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Impact of Proxymetacaine on the Dynamics of Cyclopentolate in White 6- to 7-Year-Olds

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ORIGINAL ARTICLE

Impact of proxymetacaine on the dynamics of cyclopentolate in White 6- to 7-year-olds

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Abstract

Purpose: This study compared the efficacy of cyclopentolate hydrochloride at 10-, 20- and 30-min post-instillation in White 6- to 7-year-olds, with and without prior instillation of proxymetacaine hydrochloride. The primary aim was to determine if accurate autorefraction values can be obtained sooner than the current standard of 30-min post-cycloplegia. The secondary aim was to investigate whether proxymetacaine hydrochloride enhances the efficiency of cyclopentolate.

Methods: Participants were 112 White 6- to 7-year-olds from the Child Eye Health Study. The right eye received 0.5% proxymetacaine hydrochloride and 1.0% cyclopentolate hydrochloride, and the left eye received only 1.0% cyclopentolate hydrochloride. Non-cycloplegic and cycloplegic refractive error (at 0, 10, 20 and 30 min) was measured using a binocular, open-field autorefractometer. Data were analysed through paired *t*-tests, concordance analysis, linear regression, equivalence testing and Bland–Altman analysis, using the 95% limits of agreement.

Results: Mean spherical equivalent refraction (SER) (SD) in the right eye at 0-, 10-, 20- and 30-min post-instillation was 0.62 (1.45) D, 1.52 (1.80) D, 1.64 (1.81) D and 1.72 (1.80) D, respectively. Mean left eye SER (SD) were 0.68 (1.24) D, 1.42 (1.66) D, 1.56 (1.66) D and 1.68 (1.72) D, respectively. Bland–Altman analysis showed a high level of agreement, and equivalence testing confirmed that there was no clinically significant difference in SER at 20 and 30 min in both eyes (within ±0.50 D), with mean differences of 0.08 (0.23) D in the right eye and 0.13 (0.30) D in the left eye ($p = 0.21$). However, SER at 10 and 30 min were equivalent in the right eye only.

Conclusions: Accurate autorefraction values can be obtained 20-min post-instillation of 1.0% cyclopentolate in white children aged 6–7 years, potentially reducing clinical testing times. Proxymetacaine pre-instillation allows for reliable measurements as early as 10-min post-instillation of cyclopentolate. Further research is needed to validate these findings in non-White populations and to determine the safe discharge time post-proxymetacaine instillation.

KEYWORDS
cyclopentolate, cycloplegia, proparacaine, proxymetacaine, spherical equivalent refraction

INTRODUCTION

Cycloplegic refraction is the gold standard procedure for obtaining accurate refractive values in children.[1-5] Proxymetacaine/proparacaine hydrochloride (henceforth proxymetacaine) is a topical anaesthetic which improves patient comfort upon instillation of cyclopentolate hydrochloride (henceforth cyclopentolate) and promotes the corneal absorption of cyclopentolate, theoretically improving efficacy.[6-8]

Accommodation is the ability to temporarily increase the eye's power to allow for near focus, and to compensate for hyperopia if present. Accommodative amplitude (AA) is higher in younger than in older children and adults using subjective and objective measurement techniques. For example, 6- to 10-year-old children have a median subjectively measured AA of 15.5 D compared to 12.9 D in 16-year-olds,[9] and an objectively measured AA of 8–9 D compared to 7 D in older children.[10] Doyle et al.[11] reported no clinical or statistical difference in autorefraction between measurements obtained 20- and 30-min post-instillation of 0.5% proxymetacaine and 1.0% cyclopentolate in White 12- to 13-year-olds. This study evaluates whether these findings are consistent in younger children. The secondary aim was to assess the effect of proxymetacaine on cyclopentolate efficiency.

Key points

- Accurate autorefraction can be performed 20-min post-instillation of cyclopentolate alone, regardless of proxymetacaine pre-instillation, with no clinically significant difference between spherical equivalent refraction values at 20 and 30 min after instillation.
- Proxymetacaine pre-instillation enhanced cyclopentolate efficiency and further reduced the time to accurate autorefraction to 10 min, producing equivalent spherical equivalent refraction measures at 10 and 30 min.
- Clinical testing times may be reduced by reducing the wait time between eye drop instillation and refraction in White children.

METHODS

Ethical considerations

This study was approved by the Technological University Dublin Research Ethical Committee as part of the Child Eye Health Study (CEHS). The CEHS is an ongoing 1-year longitudinal prospective study which aims to investigate the relationship between refractive error development, ocular and anthropometric growth and lifestyle factors. All research activities adhered to the tenets of the Declaration of Helsinki. Parental consent and child assent were obtained before inclusion. Inclusion criteria were: (1) children aged 6–7 years at the baseline visit, (2) White ethnicity and (3) availability of cycloplegic autorefraction measures. Participants were excluded if they had: (1) a sensitivity to cyclopentolate or (2) were using pharmacological eye drops, including for atropine penalisation or myopia control. Eligibility was confirmed at the CEHS baseline visit by the first author (MD). This was a convenience sample of children who volunteered to participate in the CEHS.

