Validity of noncycloplegic refraction in the assessment of refractive errors: the Tehran Eye Study

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ABSTRACT.

Purpose: To determine the sensitivity and specificity of noncycloplegic autorefraction for determining refractive status compared to cycloplegic autorefraction.

Methods: The target population was noninstitutionalized citizens of all ages, residing in Tehran in 2002, selected through stratified cluster sampling. From 6497 eligible residents, 70.3% participated in the study, from August to November 2002. Here, we report data on 3501 people over the age of 5 years who had autorefraction with and without cycloplegia (two drops of cyclopentolate 1.0% 5 min apart, with autorefraction 25 min after the second drop).

Results: Overall, the sensitivity of noncycloplegic autorefraction for myopia was 99%, but the specificity was only 80.4%. In contrast, the sensitivity for hyperopia was only 47.9%, but the specificity was 99.4%. At all ages, noncycloplegic autorefraction overestimated myopia and underestimated hyperopia. Overestimation of myopia was highest in the 21–30 and 31–40 year groups. Underestimation of hyperopia was high up to the age of 50 (20–40%), but decreased with age, to about 8% after the age of 50, down to almost 0% after 70. The difference in mean spherical equivalent with and without cycloplegia fell from 0.71 dioptres (D) in the 5–10 age group to 0.14D in those over 70.

Conclusion: Use of noncycloplegic autorefraction in epidemiological studies leads to considerable errors relative to cycloplegic measurements, except in those over 50–60. The difference between cycloplegic and noncycloplegic measurements varies with age and cycloplegic refractive category, and there is considerable individual variation, ruling out adjusting noncycloplegic measurements to obtain accurate cycloplegic refractions.

Key words: cycloplegic refraction – hyperopia – myopia – noncycloplegic refraction – sensitivity – specificity

Introduction

Several studies have shown that noncycloplegic and cycloplegic refractions differ in childhood (Chan & Edwards 1994; Choong et al. 2006; Fotedar et al. 2007; Fotouhi et al. 2007; Harvey et al. 2000; Liang et al. 2003; Twelker & Mutti 2001; Wesemann & Dick 2000; Williams et al. 2008a; Zhao et al. 2004), with overestimation of myopia and underestimation of hyperopia, and consequent errors in estimation of mean spherical equivalent refraction (SER). Since most samples of children are predominantly hyperopic (Morgan et al. 2009), cycloplegia is of particular importance, and cycloplegic refraction is generally regarded as the gold standard method for epidemiological studies in children. It has therefore been adopted for most studies on paediatric (Dirani et al. 2010; Giordano et al. 2009; Varma et al. 2006) and school-aged (Hashemi et al. 2003; He et al. 2006; Ip et al. 2008; Ojaimi et al. 2005a,b; Saw et al. 2002; Zadnik et al. 1993, 2003) samples, including the Refractive Error Study in Children (RESC) series (Negrel et al. 2000; Pokharel et al. 2000; Maul et al. 2000; Dandona et al. 2002; Murthy et al. 2002; Zhao et al. 2000; Naidoo et al. 2003; He et al. 2004; Goh et al. 2005; He et al. 2007; Sapkota et al. 2008).
However, cycloplegia has not always been used (see for example Quek et al. 2004; Williams et al. 1996), and some have attempted to argue that noncycloplegic and cycloplegic measurements are similar (Jungrens & Crewther 2003, 2005). Others have attempted to use more stringent cut-offs for myopia to overcome the problem of the overestimation of myopia without cycloplegia (Williams et al. 2008b).

In contrast to the general acceptance of cycloplegia for studies on children, the use of cycloplegia in adults has been less consistent. Although cycloplegia was used widely for adults in some of the early studies (Brown 1938; Slataper 1950; Sorsby et al. 1960; Fotedar et al. 2007; Goldschmidt et al. 1968; Fledelius 1983), most recent large-scale studies on older subjects, particularly from the age of 40–50, have assumed that myopia and hyperopia can be appropriately measured by objective or subjective noncycloplegic techniques (Attebo et al. 1999; Gudmundsdottir et al. 2000, 2005; Wang et al. 1994; Wong et al. 2000). The techniques used in these major eye studies on older adults have included noncycloplegic autorefractive, subjective refinement of initial noncycloplegic refraction, and subjective refraction. Some studies have attributed ametropia to those with unaided normal visual acuity, or the power of their correction to those with normal visual acuity with their presenting correction (Attebo et al. 1999; Shufelt et al. 2005; Tarcy-Hornoch et al. 2006). The assumption that cycloplegia is not necessary is open to question, given that accommodation has declined in amplitude, but has not disappeared by the age of 40–50 (Anderson et al. 2008, 2009; Duane 1912; Glasser & Campbell 1998; Hamaski et al. 1956; Hofstetter 1965; Richdale et al. 2008), and the validity of the assumption has not been systematically tested. One of the rare studies comparing cycloplegic and noncycloplegic refractions in adults reported that cycloplegia in the elderly can lead to a myopic shift in mean SER of all refractive groups (Toh et al. 2005), as high as \(-0.77\) D, in contrast to the hyperopic shifts seen in children.

