Results of Photorefractive Keratectomy plus Mitomycin-C in the Treatment of Regressed Refractive Errors after Laser in Situ Keratomileusis

Hassan Hashemi, MD1,2 • Mansour Taherzadeh, MD1 • Bijan Rezvan, DDS1

Abstract

Purpose: To investigate the application of mitomycin-C 0.02% (MMC) in the photorefractive keratectomy (PRK) procedure in correcting regressed myopia

Methods: Eighteen eyes of 11 patients with a spherical equivalent (SE) of less than -5 diopters (D) who had undergone laser in situ keratomileusis (LASIK) more than 2 years before were operated on. At the end of the PRK procedure, MMC was applied on the ablated stroma for 1 minute using a surgical sponge and then irrigated with 30 ml of cold sterile balanced salt solution. Patients had follow-up visits everyday until complete reepithelialization and then at 1st and 2nd weeks, and at 2nd, 3rd, and 6th months postoperatively.

Results: The mean preoperative sphere and cylinder were -1.23 D and -1.29 D, respectively, which improved to -0.08 D and -0.30 D, six months after surgery. Mean uncorrected and best corrected visual acuity (UCVA and BCVA) before reoperation were 0.41 and 0.06 logMAR that postoperatively changed to 0.13 and 0.04 logMAR, respectively. At 6 months after surgery, there was no sign of haze formation in any eye. The safety and efficacy indices were 1.13 and 1.06 at this time, respectively.

Conclusion: The application of MMC in PRK for the treatment of low to moderate regressed myopia after LASIK is a safe and effective option. The risk of postoperative haze formation can be reduced using this method.

Keywords: Mitomycin-C, Myopia, Laser in Situ Keratomileusis, Photorefractive Keratectomy, Refractive Error, Regressed Refractive Error

Introduction

Laser in situ keratomileusis (LASIK) is now the most common procedure used for the correction of a wide range of refractive errors.\(^1\) The advantages of this method include faster visual rehabilitation, less discomfort following surgery, better predictable results, and fewer postoperative complications.\(^2,3\) Nonetheless, this safe and effective procedure has its own problems such as intraoperative flap complications,\(^4,5\) possibility of over- or under correction, and regression as well.\(^6,7\) The rate of reoperation based on patients’ request, postoperative results, and surgeon discretion has been reported to be between 5 and 28% of LASIK cases.\(^8\) To correct residual myopia after LASIK, the surgeon considers factors such as residual stromal thickness and the amount of regressed refractive error in choosing the appropriate procedure to avoid the risk of corneal ectasia.\(^1,3,9\) There are several options are suggested as treatment of residual or regressed refractive errors. These can be performed through lifting the original flap, creating a new flap, laser epithelial keratomileusis (LASEK), or photorefractive keratectomy (PRK).\(^2\) PRK as the treatment of residual or regressed errors after LASIK is not recommended by previous studies due to reported severe corneal haze and loss of best corrected visual acuity (BCVA).\(^10\) Mitomycin-C (MMC) is used as a prophylactic agent in recent attempts to reduce these complications and to achieve better BCVA and uncorrected visual acuity (UCVA).\(^4,11,12\) The prophylactic use of MMC has been reported even with flap-related complications.\(^13-15\)

In the present study, we assessed the visual results and complications of PRK+MMC for the treatment of regressed myopia after LASIK.

Methods

In this noncontrolled clinical trial performed through 2004 to 2006, all myopic patients underwent enhancement surgery at least 2 years after their original LASIK were included. Considering refraction, the inclusion criteria were a spherical equivalent (SE) less than -5 diopters (D); spherical error less than 3.00 D and cylinder error less than 1.50 D. Moreover, patients were selected from those who were plano during the first year follow-up of their first refractive surgery. The residual stromal thickness was lower than 300 µm in some patients or was lower than 50% of the primary corneal thickness in the others. Consequently, LASIK was not applicable without the risk of corneal ectasia.

All patients were examined by a blinded examiner. These examinations included tests for UCVA, BCVA, refraction with and without cycloplegia, slit-lamp exam, fundus examination, topography (Pentacam, Oculus HR), pachymetry (ultrasound Nidec 1800). Patients with existing ocular conditions such as glaucoma, retinal or optic nerve disorders, or diabetes and collagen vascular disease were not entered in the study, unless they presented retinal degeneration due to myopia. After slit-lamp and topographic examination, patients with cataract and post LASIK ectasia were excluded.

During the surgical procedure, the corneal epithelium was scraped without the use of alcohol. After PRK, the ablated stroma was coated with MMC 0.02% for 60 seconds using a sponge, and then irrigated with 30 ml of cold sterile balanced salt solution. After completion of the procedure, a bandage contact lens (Air Optix, Cibavision) was placed. Patients were advised to use betamethasone, chloramphenicol, voltaren, and artificial eye drops every 6 hours. Voltaren was discontinued 24 hours after surgery. Once reepithelialization was complete, the contact lens was removed and chloramphenicol was discontinued. Patients continued instilling betamethasone and artificial eye drops every 4 hours for 2 weeks. Betamethasone was replaced by fluoromethalone every 6 hours, 2 weeks after surgery, which was tapered over time and discontinued at 8th postoperative week. All surgeries were done by a single surgeon (HH). In all cases the Technolas 217z Laser (Bausch & Lomb) was used to apply ablations.

