Original Article

Cycloplegic Refraction in Myopic Children with Brown Irises: Time of Maximum Cycloplegia and Difference between Retinoscopy and Autorefraction

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Objective: To evaluate time of maximum cycloplegia in myopic children with brown irises and to study differences between refractive error after maximum cycloplegia measured by retinoscopy and autorefraction.

Materials and Methods: The present study was a prospective descriptive study included myopic children with brown irises aged 5 to 14 years. Cycloplegic refraction was performed using cyclopentolate 1%, three times, ten minutes apart. Refractive error was measured by autorefraction before and at 30, 40, 50, 60, 70, and 80 minutes after the first instillation of cyclopentolate. Finally, retinoscopy was performed by a single examiner at 80 minutes. Time of maximum cycloplegia was determined from the time point at which the 95% confidence interval of the differences between the mean spherical equivalent (SE) at each point and its final value at 80 minutes was reached and remained within the equivalence limit (±0.25 D). Difference between SE of retinoscopy and autorefraction was evaluated.

Results: Sixty-eight children were recruited. The mean age was 10.5 years (SD 2.4). Thirty-seven children were male (54%). The time of maximum cycloplegia was 30 minutes after the first instillation of cyclopentolate. At 80 minutes, the degree of myopia measured by autorefraction was significantly higher compared to those measured by retinoscopy ($p<0.001$, mean difference 0.26 D).

Conclusion: Time of maximum cycloplegia in myopic children with brown irises was 30 minutes after the first instillation of cyclopentolate. Even when the maximum cycloplegia was reached, the degree of myopia measured by autorefraction was higher than that measured by retinoscopy.

Keywords: Cycloplegic refraction, Cyclopentolate, Cycloplegia, Myopia, Myopia in children, Retinoscopy, Autorefraction

Received 14 May 2020 | Revised 23 October 2020 | Accepted 29 October 2020

J Med Assoc Thai 2021;104(3):364-9

Website: http://www.jmatonline.com

Myopia in children is currently a major problem worldwide. It significantly increases globally[1], with the highest prevalence in east Asians[2]. Refraction on myopic children is therefore one of the most frequent examinations that ophthalmologists encounter.

Cyclopentolate 1% eye drop is widely used for refraction in children. It produces mydriatic and cycloplegic effects that are necessary for accurate measurement. Duration from the first instillation of the eye drop to the time point at which the maximum cycloplegic effect is reached is important to determine the best time for refraction. Previous studies found that the time of maximum cycloplegia for cyclopentolate 1% is 10 to 45 minutes[3-5]. The duration is varied between patients with light and dark irises[3], different types of refractive error[4,5], and different eye drop regimens[3-5]. However, from the previous studies, the time of maximum cycloplegia in myopic children was still inconclusive[4,5].

Measurement method also affects accuracy of refraction. A commonly used technique for refraction in children is retinoscopy. However, nowadays there is a widespread use of autorefraction in adult as it is fast and does not require physician's skill. Thus, there is doubt whether autorefraction can be used instead of retinoscopy when performing cycloplegic refraction in children. Previous studies compared cycloplegic autorefraction and retinoscopy[6-12]. They found different results.

The objectives of the present study were to determine time of maximum cycloplegia in myopic children with brown irises and to study differences in

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How to cite this article:

Pukrushpan P, Kaewpradit K, Honglertnapakul W. Cycloplegic Refraction in Myopic Children with Brown Irises: Time of Maximum Cycloplegia and Difference between Retinoscopy and Autorefraction. J Med Assoc Thai 2021;104:364-9.

doi.org/10.35755/jmedassocthai.2021.03.11414

refraction after maximum cycloplegia measured by autorefraction and retinoscopy.

Materials and Methods

The present study was a prospective descriptive study approved by the Institutional Review Board of King Chulalongkorn Memorial Hospital, Faculty of Medicine, Chulalongkorn University (IRB No. 695/59) and registered to the Thai Clinical Trials Registry (TCTR20171120003). Informed assent and informed consent were obtained from participants and their parents or guardians.

Children with brown irises, age 5 to 14 years old, who had spherical equivalent (SE) by autorefraction –0.50 diopter (D) or more, at the Refraction Clinic, King Chulalongkorn Memorial Hospital, between February 2017 and April 2018 were recruited. Exclusion criteria were uncorrected visual acuity 20/30 or better in one or both eyes, ophthalmic diseases other than refractive error or strabismus, previous ophthalmic surgery, history of allergy or sensitivity to cyclopentolate or tetracaine, history of cardiovascular disease, and insufficient cooperation interfering with instillation of eye drop or outcome measurement.

