Comparison of Single Drop versus Two Drops 0.5% Tropicamide Using Manual and Automated Refraction in Children Aged 5-7 Years: A Randomized Controlled Trial

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ABSTRACT

Background. Cycloplegia is important for obtaining accurate refractive measurements in children. However, the limited availability of cycloplegic agents in the Philippines presents challenges for pediatric mass-refraction programs.

Objective. This study evaluated the efficacy and reliability of 0.5% tropicamide administered as a single-drop versus the standard two-drop regimen for obtaining cycloplegic refraction in children.

Methods. This multicenter, randomized, single-sequence, crossover, controlled, single-blind study included children aged 5–7 years recruited from selected schools and a pediatric ophthalmology clinic in a tertiary hospital in the Philippines. Participants were randomized to receive a single drop and two drops of 0.5% tropicamide according to the study sequence. Automated refraction was performed at 5, 15, and 30 minutes, followed by manual refraction at 30–40 minutes. Another manual refraction performed 30-40 minutes after 2 drops of 0.5% tropicamide served as the reference standard. The pediatric ophthalmologists performing the reference refraction were masked to the automated refraction results.

Results. A total of 219 eyes from 111 children were included, 59% (66/111) of whom were male. Hyperopia was the most common refractive error (76%, 166/219), followed by astigmatism (62.6%, 137/219) and myopia (16%, 34/219). After a single drop of tropicamide, auto-mated refraction at 5, 15, and 30 minutes demonstrated significant differences from the reference standard in spherical equivalent (SE), sphere, cylinder, and axis (all P <0.05). The median SE values at 5, 15, and 30 minutes were 0.25 D (Interquartile Range or IQR, 1.25 D), 0.25 D (IQR, 1.50 D), and 0.375 D (IQR, 1.50 D), respectively, compared with 0.75 D (IQR, 1.75 D) for the reference refraction. In contrast, manual refraction performed 30–40 minutes after a single drop did not differ significantly from the reference standard for sphere (P = 0.479), cylinder (P = 0.470), axis (P = 0.137), or SE (P = 0.327). Following two drops, automated refraction at all time points remained significantly different from the reference standard for cylinder, axis, and SE. However, at 30 minutes, the spherical refraction did not differ significantly from the reference standard (P = 0.209).

** Dr. Torrefranca and Dr. Santiago shared first authorship for this manuscript.*

eISSN 2094-9278 (Online)
Published: September 15, 2026
https://doi.org/10.47895/amp.v60i17.14500

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Conclusion. In children aged 5–7 years, manual refraction performed 30–40 minutes after either a single- or two-drop administration of 0.5% tropicamide produced results comparable with the reference standard. Automated refraction following a single drop demonstrated greater variability and should be interpreted with caution. For mass-refraction settings, a single-drop regimen followed by manual refraction after 30–40 minutes may be a practical alternative to the standard two-drop regimen. When automated refraction is used, the sphere obtained after two drops may provide an estimate of cycloplegic refraction.

Keywords: tropicamide, single drop, autorefraction, manual refraction, Philippines

INTRODUCTION

The high frequency and impact of uncorrected pediatric refractive error impose a tremendous health burden in many countries across the world. In the Philippines, pre-pandemic estimates showed that one out of four students has uncorrected refractive error.[1] To reduce the high incidence of the disease, governments worldwide introduced large-scale population screening programs for the pediatric population. The Philippine Republic Act No. 11358, otherwise known as "The National Vision Screening Act," was signed into law to protect and promote every Filipino child's full potential through good vision and prevention of blindness. This government policy aims to screen pre-school children using a Vision Screening Kit consisting of charts with symbols or numbers and occluders. Its goal is early identification of those with eye problems, such as refractive error.