In the Tehran Eye Study, noncycloplegic and cycloplegic autorefraction has been compared on a wide age range of participants, from age 5 to over 70, in a large population-based sample (Hashemi et al. 2003, 2004, 2010). The present report quantitatively compares the results obtained with noncycloplegic and cycloplegic autorefraction over that age range, assessing the validity of noncycloplegic autorefraction compared to cycloplegic autorefraction for epidemiological purposes.

Materials and Methods

The Tehran Eye Study is a cross-sectional study that collected population-based data from August to November 2002. Details of the methodology have been published elsewhere (Hashemi et al. 2003) and are presented here only briefly.

The target population consisted of noninstitutionalized citizens of all ages, residing in Tehran in 2002, selected through stratified cluster sampling. All members of the first 10 households in each cluster were invited for a complete eye examination at Noor Vision Correction Center. All participants who presented at the eye clinic and who gave oral consent at the time of examination had complete eye examinations including tests of uncorrected and best corrected visual acuity, and objective noncycloplegic and cycloplegic autorefractive refraction, as well as slit lamp and fundus examinations. Refraction was measured by optometrists for all participants over 5 years of age using a Topcon automated refractor (Topcon KR 8000; Topcon Corporation, Tokyo, Japan) according to the instruction manual. For cycloplegic refraction, two drops of cyclopentolate (1%) were instilled 30 and 25 min before refraction. Inter-observer comparison of refraction measurements between the optometrists was carried out in 538 eyes during the study. The intra-class correlation coefficient of reliability was 0.98 (95% CI, 0.97–0.99) for noncycloplegic spherical equivalent refraction.

Given the high correlation between the left and right eyes (Pearson correlation: \(r = 0.84\), \(p < 0.001\), only data on the right eyes are presented. The mean SER values with noncycloplegic and cycloplegic autorefractive refraction in 15 age groups (5 years and above) were plotted, and the correlations between their difference and other variables were assessed through linear regression analyses and analysis of variances. In calculating the 95% confidence intervals (CI), the effect of cluster sampling was taken into account. The level of significance in statistical testing was taken as \(< 0.05\). To determine the validity of noncycloplegic refraction in comparison with cycloplegic refraction, sensitivity and specificity for detecting myopia of at least \(-0.5\) D or \(-1.0\) D and hyperopia of at least \(+0.5\) D or \(+1\) D were calculated in different gender and age groups. Sensitivity of noncycloplegic autorefractive refraction was defined as the proportion of true myopic or hyperopic participants (based on cycloplegic refraction) who were detected by noncycloplegic refraction. Specificity was defined as the proportion of those identified as myopic or hyperopic by noncycloplegic refraction who were myopic or hyperopic based on cycloplegic refraction.

The Ethics Committee of the Noor Ophthalmology Research Center and the Ethics Committee of the National Research Center for Medical Sciences approved the study, which was conducted in accord with the tenets of the Helsinki Declaration.

Results

During the study period, from August to November 2002, 1600 households and 6497 residents eligible to enter the study were selected in Tehran as the study sample. Of these, 70.3% participated in the study. Here, we report data on 3501 people who had both noncycloplegic and cycloplegic autorefractive refraction performed. The participants’ mean age was 31.6 \pm 18.11 (range, 5–95) years, and 1414 (40.4%) were men.

As shown in Fig 1A, myopia was overestimated by noncycloplegic refraction. The degree of overestimation was dependent on age, with the highest errors appearing over the age range 5–50, where 4–7% of the population was incorrectly classified as myopic. Overestimation of myopia was still seen in the older age groups, but only 1–2% of the population was incorrectly classified as myopic.