Data collection

Presented data were collected from December 2022 to June 2024 from 112 White 6- to 7-year-old children attending the CEHS (mean age (SD) 7.02 (0.59) years, $n = 60$, (53.6%) male). The sample size was calculated for a repeated measures design with three measurements, aiming to detect an effect size of 0.25 with an alpha level of 0.01 and a power of 0.99, resulting in a required sample size of 76 participants. Participants were tested at the Centre for Eye Research Ireland on the Technological University Dublin campus. An unblinded within-subjects design was employed to assess the impact of 0.5% proxymetacaine on cycloplegic efficiency. Each participant received one drop of proxymetacaine (Minims, 0.5% w/v, Bausch & Lomb, bausch.co.uk/) followed 2 min later by 1.0% cyclopentolate (Minims, 1.0% w/v, Bausch & Lomb, bausch.co.uk/) in the right eye, while the left eye served as a control, receiving one drop of cyclopentolate only. This design allowed for direct comparison of the two eye drop regimens within the same individual, controlling for inter-individual variability. Participants were advised to close their eyes gently without blinking following the instillation of each eye drop, and gentle digital pressure was applied to the participants' inner canthi to minimise systemic absorption.[12] Instilling eye drops can speed up tear drainage due to the increased fluid volume, with half of the drops draining within 30 s.[13] After 2 min (or four half-lives), only about 6% of the drop remains in the eye, minimising any dilution effect on the subsequent cyclopentolate instillation.[13] Brown/hazel irides received two drops of cyclopentolate instilled 5 min apart,[14] while blue/green/grey irides received one drop.[15] All participants received only one drop of proxymetacaine in their right eye regardless of eye colour. All children were checked at 20-min post-instillation to establish cycloplegia had been achieved (pupillary reactions non-responsive to light and accommodation amplitude <2.00 D on the push-up test).

Refractive error was measured by binocular, open-field auto-refractometry (Shin-Nippon Auto Refkeratometer NVision-K 5001, snm.co.jp) at four time points. The first measurement was taken before eye drop instillation (non-cycloplegic measurement), and subsequent cycloplegic measurements were taken at 10-, 20- and 30-min post-instillation of 1.0% cyclopentolate. Three readings were taken per eye at each time point, and the average value was recorded. The same clinician (MD) took all measurements on the same auto refractometer, measuring the right eye first. Only measurements with correct head alignment, stationary eyes and centred

autorefractor were considered valid. Measurements were taken 1–2 s after a blink to avoid interference. Spherical equivalent refraction (SER) (sphere + (cylinder/2)) was analysed for the current study. Refractive error categories were defined as myopia (SER ≤ −0.50 D, $n = 4$), emmetropia (−0.50 D < SER < +2.00 D, $n = 83$) and hyperopia (SER ≥ +2.00 D, $n = 25$) as per the Refractive Error Study in Children (RESC) protocol.[16] Iris colour was classified into three broad categories: blue (75 participants), brown (25 participants) and green (12 participants), per the classifications proposed by Mackey et al.[17] Iris colour is a good representation of overall ocular pigmentation, making it a relevant factor in this study.[18]

Statistical methods

Data were entered into the Research Electronic Data Capture (REDCap, projectredcap.org) (12.2.2) system during collection. Data were exported from REDCap as a CSV file to Microsoft Excel (Microsoft.com) and de-identified before analysis. The anonymised spreadsheet was uploaded to SPSS V.28.0 (ibm.com) for analysis.

The distribution of SER data was non-normal (Kolmogorov–Smirnov test, $p < 0.001$). However, the central limit theorem allowed the use of parametric tests due to the large sample size ($n = 112$), continuous data and mean-centred distribution.[19] This justified using parametric tests such as linear regression, paired *t*-tests, concordance analysis and equivalence/non-inferiority testing (TOST method) to compare the mean cycloplegic SER at different time points in the right and left eyes. Equivalence bounds were set at ±0.50 D.

Confidence intervals were 95%, and significance was set at $p < 0.05$. Linear regression was performed to clarify the relationship between SER measurements at 10- and 30-min post-cycloplegia, and at 20- and 30-min post-cycloplegia. Paired *t*-testing was used to compare mean SER:

1. At each time point, 0 and 10 min, 0 and 20 min, 0 and 30 min, 10 and 30 min and 20 and 30 min after cyclopentolate in both eyes. The degree of cycloplegia and differences between non-cycloplegic and cycloplegic autorefraction were compared.
2. To compare the mean difference in SER between the right and left eyes to assess the impact of 0.5% proxymetacaine on 1.0% cyclopentolate efficiency.
3. To determine whether the difference in SER at 20 and 30 min was statistically significant with and without proxymetacaine pre-instillation.

As the paired *t*-test may fail to detect poor agreement in pairs of data when the means are equal, concordance analysis (clinical concordance coefficient (CCC) and Bland–Altman plots) was also employed.[20]

One-way analysis of variance was used to determine whether iris colour affected the level of cycloplegia following eye drop instillation.

RESULTS

Figure 1 is a flowchart detailing participant selection. Two participants declined eye drops due to a previous negative experience. Table 1 displays the summary statistics for SER measurements, including the mean SER and standard deviation (SD), as well as the maximum and minimum SER recorded before eye drop instillation (0 min hereafter), and at 10-, 20- and 30-min post-instillation (cycloplegic SER). Additionally, the mean differences in SER measurements at 0, 10, 20 and 30 min in the right and left eyes were analysed for significance.

