Full Length Research Paper

Comparison of cycloplegic retinoscopy using cyclopentolate or tropicamide eye drops in an epidemiologic study of pediatric refraction among 1907 school-aged children

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Compound tropicamide eye drop (0.5% tropicamide + sodium hyaluronate) and 1% cyclopentolate eye drop were compared in an epidemiologic study of pediatric refraction in school-aged children. A total of 1907 school-aged children were divided into three age groups: 6 to 8, 9 to 12, and 13 to 15 years old. Compound tropicamide eye drop and 1% cyclopentolate eye drop were used in the same individual before conducting retinoscopy, sequentially. The administration protocols were as follows. Three drops of compound tropicamide eye drop were administrated (one drop every 10 min), followed by retinoscopy 30 to 45 min later. Three drops of 1% cyclopentolate eye drop were administrated (one drop every 10 min), followed by retinoscopy 45 to 75 min later. There was a 7-day interval between the two times of retinoscopy. Average diopter was significantly higher using cyclopentolate than tropicamide in all age groups (p<0.001). The diopter (spherical equivalent value) < 0.50 D was considered as the coincidence rate between retinoscopies using the two different cycloplegic agents. Classified by the age group, the coincidence rate was 57.14% in 6 to 8 years old group (n=595), 67.79% in 9 to 12 years old group (n=798) and 81.70% in 13 to 15 years old group (n=514). Classified by refractive status, the coincidence rate was 94.97% (n=199) in myopia population, 79.53% in emmetropia population (n=337) and 61.56% in hyperopia population (n=1371). The cycloplegic effect of cyclopentolate was stronger than that of tropicamide. The variation was even more significant with the reduction of age and increase of diopter.

Key words: Child, refractive error, tropicamide, cyclopentolate, retinoscopy.

INTRODUCTION

Compound tropicamide is widely used for epidemiologic study and clinical treatment of pediatric refraction in China. However, children always have good diopter accommodation and potent cycloplegic agent is required for retinoscopy (Wilson et al., 2009). Ideal cycloplegic agent should be characterized by rapid onset and recovery of normal regulatory capacity, complete cycloplegia and absence of regional and general side effect (Mutti et al., 1994). The commonly used cycloplegic agents include atropine sulfate, tropicamide and cyclopentolate. The main distinctions of these agents are duration of onset and function recovery, as well as the depth of cycloplegia. Atropine is the golden standard for retinoscopy because of the definite efficacy of cycloplegia, but the onset is very slow and recovery time of normal regulatory capacity is always as long as 15 to 20 days (Chen, 2002), sometimes accompanied by severe side effects (Maurice and Mishima, 1984). The recovery time as long as 15 to 20 days is too long for school-aged children and may influence their study and
life quality, thus atropine is not well tolerated. Tropicamide is a relatively safe agent used for retinoscopy. It has rapid onset duration and the maximal cycloplegia effect appears at 20 to 30 min after administration. The regulatory function always recovered to basic level within 6 h (Yolton et al., 1980). However, only partial cycloplegia effect can be induced by tropicamide and the effect lasts for less than 1 h (Crick et al., 2003). The peak time of cycloplegia is hard to capture during clinical retinoscopy.

Cyclopentolate is another choice of cycloplegic agent for patients of all ages, especially suitable for infants and children (Bartlett, 1978). The peak cycloplegic effect appears at 25 to 75 min after administration and the regulatory capacity recovers 6 to 24 h later. The cycloplegic depth is enough for retinoscopy with a residue regulation at 0. 50 to 1.75 D, mean 1.25 D (Bartlett et al., 2008). Such powerful cycloplegic effect is even similar to atropine in elder children and adults. But the onset and recovery time is much shorter than atropine. It was reported that 3 drops of cyclopentolate (one drop every 10 min) provided a similar diopter to 3 days of atropinization in children (Lin et al., 1998).

Recently, many studies were performed to compare different cycloplegic agents in retinoscopy. However there was still no agreement on the clinical effect of tropicamide and cyclopentolate. Most studies demonstrated that diopter was similar when using tropicamide or cyclopentolate for retinoscopy (Twelker and Mutti, 2001; Hofmeister et al., 2005; Proskurina, 2002). But cyclopentolate is more effective in inhibiting regulation capacity with lower residue regulation (Mutti et al., 1994; Hofmeister et al., 2005; Proskurina, 2002; Manny et al., 2001). Thus cyclopentolate is regarded as a routine and standard cycloplegic agent for both clinical and epidemiological uses (Sanchez et al., 2008). Although tropicamide was not as effective as cyclopentolate in cycloplegia, its profiles of faster onset and recovery made tropicamide more acceptable in patients (Hofmeister et al., 2005) and tropicamide might be a better cycloplegic agent for myopia and mild-to-moderate hyperopia populations.