Subnormal visual acuity in children is commonly due to amblyopia developing from neglected or undetected refractive errors. In children, the gold standard for obtaining accurate refraction entails the use of full cycloplegic refraction (FCR) to uncover all the manifest and latent refractions.[1-6] This requires the instillation of mydriatic-cycloplegic drops prior to refraction. The most important function of these drugs is cycloplegia, or the relaxation of the sphincter muscles used for accommodation.[7-9] Children are known to be strong accommodators, influencing the results of refraction without the benefit of cycloplegia. Known cycloplegic agents are atropine, homatropine, cyclopentolate, and tropicamide, with atropine being the strongest, and tropicamide, the weakest.[10] In mass refraction screening for children, a shorter-acting and less potent agent would be ideal, permitting sufficient cycloplegia for refraction purposes but allowing faster recovery from its mydriatic and cycloplegic effects. Neither the 1% tropicamide nor the 2% cyclopentolate is a registered drug in the Philippines' Food and Drug Administration (FDA) for refractive use during the conduct of the study. 1% Cyclopentolate hydrochloride, although registered since 2021, was not commercially available at the time of this study.[11] Homatropine hydrobromide 2% only received its FDA registration in June 2024 and remains commercially unavailable.[12] During the data collection period, only atropine sulfate (1%) and tropicamide (0.5%) were commercially available, both of which are in the 2022 Philippine National Drug Formulary.[13]

Although considered the least potent, tropicamide, a synthetic analog of tropic acid, is commonly used as a safe agent for cycloplegic refraction.[14] It is a short-acting drug with rare adverse events compared to atropine and cyclopentolate.[4,5] The most severe adverse reaction reported was headache.[14]

For many cases and for purposes of mass-screening, 0.5% tropicamide is a viable alternative to other cycloplegic agents. The American Academy of Ophthalmology's (AAO) recommended dosage for 1% tropicamide is instillation of two drops done 5 minutes apart, with refraction performed 30 minutes post-instillation.[11] The onset of cycloplegia from tropicamide is 25-30 minutes after administration.[14] This approximates the cycloplegic effects of cyclopentolate drops.[14] Locally, this regimen has been used for 0.5% tropicamide, sometimes combined with phenylephrine.[2-6]

Most young children are apprehensive about eyedrops.[10] Occasionally, uncooperative children may need to be sedated for purposes of refraction (usually performed with a comprehensive eye examination). Hence, if a single drop of a cycloplegic agent, albeit short-acting, proves sufficient for refraction purposes, multiple-drop instillations commonly resorted to in the clinics may not be necessary.

Realizing the need for cycloplegia in obtaining pediatric refractions, the concerns with locally available cycloplegic agents, and aligning with the aims of the National Vision Screening Act for large-scale population screening of children for amblyogenic potential, this study aimed to determine the efficacy and reliability of using single- versus the standard two-drop 0.5% tropicamide for cycloplegic refraction in 5-7 year old children. At the time of this writing, the Implementing Rules and Regulations of Republic Act 11358 have not been published in the country's Official Gazette.

This research may help improve the national guidelines for pediatric vision screening, particularly in identifying the appropriate dosage of 0.5% tropicamide as a cycloplegic agent, and the optimal timing for refraction after its instillation. It also shows an alternative to cyclopentolate and tropicamide-phenylephrine eye drops for refracting children, with fewer side effects. The results of this study will aid in the implementation of mass vision screening to prevent childhood visual impairment under the National Vision Screening Act.

This study aligns with the United Nations' third sustainable development goal of "good health and well-being". It fulfills the first two action points in the Department of Health's (DOH) agenda - (1) *Bawat Pilipino Ramdam ang Kalusugan*, [Every Filipino Experiences Health] and (2) *Ligtas, de Kalidad at Mapagkalingang Serbisyo* [Safe, Quality and Caring Service].

The results of this study will likewise guide general practitioners, comprehensive ophthalmologists, and pediatric ophthalmologists in performing pediatric vision screening. Additionally, considering the reluctance of children towards receiving eyedrops, this study explores the potential of a single-drop approach to be as effective as the two-drop approach for manual refraction. This may significantly benefit anxious and apprehensive children needing cycloplegic refraction.

OBJECTIVES

The general objective of this study was to evaluate the efficacy and reliability of using a single drop of 0.5% tropicamide versus the standard two-drop approach in obtaining cycloplegic refraction through automated refraction (AR) and manual retinoscopy (MR) by experts, among children in select institutions and schools in the National Capital Region, Philippines.

Specific objectives were to (1) assess cycloplegic autorefraction obtained with a single drop of 0.5% tropicamide at 5, 15, and 30 minutes, and compare these with manual cycloplegic retinoscopy performed 30-40 minutes after a single- and two-drop regimen (reference standard) of 0.5% tropicamide; (2) compare the measurements of manual refraction with 1 drop after 30-40 minutes, and manual refraction with 2 drops after 30-40 minutes; (3) investigate the effect of the 2-drop regimen (given 1 drop every 5 min) of 0.5% tropicamide on autorefraction at 5, 15, and 30 minutes, compared with the reference standard; and (4) determine the optimal frequency and waiting time for cycloplegia using 0.5% tropicamide in the specified age group by comparing the various autorefraction measurements against the reference standard.