Patients were scheduled to have follow-up visits every day until complete reepithelialization, and then weekly visit for two weeks, followed by 1st, 2nd, 3rd, and 6th months’ visits postoperatively. Slit-lamp exam was done at each visit to detect any corneal haze and measure the intraocular pressure (IOP). Refraction and visual acuity (VA) tests were performed in scheduled visits at 1st, 2nd, 3rd,
3rd, and 6th months. Hanna grading (in the scale of 0 to 4+) was used for the assessment of corneal haze.\textsuperscript{11} Data analysis was performed using SPSS for windows software.

**Results**

In this trial, 18 eyes of 11 patients (6 women and 5 men) were re-operated. The mean age of the patients was 39.4±5.2 (range: 28 to 48) years. Mean flap thickness cut during the original LASIK was 148±12.6 \(\mu\)m, and the mean ablation depth was 51.8±27.6 \(\mu\)m. Mean residual stromal thickness and mean corneal thickness before second surgeries were 318±32.2 \(\mu\)m and 466±26.9 \(\mu\)m, respectively. Visual and refractive results of PRK+MMC treatment at different follow-up visits are summarized in Table 1. 66.9% of the eyes were within 0.50 D of the intended SE refraction six months after surgery. Analysis of repeated measures showed that the changes between the first and last postoperative visit and the preoperative visit were statistically significant (P<0.05).

The mean UCVA at the final visit was 0.13±0.15 logMAR (Table 1) that was significantly different from the preoperative value at all visits except the first and second postoperative week (P<0.05). The efficacy index is defined as the ratio of the mean postoperative UCVA to the mean preoperative BCVA. In this series of patients, the efficacy index at six months after surgery was 1.06±0.6.

The mean BCVA at six-month measurement postoperatively was 0.04±0.06 logMAR (Table 1). Compared to the preoperative BCVA, only changes seen in the first and second postoperative weeks were statistically significant and the BCVA was worse in these eyes. The ratio of the mean postoperative BCVA at six months after surgery to the mean preoperative BCVA (Safety index) was 1.13±0.25 logMAR. Two eyes gained two lines and 3 eyes lost one line of BCVA; the others remained unchanged. There was also no sign of any haze formation in any of the studied eyes at the final visit.

**Table 1.** Mean ± standard deviation (95% confidence interval) of PRK+MMC treatment results (refraction, visual acuity, and haze formation) at different follow-up visits