Because of the disparity of opinions previously provided, a self-control study was performed to compare compound tropicamide eye drop (0.5% tropicamide + sodium hyaluronate) and 1% cyclopentolate eye drop in retinoscopy of 1907 cases of 6 to 15 years old children, so as to determine which cycloplegic agent was more reliable, and provide evidence for clinical and epidemiological examination of pediatric refraction.

MATERIALS AND METHODS

General data

Sampling was based on the total population of Yongchuan region of Chongqing city, China, and 1907 cases of children with 3814 eyes were sampled. They were aged 6 to 15 years and ratio of male to female was 1.2:1. Classified according to the age groups, there were 595 cases aged 6 to 8 years, 798 cases aged 9 to 12 years and 514 cases aged 13 to 15 years. The inclusive criteria were as follows: (1) The actual age when examining was between 6 and 15 years; (2) Their parents or guardians provided their informed consent; (3) Children were not diagnosed with systemic cardiovascular disease or neurological diseases, such as congenital heart disease, ischemic or hypoxic encephalopathy and retarded mental development. The exclusive criteria included: (1) Impaired visual function because of eye diseases (such as leukemia, cataract and retinal detachment); (2) Allergy to any components of the eye drops or children with angle closure or narrow angle glaucoma according to the medical history and anterior segment examination; (3) Refusal of any continuing examination because of discomfort in eyes after medication administration; (4) Difficulty in retinoscopy examination because of eye tampering.

Methods

Both eyes of one participant were administrated with 3 drops of compound tropicamide eye drop at first (1 drop every 10 min for three times), and 30 to 45 min later retinoscopy was performed. After 7 days, this participant was administrated with 3 drops of 1% cyclopentolate eye drop (1 drop every 10 min for three times), and 45 to 75 min later, retinoscopy was performed. Medication administration, retinoscopy, result collection and data analysis were performed by 4 persons respectively, and each task was completed by the same person to reduce the error. Triple-blind principle was complied with by the participants, examination physician and statistician.

Data analysis

All results of retinoscopy were listed and analyzed in SPSS 17.0. Diopter coincidence rate was compared using χ² test. When more than 20% of theoretical frequency in the R×C table was less than 5, Fisher definite probability method was applied to calculate the P value. When comparison of more than 2 groups were statistical significant, multiple comparison was performed, and the level of significance was α=0.05/3=0.0167. When outcome variables were used in logistic regression, we analyzed the factors such as gender, left or right eye, age, and diopter affecting the coincidence rate of diopter after retinoscopy with the two cycloplegic agents. Average diopter was compared using t test and P<0.05 was regarded as statistically significant.

RESULTS

Coincidence rate of diopter after retinoscopy with the two cycloplegic agents

As usual, the difference of spherical equivalent value in retinoscopy less than 0.50 was regarded as coincidence and that equal to or higher than 0.50 was regarded as inconformity. Coincidence was calculated using diopter of the right eye.

All subjects were classified by age stages into 6 to 8 years old group (n=595), 9 to 12 years old group (n=798) and 13 to 15 years old group (n=514). They were also classified by refractory status into myopia group (spherical equivalent value of right eye ≤ -0.50 D, n=199), emmetropia group (-0.50D < spherical equivalent value of
Figure 1. Coincidence rate of diopter after cycloplegic retinoscopy with cyclopentolate and tropicamide for (A) children in different age groups under different refractive status, and (B) children in different refractive status under different age groups. The age groups includes 6-8-year-old(n=595), 9-12-year-old(n=798), and 13-15-year-old(n=514). The refractive status includes myopia (n=199), emmetropia (n=337), and hyperopia (n=1371). Set a diopter (Spherical equivalent value) difference of <0.50D as the standard. Data were from the right eyes of 1907 children.

right eye < +0.50 D, n=337) and hyperopia group (spherical equivalent value ≥ +0.50 D, n=1371).