MATERIALS AND METHODS

Study Design

This is a multicenter, randomized, controlled, single-blind, single-sequence crossover study to evaluate the efficacy and reliability of 0.5% tropicamide administered as a single drop compared with the conventional two-drop regimen for cycloplegic refraction among children aged 5–7 years. It was conducted in selected educational institutions in Parañaque City and in the Pediatric Ophthalmology and Strabismus Clinic of a tertiary referral hospital.

A crossover design was selected to allow each participant to serve as his or her own control, thereby minimizing the influence of interindividual differences in refractive status, accommodative response, age, and other potential confounding factors. Each participant underwent autorefraction following the assigned tropicamide administration protocol, with the single-drop and two-drop regimens evaluated under standardized examination conditions. The use of a single sequence ensured that all participants underwent the study procedures in a uniform order. The investigators responsible for performing and/or interpreting the autorefraction measurements were blinded to the treatment regimen whenever feasible to minimize observer-related bias.

Study Population

The study population was drawn from two principal sources: school-aged children recruited from selected schools in Parañaque City and children presenting to the Pediatric Ophthalmology and Strabismus Clinic of a tertiary hospital. The inclusion of participants from both community-based and clinical settings was intended to provide a broader representation of children within the target age group and to improve the generalizability of the findings.

Sampling

For the community-based recruitment, a sampling frame consisting of eligible public and private schools in Parañaque City was established. From this sampling frame, one public school and one private school were selected using simple random sampling. The kindergarten classes within each selected school served as the sampling units. From the eligible kindergarten pupils, individual participants aged 5–7 years were selected through simple random sampling. The list of eligible pupils was obtained from the respective school administrators, subject to institutional approval and the parents' or legal guardians' consent.

For the hospital-based recruitment, children aged 5–7 years who presented to the Pediatric Ophthalmology and Strabismus Clinic during the study period were screened for eligibility according to the predefined inclusion and exclusion criteria. Participants were then selected using simple random sampling from the pool of eligible patients, rather than by convenience or consecutive sampling. This approach was intended to reduce selection bias and ensure that each eligible child had an equal probability of being included in the study. The multicenter approach, random selection of schools and eligible participants, standardized cycloplegic protocol, and crossover methodology were incorporated to strengthen the internal validity of the study and minimize potential sources of selection, measurement, and observer bias. By comparing the two dosing approaches within the same participants, the study aimed to determine whether a single drop of 0.5% tropicamide could provide sufficiently reliable cycloplegic autorefraction measurements while potentially reducing the amount of medication administered and simplifying the examination procedure in children.

A minimum sample size of 210 eyes was computed using R version 4.0.3, to achieve 80% power at 5% significance level in a repeated measures ANOVA with post-hoc Dunnet test for seven groups of interest: 1 drop AR at 5 mins, 1 drop AR at 15 mins, 1 drop AR at 30 mins, 1 drop MR at 30 - 40 mins, 2 drops AR at 5 mins, 2 drops AR at 15 mins, 2 drops AR at 30 mins against the reference standard (2 drops MR at 30 - 40 mins). This is to identify at least one intervention group of interest with significantly different spherical equivalent,

sphere, cylinder, or axis, from the reference group with medium effect size (Cohen's f = 0.20).

Inclusion criteria were cooperative children 5-7 years old from the 3 institutions, whose legal guardians provided informed consent. Excluded were children: (1) with other preexisting organic ocular pathology such as retinal pathology, strabismus, glaucoma, corneal pathology, media opacity, aphakia, pseudophakia, coloboma and optic nerve pathology, (2) with history of eye surgery in either eye, (3) without informed consent from guardians, (4) without an available guardian during the conduct of the study, (5) with known allergic reactions or documented hypersensitivity to tropicamide. Students whose guardians withdraw consent at any point during the study were likewise not included.

Pharmacologic Intervention

The only pharmacologic intervention is the instillation of 0.5% tropicamide, one or two drops. Study variables included demographics such as age, gender, and laterality. Study outcomes were spherical equivalents (SE) of the refraction, and the individual parts of refraction, namely, sphere, cylinder, and axis of astigmatism.