All patients underwent refraction using autorefraction (KR-800 auto kerato-refractometer, Topcon Medical Systems Inc., Tokyo, Japan), underwent instillation of tetracaine eye drop (Alcon, Inc., Switzerland), then cyclopentolate 1% eye drop (Alcon, Inc., Switzerland) three times, ten minutes apart. Any side effects were observed and recorded. Patients underwent refraction again using autorefraction starting at 30 minutes after the first drop of cyclopentolate, six times, ten minutes apart, finishing at 80 minutes after the first drop. Finally, retinoscopy was performed by a single examiner (PP). Only SE from the right eye was used for analysis.

Time of maximum cycloplegia was defined as the time point at which the SE was reached and remained within equivalent limit (±0.25 D) of the final value at 80 minutes. To determine the time of maximum cycloplegia, mean differences between the SE at each point and its final value were calculated. The time of maximum cycloplegia was determined from the time point at which the 95% confidence interval of the differences reached and remained within the equivalence limit.

All statistical analyses were performed using IBM SPSS statistics software, version 22.0 (IBM Corp., Armonk, NY, USA). The time of maximum cycloplegia was analyzed by descriptive statistics. The difference between refractive error after maximum cycloplegia measured by retinoscopy and autorefraction was analyzed by parametric test. The agreement between the two methods was analyzed by intraclass correlation coefficient (ICC) and Bland-Altman plot. The agreement within 0.50 D was used for analysis. Subgroup analysis was performed with parametric test. All p-values were two-sided and considered statistically significant when less than 0.05.

Results

Sixty-eight children were enrolled in the present study. The mean age was 10.5 years (SD 2.4, range 5 to 14). Thirty-seven children were male (54%) and 31 were female (46%). All patients had brown irises. The mean SE prior to instillation of cyclopentolate was –4.38 D (SD 2.35, range –1.25 to –10.75). The mean SE before and at each time point after instillation of cyclopentolate are shown in Figure 1.

Maximum cycloplegia was reached at 30 minutes after the first drop of cyclopentolate. This was determined by using the 95% confidence interval of the mean differences between the mean SE at each time point and its value at 80 minutes (Figure 2).

Considering the percentage of patients whose SE reached and remained within ±0.25 D of their final value, the authors found that 56 patients (82%) reached maximum cycloplegia at 30 minutes and all patients reached maximum cycloplegia at 80 minutes after the first drop of cyclopentolate. Three patients reached maximum cycloplegia at 80 minutes. One patient was an 11-year-old boy with SE –3.25 D and –2.50 D, before and after cycloplegia. The other two patients were 13 and 14-year-olds with SE –9.00 D and –7.25 D, before and after cycloplegia. All these patients had 0.50 D or less difference between SE at 30 minutes and their final value at 80 minutes.

Subgroup analysis between the two age groups (5 to 10 and 11 to 14 years) found no difference of the time of maximum cycloplegia (p=0.28). Similarly, a subgroup analyses of patients with lower and higher degrees of myopia (less than –4.00 and –4.00 D or more) also found no difference of time of maximum cycloplegia (p=0.11).

At 80 minutes, mean SE from retinoscopy was –3.70 D (SD 2.39). There was a correlation between SE measured by autorefraction and retinoscopy (ICC 0.98, 95% confident interval 0.94 to 0.99). However, the degree of myopia measured by autorefraction was significantly higher compared to those measured by retinoscopy (p<0.001, mean difference 0.26 D, 95%

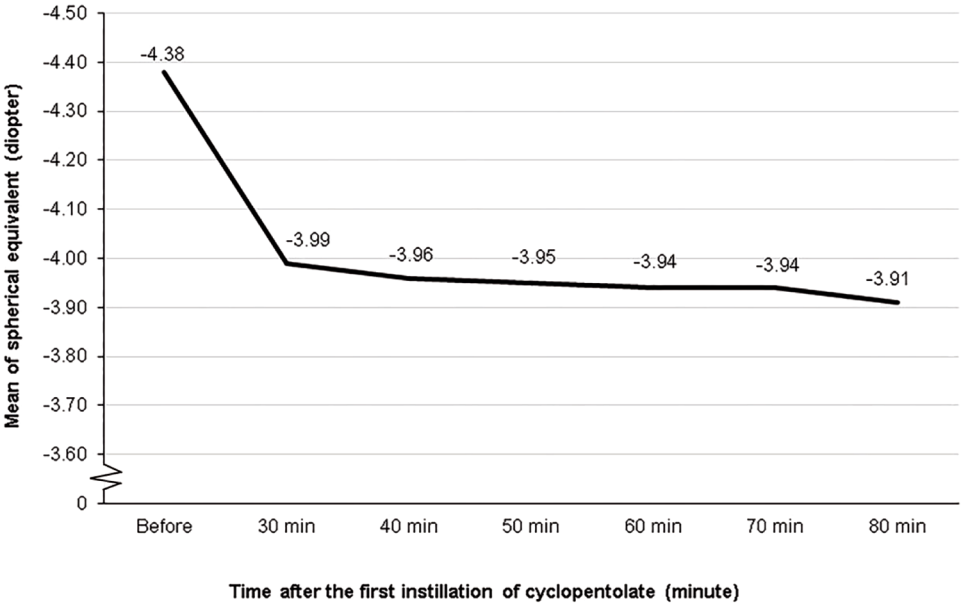

Figure 1. The mean spherical equivalent before and at each time point after instillation of cyclopentolate measured by autorefraction.