Changing trend of diopter coincidence at different age stages were shown in Figure 1A. Generally, diopter coincidence rate was reduced significantly with the decrease of age: 57.14% in 6 to 8 years old group, 67.79% in 9 to 12 year old group and 81.7% in 13 to 15 year old group ($\chi^2=76.902$, $P<0.001$). The multiple comparisons showed that the coincidence rate was also significantly different between any two groups (6 to 8 years old group vs. 9 to 12 years old group; 6 to 8 years old group vs. 13 to 15 year old group; 9 to 12 years old group vs. 13 to 15 year old group ($P<0.001$). Similar trends with changes of age stages were also observed in emmetropia and hyperopia groups with statistical significance, but not in myopia group (Fisher definite probability method, $P=0.140$).

Diopter coincidence in population with different refractory status was shown in Figure 1B. Generally, coincidence was lowest in hyperopia group (61.56%),
Table 1. The diopter after using the two cycloplegic agents in different age stages.

<table>
<thead>
<tr>
<th>Group (Years)</th>
<th>N</th>
<th>Tropicamide</th>
<th>Cyclopleolate</th>
<th>Cyclopleolate - Tropicanide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Total</td>
<td>1907</td>
<td>0.19 ± 1.18</td>
<td>0.25 ± 1.10</td>
<td>0.50 ± 1.23***</td>
</tr>
<tr>
<td>6 - 8</td>
<td>595</td>
<td>0.67 ± 0.86</td>
<td>0.75 ± 0.72</td>
<td>1.07 ± 0.85***</td>
</tr>
<tr>
<td>9 - 12</td>
<td>798</td>
<td>0.13 ± 0.98</td>
<td>0.16 ± 0.99</td>
<td>0.43 ± 1.04***</td>
</tr>
<tr>
<td>13 - 15</td>
<td>514</td>
<td>-0.28 ± 1.53</td>
<td>-0.20 ± 1.35</td>
<td>-0.05 ± 1.57***</td>
</tr>
</tbody>
</table>

*** P<0.001 vs Tropicamide

Table 2. Comparison of diopter in myopia population.

<table>
<thead>
<tr>
<th>Group (Years)</th>
<th>N</th>
<th>Tropicamide</th>
<th>Cyclopleolate</th>
<th>Cyclopleolate - Tropicanide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Total</td>
<td>199</td>
<td>-2.10 ± 1.99</td>
<td>-1.88 ± 1.86</td>
<td>-2.00 ± 1.97***</td>
</tr>
<tr>
<td>6 - 8</td>
<td>10</td>
<td>-2.44 ± 2.50</td>
<td>-1.49 ± 1.47</td>
<td>-2.24 ± 2.51**</td>
</tr>
<tr>
<td>9 - 12</td>
<td>91</td>
<td>-1.73 ± 1.45</td>
<td>-1.71 ± 1.56</td>
<td>-1.63 ± 1.43***</td>
</tr>
<tr>
<td>13 - 15</td>
<td>98</td>
<td>-2.39 ± 2.32</td>
<td>-2.04 ± 2.14</td>
<td>-2.32 ± 2.31**</td>
</tr>
</tbody>
</table>

** P<0.01 vs Tropicamide; *** P<0.001 vs Tropicamide

followed by emmetropia group (79.53%) and myopia group (94.97%). The difference between these groups was statistically significant ($\chi^2=113.617, P<0.001$). The multiple comparisons showed that the coincidence rate was significantly different between any two groups (myopia group vs. emmetropia group, myopia group vs. hyperopia group, emmetropia group vs. hyperopia group, $P<0.001$). Similar trends with changes of refractory status were also observed in 9 to 12 and 13 to 15 years old group, but not in 6 to 8 years old group ($\chi^2=2.485, P=0.289$), which has the lowest coincidence among all age stages.

In order to analyze the possible factors influencing coincidence rate of diopter, multiple logistic regression analyses were performed with children’s gender, left or right eye, age, and diopter as covariates (Table 1). It was found that coincidence rate of diopter was correlated with age ($OR=1.104, P<0.001$) and diopter ($OR = 0.515, P<0.001$). Gender ($P=0.29$) and left or right eye ($P=0.644$) did not correlate with coincidence rate of diopter.

Comparison of diopter in population of different age stages

The diopter of retinoscopy after using cyclopentolate was higher than that using tropicamide. The differences after using the two agents were statistically significant in the total population as well as all age stages. (Total: Right eye, t=-36.949, P<0.001, left eye, t=-33.752, P<0.001; 6 to 8 year old group: Right eye, t=-23.470, P<0.001, left eye, t=-19.197, P<0.001; 9 to 12 year old group: Right eye, t=-28.480, P<0.001, left eye, t=-24.713, P<0.001; 13 to 15 year old group: Right eye, t=-18.240, P<0.001, left eye, t=-16.944, P<0.001) (Table 1).