Ethical Considerations

Upon approval of the local Institutional Research Ethics Board, an orientation was conducted with involved primary school teachers and their principals about the study protocol, methodologies, benefits and risks, significance, and the process of data usage and disposal. For children from the Pediatric Ophthalmology Clinic, the guardians were briefed during the consultation. During data collection in the schools, the informed consent form (written in both English and Filipino) was signed by the guardian after complete understanding of the document. Participation was completely voluntary. Additionally, an assent form was signed by the participant if they were aged 7 years old.

Process Flow

The minimum requirement for inclusion was the presence of the child and a guardian, provided the latter was more than 18 years of age. During the entire process (Figure 1), the child was accompanied by a guardian. All children were screened for eligibility using the inclusion and exclusion criteria. The participants were identified only by a number and underwent baseline autorefraction (AR 0 min) using a pre-calibrated Huvitz HRK-7000 (South Korea, 2014). Thereafter, tropicamide 0.5% 1 drop was instilled in each eye. After instillation, compression of the lacrimal sac was done to diminish the risk of systemic side effects. One pediatric ophthalmologist was assigned to instill the drops.

Automated refraction was then obtained 5-, 15-, and 30-minutes after the first drop of tropicamide. Manual refraction was performed by any of three masked pediatric ophthalmologists after the 30 min automated refraction was obtained. All refractionists were board-certified pediatric ophthalmologists who trained in comprehensive ophthalmology from the same institution, but subspecialty trained in pediatric ophthalmology in various institutions.

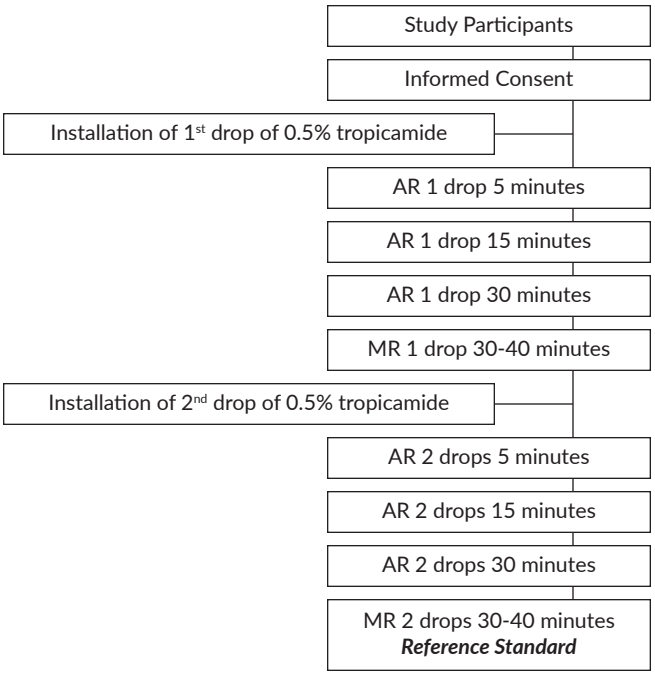

Figure 1. Process flow of the data collection.

AR – autorefraction, MR – manual refraction

A second drop of tropicamide was instilled 40 min after the initial instillation with lacrimal sac compression. Automated refraction was again obtained at 5-, 15-, and 30-minutes after the 2nd drop of tropicamide. Finally, one of three pediatric ophthalmologists performed a refraction that served as the reference standard for all obtained refractions. The reference standard for obtaining the short-acting cycloplegic refraction was slightly different from the recommended protocol for tropicamide 1% by the AAO, as the 2 drops were given 30-40 minutes apart, with final refraction obtained 30-40 minutes after the 2nd drop.[11] The AAO regimen for refraction was to give 2 drops of tropicamide 5 minutes apart, with refraction obtained 30 minutes after the 2nd drop.[11]

Manual refraction was performed via retinoscopy in a semi-dim room. In the schools, this was done in a classroom with the lights off, and for the tertiary care facility, a standard refracting lane with lights off or dimmed was used. Manual retinoscopy objectively measures refractive errors. This is performed by observing the movement of reflected light in the child's pupil through an optical instrument called a retinoscope. Children were instructed to fixate at a non-accommodative target – the 20/200 line or the largest letter optotype in the visual acuity chart. In the classroom, a surrogate distant, non-accommodative target was chosen by the refractionist. After neutralization of the reflex using the retinoscope, refraction was recorded for the eye. Manual refraction performed by the pediatric ophthalmologists

30-40 min after the 2nd instillation of 0.5% tropicamide was set as the reference standard, based on the AAO's recommendation.[31] At the end of data collection, all children were observed for an additional 15 minutes for adverse effects. All refraction results were encoded in an Excel worksheet.