In contrast, as shown in Fig. 1B, hyperopia was more markedly under-
The validity of noncycloplegic autorefraction for the determination of categorical refractive error is assessed in Table 1. For this analysis, two commonly used cut-offs for myopia (≤0.5D or ≤−1.0D) and hyperopia (> +0.5D or > +1.0D) were used. Irrespective of the cut-offs, noncycloplegic autorefraction detected almost all myopes, but erroneously classified some participants as myopic, particularly in the age range 21–50. In contrast, noncycloplegic autorefraction had high specificity, but low sensitivity for hyperopia. In other words, most participants classified as hyperopic were genuine hyperopes, but many hyperopes were misclassified as either emmetropes or even myopes. The impact of these differences is shown in Fig. 2. With the lower cut-offs (Fig. 2A), the categorical distributions of refractive error were completely transformed from predominantly emmetropic without cycloplegia, to predominantly hyperopic after cycloplegia. Less marked changes were seen with the higher cut-offs (Fig. 2B).

The difference in mean SER between the two refraction methods also varied according to age (Fig. 3). The difference decreased with age, starting with 0.71 D in the 5–10 year age group and decreasing to 0.14 D in the 71–75 year age group. The difference reached a value of around 0.4D in the 16–20 age group and remained at approximately that level until the 46–50 age group, where it declined to about 0.2D. A linear regression plot for the inter-method difference with age (years) indicated an inverse correlation with a coefficient of −0.007D/year (p < 0.001). There were no significant gender differences in the correlation between age and difference in refraction between the two measurement methods, and there was no significant interaction between age and gender in the amount of difference between the two measurement methods. Although simple regression models showed the inter-method difference was lower among people with cataracts and diabetes, using multiple regression, age and gender were the only significant variables in the final model.

For further analysis, data were examined for three groups, < 25, 25–49 and ≥50, based on common patterns of refractive change during development. Attributing emmetropia to those with normal visual acuity leads to considerable error, as shown in Table 2. Only a low percentage (<10%) of those identified as myopic with cycloplegia had 6/6 visual acuity, but over 80% of those identified as hyperopic with cycloplegia had 6/6 vision and would have been identified as emmetropic under some protocols. The effect of this assumption also varied with age, but was high until the age of 60.

For each age group, there was a considerable individual variation in the magnitude of the difference between the cycloplegic refraction and the noncycloplegic refraction, as shown in Fig. 4. In almost all cases, the cycloplegic refractions were more positive than the noncycloplegic, and most of the few that were not were within the limits of instrument error. Most differences were in the range 0.00D–+1.00D, with a tail extending to almost +2.00D for the <25 and 25–49 age groups. However, in the ≥50 age group, the tail was largely eliminated, and the data were more tightly clustered between 0.00D and +0.50D.

Within each age group, the mean differences also depended on the type of refractive error determined from the cycloplegic refraction (Fig. 5). In the < 25 age group, analysis of variance showed that the difference between cycloplegic and noncycloplegic refractive errors was higher for cycloplegic hyperopes, than for cycloplegic emmetropes, and cycloplegic myopes (p < 0.001). In the 25–49 age group, the difference in the two measures was still larger than for cycloplegic emmetropes and cycloplegic myopes (p < 0.001), and in the ≥50 age group, the error was not significantly different between the three.
Table 1. The validity of noncycloplegic refraction compared to cycloplegic refraction in the assessment of refractive errors equal to or more than 0.5 or 1.0 D.