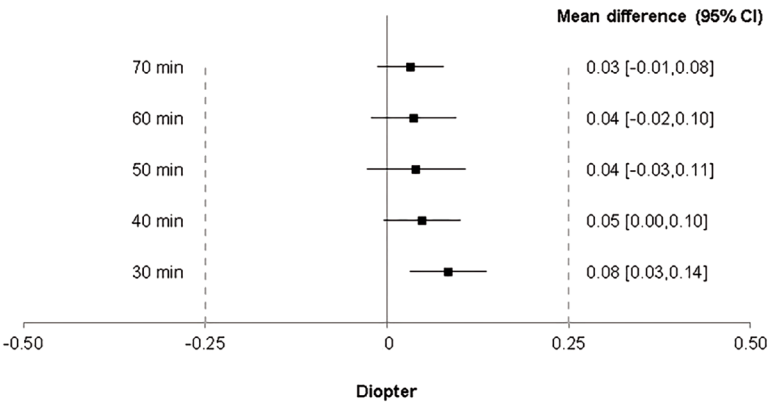

Figure 2. Mean differences between mean spherical equivalent at each time point and its value at 80 minutes, and its 95% confidence interval (CI).

limits of agreement –1.12 to 0.60 D, range 0.50 lower to 2.00 D higher than retinoscopy) (Figure 3). Twenty-two patients (32%) and 11 patients (16%) had a difference of more than 0.25 D and 0.50 D, respectively, between the two methods. Six patients whose myopia was measured by autorefraction were at least 1 D higher than that measured by retinoscopy. All patients who had a difference of more than 0.50 D underwent subjective refraction. Glasses were prescribed according to their retinoscopy result, which produced good vision within the range of 20/20 to 20/25-2. Subgroup analysis showed that the degree of difference between the two methods did not differ between two age groups (5 to 10 and 11 to 14 years, p=0.18). No serious side effects were recorded.

Discussion

The present study was a study evaluating time of maximum cycloplegia among the largest group of myopic children. The researchers found that maximum cycloplegia in myopic children with brown irises occurred at 30 minutes after the first instillation of cyclopentolate 1%. Subgroup analyses of patients at different age groups or different degrees of myopia also found the same result.

There was a previous study by Lin et al who reported the cycloplegic effect in 37 myopic Taiwanese children receiving either cyclopentolate

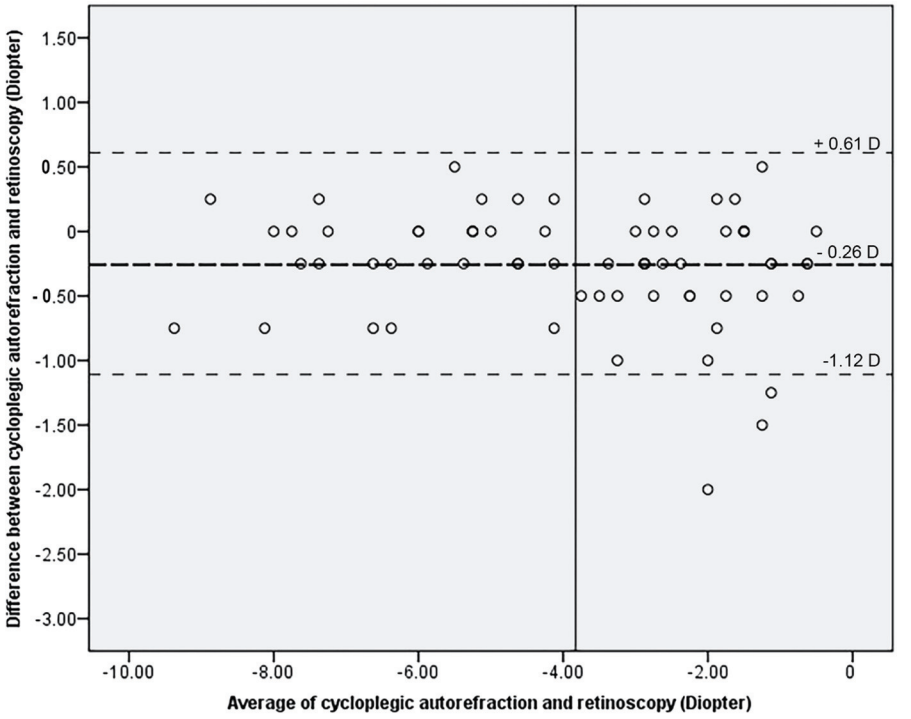

Figure 3. Spherical equivalent: difference versus average of values measured by autorefraction and retinoscopy (Bland-Altman plot).

