Myopia correction in children: a meta-analysis

Abstract

Purpose: The purpose of this study was to conduct a meta-analysis comparing rigid gas permeable lenses (RGP) with soft contact lenses (SCL), spectacles and orthokeratology (OK) lenses for myopia control with respect to axial length elongation, spherical equivalent and measures of corneal curvature.

Methods: Medline, Cochrane, EMBASE, and Google Scholar databases were searched to September 29, 2015 using the following keywords: rigid gas permeable contact lens; refractive error; and refractive abnormalities. Randomized controlled trials, two-arm prospective studies and retrospective studies of children with myopia treated with RGP lenses compared with spectacles, SCL, and OK lenses were included. Outcome measures were changes of axial length, spherical equivalent, flatter meridian, steeper meridian and corneal apical radius.

Results: Five studies were included. Three studies reported axial length change after 2-3 years of treatment with RGP lenses and SCL/spectacles and no difference between the groups was noted (pooled mean difference = -0.077, 95% confidence interval [CI]: -0.120 to 0.097, \( p = 0.840 \)). Two studies reported a change of spherical equivalent after 2-3 years of treatment with RGP lenses and SCL/spectacles, and no difference between the groups was noted (pooled mean difference = 0.275, 95% CI: -0.390 to 0.941, \( p = 0.417 \)). Two studies compared corneal curvature measures between RGP and OK lenses after 3-6 months of treatment and no differences in any measures of corneal curvature were seen.

Conclusions: The effect of RGP lenses and SCL/spectacles on axial length elongation and spherical equivalent and of RGP and OK lenses on corneal curvature in children with myopia was similar.
Refractive errors that are uncorrected are a leading cause of visual impairment worldwide [1] and myopia is the most common refractive error [2]. It has been estimated that up to 30% of the United States’ population and over 90% of some East Asian populations are affected by myopia [2]. Myopia is typically progressive in children and early onset myopia can be associated with the development of high myopia, which can result in a large number of pathological complications including cataracts, peripheral retinal tears and retinal detachment, myopic foveoschisis, peripapillary deformation, dome-shaped macula, choroidal/scleral thinning, myopic choroidal neovascularization, glaucoma and macular degeneration [3-6]. Thus, treatment of myopia and controlling its progression is of importance to avoid later ocular pathologies.

Myopia is typically cause by increased axial length of the eye which causes light from objects at a distance to focus in front of the retina, resulting in blurred distance vision. Many approaches have been examined to treat and/or slow the progression of myopia [7,8]. Pharmacological approaches included timolol and atropine drops [7, 8] Ocular methods include bifocal and progressive addition spectacles, and soft, rigid gas permeable (RGP), and orthokeratology (OK) contact lenses [7,8]. Individual studies, and reviews of the literature, have indicated that all of the aforementioned methods are effective to some degree [7-15]; however, there remains no consensus on the best method to control myopia progression.

Both RGP and OK lenses attempt to reshape the cornea to reduce refractive error and correct myopia [16]. RGP lenses are worn during the day, whereas OK lenses are worn at night (during sleep) and provide for adequate vision during the day [17]. Studies have suggested that both methods can achieve myopia correction and control [16,17]; however, few studies have compared the two methods, or compared RGP lenses with other methods of myopia control.

Thus, the purpose of this study was to conduct a meta-analysis comparing RGP and soft contact lenses (SCL) and spectacles, and RGP and OK lenses for myopia control with respect to axial length elongation, spherical equivalent and measures of corneal curvature.

**Methods**

**Literature search strategy, study selection, and data extraction**

This systematic review and meta-analysis was conducted in accordance with PRISMA guidelines [18]. Medline, Cochrane, EMBASE and Google Scholar databases were searched from inception to September 29, 2015 using combinations of the following keywords: rigid gas permeable contact lens; refractive error; and refractive abnormalities. Reference lists of relevant studies were also searched for potentially relevant articles. Searches were conducted independently by two reviewers, and a third was consulted for resolution of any disagreements.