Data Collection

The pediatric ophthalmologists performing the cycloplegic refraction were masked to the treatment regimen during the assessment. A data collection form was used, where, for each station, the results were cut from the original piece of paper. This was done to ensure blinding and to avoid bias from the examiners. To minimize the potential for observer bias, the examiner was not provided with information regarding the study hypothesis or the expected direction of the difference between the two regimens. The AR measurements were obtained using a standardized examination protocol, and the examiner followed the same procedures and timing for both assessments. The examiner was also instructed to record the refraction measurements independently and without reference to the participant's previous measurements. Where feasible, the refraction measurements were performed by different pediatric ophthalmologists who were not informed of the participant's previous measurement or treatment allocation. The identity of the examiner was recorded for each measurement, allowing assessment of potential examiner-related variability.

Data Analysis

Demographic characteristics of the participants were summarized using descriptive statistics. Numerical variables were described using median and interquartile range (IQR), depending on the normality of the distribution. The IQR was used in this study to describe the variability of the continuous refraction measurements. The IQR, calculated as the difference between the 75th percentile (Q3) and the 25th percentile (Q1), represents the middle 50% of the observed values. It was selected as an appropriate measure of dispersion because the refraction data were summarized using the median and were not assumed to follow a normal distribution. Compared with the range, which is strongly influenced by extreme minimum and maximum values, the IQR provides a more robust representation of the distribution of the data. Similarly, the IQR is preferable to the standard deviation (SD) for skewed or non-normally distributed data, as it is less affected by outliers. Thus, reporting the median with IQR provides a more appropriate summary of the central tendency and variability of the refraction measurements in this study. On the other hand, categorical variables were described as frequencies and percentages.

There were seven intervention groups of interest (1 drop AR at 5 minutes, 1 drop AR at 15 minutes, 1 drop AR at 30 minutes, 1 drop MR at 30-40 minutes, 2 drops AR at 5 minutes, 2 drops AR at 15 minutes, and 2 drops AR at 30 minutes) which were compared to the reference standard (2 drops MR at 30-40 minutes). Significant differences in median/mean-rank spherical equivalent, sphere, cylinder, and axis of each intervention group of interest with the reference standard were determined by the Kruskal-Wallis H test with post-hoc Dunn test. Data analysis was performed using Stata version 17. Normality of distribution of numerical variables was assessed by the Shapiro-Wilk test of normality. The tests of hypotheses were evaluated at a significance level set at $\alpha = 0.05$.

RESULTS

Data were collected from 219 eyes of 111 children aged 5-7 years pooled from the study sites. Seven children were excluded from the study for various reasons, including age, absence of a guardian during data collection, and presence of an ocular co-morbidity. The majority were males (59%, n = 66). The most common refractive error was hyperopia (76%, n = 166), followed by astigmatism (62.56%, n = 137) and myopia (16%, n = 34). With-the-rule astigmatism was the most predominant astigmatism (61.54%, n = 135). Those who had refractive errors with risk for amblyopia were identified. The majority of the refractive errors that were amblyogenic for age were from astigmatism (85.45%, n = 47). The reference table used to identify amblyogenic refraction was based on the AAO's published treatment guidelines for refractive correction in infants and young children.[31] The rest of the details are summarized in Table 1.

Table 1. Characteristics of Study Participants (n = 219 eyes, 111 children)

Characteristics	Mean (SD); Frequency (%)
Number of participants	111
Age, years	5.61 (5-7 years)
Sex	
Male	66 (59.46%)
Female	45 (40.54%)
Number of eyes	219
Laterality	
Left	109 (49.77%)
Right	110 (50.23%)
Location	
Public School	90 (41.06%)
Private School	70 (31.96%)
Local Institution	59 (26.94%)
Error of refraction	200 (91.32%)
Hyperopia	166 (76%)
Myopia	34 (16%)
Astigmatism	137 (62.56%)
With-the-rule	135 (61.54%)
Against-the-rule	2 (0.91%)
Oblique	0 (0%)
Amblyogenic for age	55 (28%)
Hyperopia	6 (10.90%)
Myopia	17 (30.91%)
Astigmatism	47 (85.45%)

