Efficacy of a pediatric cycloplegic administered as a spray

Topical administration of mydratic and cycloplegic eyedrops is often an unpleasant procedure associated with significant side effects such as burning, stinging, and tearing. This is especially true in the pediatric population, in which avoidance of drug administration is common. A more acceptable alternative to eyedrop application may be use of the same mydratic and cycloplegic agents delivered to the eye as a spray. Sharp and Hanna7 previously reported the efficacy of a mydratic spray, but this study was not specifically directed at the pediatric population and had several methodological problems. We have shown, however, that mydratic combinations, when delivered as a spray, can be as efficacious and safe as the same mydratic solutions administered in conventional eyelid form.

In the pediatric age group, manifest subjective refractive techniques are often difficult at best. The clinician frequently relies on objective refractive procedures such as cycloplegic retinoscopy. We wished to learn whether administration of a mydratic-cycloplegic combination spray to the pediatric patient would have the same cycloplegic efficacy as a solution administered in conventional eyelid form. Since drug administration can be greatly enhanced if cyclopejics could be applied to the closed eyes of the pediatric patient, we further investigated if the cycloplegic spray would have the same efficacy as cycloplegic eyedrops applied to either open or closed eyes.

Methods

Potential subjects were screened for participation in the study according to the criteria listed in Table 1. After screening, 38 subjects were entered into the study, 20 (53 percent) of whom were male, and 23 (61 percent) were Caucasian. Subjects ranged in age from 6 months to 12 years (mean=7.3 years). Of the 38 subjects, 9 (24 percent) had blue irides, 26 (68 percent) brown irides, and 3 (8 percent) were classified as “other.”

We conducted an examiner-masked (by third-party drug administration), parallel-group study approved by the Institutional Review Board of the University of Alabama at Birmingham. The parent or guardian of each subject signed an appropriate informed consent in which the nature and possible consequences of the study were explained. The cycloplegic solution was prepared by mixing 3.75 ml cyclopentolate 2.0%, 3.75 ml phenylephrine 10%, and 7.5 ml tropicamide 1.0%, yielding a final 15 ml solution consisting of cyclopentolate 0.5%, phenylephrine 2.5%, and tropicamide 0.5%.

This solution was introduced into the original tropicamide droptainer and labeled “combination drops.” Before introducing the combination drops into the droptainer, the container was rinsed several times using sterile saline and then air dried. A second bolus of the same solution was prepared and added to a commercially available pump atomizer (Duray-Pretty Neat, Kearny, N.J.) that had been aseptically filled with 3% hydrogen peroxide. When activated, the atomizer delivered a spray volume of approximately 30 μl.
The subjects were randomized into one of four groups to receive: 1) one drop of combination solution to both open eyes; 2) one drop of combination solution to both closed eyes; 3) one “pump” of spray to both open eyes; and 4) one “pump” of spray to both closed eyes. Each subject received the cycloplegic under only one condition. Under both “drop” conditions, the subject’s head was inclined backward, and the combination solution was applied either to the interpalpebral fissure under “closed-eye” conditions or to the inferior cul-de-sac under “open-eye” conditions. For both “spray” conditions, the subject’s head was maintained in an upright position, and the spray atomizer was held approximately 10 cm from the subject’s eyes. A few moments after the cycloplegic combination was administered to the closed eyes under either drop or spray conditions, the subject was instructed to blink several times. Excess drug on the skin surfaces of the eyelids or adnexa was blotted dry. Immediately following drug instillation, the subject was asked to respond to questions about discomfort, burning, and stinging. Tearing and avoidance of drug instillation were objectively noted by the investigator. These five parameters were recorded using a magnitude estimation scale from “0” to “3,” with 3 being the most severe response.

Cycloplegic response was assessed by measuring residual accommodation under two conditions. In subjects who could reliably respond subjectively, amplitude of accommodation was measured by instructing the subject to read 0.5 M optotypes while they were moved along a Prince rule from 40 cm toward the subject to the point at which the optotypes were perceived as the first sustained blur. This procedure was performed by occluding the eye not tested. Each measurement was repeated two times through the subject’s best refractive correction or, if uncorrected, amplitude of accommodation was calculated using the subject’s refractive error. Amplitude of accommodation also was assessed monocularly in all subjects using an objective retinoscope technique in which the subject was instructed to fixate various size optotypes at the plane of the retinoscope as the examiner continually decreased the retinoscopic distance starting at approximately 40 cm. The point was noted at which a rapid change from

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<th>Table I: Eligibility criteria</th>
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<td>- Male of female</td>
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<td>- 0–12 years of age</td>
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<td>- Any refractive error</td>
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<td>- Normotensive</td>
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<td>- Open anterior chamber angles</td>
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<td>- Taking no ocular or systemic medications known to affect pupil size or accommodation</td>
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![Figure 1: Amplitude of accommodation using pushup procedure for the four methods of drug delivery. Data points represent means ±S.E.](image1)

![Figure 2: Amplitude of accommodation using retinoscopy procedure for the four methods of drug delivery. Data points represent means ±S.E.](image2)

Results

Figures 1 and 2 show the change in residual amplitude of accommodation using the two measurement techniques for the four methods of drug delivery. Repeated measures analysis of covariance (ANCOVA), correcting for differences in accommodation at time zero, revealed no statistically significant difference in amplitude of
accommodation among the four methods of drug administration for either of the two amplitude measures [Pushup (PU): F=0.971; df=3, 26; p=0.422; Retinoscopy (RE): F=0.619; df=3, 32; p=0.608].