Inclusion criteria for the meta-analysis were as follows: 1) randomized controlled trials (RCTs), two-arm prospective studies and retrospective studies; 2) examined children with myopia; and 3) outcomes with RGP lenses, compared with those of other treatments such as spectacles, SCL and OK lenses, were reported. Cohort studies, letters, comments, editorials, case reports, proceedings, personal communications and one-arm studies were excluded, as were studies that did not provide quantitative outcome data.

The following information/data were extracted from studies that met the inclusion criteria: the name of the first author; year of publication; study design; number of participants in each group; participants’ age and gender; treatments; and outcomes of interest.

**Quality assessment**

The methodological quality of the included studies was assessed using the risk-of-bias assessment tool outlined in the Cochrane Handbook for Systematic Reviews of Interventions [19]. Briefly, six domains are evaluated: random sequence generation; allocation concealment; blinding of patients and personnel; blinding of outcome assessment; incomplete outcome data; and selective reporting risk.

**Outcome measures and data analysis**

Outcome measures of the analysis were mean differences of changes from baseline of axial length, spherical equivalent, flatter meridian, steeper meridian and corneal apical radius. Outcomes were compared between patients who wore RGP lenses and those who wore SCL or spectacles, and those who wore RGP lenses and OK lenses. Pooled mean differences with 95% confidence intervals (CIs) were calculated. For each study, a mean difference >0 indicated greater improvement of spherical equivalent, greater axial length elongation and greater increases in measures of corneal curvature (i.e., apical radius and steeper/flatter meridian) in subjects using RGP lenses as compared with those using SCL or spectacles, or with those using OK lenses. A mean difference <0 indicated greater decreases in spherical equivalent, lesser axial length elongation and greater decreases in measures of corneal curvature in subjects using RGP lenses as compared those using SCL or spectacles or OK lenses.
Heterogeneity between studies was evaluated using the Cochran Q statistic and the \( I^2 \) statistic, which indicates the percentage of the observed between-study variability caused by heterogeneity. A Cochran Q statistic with a value of \( p < 0.1 \) or \( I^2 \) statistic >50% was considered to indicate significant heterogeneity. If significant heterogeneity was present, a random-effects model (DerSimonian-Laird approach) of analysis was used; otherwise a fixed-effect model was performed (Mantel-Haenszel approach). Sensitivity analysis based on the leave-one-out approach was performed if three or more studies were included in the meta-analysis to determine the effect of any one study on the pooled outcome, and thus evaluate the robustness of the pooled effect size. Sensitivity analysis is not informative if there are fewer than than three studies. All statistical analyses were performed by using Comprehensive Meta-Analysis software, version 2.0 (Biostat, Englewood, NJ, USA).

Results

Literature search and study characteristics

A flow diagram of study selection is presented in Figure 1. A total of 231 potentially relevant articles were identified via the database searches and 12 were identified from a review of the reference lists of the articles identified in the searches. After duplicates were removed, 243 articles remained. These were screened by title and abstract and 215 were excluded. The full texts of the remaining articles were reviewed, and 23 were excluded, the reasons for which are shown in Figure 1. Thus, five studies were included in the meta-analysis [12,13,20-22].

The basic characteristics of the five studies are summarized in Table 1, and the inclusion criteria and intervention protocols in Table 2. Of the five studies, three compared RGP lenses to SCL or spectacles and included a total of 589 children (285 males) and two studies compared RGP lenses with OK lenses and contained a total of 42 teenagers (21 males).
FIGURE 2. Meta-analysis of rigid gas permeable (RGP) lenses vs. soft contact lenses/spectacles for (A) axial length elongation and (B) spherical equivalent.

FIGURE 3. Sensitivity-analysis of rigid gas permeable (RGP) lenses vs. soft contact lenses/spectacles on axial length elongation.
FIGURE 4. Meta-analysis of rigid gas permeable (RGP) lenses vs. orthokeratology (OK) lenses for (A) spherical equivalent, (B) corneal apical radius, (C) flatter meridian, and (D) steeper meridian.
Three studies [13,20,22] reported a change of axial length after 2-3 years of treatment with RGP lenses and SCL/spectacles; two of which reported greater, but not statistically significant, axial length elongation for RGP lens patients. A random-effects model of analysis was performed since large heterogeneity was present between studies ($I^2 = 66.2\%$, Cochran Q = 5.9, $p=0.052$) (Figure 2A).

