Topical Mydriatic and Cycloplegic Spray for Chinese Children

Chun-yu Wong, FRCS; Dorothy S. P. Fan, FRCS; Christopher B. O. Yu, FRCOphth; and Dennis S. C. Lam, FRCS, FRCOphth

ABSTRACT

**Purpose:** To assess the efficacy and tolerance of mydriatic and cycloplegic spray versus drops for Chinese children.

**Methods:** The effects of the spray (cyclopentolate 0.25%, phenylephrine 0.625%, and tropicamide 0.5%) and the drops (cyclopentolate 1%, phenylephrine 0.5%, and tropicamide 0.5%) were evaluated in 29 children (58 eyes) in two separate sessions. There was a 1-week period between the applications of the spray and the drops. Dilated pupil size and refraction after cycloplegia were the primary outcome variables used to assess the efficacy. A subjective discomfort score was used to assess acceptance of the spray and the drops.

**Results:** The mean age of the study population was 4.33 ± 1.39 years (range, 3 to 8 years). The mean pupil size was 6.9 mm for the spray and 6.6 mm for the drops. The spray appeared to be slightly more effective than the drops, with a mean difference of 0.3 mm that was statistically significant ($P = .001$, two-tailed t test). No statistically significant difference in cycloplegic response was found between the spray and the drops ($P = .535$, two-tailed t test). Administration of the spray caused less discomfort than did administration of the drops ($P < .001$, Wilcoxon signed-rank test).

**Conclusions:** The spray system appears to be clinically equivalent to the drops for achieving effective pupil dilation and cycloplegia, even in a population with dark irides such as ours. Tolerability and acceptance improved because the spray was applied to the closed eyelids.


INTRODUCTION

Fundal examination and cycloplegic refraction are essential components of any pediatric eye examination, but the administration of topical mydriatic and cycloplegic eyedrops can be an unpleasant procedure for some children, parents, and healthcare workers. Children often experience discomfort during the application of eyedrops. The use of a topical spray delivery system may be a more acceptable alternative to eyedrops and has been proven to be effective in several studies.2-4 Chinese patients tend to have darkly pigmented irides, which are more difficult to dilate and tend to have a delay in onset and decreased magnitude of the cycloplegic effect due to pigment binding of the cycloplegic drugs.5,6 The purpose of this comparative study was to further...
TABLE
RESULTS OF MYDRIASIS, CYCLOPLEGIA, AND
COMFORT LEVEL WITH DROPS AND SPRAY

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Drops</th>
<th>Spray</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupil size</td>
<td>6.61 ± 0.57* (5.5 to 7.5)</td>
<td>6.91 ± 0.58 (5.0 to 8.0)</td>
<td>.001</td>
</tr>
<tr>
<td>Pre-SE</td>
<td>-0.86 ± 0.23 (-5.75 to 5.00)</td>
<td>-0.91 ± 2.15 (-6.25 to 3.75)</td>
<td>.702</td>
</tr>
<tr>
<td>Post-SE</td>
<td>-0.61 ± 2.33 (-6.00 to 6.25)</td>
<td>-0.60 ± 2.42 (-5.75 to 6.00)</td>
<td>.969</td>
</tr>
<tr>
<td>Cyclo*</td>
<td>0.38 ± 0.58 (-1.50 to 1.50)</td>
<td>0.31 ± 0.64 (-0.75 to 2.25)</td>
<td>.535</td>
</tr>
<tr>
<td>Comfort</td>
<td>1.48 ± 1.19 (0 to 3)</td>
<td>0.55 ± 0.83 (0 to 2)</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

SE = spherical equivalent.
*Mean ± standard deviation.
*Range.
*Change in SE refraction after cycloplegia.

0.5% tropicamide, and 1% cyclopentolate instilled in the inferior conjunctival sac or two applications of topical spray administered to the closed eyelid. The Colvard Pupillometer (Oasis Medical, Glendora, CA) was used to measure the size of the pupils in a standardized environment 30 minutes after the application of the last medication. Autorefraction was performed before and 45 minutes after drug application. An independent observer who was masked from the randomization measured pupil size and refraction. Immediately following the application of the drug, the subject was asked to respond to questions about his or her discomfort. Answers were recorded using a semiquantitative estimation scale from “0” to “3,” 0 being no discomfort and 3 being the maximum. In part 2, the procedure was repeated 1 week later with the other method of application.

The mydriatic-cycloplegic solution was prepared by mixing 7.5 mL of cyclopentolate 1.0%, 7.5 mL of phenylephrine 2.5%, and 15 mL of tropicamide 1.0%, yielding a final 30-mL solution composed of cyclopentolate 0.25%, phenylephrine 0.625%, and tropicamide 0.5%. The solution was introduced into a sprayer that had been asepticized with 6% hydrogen peroxide. The sprayer was held approximately 10 cm from the subject’s eyes. A few moments after the mydriatic combination was administered to the closed eyelids, the subject was instructed to blink several times. Excess drug on the surface of the skin was blotted dry.

The main outcome measures used were the pupil size 30 minutes after the application of the last medication (using the Colvard Pupillometer), refraction (using the Topcon KR-7100 autorefractometer, Topcon Corp., Itabashi-ku, Japan) before and after the application of the drug, and discomfort due to the application. Side effects occurring after the administration of the drug were ascertained during follow-up. The two-tailed t test and Wilcoxon signed-rank test were used for statistical analysis.

