et al. Tropicamide 1% an effective cycloplegic agent for myopic children. Invest Ophthalmol Vis Sci 2001;42:1728-35.
19. Ichiro Hamasaki et al. Evaluation of the cycloplegic effect of mixed drops. Jpn J Ophthalmol. 2007;51:111-115.