Two studies reported changes of spherical equivalent after 2-3 years of treatment with RGP lenses and SCL/spectacles. One study [22] reported greater improvement of spherical equivalent with RGP lenses while the other did not find a difference [21]. A random-effects model was performed since large heterogeneity was present ($I^2 = 91.6\%$, Cochran Q = 11.9, $p=0.001$). The results showed that change of spherical equivalent from baseline was not different between the two groups (pooled mean difference = 0.275, 95% CI: -0.390 to 0.941, $p=0.417$) (Figure 2B).

Sensitivity analysis for axial length based on the leave-one-out approach showed that the pooled effect size became positive when the study by Khoo et al. [13] was removed; however, the significance of the association between axial length elongation and use of RGP lenses did not change (Figure 3).
TABLE 1. Basic characteristics of studies included in the meta-analysis

<table>
<thead>
<tr>
<th>First author (publication year)</th>
<th>Intervention</th>
<th>Number of patients</th>
<th>Age, years</th>
<th>Male, N (%)</th>
<th>Drop-out, N (%)</th>
<th>Time point of outcome measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swarbrick (2015)</td>
<td>OK</td>
<td>26</td>
<td>13.4 ± 1.9</td>
<td>14</td>
<td>8</td>
<td>6 months</td>
</tr>
<tr>
<td></td>
<td>RGP</td>
<td>26</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kang (2011)</td>
<td>OK</td>
<td>16</td>
<td>Range: 11 to 16</td>
<td>7</td>
<td>NR</td>
<td>3 months</td>
</tr>
<tr>
<td></td>
<td>RGP</td>
<td>16</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walline (2004)</td>
<td>RGP</td>
<td>59</td>
<td>10.5 ± 1.2</td>
<td>24 (41)</td>
<td>0</td>
<td>3 years</td>
</tr>
<tr>
<td></td>
<td>SCL</td>
<td>57</td>
<td>10.5 ± 1.1</td>
<td>23 (40)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Katz (2003)</td>
<td>RGP</td>
<td>105/158*</td>
<td>8.4 ± 1.5</td>
<td>71 (45)†</td>
<td>53 (35)†</td>
<td>24 months</td>
</tr>
<tr>
<td></td>
<td>Spectacles</td>
<td>192/225*</td>
<td>8.3 ± 1.6</td>
<td>133 (60)†</td>
<td>33 (15)†</td>
<td></td>
</tr>
<tr>
<td>Khoo (1999)</td>
<td>RGP</td>
<td>45</td>
<td>Range: 10-12</td>
<td>18</td>
<td>60 (57)</td>
<td>3 years</td>
</tr>
<tr>
<td></td>
<td>Spectacles</td>
<td>45</td>
<td></td>
<td>16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Number of patients at 24 months/number of patients after adaptation.  
† After adaptation.  
OK, orthokeratology lenses; NR, not reported; RGP, rigid gas permeable lenses; SC, soft contact lenses.  
Age reported as mean ± standard deviation, unless otherwise stated.

Meta-analysis of RGP vs. OK lenses

Two studies [12,20] reported comparisons of changes of corneal curvature measures (i.e., apical radius, flatter meridian, spherical equivalent and steeper meridian) after 3-6 months of treatment with RGP and OK contact lenses. Swarbrick et al. [12] reported no significant differences between RGP vs. OK contact lenses in apical radius, flatter meridian, spherical equivalent and steeper meridian, while Kang et al. [20] reported significant differences. A random-effects model of analysis was used when pooling the results of the two studies as significant heterogeneity was present with respect to all measures (Figure 4). The results revealed no differences in all of the measures of corneal curvature between RGP vs. OK lens wear (spherical equivalent: pooled mean difference = -1.185, 95% CI: -2.734 to 0.363, p=0.134; apical radius: pooled mean difference = -0.198, 95% CI: -0.512 to 0.115, p=0.215; flatter meridian: pooled mean difference = 0.743, 95% CI: -0.246 to 1.733, p=0.141; steeper meridian: pooled mean difference = 0.891, 95% CI: -0.048 to 1.831, p=0.063) (Figure 4).

