Cycloplegic effect of atropine compared with cyclopentolate-tropicamide combination in children with hypermetropia

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INTRODUCTION

Cycloplegic refraction is important in assessing patients with decreased vision or ocular deviation. Hypermetropia is a refractive error that causes decreased vision in children. This condition is associated with reading disabilities, learning difficulties, low intelligence, and slow development of visual perceptual skills in children. Cycloplegic refraction is necessary in children because of their high amplitude of accommodation and inability to give reliable subjective responses.

Cycloplegia is the paralysis of the ciliary muscle of the eye resulting in dilatation of the pupil and paralysis of accommodation. This can be achieved by instilling cycloplegic agents such as atropine, cyclopentolate, and tropicamide into the conjunctival sac.

Atropine is an organic compound derived from tropic acid and tropine. Atropine is the most potent of the cycloplegic agents and has a slow onset of effect with duration of action lasting up to 2 weeks. Preparations are available in 0.5% or 1% eye drops or eye ointment. Adverse effects may be ocular or systemic. These include allergic contact dermatitis of the lids, allergic conjunctivitis, keratitis, and increase in intraocular pressure.

ABSTRACT

Background: Cycloplegic refraction is important in assessing children with hypermetropia. Atropine, though the gold standard cycloplegic agent for refraction in children, has a long duration of action and more severe side effects compared to short-acting cycloplegic agents. The aim of the study was to compare the cycloplegic effect of atropine with cyclopentolate and tropicamide combination in children with hypermetropia. Subjects and Methods: This was a crossover interventional study in children with hypermetropia. Cycloplegic refraction using two separate regimens of cycloplegic drugs was done on all subjects. Data were analyzed using the statistical software SPSS version 22.0. The mean spherical equivalent values of regimen 1 (atropine 1%) and regimen 2 (cyclopentolate 1% and tropicamide 1%) were presented as mean and standard deviation. A P ≤ 0.05 was considered statistically significant. Results: One hundred and twenty-six eyes of 63 subjects aged 5–12 years were examined. The mean spherical equivalent values for regimen 1 and regimen 2 for the right eyes were 4.73 ± 2.1 DS and 4.54 ± 1.9 DS, respectively (P = 0.59). The mean spherical equivalent values for regimens 1 and 2 for the left eyes were 4.74 ± 2.0 DS and 4.54 ± 1.8 DS, respectively (P = 0.56). Conclusion: The combination of 1% cyclopentolate and 1% tropicamide could be a useful alternative to atropine 1% for cycloplegic refraction in children with hypermetropia.

Key words: Atropine, cyclopentolate, cycloplegic refraction, hypermetropia, tropicamide

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secretions, fever, irritability, tachycardia, convulsions, and possibly death.\textsuperscript{2,4}

Cyclopentolate is a synthetic antimuscarinic cycloplegic agent with an onset of action of 30–45 min and duration of action of 24 h. Preparations are available in 0.5% and 1% solutions. Ocular side effects may include irritation, lacrimation, allergic blepharoconjunctivitis, conjunctival hyperemia, and increase in intraocular pressure. Systemic side effects include drowsiness, ataxia, disorientation, incoherent speech, restlessness, and visual hallucinations.\textsuperscript{5,6}

Tropicamide is a synthetic analog of tropic acid. The onset of action is 15–30 min and lasts 4–6 h. It is available in 0.5% and 1% solutions. Ocular side effects include dry mucus membranes, flushing, and tachycardia.\textsuperscript{6} Having mentioned the cycloplegic agents above and their characteristics, notwithstanding, an ideal cycloplegic agent should have a rapid onset of action, complete cycloplegic effect, quick reversal of cycloplegic effect, and absence of ocular and systemic side effects.\textsuperscript{7}

The aim of the study was to compare for the purpose of refraction, the cycloplegic effect of atropine with cyclopentolate and tropicamide combination in children with hypermetropia. This would ascertain if tropicamide and cyclopentolate, which have shorter duration of action and less severe adverse effects, could be used instead of atropine, a drug with a long duration of action and more severe adverse effects.\textsuperscript{2,4,6}

SUBJECTS AND METHODS

The study adhered to the tenets of the Declaration of Helsinki. Ethical approval was obtained from the Ethics Review Board of Aminu Kano Teaching Hospital, Kano, Nigeria. This crossover interventional study was carried out from November 2014 to March 2015. Sixty-three subjects took part in the study. Consent was obtained from parents of subjects. Criteria for inclusion were children aged between 5 and 12 years with hypermetropia of at least 1 D in each eye. Children outside this age range, those with other refractive errors or other eye diseases and history of cardiovascular disease were excluded from the study. Subjects with a history suggestive of allergy to atropine, cyclopentolate, or tropicamide were also excluded from the study.