Cycloplegic SER was more hyperopic or less myopic than non-cycloplegic SER at 10, 20 and 30 min (Table 2). The change between pre- and post-cycloplegic SER was greater in participants classified as emmetropic and hyperopic than myopic. For myopes (SER ≤ −0.50 D), the mean (SD) SER change was 0.21 D. However, the mean SER change for emmetropes, categorised by cycloplegic SER as −0.49 D to +0.50 D, +0.51 D to +0.99 D and +1.00 D to +1.99 D, was 0.40 D, 0.58 D and 1.03 D, respectively. For hyperopes (≥+2.00 D), the mean SER change was 1.76 D.

This is illustrated in Figure 2, where the best-fit line (blue dotted line) is closely aligned with the $y = x$ line (orange solid line, indicating perfect agreement). In contrast, the weaker correlation (CCC = 0.97) between the left eye's 10- and 30-min SER measurements is shown in Figure 3, where the best-fit line deviates from the $y = x$ line.

The agreement indices for SER measurements at 0 and 10 min, 10 and 30 min and 20 and 30 min for the right and left eyes are presented in Table 3. The poorest correlation

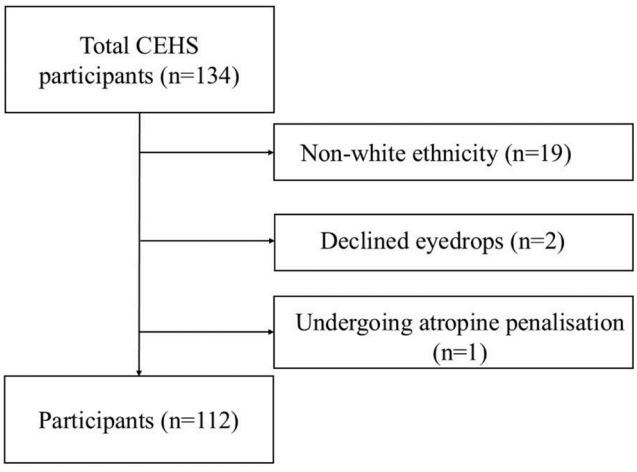

FIGURE 1 Flowchart of participant selection for the current study from the Child Eye Health Study (CEHS).

TABLE 1 Summary statistics of SER measurements without cycloplegia (0 min) and with cycloplegia at 10, 20 and 30 min in the right (proxymetacaine and cyclopentolate) and left (cyclopentolate only) eyes.

	Right eye SER (D)				Left eye SER (D)			
	0 mins[a,*]	10 mins[b,*]	20 mins[c,*]	30 mins[d,*]	0 mins[a,*]	10 mins[b,*]	20 mins[c,*]	30 mins[d,*]
Mean (SD)	0.62 (1.45)	1.52 (1.80)	1.64 (1.81)	1.72 (1.80)	0.68 (1.24)	1.42 (1.66)	1.56 (1.66)	1.68 (1.72)
Max	11.19	11.75	12.69	12.50	9.75	11.38	11.69	11.62
Min	−2.31	−2.25	−2.18	−2.25	−1.81	−1.75	−1.68	−1.69

Abbreviations: D, dioptre; mins, minutes; SD, standard deviation; SER, spherical equivalent refraction.

[a]Comparing mean differences in SER pre-instillation (0 min) and at 10 min.

[b]Comparing mean differences in SER at 10 and 30 min.

[c]Comparing mean differences in SER at 20 and 30 min.

[d]Comparing mean differences at 0 and 30 min.

*$p < 0.001$.

TABLE 2 Paired *t*-test difference in mean SER without cycloplegia (0 min) and with cycloplegia at 10 & 30 min and 20 & 30 min in 112 white 6- to 7-year-old participants.

	Min SER difference (D)	Max SER difference (D)	Mean SER difference (D)	SD	*t*
RE SER at 10 mins – SER at 0 mins	−0.25	4.94	0.84	0.78	11.19*
LE SER at 10 mins – SER at 0 mins	−0.50	4.56	0.68	0.84	8.41*
RE SER at 20 mins – SER at 0 mins	−0.31	4.87	0.95	0.80	12.41*
LE SER at 20 mins – SER at 0 mins	−0.31	4.49	0.82	0.87	9.82*
RE SER at 30 mins – SER at 0 mins	0.06	4.94	1.03	0.78	13.74*
LE SER at 30 mins – SER at 0 mins	−0.25	4.69	0.93	0.87	11.23*
RE SER at 30 mins – SER at 10 mins	−0.50	0.94	0.19	0.27	7.61*
LE SER at 30 mins – SER at 10 mins	−0.56	1.31	0.27	0.30	9.37*
RE SER at 30 mins – SER at 20 mins	−0.55	0.63	0.08	0.23	3.64*
LE SER at 30 mins – SER at 20 mins	−0.75	1.43	0.13	0.30	4.19*

Note: Cycloplegic SER measurements at 20 min were well-correlated overall with those at 30 min in both eyes (RE CCC = 0.99, LE CCC = 0.98). However, SER measurements taken at 10 min showed a stronger correlation with those at 30 min in the right eye (CCC = 0.98) compared to the left eye (CCC = 0.97).