RESULTS

Twenty-nine Chinese children (58 eyes) comprised the study population. The gender ratio was 10 males to 19 females. The ages ranged from 3 to 8 years, with a mean age of 4.33 ± 1.39 years. The pupil size, change in spherical equivalent refraction after cycloplegia, and level of discomfort were reported (Table).
The mean pupil size after the application of the spray was 6.9 mm and 6.6 mm after the application of the drops. No eye failed to dilate with either drug. The spray appeared to be slightly more effective than the drops; the mean difference was 0.3 mm, which was statistically significant \( (P = .001, \text{two-tailed } t \text{ test}) \).

The change in the spherical equivalent for the drops and the application of the spray was 0.38 ± 0.58 and 0.31 ± 0.64, respectively. No statistically significant difference in cycloplegic response was found between the spray and the drops \( (P = .535, \text{two-tailed } t \text{ test}) \).

The difference in discomfort scores between the application of the drops and the spray was statistically significant. The spray caused less discomfort than did the drops \( (P < .001, \text{Wilcoxon signed-rank test}) \). No major side effects or complications were reported with the use of either of the drugs.

**DISCUSSION**

The mydriatic and cycloplegic medications used in this study have been widely used and considered to be safe. However, central nervous system toxicity and gastrointestinal disturbances can occur with cyclopentolate.\(^7\)-\(^{12}\) On the other hand, phenylephrine 2.5% can cause adverse cardiovascular effects.\(^13\) Phenylephrine 1% with either tropicamide 1% or cyclopentolate 0.2% had been shown to be safe and effective.\(^14\) For these reasons, a mydriatic-cycloplegic solution comprising cyclopentolate 0.25%, phenylephrine 0.625%, and tropicamide 0.5% was prepared instead of using the more highly concentrated preparation (cyclopentolate 0.5%, phenylephrine 2.5%, and tropicamide 0.5%) described by Wesson et al.\(^15\) Neither the drops nor the spray produced side effects during our study. The spray appeared to be safer than the drops because it had a lower concentration of cyclopentolate and phenylephrine.

Before administering eyedrops to children, healthcare workers frequently need to force open the eyelid, especially in uncooperative children. The parents are usually asked to help by holding the child still. This can be an unpleasant procedure for some patients, parents, and healthcare workers. Children often experience considerable discomfort during the administration of the eyedrops, which may result in alienating the child and reducing cooperation during subsequent examinations, and some may eventually need to be examined under general anesthesia. With the spray system, medication is delivered to the closed eyelids, obviating the need for healthcare workers to touch the eyelids. The topical medication on the eyelashes is then transferred to the tear film through subsequent blinking. In this study, higher discomfort scores that were statistically significant \( (P < .001, \text{Wilcoxon signed-rank test}) \) were recorded for the drops. The spray appeared to cause less discomfort and was regarded as more acceptable.

Our study demonstrates that both the spray and the drops produce good mydriasis in darkly pigmented irides. Pupil sizes of 6.6 and 6.9 mm were achieved with the drops and the spray, respectively. The spray was statistically superior to the drops regarding mydriatic effect.

Cycloplegia allows for a true estimate of the refractive error of the eye by relaxing accommodation. Most clinicians agree that cycloplegia is necessary when performing refraction in young children, for high hyperopia, and in patients with strabismus.\(^1\) The cycloplegic effect achieved by the drops and the spray was 0.38 and 0.31, respectively. There was no statistically significant difference in the cycloplegic response between the spray and the drops, but the magnitude of cycloplegic effect appeared to be low for both drugs. Iris pigmentation affects the extent\(^15,16\) and rate of accommodative loss in eyes with dark irides especially when using cyclopentolate and tropicamide.\(^16\) In our population, darkly pigmented eyes were common, and the decreased magnitude of the cycloplegic effect was due to pigment binding of the cycloplegic medications.

A recent study\(^17\) compared the effectiveness of cyclopentolate 1% and tropicamide 1% in African American children and concluded that the combination used was adequate for ocular biometry and cycloplegic refraction in the study population. We used a lower concentration of the cyclopentolate and tropicamide in our study for both the drops and the spray, which may be the reason for the limited cycloplegia achieved.

Tropicamide 1% takes approximately 30 minutes to be effective and useful accommodation is recovered in 2 to 4 hours.\(^18\) With cyclopentolate 1%, the maximal cycloplegic effect is attained at 45
minutes and remains stable for 90 minutes.\textsuperscript{19} In this study, we measured the autorefraction 45 minutes after the drug application. Perhaps we need to wait longer for the medication to work because of the lower concentration of medications used in darkly pigmented irides.

Finally, most of our subjects were low myopes (mean refractive error, -0.86 for drops and -0.91 for spray). Myopic children may be expected to experience a less cycloplegic effect than would hyperopic children.

The spray system appears to be clinically equivalent to the drops in achieving effective pupil dilation and adequate cycloplegia, even in a population with dark irides such as ours. The spray is safe and causes less discomfort than do the drops. Tolerability and acceptance improved in our study group because the spray was applied to the closed eyelids. This method of drug application appears to be practical for the pediatric population as well as for patients with limited cooperation.

REFERENCES

15. Miranda MN. Residual accommodation: a comparison between cyclopentolate 1% and a combination of cyclopentolate 1% and tropicamide 1%. Arch Ophthalmol 1972;87:515-517.