All subjects had routine ophthalmic evaluation and cycloplegic refraction. Two separate regimens of cycloplegic drugs were used for all subjects. These were instilled into the conjunctival sac of the subjects.

Regimen 1 comprised instillation of one drop of 1% atropine twice daily for 3 days before and on the day of refraction. Regimen 2 comprised instillation of 1% cyclopentolate and 1% tropicamide. Cyclopentolate (1%) was instilled twice at 5 min intervals followed by tropicamide (1%) also instilled twice at 5 min intervals.

Refraction was done 30 min after instillation of the last drop of tropicamide. For both regimens, cycloplegic effect of the drugs was noted when the pupils did not react to light and were fully dilated and when retinoscopic reflex did not fluctuate.\textsuperscript{4} Each of the subjects had both regimens of the cycloplegic drugs. However, there was a 5-week interval between regimen 1 and regimen 2 to allow for the cycloplegic effect of atropine to wear off. The refraction was carried out in a dark room using a Keeler retinoscope and at a working distance of 66 cm (equivalent to 1.5 D). A single refractionist carried out all refraction procedures.

The results of the refraction were converted to the spherical equivalent of the values obtained. This was done by calculating the sphere plus half of the cylinder.\textsuperscript{8} Parents of the subjects were informed about possible postinstillation side effects of the drugs and were told to present to the hospital immediately should any of these be observed.

Data analysis

Data were analyzed using the statistical software Statistical Package for the Social Sciences (SPSS) version 22.0, International Business Machines Corporation, Armonk, New York, United States of America. The mean spherical equivalent values of atropine (regimen 1) and tropicamide with cyclopentolate combination (regimen 2) were presented as a mean and standard deviation. A $P \leq 0.05$ was considered statistically significant.

RESULTS

A total of 63 subjects participated in the study. One hundred and twenty-six eyes of these were examined. There were 26 females and 37 males (male: female = 1.4:1). Table 1 gives a summary of the sex distribution of the subjects.

Their ages ranged from 5 to 12 years with a mean age of 8.23 ± 1.88 years.

The cycloplegic refraction procedures using atropine 1% (regimen 1) and tropicamide 1%-cyclopentolate 1% combination (regimen 2) were recorded. Table 2 shows the spherical equivalent values of these procedures done on all subjects using both regimens.

The mean spherical equivalent values for regimen 1 and regimen 2 for the right eyes were 4.73 ± 2.1 D and

| Table 1: Sex distribution of subjects |
|--------------------------------------|
| Sex      | Frequency | Percentage | Cumulative percentage |
|----------|-----------|------------|-----------------------|
| Female   | 26        | 41.3       | 41.3                  |
| Male     | 37        | 58.7       | 100.0                 |
| Total    | 63        | 100.0      |                       |
Table 2: Spherical equivalent values of refraction procedures in all subjects