Diopter in population with different refractory status

The children were classified into myopia (n=199), emmetropia (n=337) and hyperopia (n=1371) groups by refractory status, and the average diopter of these population was listed in Tables 2 to 4, respectively.

Table 2 showed that in myopia population, diopter was significantly higher using cyclopentolate than using tropicamide in total population and also 9 to 12 year old group (Total: Right eye, t=-5.709, P<0.001, left eye, t=-5.630, P<0.001; 9 to 12 year old group: Right eye, t=-4.37, P<0.001, left eye, t=-5.86, P<0.001). However, in 6 to 8 and 13 to 15 year old group, diopter of right eye was significantly higher using cyclopentolate than using tropicamide (6 to 8 year old group, t=-3.536, P=0.008; 13 to 15 year old group: t=-2.875, P=0.005), but not left eye (6 to 8 year old group, t=-2.229, P=0.056; 13 to 15 year old group: t=-1.867, P=0.065).

Table 3 showed that in emmetropia population, diopter was significantly higher using cyclopentolate than using tropicamide in total population, 9 to 12 and 13 to 15 groups (Total: Right eye, t=-5.224, P<0.001, left eye, t=-5.368, P<0.001; 9 to 12 year old group: Right eye, t=-3.993, P<0.001, left eye, t=-3.851, P<0.001; 13 to 15 year old group: Right eye, t=-6.971, P<0.001, left eye, t=-6.945, P<0.001). However, there was no statistical significance of diopter in 6 to 8 year old group (Right eye, t=1.981, P=0.058; left eye, t=2.054, P=0.05).
Table 3. Comparison of diopter in emmetropia population.

<table>
<thead>
<tr>
<th>Group (Years)</th>
<th>N</th>
<th>Tropicamide</th>
<th>Cyclopentolate</th>
<th>Cyclopentolate - Tropicamide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Total</td>
<td>337</td>
<td>-0.05 ± 0.42</td>
<td>0.02 ± 0.46</td>
<td>0.06 ± 0.16***</td>
</tr>
<tr>
<td>6-8</td>
<td>29</td>
<td>0.30 ± 0.67</td>
<td>0.39 ± 0.64</td>
<td>0.08 ± 0.15</td>
</tr>
<tr>
<td>9-12</td>
<td>154</td>
<td>-0.03 ± 0.33</td>
<td>0.01 ± 0.36</td>
<td>0.08 ± 0.16***</td>
</tr>
<tr>
<td>13-15</td>
<td>154</td>
<td>-0.14 ± 0.41</td>
<td>-0.05 ± 0.48</td>
<td>0.04 ± 0.17***</td>
</tr>
</tbody>
</table>

*** P<0.001 vs Tropicamide.

Table 4. Comparison of diopter in hyperopia population.

<table>
<thead>
<tr>
<th>Group (Years)</th>
<th>N</th>
<th>Tropicamide</th>
<th>Cyclopentolate</th>
<th>Cyclopentolate - Tropicamide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Total</td>
<td>1371</td>
<td>0.58 ± 0.57</td>
<td>0.62 ± 0.56</td>
<td>0.98 ± 0.57***</td>
</tr>
<tr>
<td>6 - 8</td>
<td>556</td>
<td>0.76 ± 0.53</td>
<td>0.82 ± 0.61</td>
<td>1.19 ± 0.51***</td>
</tr>
<tr>
<td>9 - 12</td>
<td>553</td>
<td>0.47 ± 0.47</td>
<td>0.52 ± 0.51</td>
<td>0.87 ± 0.46***</td>
</tr>
<tr>
<td>13 - 15</td>
<td>262</td>
<td>0.40 ± 0.58</td>
<td>0.40 ± 0.36</td>
<td>0.73 ± 0.54***</td>
</tr>
</tbody>
</table>

*** P<0.001 vs Tropicamide.

Table 4 showed that in hyperopia population, diopter was significantly higher using cyclopentolate than using tropicamide in total population and all age stages (Total: Right eye, t=-47.002, P<0.001, left eye, t=-37.042, P<0.001; 6 to 8 year old group: Right eye, t=-27.747, P<0.001, left eye, t=-21.535, P<0.001; 9 to 12 year old group: right eye, t=-35.202, P<0.001, left eye, t=-26.950, P<0.001; 13 to 15 year old group: Right eye, t=-21.703, P<0.001, left eye, t=-20.812, P<0.001).

