Evaluation of Results of Photorefractive Keratectomy (PRK) With Mitomycin in Selected Refractive Cases

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Abstract: Purpose: To evaluate the accuracy of postoperative refraction, UCVA, BCVA and possible complications after Photorefractive keratectomy (PRK) using mitomycin C in moderate to high myopia in selected refractive cases that are considered unsuitable for lasik. Methods: twenty one eyes (of 14 myopic patients) were subjected to Photorefractive keratectomy (PRK) using the The ALLEGRETTO WAVE EYE-Q 1010 with application of mitomycin C 0.02%. for one and half minutes after excimer laser ablation. All patients were examined 1,4,7,14 days and 1,3 months after surgery. Results: The age ranged from 20-46 years with a mean of 26.10±5.91 years. The preoperative spherical equivalent refraction (Sph.EQ) ranged from (-2.50 to -9.50D) with a mean of -5.23 ± 2.09 diopters (D). The preoperative central pachymetry ranged from 489-581µ with a mean of 518.11±26.08µ. The preoperative average keratometric readings ranged from 39.8-45.9D with a mean of 43.02±1.63D. The postoperative spherical equivalent ranged from 0.5 to -1.25D with a mean value of -0.26 ±0.49D at 3 months after surgery. The UCVA increased from 0.06±0.03(range 0.017-0.1) preoperatively to 0.76±0.17(range 0.5-1.0) at 3 months postoperatively. The BCVA increased from 0.84±0.17(range 0.5-1.0) preoperatively to 0.89±0.21(range 0.5-1.2) at 3 months postoperatively. Three months after surgery, all eyes had uncorrected visual acuity (UCVA) of 20/40 or better, 14 eyes (81.0%) had uncorrected visual acuity of 20/30 and 4 eyes (19.05 %) achieved UCVA of 20/20. Regarding the BCVA, all cases gained 1 or more lines except 1 eye. Grade 1 corneal haze developed in 5 cases (23.81%) but disappeared completely by 1 month after surgery by which time topical steroid drops was discontinued. Conclusion: PRK with Mitomycin-C provides a promising treatment line for moderate to high myopia in patients that are considered unsuitable for laser in situ keratomileusis (LASIK). However, further research with longer follow-up is suggested. Financial disclosure(s): The authors have no financial interest in any of the materials discussed in this article. Key words: PRK mitomycin-moderate to high myopia –UCVA-BCVA-spherical equivalent (Sph.EQ) corneal haze.

INTRODUCTION

Excimer laser ablation of the corneal stroma is popularly used to correct a refractive error by altering the anterior corneal curvature. Currently, 2 procedures are performed to treat myopia: surface ablation like photorefractive keratectomy (PRK) and laser in situ keratomileusis LASIK (Pop M, Payette Y 2000, Ambrosio R Jr, Wilson SE et al 2001). Although LASIK is becoming more popular than PRK, it can result in various complications associated with the creation of an anterior corneal flap(Tham VM-B, Maloney RK 2000; Stulting RD, Carr JD, et al 1999 and Shah MN, Misra M, et al 2000). There are also cases with insufficient corneal thickness leaving the cornea with an unacceptable residual bed makes LASIK unsafe or limits it to smaller ablation zones that may cause disturbances in night vision when the pupil dilates, or halos and glare (Holladay JT, Dudeja DR, et al 1999). PRK for correcting intermediate to high levels of myopia may result in a strong wound-healing reaction, leading to haze formation and suboptimal refractive outcomes (Wallau AD, Campos M; 2000). MMC is an antimetabolite used in ophthalmology for cases of corneal and conjunctival intraepithelial neoplasms, ocular pemphigoid and during surgical treatment of glaucoma and pterygium. It employs its cytotoxic effects through inhibition of DNA synthesis. The rationale for its use in PRK is based on prevention of keratocyte proliferation and deposition of irregularly generated material leading to scar formation(Sadeghi HM, Seitz B, et al 1998, Schipper I, Suppelt C, et al 1997). Several studies showed the effects of mitomycin C application on the reduction of PRK postoperative haze formation in animal model(Netto MV, Mohan RR, et al 2006, Huizhuo Xu, MD; Shuangzhen Liu, MD; et al 2001). A part from patients with thin corneas, some lasik patients are more liable to flap complications than others; Patients with flat corneas with mean keratometry below 41.00 are at a higher risk of encountering a free cap (Slade SG, 1999), steep corneas are thought to offer higher resistance to the blade excision when applied, resulting in a more superficial pass...
resulting in button hole (Taneri S, Koch JM, et al 2005). In cases of previous button holes, a new LASIK flap after 3 to 6 months may interfere with the first pass and lead to the development of a second buttonhole or other flap abnormality (Tekwani NH, Chalita MR, et al., 2003), different ablation patterns as a result of altered laser ablation rate through the scar of previous button hole resulting in irregular astigmatism and loss of BSCVA. In these cases, a transepithelial PTK/PRK technique is effective before the onset of scarring (Vajpayee RB, Gupta V, et al., 2003; Weisenthal RW, Salz J, et al., 2003).