| Patient number | Age (years) | Gender | Regimen 1 (D) (atropine 1%) | Regimen 2 (D) (tropicamide 1% and cyclopentolate 1%) | Difference between regimen 1 right eye and regimen 2 right eye (D) | Difference between regimen 1 left eye and regimen 2 left eye (D) |
|----------------|-------------|--------|-----------------------------|------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| 1              | 9           | Male   | +11.00                      | +11.00                                               | +10.50                                                         | 0.00                                                          |
| 2              | 10          | Female | +4.50 +4.50                 | +4.50 +4.50                                          | 0.00                                                          | 0.00                                                          |
| 3              | 7           | Male   | +8.50 +6.25                 | +8.00 +6.25                                          | 0.50                                                          | 0.00                                                          |
| 4              | 9           | Male   | +5.25 +6.00                 | +5.25 +6.00                                          | 0.00                                                          | 0.00                                                          |
| 5              | 9           | Male   | +4.50 +4.50                 | +4.50 +4.50                                          | 0.00                                                          | 0.00                                                          |
| 6              | 8           | Male   | +4.50 +4.25                 | +3.75 +4.00                                          | 0.75                                                          | 0.25                                                          |
| 7              | 7           | Male   | +4.00 +3.50                 | +3.75 +3.75                                          | 0.25                                                          | 0.25                                                          |
| 8              | 9           | Male   | +4.25 +3.75                 | +4.25 +3.75                                          | 0.00                                                          | 0.50                                                          |
| 9              | 6           | Female | +3.75 +3.50                 | +3.25 +3.25                                          | 0.50                                                          | 0.25                                                          |
| 10             | 10          | Female | +4.25 +3.50                 | +3.25 +3.25                                          | 1.00                                                          | 0.25                                                          |
| 11             | 8           | Female | +3.00 +3.25                 | +3.25 +3.75                                          | 0.00                                                          | 0.00                                                          |
| 12             | 8           | Female | +7.00 +7.50                 | +6.75 +7.25                                          | 0.25                                                          | 0.25                                                          |
| 13             | 8           | Female | +3.50 +3.50                 | +3.00 +3.25                                          | 0.50                                                          | 0.25                                                          |
| 14             | 5           | Female | +6.00 +4.50                 | +5.75 +4.50                                          | 0.25                                                          | 0.00                                                          |
| 15             | 10          | Male   | +3.25 +3.25                 | +3.25 +3.25                                          | 0.00                                                          | 0.00                                                          |
| 16             | 10          | Male   | +3.00 +3.50                 | +3.00 +3.25                                          | 0.25                                                          | 0.25                                                          |
| 17             | 9           | Female | +4.50 +4.75                 | +4.50 +4.75                                          | 0.00                                                          | 0.00                                                          |
| 18             | 5           | Male   | +5.25 +6.00                 | +4.50 +6.00                                          | 0.75                                                          | 0.00                                                          |
| 19             | 12          | Male   | +7.75 +7.50                 | +7.50 +7.25                                          | 0.25                                                          | 0.25                                                          |
| 20             | 5           | Male   | +2.50 +2.50                 | +2.50 +2.50                                          | 0.00                                                          | 0.50                                                          |
| 21             | 11          | Male   | +9.75 +9.75                 | +8.50 +8.25                                          | 1.25                                                          | 1.50                                                          |
| 22             | 8           | Female | +3.50 +3.50                 | +3.50 +3.25                                          | 0.00                                                          | 0.25                                                          |
| 23             | 8           | Male   | +2.00 +2.00                 | +2.50 +2.00                                          | 0.00                                                          | 0.00                                                          |
| 24             | 11          | Female | +4.25 +4.25                 | +3.75 +4.00                                          | 0.50                                                          | 0.25                                                          |
| 25             | 8           | Female | +3.75 +4.00                 | +3.75 +3.75                                          | 0.00                                                          | 0.25                                                          |
| 26             | 7           | Male   | +4.00 +4.25                 | +4.00 +4.25                                          | 0.00                                                          | 0.00                                                          |
| 27             | 8           | Male   | +3.75 +4.00                 | +3.75 +4.00                                          | 0.00                                                          | 0.00                                                          |
| 28             | 9           | Female | +4.00 +3.50                 | +4.00 +3.50                                          | 0.00                                                          | 0.00                                                          |
| 29             | 6           | Male   | +2.50 +2.50                 | +2.50 +2.25                                          | 0.00                                                          | 0.25                                                          |
| 30             | 12          | Male   | +3.00 +3.50                 | +3.00 +3.50                                          | 0.00                                                          | 0.00                                                          |
| 31             | 10          | Male   | +3.00 +3.50                 | +3.00 +3.50                                          | 0.00                                                          | 0.00                                                          |
| 32             | 11          | Female | +2.75 +3.25                 | +2.75 +3.25                                          | 0.00                                                          | 0.00                                                          |
| 33             | 7           | Male   | +4.75 +4.50                 | +4.75 +4.50                                          | 0.00                                                          | 0.00                                                          |
| 34             | 7           | Female | +4.00 +3.75                 | +4.00 +3.75                                          | 0.00                                                          | 0.25                                                          |
| 35             | 8           | Male   | +4.50 +4.50                 | +4.50 +4.50                                          | 0.00                                                          | 0.00                                                          |
| 36             | 9           | Male   | +3.00 +3.25                 | +2.75 +2.75                                          | 0.25                                                          | 0.50                                                          |
| 37             | 10          | Male   | +2.75 +3.25                 | +2.75 +3.25                                          | 0.00                                                          | 0.00                                                          |
| 38             | 6           | Female | +2.50 +2.50                 | +2.50 +2.25                                          | 0.00                                                          | 0.00                                                          |
| 39             | 10          | Male   | +6.75 +6.75                 | +6.50 +6.50                                          | 0.25                                                          | 0.25                                                          |
| 40             | 9           | Female | +3.75 +3.75                 | +3.75 +3.75                                          | 0.00                                                          | 0.00                                                          |
| 41             | 9           | Male   | +9.75 +9.75                 | +9.50 +9.00                                          | 0.25                                                          | 0.75                                                          |
| 42             | 5           | Female | +4.50 +5.25                 | +4.50 +5.25                                          | 0.00                                                          | 0.00                                                          |
| 43             | 10          | Female | +11.50 +10.50               | +9.25 +9.25                                          | 1.75                                                          | 1.25                                                          |
| 44             | 5           | Male   | +3.50 +2.75                 | +2.50 +2.25                                          | 0.50                                                          | 0.50                                                          |
| 45             | 10          | Female | +6.50 +7.25                 | +6.50 +7.25                                          | 0.00                                                          | 0.00                                                          |
| 46             | 10          | Male   | +6.50 +6.75                 | +6.50 +6.50                                          | 0.25                                                          | 0.25                                                          |
| 47             | 8           | Male   | +3.50 +4.75                 | +3.50 +4.50                                          | 0.00                                                          | 0.25                                                          |
| 48             | 6           | Male   | +3.75 +3.75                 | +3.50 +3.50                                          | 0.25                                                          | 0.25                                                          |
| 49             | 9           | Female | +3.50 +3.50                 | +3.50 +3.50                                          | 0.00                                                          | 0.00                                                          |
| 50             | 8           | Female | +5.25 +4.75                 | +5.25 +4.75                                          | 0.00                                                          | 0.00                                                          |
| 51             | 8           | Male   | +3.25 +3.00                 | +3.25 +3.00                                          | 0.00                                                          | 0.00                                                          |
| 52             | 8           | Male   | +3.25 +4.25                 | +3.25 +4.25                                          | 0.00                                                          | 0.00                                                          |
| 53             | 10          | Male   | +4.25 +3.75                 | +4.00 +3.50                                          | 0.25                                                          | 0.25                                                          |
| 54             | 11          | Female | +4.25 +4.50                 | +4.25 +4.25                                          | 0.00                                                          | 0.00                                                          |
| 55             | 5           | Male   | +6.50 +6.25                 | +6.00 +6.00                                          | 0.50                                                          | 0.25                                                          |