Abbreviations: CCC, clinical concordance coefficient; D, dioptre; LE, left eye; Max, Maximum; Min, minimum; mins, minutes; RE, right eye; SD, standard deviation; SER, spherical equivalent refraction.

*$p < 0.001$.

was found when comparing non-cycloplegic to cycloplegic measures.

The differences in mean SER measurements at 20 and 30 min in the right eye (0.08 (0.23) D) and those in the left eye (0.13 (0.30) D) were not significantly different ($t(111) = -1.27$, $p = 0.21$; Table 3).

Equivalence testing further confirmed that the right eye measurements at 10 and 30 min were equivalent. Upper and lower bounds of +0.50 D and −0.50 D, respectively, were used for this testing. As can be seen in Figure 4a, SER measurements were equivalent in the right eye, as the 90% confidence interval (CI) of −0.26 to 0.48 lies entirely within the ±0.50 D equivalence bounds. SER measurements at 10 and 30 min were not equivalent in the left eye (CI: −0.22, 0.53) (Figure 4c).

Equivalence was confirmed for both the right eye (TOST: 90% CI = −0.33, 0.42) and left eye (TOST: 90% CI = −0.30, 0.44) measurements at 20 and 30 min (Figure 4b,d).

Bland–Altman plots were used to compare the mean differences and 95% confidence intervals for SER measures between time points (see Figure 5). The Bland–Altman plots showed minimal difference between readings at 20 and 30 min in both eyes, as the mean-of-all-differences lines were close to zero (Figure 5b,d). The Bland–Altman plot comparing readings at 10 and 30 min in the left eye (Figure 5c) showed poor agreement. The limits of agreement ranged from −0.32 to 0.86 D.

Myopic participants showed no significant SER changes between 10 and 30 min or 20 and 30 min in either eye. There was no significant difference in SER change at 10 and 30 min between hyperopes and emmetropes in the right eye with proxymetacaine and cyclopentolate (0.17 D vs. 0.21 D, $t(106) = 0.66$, $p = 0.51$). In contrast, in the left eye (cyclopentolate alone), hyperopes had significantly larger differences compared to emmetropes between 10 and 30 min (0.39 D vs. 0.23 D, $t(106) = -2.44$, $p = 0.02$). This significant difference between hyperopic and emmetropic SER change did not persist at 20 and 30 min (0.17 D vs. 0.09 D, $t(106) = -1.14$, $p = 0.26$).

Eye colour did not significantly affect the difference in SER measures in the right (10 and 30 min: $F(2) = 0.90$, $p = 0.41$)

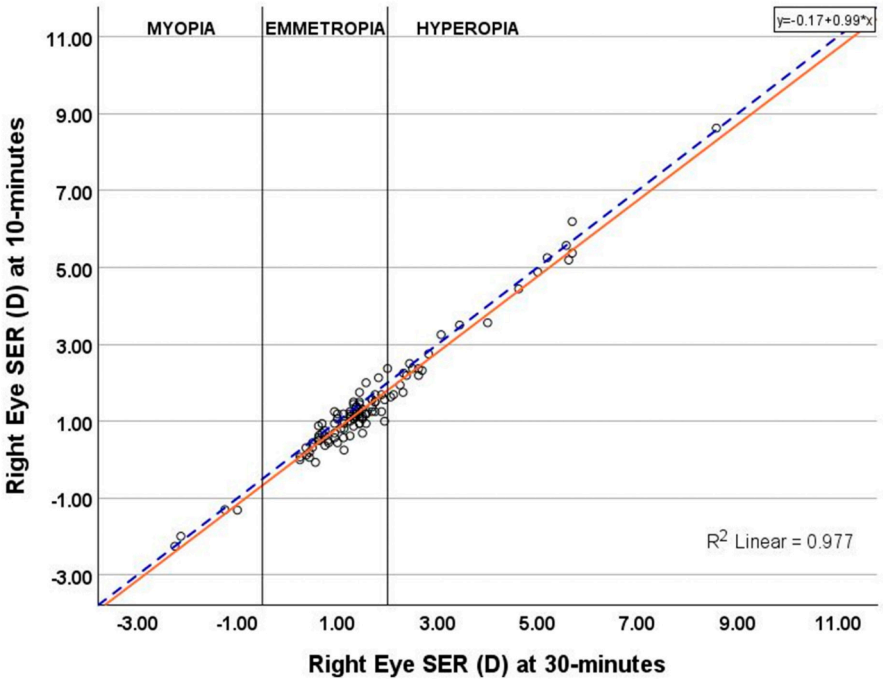

FIGURE 2 Scatter plot showing SER measures at 10- (*y*-axis) and 30-min (*x*-axis) post-instillation of 0.5% proxymetacaine and 1.0% cyclopentolate. It includes the best-fitting regression line (solid orange) and $y = x$ line (dotted blue) to assess the agreement between SER measurements. D, dioptre; SER, spherical equivalent refraction.