Table 2. Automated Refraction (AR) and Manual Refraction (MR) Results following 1-drop and 2-drops of 0.5% Tropicamide

Refraction Parameters	Noncyclo-plegic AR	1 drop				2 drops			
		AR at 5 mins	AR at 15 mins	AR at 30 mins	MR at 30-40 mins	AR at 5 mins	AR at 15 mins	AR at 30 mins	MR at 30-40 mins (Reference Standard)
	Median (IQR)								
Sphere	0.5 (1)	0.75 (1.5)	0.75 (1.25)	0.75 (1.5)	1 (1)	1 (1.5)	1 (1.5)	1 (1.5)	1 (1.5)
Cylinder	-1 (1.5)	-1 (1.5)	-1 (1.25)	-1 (1.25)	-0.5 (1.5)	-0.75 (1.75)	-1 (1.5)	-1 (1.5)	-0.5 (1)
Axis	162 (167)	167 (169)	162 (168)	154 (165)	180 (180)	36 (167)	161 (170)	164 (172)	180 (180)
SE	-0.25 (0.875	0.25 (1.25)	0.25 (1.5)	0.375 (1.5)	0.75 (1.75)	0.5 (1.25)	0.375 (1.5)	0.375 (1.375)	0.75 (1.5)
	Post-hoc Dunn test *p*-value								
Sphere	<0.0001*	0.0039*	0.0492*	0.0273*	0.4793	0.0412*	0.0159*	0.2089	Reference
Cylinder	<0.0001*	<0.0001*	<0.0001*	<0.0001*	0.4697	<0.0001*	<0.0001*	<0.0001*	Reference
Axis	<0.0001*	0.0067*	0.0003*	<0.0001*	0.1367	<0.0001*	0.0003*	<0.0001*	Reference
SE	<0.0001*	<0.0001*	0.0001*	<0.0001*	0.3273	0.0050*	0.0011*	0.0028*	Reference

*Note: * Significant (p-value <0.05) Kruskal-Wallis H test for sphere, cylinder, axis, and SE.*

IQR – interquartile range

Table 2 summarizes the automated refraction (AR) and manual refraction (MR) results following one- and two-drop administration of 0.5% tropicamide. Refraction parameters included sphere, cylinder, axis, and spherical equivalent (SE), with results presented as median (IQR). Following the one-drop regimen, AR measurements obtained at 5, 15, and 30 minutes differed significantly from the reference standard across all refraction parameters. Significant differences were observed in sphere, cylinder, axis, and SE at all time points, with the largest and most consistent differences observed for cylinder and SE (all P <0.001 at the corresponding time points). In contrast, manual refraction performed at 30–40 minutes following one drop did not differ significantly from the reference standard for sphere (P = 0.4793), cylinder (P = 0.4697), axis (P = 0.1367), and SE (P = 0.3273).

Following the two-drop regimen, AR measurements remained significantly different from the reference standard for cylinder, axis, and SE at all time points (P ≤0.05). However, for sphere, significant differences were observed at 5 minutes (P = 0.0412) and 15 minutes (P = 0.0159), but the 30-minute measurement did not differ significantly from the reference standard (P = 0.2089).

Comparison of manual refraction following one versus two drops of 0.5% tropicamide showed no statistically significant differences in sphere, cylinder, axis, or SE, indicating that increasing the dose from one to two drops did not materially alter the manual refraction results. These findings suggest that, although statistically significant differences were observed in several automated refraction measurements compared with the reference standard, the final manual refraction measurements obtained at 30–40 minutes after one drop were comparable with the two-drop reference standard (Table 2).

Table 3 compares automated refraction obtained at 5, 15, and 30 minutes with manual refraction performed at 30–40 minutes following a single drop of 0.5% tropicamide. Statistically significant differences were observed across the four refraction parameters at all time points (all with P <0.05).

Despite these statistically significant differences, the magnitude of the observed differences should be considered in terms of clinical relevance. The reported differences were approximately 0.25 D for sphere, 0.52 D for cylinder, 0.38 D for spherical equivalent, and 23 degrees for axis. These differences indicate measurable variation between automated and manual refraction; however, statistical significance alone does not establish that the differences are clinically meaningful. In particular, the relationship between a change in refractive power and visual acuity is not linear and may vary according to the magnitude and type of refractive error, age, accommodation, and the presence of other visual factors. Therefore, the observed dioptric differences should be interpreted in conjunction with their potential effect on visual acuity and clinical decision-making rather than on statistical significance alone.