Quality assessment

Results of the quality assessment are shown in Figure 5. All of the included studies had low risk in reporting bias and four studies had low risk of bias in random sequence generation; however, three studies had high risk in selection bias and all the studies had high risk of bias in performance bias. Overall, the quality of included studies was limited by study design and the characteristics of the treatments.

Discussion

The objective of this meta-analysis was to compare RGP lenses and soft contact lenses (SCL) and spectacles, and RGP and OK lenses for myopia control with respect to axial length elongation, spherical equivalent, and measures of corneal curvature. The results indicated that axial length elongation and change of spherical equivalent from baseline was not different between RGP lenses and SCL/spectacles, nor were there differences between RGP and OK lenses with respect to measures of corneal curvature (flatter meridian, steeper meridian and corneal apical radius). This analysis, however, is limited by the small number of included studies and the results should be interpreted with considerable caution. These findings highlight the need for high-quality studies examining these various methods for controlling myopia.

Myopia is a common condition affecting a significant percentage of the population [2]. A high degree of myopia is associated with severe ocular pathologies and, thus, control of myopia is of marked clinical importance. To date, very few of
 superficial chamber depth between the two groups was 0.22 mm
pooled estimate of axial length change in the OK group was
the daytime
reshape the cornea and thus provide adequate vision during
the many methods proposed for myopia control have been shown to be effective and studies comparing different methods are extremely heterogeneous.
OK is a relatively new technique in which a reverse geometry gas permeable contact lens is worn overnight to reshape the cornea and thus provide adequate vision during the daytime [23]. A 2015 meta-analysis by Sun et al.[17] on the use of OK for myopia control included seven studies. The pooled estimate of axial length change in the OK group was 0.27 mm less than in the control group, the difference in vitreous chamber depth between the two groups was 0.22 mm and OK lenses reduced myopia progression by approximately 45%.
A recent Cochrane Database Systematic review by Walline et al. [7] examined a number of interventions for myopic control including multifocal lenses, rigid and soft contact lenses, timolol drops and topical muscarinic receptor antagonists and reported that muscarinic receptor agonists were the most effective. At the time of publication, however, topical antimuscarinic medications were not commercially available. The analysis was limited by the number of available studies examining the different treatments; for example, only

OK, orthokeratology lenses; NR, not reported; RCT, randomized controlled trial; RGP, rigid gas permeable lenses; SC, soft contact lenses

<table>
<thead>
<tr>
<th>First author (publication year)</th>
<th>Country</th>
<th>Study design</th>
<th>Intervention</th>
<th>Intervention protocol</th>
<th>Inclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swarbrick (2015)</td>
<td>East Asian</td>
<td>Crossover RCT</td>
<td>OK</td>
<td>Subjects were fitted with overnight OK in 1 eye, chosen at random, and RGP lenses for daytime wear in the contralateral eye. Lenses were worn for 6 months. After a 2-week recovery period without lens wear, lens eye combinations were reversed and continued for a further 6 months, followed by another 2-week recovery period without lens wear.</td>
<td>Myopia between -1.00 and -4.00 D spherical equivalent, evidence of progression of myopia in the previous 12 months (based on a reported increase in spectacle prescription), &lt;1.50 D of corneal toricity, &lt;1.00 D difference in spherical equivalent refraction between the two eyes.</td>
</tr>
<tr>
<td>Kang (2011)</td>
<td>East Asian</td>
<td>RCT</td>
<td>OK</td>
<td>Subjects were randomly fitted with an OK lens in one eye for overnight wear and a conventional RGP lens in the other eye for daily wear.</td>
<td>Central refraction between -1.00 DS and -4.00 DS with ≤1.50 DC.</td>
</tr>
<tr>
<td>Walline (2004)</td>
<td>US</td>
<td>RCT</td>
<td>RGP</td>
<td>Adaptation to RGP wear was determined by the subject reporting a wearing time of at least 40 hours/week and contact lenses that were “usually comfortable” or “always comfortable” after 1 to 2 months of contact lens wear. A total of 116 (78.9%) patients successfully adapted to RGP wear and were randomly assigned to wear RGP (n=59) or SCL (n=57) for the clinical trial.</td>
<td>Visual acuity of 20/20 or better both eyes. Both eyes had a spherical component of -0.75 to -4.00 D. Both eyes had &lt;1.50 D astigmatism by cycloplegic autorefraction and &lt;1.00 D astigmatism by noncycloplegic manifest refraction, and there was &lt;1.00 D difference between the spherical components of the two eyes.</td>
</tr>
<tr>
<td>Katz (2003)</td>
<td>Singapore</td>
<td>RCT</td>
<td>RGP</td>
<td>Median of 7 hours per day, but no more than 40% wore them at least 8 hours per day, 7 days per week. Spectacles For a median of 15 hours per day at the time of the 24-month follow-up.</td>
<td>Myopia between -1 and -4 D, astigmatism ≤2 D</td>
</tr>
<tr>
<td>Khoo (1999)</td>
<td>Singapore</td>
<td>Prospective</td>
<td>RGP</td>
<td>The children were randomly selected from various schools in Singapore, and then were randomly selected for contact lens wear. Spectacles NR</td>
<td>Corrected visual acuity of 6/6 or better for each eye. Myopia with ≤3 D astigmatism.</td>
</tr>
</tbody>
</table>
two studies examined RGP lenses and neither showed evidence of an effect on myopia. Progressive addition lenses (four studies) and bifocal spectacles (four studies) showed only a small slowing of myopic progression. The review did not assess the effect of OK lenses.