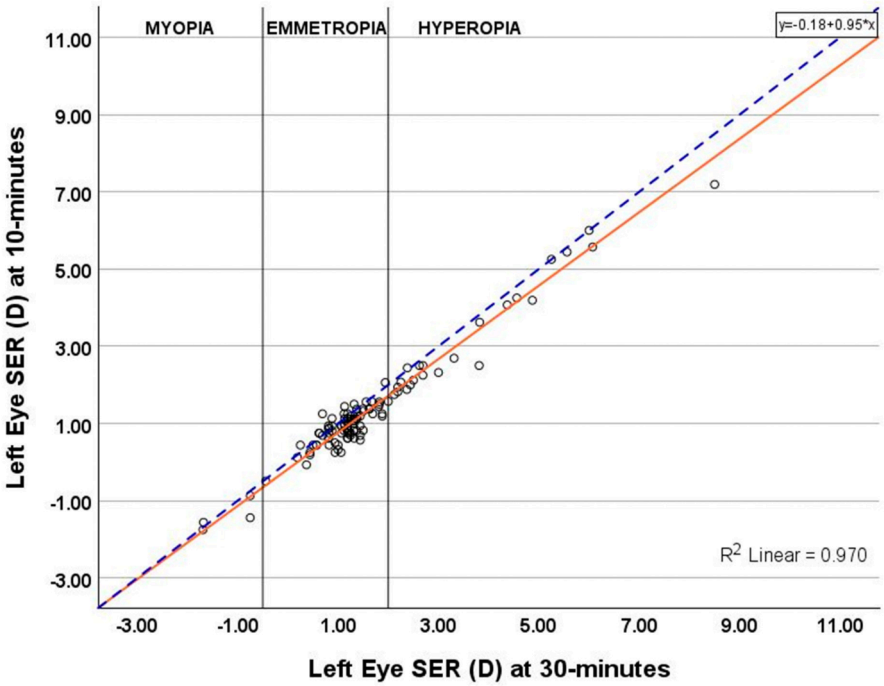

FIGURE 3 Scatter plot showing SER measures at 10- (*y*-axis) and 30-min (*x*-axis) post-instillation of 1.0% cyclopentolate only. It includes the best-fitting regression line (solid orange) and $y = x$ line (dotted blue) to assess the agreement between SER measurements. SER, spherical equivalent refraction; D, dioptre.

or left eyes (F (2) = 0.91, $p = 0.41$). There was no significant difference in SER change between participants with brown irides (two drops of cyclopentolate) and those without (one drop). For example, the mean (SD) SER difference between 10 and 30 min in participants with brown and non-brown irides was 0.02 (0.06) D ($t(110) = 0.40$, $p = 0.69$) in the right eye.

No adverse effects following instillation of eye drops were observed.

TABLE 3 Agreement indices for spherical equivalent refraction (SER) measurements (between 0 and 30 min, 10 and 30 min and 20 and 30 min) in the right (proxymetacaine and cyclopentolate) and left (cyclopentolate only) eyes separately. All precision values were significant ($p < 0.01$).

	Right eye				Left eye			
	0 & 10 mins	10 & 30 mins	20 & 30 mins	0 & 30 mins	0 & 10 mins	10 & 30 mins	20 & 30 mins	0 & 30 mins
Precision	0.886	0.989	0.992	0.887	0.851	0.985	0.984	0.848
Accuracy	0.814	0.994	0.999	0.797	0.797	0.988	0.997	0.776
Concordance	0.721	0.983	0.991	0.707	0.678	0.973	0.981	0.658

Abbreviation: Mins, minutes.