The maximum disparity using tropicamide or cyclopentolate occurred in hyperopia group (+2.50 D), while the minimum disparity occurred in myopia group (-0.25 D).

The most common complications of cyclopentolate were eye irritant syndrome and bulbar conjunctiva hyperemia. Increase of intraocular pressure and central nervous system syndrome were not observed in any cases.

DISCUSSION

The two cycloplegic agents used most frequently in mainland China were 0.5% tropicamide + sodium hyaluronate and 1% cyclopentolate (currently there are 0.25% and 0.5% tropicamide in China and the latter was used more frequently. No 1% tropicamide was available in China. Cyclopentolate in China has only one concentration of 1%. The present study demonstrated that diopter of retinoscopy was significantly higher using cyclopentolate than using tropicamide in 6 to 15 years old group children. Thus cycloplegic effect of cyclopentolate is more complete than tropicamide. It may reduce the error of retinoscopy under cycloplegic condition and provides more accurate results of retinoscopy as the basis of pediatric refraction correction. These results are similar to the study of Egashira et al. (1993).

Diopter in 6 to 8 and 13 to 15 years old group of myopia population was significantly higher using cyclopentolate than using tropicamide in right eyes, but not left eyes. The possible reasons included: (1) Operating error of nurse when administrating the drops, and (2) Error resulted from the poor cooperation of subjects. As usual eye drops were administrated firstly in the right eyes and then in the left eyes. The relatively small sample size in 6 to 8 years old group (n=29) might have resulted in the similarity of diopter.

The maximum disparity occurred in the hyperopia group (+2.50 D) while the minimum occurred in the myopia group (-0.25 D). It was speculated that regulatory capacity was stronger in hyperopia status than in myopia status. Inhibition of regulatory capacity was more effective using cyclopentolate than tropicamide. Therefore, 1% cyclopentolate provided stronger inhibitory effect in hyperopia and emmetropia status than in myopia status.

It was also demonstrated that coincidence rate of tropicamide and cyclopentolate was lower in younger children. In all refractory status, the coincidence rate was lowest in 6 to 8 years old group but no statistical significance was observed. These results showed that cyclopentolate provided stronger cycloplegic effect in younger age stage in all refractory status. The reason might be that younger children had stronger regulatory capacity (Rosenfield and Benzoni, 2007) and the capacity was inhibited more effectively by cyclopentolate with
higher diopter in retinoscopy. These results were similar to the study of Owens et al. (1998), in which cyclopentolate showed stronger cycloplegic effect in younger children than elder children. Thus it was believed that 1% cyclopentolate provided stronger cycloplegic effect in younger age stage than in elder age stage.

The phenomenon that coincidence was lower in younger children was even more obvious in hyperopia and emmetropia population than myopia population. According to the pathogenesis of myopia, regulatory capacity in myopia population was attenuated but not enhanced (Li, 2005). Thus the inhibited effect of cyclopentolate was more obvious in hyperopia children because of the stronger inhibitory effect than tropicamide. Therefore, it was believed that cyclopentolate provided more accurate results of retinoscopy than tropicamide in younger children with hyperopia. For the newly diagnosed young children, cyclopentolate should be adopted in preference.

Besides, it was speculated that the relatively shorter peak time of 0.5% tropicamide might be another reason of diopter disparity using the two different cycloplegic agents. The cycloplegic effect was attenuated rapidly after peak time. On the other hand, poor cooperation of children during examination prolonged the duration of retinoscopy. It was hard to perform examination exactly at peak time of cycloplegic effect in clinical conditions. Cyclopentolate provided less residue regulation and accommodation amplitude, as well as longer duration of peak cycloplegic effect. Therefore, it was more suitable for children in retinoscopy. The speculation was in accordance of the study of Lin et al. (1998) in which they found that although onset of tropicamide was rapid, it had shorter duration of peak effect than cyclopentolate.

In conclusion, cycloplegic effect of cyclopentolate is stronger than tropicamide. But this effect varies among different age stages. The stronger effect is more obvious in younger children. Therefore, 1% cyclopentolate should be used for retinoscopy under cycloplegic condition as an international unification measure in epidemiological study of refraction in young children. The stronger cycloplegic effect of cyclopentolate is also more obvious in hyperopia and emmetropia status. Therefore, it is recommended that cyclopentolate should be used for retinoscopy in hyperopia and emmetropia children. The limitation of this study was that no examination of accommodation was performed as further reference for the present study.

ACKNOWLEDGMENT

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