Contd...
The findings of this study support previous studies which have shown that atropine can be replaced with cyclopentolate either alone or in combination with other short-acting cycloplegic agents to achieve effective cycloplegia in children.

There are known side effects associated with cycloplegic agents. Reported cases of systemic side effects of these include acute midbrain hemorrhage, ataxia, restlessness, hallucinations, seizures, fever, dryness of the mouth and skin, tachycardia, delirium, and death. Our study did not record any adverse effects. This may be due to the age range of our study population. Toxic effects of cycloplegic agents occur more in younger children.

The results of this study are of great relevance clinically. The use of atropine to achieve cycloplegia is usually started by parents at home. This may not be favorable as compliance may not be adequate and complete cycloplegia may not be achieved. Another disadvantage of atropine is its long duration of action and possible toxic effects. Our results suggest that the use of atropine can be replaced with tropicamide and cyclopentolate for cycloplegic refraction with comparable cycloplegic effects. Second, these two drugs are short acting with benefits of complete reversal of cycloplegic effects within hours.

On the whole, evidence suggests that atropine, though the gold standard cycloplegic agent for refraction in children, can be replaced by cyclopentolate alone or in combination with other short-acting cycloplegic agents to achieve effective cycloplegia in children with hypermetropia. The combination of cycloplegic agents used in this study is therefore recommended for the use in refraction by eye care providers to achieve effective cycloplegia in children with hypermetropia.

Future studies should include younger children because they have a higher amplitude of accommodation. This may further establish the similar effectiveness of atropine in comparison with other short-acting cycloplegic agents for refraction in children, thereby further strengthening available evidence.
A limitation of this study is that the subjects were children aged 5–12 years. If younger children were included in the study, the results may have been more reliable because they have a higher amplitude of accommodation.

CONCLUSION

This study has shown that the combination of 1% tropicamide and 1% cyclopentolate can give results of cycloplegia comparable to 1% atropine with benefits of less severe side effects and a shorter duration of action of the drugs.

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Conflicts of interest

There are no conflicts of interest.

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