<table>
<thead>
<tr>
<th>Age</th>
<th>Myopia ≤ 0.5D</th>
<th>Myopia ≤ 1.0D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity (%)</td>
<td>Specificity (%)</td>
</tr>
<tr>
<td>5–20</td>
<td>98.1</td>
<td>80.3</td>
</tr>
<tr>
<td>21–30</td>
<td>100</td>
<td>74.9</td>
</tr>
<tr>
<td>31–40</td>
<td>100</td>
<td>76.5</td>
</tr>
<tr>
<td>41–50</td>
<td>99.1</td>
<td>84.1</td>
</tr>
<tr>
<td>51–60</td>
<td>96.2</td>
<td>86.4</td>
</tr>
<tr>
<td>61–70</td>
<td>100</td>
<td>89.7</td>
</tr>
<tr>
<td>&gt; 70</td>
<td>100</td>
<td>92.9</td>
</tr>
<tr>
<td>Male</td>
<td>98.6</td>
<td>81.5</td>
</tr>
<tr>
<td>Female</td>
<td>99.3</td>
<td>79.8</td>
</tr>
<tr>
<td>Total</td>
<td>99.0</td>
<td>80.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Hyperopia ≥ +0.5D</th>
<th>Hyperopia ≥ +1.0D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity (%)</td>
<td>Specificity (%)</td>
</tr>
<tr>
<td>5–20</td>
<td>38.9</td>
<td>99.4</td>
</tr>
<tr>
<td>21–30</td>
<td>22.8</td>
<td>100</td>
</tr>
<tr>
<td>31–40</td>
<td>29.9</td>
<td>98.7</td>
</tr>
<tr>
<td>41–50</td>
<td>59.4</td>
<td>98.1</td>
</tr>
<tr>
<td>51–60</td>
<td>87.1</td>
<td>99.4</td>
</tr>
<tr>
<td>61–70</td>
<td>88.7</td>
<td>99.0</td>
</tr>
<tr>
<td>&gt; 70</td>
<td>96.4</td>
<td>98.1</td>
</tr>
<tr>
<td>Male</td>
<td>49.3</td>
<td>99.3</td>
</tr>
<tr>
<td>Female</td>
<td>46.8</td>
<td>98.8</td>
</tr>
<tr>
<td>Total</td>
<td>47.9</td>
<td>99.0</td>
</tr>
</tbody>
</table>

groups, although the difference for the cycloplegic hyperopes remained marginally higher (p = 0.111).

Discussion

Overall, our results show that attempts to estimate refractive error without cycloplegia can produce major errors. Noncycloplegic autorefraction identifies all those with significant myopia, but includes some nonmyopes in the myopic category. It includes in the hyperopic category only those with cycloplegic hyperopia, but includes many cycloplegic hyperopes in the emmetropic category. The tendency to overestimate myopia and emmetropia and underestimate hyperopia decreased with age, but there were significant errors in refractive classification in age groups up to age 50. Mean SER estimates are particularly subject to error, because they are contributed to by both the overestimation of myopia and the underestimation of hyperopia. Even in the oldest age group, there was still some difference between cycloplegic and noncycloplegic measurements. Attributing emmetropia or habitual correction power to those with normal visual acuity compounds the errors associated with lack of cycloplegia, because, in all but those aged ≥65, many subjects with identified hyperopia with cycloplegia autorefraction had normal visual acuity. Our results suggest that cycloplegia is crucial for accurate determination of refractive error up to the age of 50 and that smaller errors are associated with lack of cycloplegia after that age.

In the case of school-aged children, it is clear from our results that cycloplegia is required for accurate assessment of the prevalence of refractive error, confirming previous reports, and consistent with prevailing practice. Fotedar et al. (2007) found that the difference between noncycloplegic and cycloplegic refraction among 12-year-olds was 0.84 D. Our results showed a very similar difference of 0.71 D in a broader age group.

In the young adult to middle age group, from 20 to 50, our results showed a similar pattern to that seen in children, with some overestimation of myopia, more marked overestimation of emmetropia, and underestimation of hyperopia with noncycloplegic refractions. After the age of 40, there was some reduction in the difference between estimates based on cycloplegic and noncycloplegic refractions, but they were still significant. There are very few studies on the impact of cycloplegia over this age range, but similar results have been reported on young adults (Jorge et al. 2005). After the age of 50, the differences in prevalence estimates without and with cycloplegia were smaller, but they remained detectable even in the oldest age group studied.

In terms of mean SER, the difference between the cycloplegic and noncycloplegic measures was highest in the 5–10 age group, probably due to the high amplitude of accommodation in this age group (Anderson et al. 2008). The difference decreased with age, but there were still significant differences between the results obtained with two methods in older age groups. There was an increase in the mean SER with age, but the results without cycloplegia were consistently lower, i.e. shifted in a myopic direction. The difference between noncycloplegic and cycloplegic measurements reduced markedly around the age of 45 years and continued with an almost constant difference after that, even up to the age of 75 years. We did not find the myopic shift in refraction reported by Toh et al. (2005).