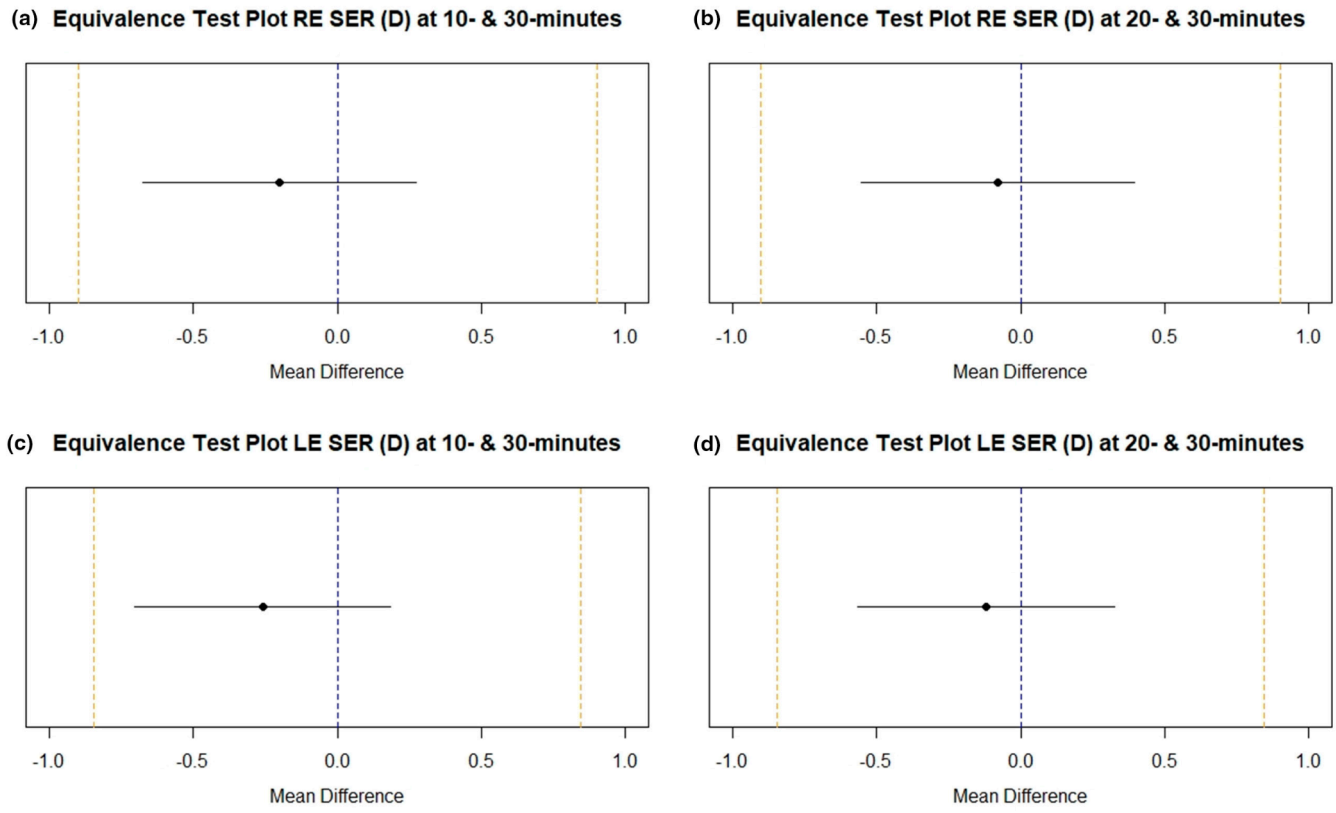

FIGURE 4 Plots presenting the equivalence bounds (−0.50 D, 0.50 D) with the 90% CI in right eyes (proxymetacaine and cyclopentolate) (a) and (b) and left eyes (cyclopentolate only) (c) and (d). SER measurements at 10 and 30 min were equivalent in right eyes (CI: −0.26, 0.48) as the 90% CI lay entirely within equivalence bounds but were not equivalent in left eyes (CI: −0.22, 0.53). Measurements at 20 and 30 min were equivalent in right (CI: −0.30, 0.44) and left eyes (CI: −0.33, 0.42). CI, confidence interval; D, dioptre; LE, left eye; RE, right eye; SER, spherical equivalent refraction.

DISCUSSION

The current study found no clinically significant difference in SER at 20 and 30 min in either eye, indicating that proxymetacaine is not necessary to reduce the wait time from the current gold standard of 30–20 min.[3-5] However, the 10- and 30-min SER measurements were only equivalent in the right eye, indicating that the pre-instillation of 0.5% proxymetacaine enhanced the cycloplegic effect of 1.0% cyclopentolate in the first 10 min when compared to 1.0% cyclopentolate alone. This study, along with prior research involving white 12- to 13-year-olds in Ireland,[11] provides a quantitative assessment of the impact of proxymetacaine on cyclopentolate action in a clinical setting in Ireland.

Non-cycloplegic autorefraction measurements were more myopic or less hyperopic than cycloplegic SER as early as 10 min following cyclopentolate instillation. Non-cycloplegic measurements overestimated the degree of myopia or underestimated hyperopia, aligning with previous research.[1] This difference highlights the importance of cycloplegic autorefraction for precise measurements. Of the sample, 22% had clinically significant hyperopia. In this group, the difference between non-cycloplegic and cycloplegic SER was 1.76 D, aligning with the 1.28 D difference in 4- to 15 year-olds observed by Sankaridurg et al.[21]