Therefore PRK with application of mitomycin C to inhibit haze formation might provide a good refractive alternative in cases that does not seem suitable for Lasik.

**Purpose:** To evaluate the refractive outcomes and possible complications after PRK using mitomycin C in moderate to high myopia in selected refractive cases that are considered unsuitable for lasik.

**Methods:** twenty one eyes (of 14 myopic patients) were subjected to Photorefractive keratectomy (PRK) with application of mitoycin C 0.02%. for one and half minutes after excimer laser ablation.

**Technique:**
After topical anaesthesia, mechanical debridement for the central 8mm diameter epithelium was done in all cases (except post-button hole) starting 3mm away from visual axis with a blunt end of spatula and continued to reach the planned diameter while keeping the cornea wet all the time to enable smooth debridement. PTK with 50 μ depth was used for epithelial debridement post-button hole to obtain a regular surface prior to excimer laser ablation by the The ALLEGRETTO WAVE EYE-Q 1010 using a nomogram where 10% undercorrection was used in all cases (to avoid overcorrection associated with mitomycin C usage). Mitomycin C 0.02% is applied for 1.5 minutes to the ablation site following laser ablation and then washed thoroughly with cold BSS with meticulous washing of the fornices, the lid margins and the puncti to remove any traces of mitomycin C to avoid endothelial toxicity and conjunctival toxicity followed by application of a drop of antibiotic—steroid combination and the applying a bandage contact lens for 4 days.

**Post-operatively:**
Antibiotics (morfolaxin 0.5%) eye drops 6 times daily for 1 week, NSAID (diclofenac sodium 0.1%) eye drops 4 times daily for 1 week, Steroid drops (Prednisolone Acetate 1%) eye drops 4 times daily for 1 month and GABA analogue (gabapentin 300mg tablets) twice daily as a pain killer for 2 days.

All patients were examined 1, 4, 7, 14 days and 1, 3 month after surgery. Of the 21 eyes performed, 13 eyes were performed because of thin cornea (<500 μ) to decrease the risk of ectasia, 4 cases because of extensive retinal weakness (to avoid suction on the globe by the suction ring in Lasik), 2 cases because of previous button hole (to avoid irregular cut by the microkeratome and to get rid of the haze from the previous button hole), 1 case because of irregular cornea with facet (following pterygium removal) avoiding good application of Suction ring) and 1 case because of flat cornea (mean K <40D) to decrease the risk of free cap (Table 1 & fig 1).

![Fig. 1: Photos of some cases included in the study.](image-url)
Table 1: number and percentage of cases done as PRK with mitomycin in the study according to the various reasons.

<table>
<thead>
<tr>
<th>Reason for PRK</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>thin cornea (&lt;500 µ)</td>
<td>13</td>
<td>61.91%</td>
</tr>
<tr>
<td>extensive retinal weakness</td>
<td>4</td>
<td>19.04%</td>
</tr>
<tr>
<td>previous button hole</td>
<td>2</td>
<td>9.52%</td>
</tr>
<tr>
<td>IRregular cornea with facet</td>
<td>1</td>
<td>4.76%</td>
</tr>
<tr>
<td>flat cornea (mean K &lt;40D)</td>
<td>1</td>
<td>4.76%</td>
</tr>
</tbody>
</table>

Results:
The age ranged from 20-46 years with a mean of 26.10±5.91 years. The preoperative spherical equivalent refraction (Sph.EQ) ranged from (-2.50 to -9.50D) with a mean of -5.23 ± 2.09 diopters (D). The preoperative central pachymetry ranged from 489 to 581µ with a mean of 518.11±26.08µ. The preoperative mean keratometric readings ranged from 39.8 to 45.9D with a mean of 43.02±1.63D.