Overall, our results suggest that cycloplegia is required for epidemiological studies, up to at least the age of 50. In particular, studies on refractive errors in the high school years or in adults in the 20–50 age bracket will have significant errors using noncycloplegic techniques. Even in older age groups, there is some overestimation of myopia and underestimation of hyperopia, with a corresponding shift in mean SER. The errors caused by lack of cycloplegia affect estimates of prevalence of myopia, emmetropia and hyperopia, mean SER, and the categorical and continuous distributions of spherical equivalent refraction.

A somewhat similar, but more limited, analysis has recently been reported by Krantz et al. (2010) on participants with an age range of 22–84, and a mean age of 49. The authors concluded that cycloplegia may not be necessary in epidemiological studies of refraction in adults, whereas we reached a different conclusion.

The difference in conclusions is surprising, because the results obtained in the two studies appear to be quite similar. However, Krantz et al. (2010)
qualified their conclusion, pointing out that differences between SEs before and after cycloplegia were statistically significant for most subgroups defined by age and refractive status, but if hyperopia or refractive error were not primary end-points, if the study targeted older populations, if the expected number of young participants with hyperopia was low, or if the study was measuring the prevalence of myopia, then cycloplegia may not be necessary. We believe that it is important to start with the recommendation that refraction with cycloplegia is the gold standard, and to then justify the non-use of cycloplegia where appropriate. The restrictions on the usefulness of epidemiological studies without cycloplegia proposed by Krantz et al. (2010) seem to preclude significant analysis of hyperopia and hyperopic shifts (Morgan et al. 2009).

A further difference between the analyses is that Krantz et al. (2010) used only $+1.0\text{D}$ as a cut-off for myopia and $+1.0\text{D}$ as a cut-off for hyperopia. These cut-offs lead to smaller errors, but if the commonly used cut-offs of $+0.5\text{D}$ and $+0.5\text{D}$ are used, then the errors in classification are much more marked. It should be noted that many of the major epidemiological studies on adults (Wang et al. 1994; Attebo et al. 1999; Wong et al. 2000; Shufelt et al. 2005) used $+0.5$ and $+0.5\text{D}$ as cut-offs, and thus, the results reported in these studies are subject to greater error than documented by Krantz et al. (2010).

While the magnitude of errors on older people owing to lack of cycloplegia is small after the age of 50, and particularly after the age of 60, studies on refractive error are now starting to fill in the gap between studies on children and older adults, to elucidate the pattern of lifelong changes in refractive error (Bourne et al. 2004; Shah et al. 2008; Saw et al. 2008; Vitale et al. 2008), and caution in interpreting their results is required. It will be necessary in future epidemiological studies on younger adults to measure cycloplegic refraction over this important age range to avoid significant errors.

Given that there are many studies that have used noncycloplegic techniques for studies on both children and adults, including large studies such as the Avon Longitudinal Study of Par-

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Table 2. The prevalence of UCVA 20/20 by refractive errors and age.

<table>
<thead>
<tr>
<th>Refractive error</th>
<th>Refraction type</th>
<th>Age group</th>
<th>5–24</th>
<th>25–44</th>
<th>45–64</th>
<th>65 or more</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myopia</td>
<td>Noncycloplegic (%)</td>
<td></td>
<td>9.4</td>
<td>8.9</td>
<td>3.5</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>Cycloplegic (%)</td>
<td></td>
<td>4.2</td>
<td>4.1</td>
<td>4.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Hyperopia</td>
<td>Noncycloplegic (%)</td>
<td></td>
<td>82.7</td>
<td>67.7</td>
<td>27.8</td>
<td>4.9</td>
</tr>
<tr>
<td></td>
<td>Cycloplegic (%)</td>
<td></td>
<td>90.7</td>
<td>81.9</td>
<td>35.9</td>
<td>6.6</td>
</tr>
</tbody>
</table>
ents and Children (Williams et al. 1996) and the British Birth Cohort studies (Cumberland et al. 2007, 2008), an important question is whether non-cycloplegic refractions can be adjusted to give an accurate cycloplegic refraction. Cycloplegic refraction is therefore essential for determination of the basic optical properties of the eye. Even at a population level, the variation with age and refractive status means that adjustment of group results would need to be age-specific and would need to be refraction-specific as well. Non-cycloplegic refractions will be closer to cycloplegic refractions in highly myopic and older populations, but for really comparable results, cycloplegic refractions are essential.

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