A 2013 literature review (but no meta-analysis) by Koffler and Sears [16] sought to compare the effectiveness of OK lenses vs. SCL, RGP lenses and spectacles for myopia control in children. The authors concluded that OK was as effective as the other methods for treating myopia and was more effective at treating axial elongation. No major adverse events were associated with the use of OK lenses. A more recent review of the literature reported that the most effective methods for controlling myopia were OK lenses, soft bifocal contact lenses and topical pharmaceutical agents, such as atropine or pirenzepine, and that these interventions can slow the progression by up to 50%, and that contact lenses and bifocal and multifocal spectacles were not effective at controlling myopia [8]. Similarly, another recent review concluded that atropine eye drops had the largest effect on slowing myopia progression, undercorrection increased myopia progression, progressive or bifocal lenses (spectacles or contacts) may slow progression and RGP lenses had little effect on slowing myopia progression [15].

It is difficult to draw definitive conclusions from the aforementioned studies because of the large heterogeneity in the study methods, and in individual studies examining different methods for controlling myopia. In 2016, Huang et al. [24] conducted a network meta-analysis to compare the efficacy of 16 interventions for myopia control in children with respect to single vision spectacles or placebo. Thirty RCTs (with 5422 eyes) were analyzed and the overall results indicated that atropine, pirenzepine and progressive addition spectacle lenses were effective with respect to refraction, and that atropine, OK lenses, peripheral defocus modifying contact lenses, pirenzepine and progressive addition spectacle lenses were effective with respect to axial length. The most effective interventions were pharmacological agents, such as atropine and pirenzepine, followed by OK and peripheral defocus-modifying contact lenses.

It should be noted that the five studies included in this analysis were generally restricted to patients with moderate myopia and that treatment results can vary in patients with different degrees of myopia. In a study that did not meet the criteria for the current analysis, Charm et al. [25] studied children with high myopia (-5.00 D or more) and compared the results of partial reduction OK lenses with those of controls wearing spectacles. At 24 months of follow-up, axial length elongation was 63% slower in the children with OK lenses compared with those wearing spectacles.

There are limitations of this analysis, the first of which is the small number of available studies to be included. Time points of outcome measurement varied between some studies, and in some studies the drop-out percentage was not reported. This analysis was limited to comparing the results of certain types of optical correction methods and did not examine pharmacological methods.

Conclusions

Axial length elongation and change of spherical equivalent from baseline was not different in patients with myopia when treated with RGP lenses vs. SCL/spectacles, nor are there differences with respect to measures of corneal curvature (flatter meridian, steeper meridian and corneal apical radius) when myopia is treated with RGP and OK lenses. These results should be interpreted with caution due to the small number of studies included in the analysis.

Competing Interest

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References