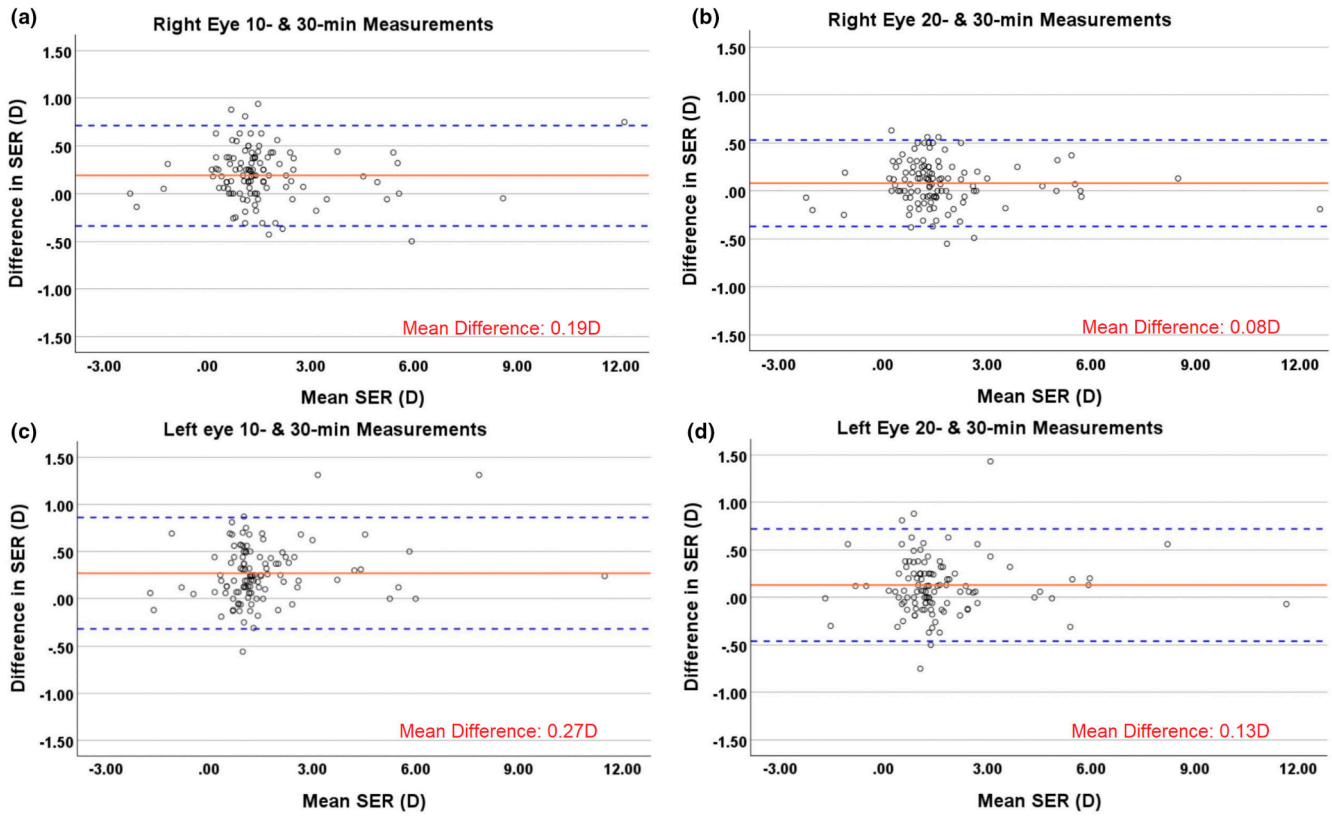

FIGURE 5 Bland–Altman plots of the difference in mean readings post-instillation of 0.5% proxymetacaine and 1.0% cyclopentolate (a) and (b) and 1.0% cyclopentolate only (c) and (d). The solid orange lines represent the mean differences, and the dotted blue lines represent upper and lower 95% confidence intervals. D, dioptre; LE, left eye; RE, right eye; SER, spherical equivalent refraction.

The marginal difference (<0.50 D) to the current findings is likely due to their inclusion of older children, whose non-cycloplegic and cycloplegic SER change reduced from 0.89 D to 0.33 D between 6 and 15 years of age.[21] The SER differences in participants with low hyperopia (+0.50 D to <+2.00 D) in the current study were comparable to those in Sankaridurg et al.[21] the current study found changes of 0.58 D for the +0.50 D to +0.99 D group, 0.92 D for the +1.00 to +1.49 D group and 1.19 D for the +1.50 D to +1.99 D group, closely matching the Sankaridurg values (0.59 D, 0.72 D and 1.03 D, respectively).

The pre-instillation of proxymetacaine enabled accurate autorefraction to be performed 10 min after cyclopentolate in White 6- to 7-year-old children. The mean difference between SER measurements at 10 and 30 min is close to zero in the right eye supporting the equivalence findings, but not in the left eye. Proxymetacaine is known to enhance the efficacy of cyclopentolate by increasing corneal absorption.[22] Significant SER differences between emmetropes and hyperopes were found in the left eye between 10 and 30 min, with hyperopes showing larger changes. However, no significant difference was observed between hyperopes and emmetropes at 20 and 30 min, indicating a 20-min wait after cyclopentolate alone is sufficient for cycloplegia in all refractive groups. The current study findings align with the larger Sankaridurg et al.[21] study ($n = 6017$) where hyperopes (43.1% of sample) experienced more significant SER changes with cycloplegia than emmetropes or myopes, to a similar magnitude as in the current work. Reducing testing times for children aged 6 years and above would improve the efficiency of ophthalmology and optometry-based practices by allowing more children to be seen daily.

Equivalence of the 20- and 30-min measurements in both eyes indicates that accurate autorefraction can be performed 20 min after cyclopentolate instillation in White 6- to 7-year-old children, regardless of proxymetacaine pre-instillation. Rosenfield et al.[23] suggested that daily variability in refraction measures of ±0.50 D was expected in patients, hence making 0.50 D the minimum clinically significant change in refraction. Davies et al.[24] and Lee and Cho[25] examined the repeatability and accuracy of the autorefractor used in the current study and found test–retest differences of (mean difference (SD)) 0.14 (0.35) D. In the present study, the mean differences between SER measurements at 20 and 30 min were close to zero in both eyes (Figure 5) and fell within the repeatability of the autorefractor. Some of the statistically insignificant discrepancies in measured SER values may be partly due to instrument repeatability or daily variations in refraction measures.[23-25]