As to the optimal frequency of instillation and time to achieve cycloplegia, using a single drop of 0.5% tropicamide and waiting 30-40 minutes (p-values: sphere = 0.4793, cylinder = 0.4697, axis = 0.1367, and spherical equivalent = 0.3273) and two drops using automated refraction (sphere only, p-value = 0.2089) at 30 minutes showed comparable results with the reference standard.

DISCUSSION

Because children cannot verbalize problems with vision and are strong accommodators, cycloplegic refraction needs to be performed to uncover the true refractive errors.

Table 3. Comparison of Automated Refraction (AR) and Manual Refraction (MR) after Using Single Drop of 0.5% Tropicamide Compared against MR Using 1 Drop of 0.5% Tropicamide

Refraction Parameters	1 drop			
	AR at 5 mins	AR at 15 mins	AR at 30 mins	MR at 30-40 mins
	Median (IQR)			
Sphere	0.75 (1.5)	0.75 (1.25)	0.75 (1.5)	1 (1)
Cylinder	-1 (1.5)	-1 (1.25)	-1 (1.25)	-0.5 (1.5)
Axis	167 (169)	162 (168)	154 (165)	180 (180)
SE	0.25 (1.25)	0.25 (1.5)	0.375 (1.5)	0.75 (1.75)
	Post-hoc Dunn test *p*-value			
Sphere	0.0039*	0.0312*	0.0293*	Reference
Cylinder	<0.0001*	<0.0001*	<0.0001*	Reference
Axis	0.0051*	0.0040*	0.0008*	Reference
SE	<0.0001*	<0.0003*	0.0001*	Reference

*Note: * Significant (p-value <0.05) Kruskal-Wallis H test for sphere, cylinder, axis, and spherical equivalent (SE).*

IQR – interquartile range

Cycloplegia, which relaxes accommodation, is essential because accommodation interferes with accurate retinoscopy.[2]

Baseline local demographics can be obtained from various studies of pediatric refractive errors. A 2015 study in Nepal showed that of 219 children aged 3 to 16, 70 (31.96%) were ametropic, of which 21.92% had hyperopia and 10.05% myopia.[2] A Mexican study of 12- to 13-year-olds showed 6% of 1035 children had hyperopia.[3] The overall prevalence of hyperopia in Malaysia was higher for children aged 6-10 years of age (15.7%) than those more than 12 years of age (6.8%). Myopia prevalence was only at 5%, while hyperopia was at 7.7%.[4] Surprisingly, a Nepal study in 2008of children aged 5-9 years living in urban cities showed 93.3% ametropia in children with uncorrected visual impairment.[5] In our study, the overall prevalence of refractive error was 92% (n = 100), the majority of which were hyperopic (76%, n = 83), while 34% (n = 17) were myopic. Around 27 (28%) were considered to have amblyogenic refractive errors.

Properly performed manual cycloplegic retinoscopy provides an acceptable method of identifying refractive errors among children. This remains the gold standard for detecting refractive errors in this population.[2,3] Ideally, a skilled and well-trained ophthalmologist or optometrist performs the test to obtain the most accurate results. While the cycloplegic agents themselves present variability in cycloplegic effects, using a long-acting agent such as atropine, an intermediate-acting agent such as cyclopentolate, and a short-acting agent such as tropicamide are the commonly available options.[8] Cycloplegia is attained by topical instillation using one to three drops. In the Philippines, the commercially available drops are tropicamide (0.5%) and atropine (1%). Other cycloplegic agents such as homatropine and cyclopentolate received FDA approval recently.[12,15] Although the gold standard atropine provides the greatest amount of cycloplegia, its potential systemic adverse effects caution against widespread use in children.[16] Other challenges with atropine are the delay in cycloplegia onset and prolonged recovery for restoration of normal accommodative function, posing difficulty for children in school.[16] Hence, ophthalmologists prefer using cyclopentolate and tropicamide as alternative drugs. Of these, tropicamide is less potent and less effective in achieving cycloplegia, and is considered by some as an inferior drug for cycloplegic refraction, especially for pediatric patients with strabismus.[14-17] These earlier reports were refuted by later studies where tropicamide replicated accommodation paralysis observed with cyclopentolate.[18] The Correction of Myopia Evaluation Trial (COMET) provided additional evidence supporting the efficacy of tropicamide by evaluating 469 children aged 6-11 years, who underwent cycloplegic assessment with 2 drops of 1% tropicamide. The study found minimal residual accommodation following cycloplegia and concluded that 1% tropicamide was an effective option as a cycloplegic agent in myopic children.[19] Furthermore, a 2015 study in Iran consisting of 50 eyes of 25 adult patients aged 28-67 years showed that 0.5% tropicamide provided comparable results with 1% in achieving pupillary dilation and cycloplegia, and thus was recommended for use to reduce and prevent possible adverse effects.[20-24]