1% or tropicamide 1% twice[4]. They found that time of maximum cycloplegic effect was about 45 minutes for cyclopentolate and about 30 minutes for tropicamide. Manny et al showed that the time of maximum cycloplegia were different among people who have different iris color[3]. They studied the effect of cyclopentolate 1% one drop in 35 adults with any type of refractive error and found that the time of maximum cycloplegia was 10 to 20 minutes among patients with light irises and 30 to 40 minutes among patients with dark irises.

A previous study by one of the present authors studied 60 children with brown irises, using cyclopentolate 1% three times, a similar regimen to the present study[5]. The result was maximum cycloplegia occurred at 30 minutes. However, subgroup analysis suggested that the result in myopic group might be dissimilar from other types of refractive error since the time of maximum cycloplegia in emmetropic and hyperopic groups were 30 minutes, whereas, in myopic group was 50 minutes. Nevertheless, results on the myopic group were inconclusive due to small sample size in the study. Therefore, the present study clarified that in myopic children, the time of maximum cycloplegia was also 30 minutes after the first drop of cyclopentolate, coinciding with results on children with emmetropia or hyperopia from the previous study[5].

The previous study found that mean pupil size after using cyclopentolate 1%, three times, in children with brown irises was only 3.7 mm at 30 minutes, and further dilation occurred thereafter[5]. Accordingly, although maximum cycloplegia occurred at 30 minutes, physicians may find it difficult to perform retinoscopy in small pupil size. The authors would recommend using tropicamide 1% in conjunction with cyclopentolate to facilitate the retinoscopy.

The present study found that, after maximum cycloplegia, there was a significant difference in the degree of myopia measured by autorefraction and retinoscopy. Autorefraction overestimated myopia, with mean difference of 0.26 D, range from 0.50 lower to 2.00 D higher than retinoscopy. The authors also found that 16% of patients had a difference of more than 0.50 D, and 9% of patients had the difference 1.00 D or more between the two methods. This is comparable to study of Guha et al who reported that 13.2% of myopic children had a difference of more than 0.50 D between those methods[10]. This is supported by evidence from Ebri et al who evaluated residual accommodation in children after receiving cyclopentolate 1%[13]. They found mean residual

accommodation of 0.63 D and 46% of children had residual accommodation of more than 0.50 D. In contrary, other previous studies did not find clinically significant differences between those two methods[6-8,12]. There was also a report showing that a significant difference between the two methods was found only in hyperopic children, not in myopic children[11]. However, the effect of cyclopentolate has been reported to vary according to eye drop regimens[14,15] and iris colors[3]. This may explain the different results between studies.

Even though the authors postulated that cycloplegic autorefraction might overestimate myopia, the authors still had to use autorefraction to investigate time of maximum cycloplegia. Retinoscopy takes much more time, so it cannot be used to measure SE at every time point. Furthermore, the present study regimen used cyclopentolate 1% at time points 0, 10, and 20 minutes, and then began to measure SE at 30 minutes. Therefore, there was a possibility that the time of maximum cycloplegia could have been earlier than 30 minutes. Future study with lower frequency of cyclopentolate and shorter duration of measurement would answer that question.

In conclusion, the present study found that maximum cycloplegia in myopic children with brown irises occurred at 30 minutes after the first instillation of cyclopentolate 1%. This could help ophthalmologists determine the most appropriate time of cycloplegic refraction to get more accurate measurements and shorten patient waiting times. When maximum cycloplegia is reached, measuring refraction with autorefraction can overestimate myopia. Retinoscopy is still recommended.

What is already known on this topic?

Myopia in children is currently a major problem worldwide. It has the highest prevalence in east Asians. Refraction on myopic children is therefore one of the most frequent examinations in ophthalmology service. However, previous results on time of maximum cycloplegia in myopic children with brown irises was still inconclusive.

What this study adds?

This study found that maximum cycloplegia in myopic children with brown irises occurred at 30 minutes after the first drop of cyclopentolate. The results of this study could help ophthalmologists determine the best time to perform cycloplegic refraction. In addition, the authors still recommend retinoscopy over autorefraction when maximum cycloplegia is reached since the latter can overestimate myopia.

Acknowledgement

This study was supported by the Ratchadaphisek Sompoch Fund (grant number RA60/021).

Conflict of interested

The authors disclose no conflicts of interest.

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