<table>
<thead>
<tr>
<th></th>
<th>Sphere</th>
<th>Cylinder</th>
<th>UCVA</th>
<th>BCVA</th>
<th>Haze</th>
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<tbody>
<tr>
<td>Preoperative</td>
<td>-1.23±1.42</td>
<td>-1.29±0.80</td>
<td>0.41±0.27</td>
<td>0.06±0.13</td>
<td>-</td>
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<tr>
<td></td>
<td>(-1.992 to -0.477)</td>
<td>(-1.714 to -0.861)</td>
<td>(0.265 to 0.547)</td>
<td>(-0.005 to 0.130)</td>
<td>-</td>
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<tr>
<td>Week 1</td>
<td>0.59±0.77</td>
<td>-0.79±0.50</td>
<td>0.25±0.35</td>
<td>0.19±0.20</td>
<td>0.85±0.54</td>
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<tr>
<td></td>
<td>(0.181 to 1.006)</td>
<td>(-1.064 to -0.529)</td>
<td>(0.069 to 0.438)</td>
<td>(0.083 to 0.292)</td>
<td>(0.576 to 1.130)</td>
</tr>
<tr>
<td>Week 2</td>
<td>0.45±0.67</td>
<td>-0.62±0.50</td>
<td>0.26±0.18</td>
<td>0.18±0.12</td>
<td>0.71±0.28</td>
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<tr>
<td></td>
<td>(0.098 to 0.808)</td>
<td>(-0.988 to -0.419)</td>
<td>(0.169 to 0.356)</td>
<td>(0.114 to 0.242)</td>
<td>(0.560 to 0.851)</td>
</tr>
<tr>
<td>Week 4</td>
<td>0.42±0.64</td>
<td>-0.42±0.33</td>
<td>0.23±0.19</td>
<td>0.13±0.14</td>
<td>0.36±0.22</td>
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<tr>
<td></td>
<td>(0.079 to 0.765)</td>
<td>(-0.882 to -0.349)</td>
<td>(0.133 to 0.330)</td>
<td>(0.062 to 0.213)</td>
<td>(0.241 to 0.465)</td>
</tr>
<tr>
<td>Month 2</td>
<td>0.22±0.52</td>
<td>-0.36±0.26</td>
<td>0.18±0.15</td>
<td>0.11±0.14</td>
<td>0.25±0.09</td>
</tr>
<tr>
<td></td>
<td>(-0.060 to 0.498)</td>
<td>(-0.595 to -0.248)</td>
<td>(0.040 to 0.185)</td>
<td>(0.040 to 0.185)</td>
<td>(0.205 to 0.295)</td>
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<tr>
<td>Month 3</td>
<td>0.016±0.36</td>
<td>-0.33±0.29</td>
<td>0.13±0.13</td>
<td>0.07±0.07</td>
<td>0.04±0.10</td>
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<tr>
<td></td>
<td>(-4.871 to 1.809)</td>
<td>(-0.497 to -0.222)</td>
<td>(0.062 to 0.201)</td>
<td>(0.031 to 0.106)</td>
<td>(-0.006 to 0.995)</td>
</tr>
<tr>
<td>Month 4</td>
<td>-0.16±0.32</td>
<td>-0.33±0.29</td>
<td>0.13±0.12</td>
<td>0.08±0.09</td>
<td>0.01±0.06</td>
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<tr>
<td></td>
<td>(-1.871 to 0.156)</td>
<td>(-0.480 to -0.176)</td>
<td>(0.072 to 0.196)</td>
<td>(0.029 to 0.121)</td>
<td>(-0.016 to 0.046)</td>
</tr>
<tr>
<td>Month 6</td>
<td>-0.08±0.45</td>
<td>-0.30±0.26</td>
<td>0.13±0.15</td>
<td>0.04±0.06</td>
<td>0.00±0.00</td>
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<tr>
<td></td>
<td>(-0.315 to 0.159)</td>
<td>(-0.436 to -0.157)</td>
<td>(0.057 to 0.211)</td>
<td>(0.010 to 0.077)</td>
<td>(0.000 to 0.000)</td>
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</table>
Discussion
Performing a second surgery after LASIK is occasionally necessary to correct residual refractive errors due to under correction or regression. A variety of techniques such as ablating the residual stroma after lifting the original flap or creating a new one, ablating the flap, PRK, intrastromal corneal rings, anterior chamber or posterior intraocular lenses (IOLs), and conductive keratoplasty in hyperopic cases. To minimize the risk of associated complications, the surgeon needs to choose the best option of reoperation for each case. For example, although lifting the old LASIK flap or creating a new one have been reported suitable to improve long term UCVA, there may be an increased risk of epithelial ingrowth, perforation, induced irregular astigmatism, or other issues. Moreover, when high amounts of correction have been done during the first LASIK, the residual stromal thickness must be noted. In creating a new flap, keeping the old flap intact, although not impossible, can be problematic. Flap wrinkling and the risk of diffuse lamellar keratitis are other complications of lifting the old flap or creating a new one. In contrast, ablating the flap surface is a simple and effective procedure. According to the previous researches, PRK could be a suitable alternative for reoperation after LASIK, but in this case, the risk of corneal haze and loss of BCVA should be considered. In one study, severe haze was observed in 14 out of 17 patients who had PRK after LASIK. In the present study, we aimed to apply MMC 0.02% on the ablated flap for 1 minute after PRK in order to challenge this concern. Our findings indicated that PRK+MMC can improve UCVA and maintain BCVA. After the second postoperative week, there was a significant decrease in the amount of haze, and eventually, there were no cases of corneal haze at 6 months after reoperation. The mean sphere and cylinder error and UCVA in these patients showed a similar significant improvement starting two weeks after surgery until the sixth postoperative month. BCVA worsened in patients during the first two weeks after surgery, which was due to the effect of surgery or reepithelialization. Then, some improvement was seen in the BCVA which was not statistically significant compared to the preoperative value. An efficacy index of 1.06 and a safety index of 1.13 are in favor of the procedure. In a similar study, Srivasan et al performed PRK+MMC on 30 eyes of 23 patients who had residual refractive error after myopic LASIK. They used a similar concentration of MMC but the application time varied in the range of 30 seconds to two minutes. The authors concluded that the procedure is safe and effective in the treatment of regressed myopia after LASIK, and they found no signs of haze in any cornea. In another study, MMC was used prophylactically to prevent haze formation in the correction of moderate to severe myopia with PRK, and acceptable results were achieved. Hashemi et al also reported that PRK+MMC was effective in preventing corneal haze in the treatment of high myopia with PRK. In the present study, we found no haze at six months after reoperation. This result indicates that technique of intraoperative MMC application in conjunction with PRK can be a safe and effective treatment for regressed myopia after LASIK. One limitation though, is the limited correctable refractive error. Here we studied cases where the SE was up to -5 D. Studies on higher amounts of refractive error with larger sample sizes are warranted.

Conclusion
The intraoperative application of MMC with PRK is safe and effective in the treatment of low to moderate myopia after LASIK. This technique would reduce the risk of corneal haze formation.
References