Lovasik et al. reported that one drop of 1.0% cyclopentolate was less effective and slower in producing cycloplegia in brown eyes than blue or green, with significantly deeper

cycloplegia observed in lighter irides.[26] The current study supports the use of Mohan et al.'s criteria for optimal dosage of cyclopentolate in dark irides,[15] as one drop in blue and green irides and two drops in brown irides resulted in no significant impact on the difference in SER between measurements based on iris colour.[15]

Reports of the duration of action of proxymetacaine are inconsistent. A 2009 study with a small sample size ($n = 17$) found that corneal sensation did not fully return by 60-min post-instillation in young adults.[27] Conversely, Lawrenson et al.[28] ($n = 28$), Kyei et al.[29] ($n = 240$) and Basso Dias et al.[30] ($n = 21$) found that adult participants regained corneal sensation within 20–30 min after 0.5% proxymetacaine eye drops. Further study is warranted to determine how quickly the anaesthetic effect of proxymetacaine wears off in children to determine a safe discharge time for patients following cycloplegia.

Painful procedures cause distress and anxiety in children, leading to reduced cooperation in future healthcare appointments.[31] Hence, it is essential to minimise distress where possible. Hirji et al.[32] found that the two main causes of distress in children (aged 4–10 years) receiving cyclopentolate drops were: (1) cyclopentolate-induced stinging and (2) longer wait times between eye drop instillation and examination. The duration of proxymetacaine-induced stinging is 3.2 s on average compared to 63 s after cyclopentolate.[33] Although adding proxymetacaine before cyclopentolate may initially seem challenging in children, it offers significant benefits by greatly reducing discomfort. Shah et al.[7] found that 91% of children ($n = 88$, mean age 4.8 years) had no adverse reaction after using proxymetacaine, enabling atraumatic cycloplegia. Seventy per cent of children cried or refused cyclopentolate alone, while only 6% cried with pre-instillation of proxymetacaine and none refused the eye drops. This shows how well children tolerate the two-drop regimen. In adults, cyclopentolate with proxymetacaine had a similar pain score to saline (0.36 vs. 0.16), compared to a higher score of 4.19 for cyclopentolate alone.[6]

Effective communication and behavioural techniques, like 'Tell-Show-Do', are key to managing anxious children.[34] Simple explanations, distraction and positive reinforcement (e.g., praise or stickers) ease anxiety. Involving parents and using pre-visit imagery also enhance cooperation. As distraction techniques are essential when administering cyclopentolate alone, adding proxymetacaine does not significantly alter examination procedures. Whether pre-instilling proxymetacaine or using cyclopentolate alone, the approach to managing children and reducing their perceived discomfort stays the same, as these techniques are effective across medical settings.[35] Ultimately, the initial effort of using two drops is outweighed by the long-term benefits of reducing distress and fostering positive associations with eye care, leading to smoother future examinations.

A limitation of the current study was that post-cycloplegia pupil size was not measured. However, it has been found that pupil dilation does not coincide with maximum cycloplegia.[36,37] Another limitation was that accommodation was not measured. However, previous studies have concluded that cyclopentolate can result in sufficiently reduced residual accommodation 10- to 30-min post-instillation.[36] Additionally, systematically choosing the right and left eyes for the two eye drop regimes may affect results due to potential differences in timing, tearing and eyelid squeezing.

This study is the first to investigate the effect of proxymetacaine on cyclopentolate efficacy in vivo in a cohort of children. A strength of the study was using the fellow eye as a control, which allowed for within-subject analysis. Findings indicate that accurate autorefraction values can be obtained 20-min post-instillation of 1.0% cyclopentolate alone, and reliable measures as early as 10 min after the instillation of 0.5% proxymetacaine and 1.0% cyclopentolate in children aged 6 years and above. These results fill a gap in the literature by confirming that the findings of Doyle et al.[11] persist in younger children. The current study also investigated the effect of eye colour and SER category on the difference in SER between time points after cycloplegia.

The clinical implications of these findings are significant. Reducing waiting times for cycloplegia from the standard 30–20 min can enhance the efficiency of paediatric eye care, allowing more children to be examined daily. This can increase patient throughput in optometric and ophthalmic practices, minimising distress and discomfort for young patients.[38]

CONCLUSION

Study findings indicate that accurate autorefraction values can be obtained 20-min post-instillation of 1.0% cyclopentolate alone and that it is possible to achieve reliable measures as early as 10 min after the instillation of 0.5% proxymetacaine and 1.0% cyclopentolate in children aged 6 years and above. The clinical implication of these findings is that paediatric testing times may be reduced in practice. Further research involving non-White participants is needed to determine if the findings are consistent across different ethnicities. Additionally, more research is required to ascertain the duration of proxymetacaine's anaesthetic effect and to establish safe discharge times for patients from clinics.

AUTHOR CONTRIBUTIONS

Megan Doyle: Conceptualization (supporting); data curation (equal); formal analysis (equal); investigation (equal); methodology (lead); project administration (equal); resources (supporting); software (equal); validation (equal); visualization (equal); writing – original draft (lead); writing – review and editing (equal). **Veronica O'Dwyer:** Conceptualization (equal); data curation (supporting); formal analysis (supporting);

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest related to this publication.

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