Several studies investigated the optimal number and frequency of drops for cycloplegic agents, with the main goal of administering the least amount and frequency of medication that will achieve the cycloplegic effect closest to the gold standard, while causing minimal discomfort and side effects. Manny et al in 2001 demonstrated the effectiveness of 1 drop of 1% cyclopentolate versus 2 drops, finding no significant difference in achieving cycloplegia.[25] The addition of a second drop did not result in significantly higher cycloplegia, but increased the risk of systemic side effects such as tachycardia and flushing.[24,25] In our study, no side effects were reported. Several studies have identified the effectiveness of 0.5%

tropicamide alone in comparison to 1% cyclopentolate. The studies concluded that while 2 drops of 0.5% tropicamide were less potent than cyclopentolate, it was useful for quick assessments where full cycloplegia was not required.[26-30] In comparison to published results, our study showed that while 1 drop of 0.5% tropicamide was not effective to achieve cycloplegia for purposes of autorefraction after 30-40 min, manual refraction by trained pediatric ophthalmologists after 30-40 min was consistent with the reference standard. Refraction was carried out with distance fixation at a non-accommodative target, relaxing accommodation. While all the components of refraction were statistically different, it seemed that the sphere component with 2 drops of 0.5% tropicamide using autorefraction after 30-40 minutes was similar to its manual refraction counterpart.[29-34]

It is widely perceived that a single drop may have questionable utility in uncooperative children, especially since washout effects of crying and the limited surface area of the fornices need to be contended with.[19] Most ophthalmologists resort to repeated instillation of drops to ensure drug absorption. In difficult scenarios and uncooperative patients, however, where only one drop can be instilled, it may be more prudent to wait longer for cycloplegia to set in, rather than instill a second drop.

This study was undertaken in line with the goals of the Philippine government in establishing a National Vision Screening Act for kindergarten pupils to decrease the incidence of blindness in children. The ideal cycloplegic agent for mass refraction screening is the shortest-acting cycloplegic agent achieving similar levels of cycloplegia compared to the gold standard agents, but with the least adverse side effects. This study was inspired by The Baltimore Vision Screening Project, which was done among pre-kindergarten and kindergarten pupils.[23] The goal was to assess the level of visual morbidity in this population. In two hundred eighty-five children aged 3-5 years old, 5.3% of pupils had amblyopia, 3.2% had strabismus, and 7.4% had refractive errors. Compliance with recommended treatment was poor in about 30%, with only 20% of the students passing the vision screening the following year.[15,16,21] The results of the screening project showed the necessity for regular and timely screening across the globe.

Our study showed that even with 1 drop of 0.5% tropicamide, refraction performed by trained specialists can achieve cycloplegia comparable to the reference standard. The investigators aimed to supplement information for the national guidelines in vision screening, particularly the identification of the appropriate dosage of cycloplegic agent and the timing of refraction. This study also hopes to guide general practitioners, comprehensive ophthalmologists, and pediatric ophthalmologists in performing vision and refraction screening among Filipino children.[35]

CONCLUSION

Autorefraction following a single drop of 0.5% tropicamide demonstrated significant differences from the reference standard and should therefore not be relied upon as the sole method for accurate cycloplegic refraction in children. In contrast, manual refraction performed 30–40 minutes after either a single- or two-drop instillation of 0.5% tropicamide produced results comparable to the reference standard. Thus, for mass-refraction settings, a single drop of 0.5% tropicamide followed by skilled manual refraction after a 30–40-minute waiting period may provide a practical alternative to the standard two-drop regimen. When autorefraction is used, the two-drop regimen should be interpreted with caution. Although the spherical component at 30 minutes was not significantly different from the reference standard, the cylinder, axis, and spherical equivalent remained significantly different.

Data Availability Statement

The study used primary data collected directly from the institutions. A password-protected spreadsheet holds all the data. This sheet is readily available only upon request.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

Funding Source

None.

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