To evaluate the relative ability of the pushup and retinoscopic methods to assess amplitude of accommodation, the slopes of the curves for each method were compared (Fig. 3). This analysis showed each method to be similar in its ability to assess amplitude of accommodation (p>0.05).

An ANCOVA revealed no statistically significant difference in cycloplegic response for either amplitude measure based on eye color (i.e., blue vs. non-blue) (Fig. 4) [PU: F=1.837; df=1, 28; p=0.186; RE: F=1.405; df=1, 34; p=0.244]. For each eye color there was no statistically significant difference in cycloplegic response between drops and spray (Fig. 5). [PU/Blue eyes: F=0.014; df=1, 4; p=0.912; PU/non-blue eyes: F=1.691; df=1, 21; p=0.208; RE/Blue eyes: F=0.636; df=1, 5; p=0.461; RE/non-blue eyes: F=1.662; df=1, 26; p=0.209].

We also found no statistically significant difference in cycloplegic response based on age (<8 years versus ≥8 years) (Fig. 6) [PU: F=0.182; df=1, 28; p=0.673; RE: F=1.807; df=1, 34; p=0.188]. Within each age range there was no difference in cycloplegic response between drops and spray [PU<8: F=0.551; df=1, 8; p=0.479; PU≥8: F=3.086; df=1, 17; p=0.097; RE/<8: F=0.486; df=1, 14; p=0.497; PU/≥8: F=1.164; df=1, 17; p=0.296].

The subjective and objective responses to the four drug administration methods have been reported elsewhere.²

Discussion

Topically applied sprays represent an alternative method of administering ophthalmic solutions. Sprays can be less irritating and less objectionable when compared with solutions given in conventional eyedrops. Various antiglaucoma medications were once commercially prepared in mist-dispensing bottles, but these are
no longer available. Combinations of mydriatics and cycloplegics have been used as sprays for routine mydriasis or cycloplegia in adults and children.\textsuperscript{1,2} The spray can be produced by using a refillable perfume atomizer that has first been asepticized by ethylene oxide gas or hydrogen peroxide before filling with the appropriate mydriatic or cycloplegic combination. The unit is held 5–10 cm from the eye before activating the spray. The volume of a single spray emanating from our system (105 μl) was greater than the volume of a drop obtained from a standard eyedropper.\textsuperscript{3}

High uncorrected refractive errors during the neonatal period or early childhood years may increase the risk of amblyopia or strabismus.\textsuperscript{5} It is therefore important for refractive examinations of children to be performed carefully, and it is generally recognized that refractive examinations performed under cycloplegia yield the most reliable and valid results.\textsuperscript{6} An important disadvantage of cycloplegic refraction, however, is that the pediatric patient often experiences discomfort upon instillation of the eyedrops, which may result in alienating the child and reducing subsequent cooperation during the examination. Traditionally, cycloplegic refraction in the pediatric age group has been accomplished by using solutions of tropicamide, cyclopentolate, and phenylephrine, instilled separately.\textsuperscript{6,7} This combination of agents produces adequate mydriasis for fundus evaluation and allows effective cycloplegia for retinoscopy or subjective refraction.\textsuperscript{6,7} Caputo and Lingua\textsuperscript{8} have recommended a combination mydriatic-cycloplegic solution that minimizes ocular irritation and provides acceptable mydriasis and cycloplegia with a single-encounter medication. We used a solution prepared by combining 3.75 ml cyclopentolate 2.0% with 7.5 ml tropicamide 1.0% and 3.75 ml phenylephrine 10.0%. The final, mixed solution contains cyclopentolate 0.5%, tropicamide 0.5%, and phenylephrine 2.5%. No major side effects have been reported from use of this combination mydriatic-cycloplegic solution.\textsuperscript{3}

The results of our study revealed no statistically significant difference in cycloplegic response for the four methods of drug administration. It is interesting to note, however, that the maximum effect was achieved by 20–30 minutes for each of the methods. This is of practical significance since it implies that clinicians need not wait 30–45 mins following cycloplegic instillation before the refractive procedures begin, as is the traditional recommendation.\textsuperscript{6} Although this finding is in contrast to that reported by several previous investigators,\textsuperscript{8,9,10} Manny and associates\textsuperscript{11} have recently obtained similar results using cyclopentolate in the pediatric age group.

We have reported\textsuperscript{2} that adverse drug instillation responses among these four methods of drug delivery are not significantly different. There is less burning sensation and less avoidance reaction on the part of the child, however, when the cycloplegic solution is applied using the spray under closed-eye conditions. This would strongly suggest, therefore, that application of a cycloplegic spray to closed eyes is as efficacious yet more tolerable compared to the other methods of drug administration.

It is of interest that the two methods of measuring amplitude of accommodation revealed significantly different results. The pushup method appears to demonstrate about 5D residual accommodation, whereas the retinoscopic method revealed little or no residual accommodation. This may be due to greater interpretive variability on the part of the child, differences in blur interpretation, or difficulty in understanding the pushup test. The greater variability inherent in the pushup method suggests that retinoscopy should be employed as the procedure of choice to ascertain residual accommodation prior to cycloplegic retinoscopy or subjective refraction in children.

Due to its ease and rapidity of administration, use of a cycloplegic spray appears to be a viable alternative to conventional eyedrops for routine cycloplegic refraction in the pediatric population. The results of our study suggest, moreover, that the spray can be applied to the closed eyelids, which improves tolerability and acceptance by the pediatric patient.

References


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