The postoperative spherical equivalent ranged from 0.5 to -1.25D with a mean value of -0.26 ±0.49D at 3 months after surgery. The UCVA increased from 0.06±0.03(range 0.017 to 0.1) preoperatively to 0.76±0.17 (range 0.5 to 1.0) at 3 months postoperatively. The BSCVA increased from 0.84±0.17 (range 0.5 to 1.0) preoperatively to 0.89±0.21(range 0.5 to 1.2) at 3 months postoperatively. Three months after surgery, all eyes had uncorrected visual acuity (UCVA) of 20/40 or better, 14 eyes (81.0%) had uncorrected visual acuity of 20/30 and 4 eyes (19.05%) achieved UCVA of 20/20. Regarding the BSCVA 3 months postoperatively, 1 eye (4.76%) gained 4 Snellen lines, 5 eyes (23.8%) gained 2 lines, 4 eyes (19.04%) gained 1 line, while 11 eyes (52.36%) showed no change in BSCVA. No eyes had lost any line of BSCVA. Grade 1 corneal haze developed in 5 cases (23.81%) but disappeared completely by 1 month after surgery by which time topical steroid drops was discontinued (Table 2).

Table 2: number and percentage of cases that postoperatively gained or lost Snellen lines of BSCVA in in the study.

<table>
<thead>
<tr>
<th>Change in BSCVA</th>
<th>No change</th>
<th>Gained 1 line</th>
<th>Gained 2 lines</th>
<th>Gained 4 lines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>11</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Percentage</td>
<td>52.36%</td>
<td>19.04%</td>
<td>23.8%</td>
<td>4.76%</td>
</tr>
</tbody>
</table>

The mean value for the spherical equivalent decreased from -5.23 ± 2.09 diopters (D) preoperatively to a of -0.26 ±0.49D at 3 months after surgery with t-test showing a value of 3.35(P=0.01) denoting a significant difference (Table 3 & chart 1).

Table 3: Comparison of the mean change between preoperative and postoperative 3rd for the Spherical equivalent among patients in the study.

<table>
<thead>
<tr>
<th>Spherical Equivalent in Diopters (D)</th>
<th>Preop. Mean ± S.D.</th>
<th>Postop.3 month Mean ± S.D.</th>
<th>&quot;t&quot; test</th>
<th>P value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-5.23 ± 2.09</td>
<td>-0.26 ±0.49</td>
<td>3.35</td>
<td>&lt; 0.05</td>
<td>Significant</td>
</tr>
</tbody>
</table>

Chart 1: Showing the mean value of the Spherical equivalent (Sph.EQ) in diopters preoperatively and 3 month postoperatively.

The mean value for the uncorrected visual acuity (UCVA) in snellen lines increased from 0.06±0.03 preoperatively to a of 0.76±0.17 at 3 months after surgery with t-test showing a value of 3.47 (P=<0.01) denoting a significant difference (Table 4 & chart 2).

Table 4: Comparison of the mean change between preoperative and postoperative 3rd for the uncorrected visual acuity (UCVA) in snellen lines among patients in the study.

<table>
<thead>
<tr>
<th>Item</th>
<th>Preop. Mean ± S.D.</th>
<th>Postop.3 month Mean ± S.D.</th>
<th>&quot;t&quot; test</th>
<th>P value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>uncorrected visual acuity</td>
<td>0.06±0.03</td>
<td>0.76±0.17</td>
<td>3.47</td>
<td>&lt; 0.05</td>
<td>Significant</td>
</tr>
</tbody>
</table>
The mean value for the best spectacle corrected visual acuity (BSCVA) in snellen lines increased from 0.84±0.17 preoperatively to a of 0.89±0.2 at 3 months after surgery with t-test showing a value of 0.18 (P=>0.05) denoting a non significant difference (Table 5 & chart 3).

Table 5: Comparison of the mean change between preoperative and postoperative 3rd for the best spectacle corrected visual acuity (BSCVA) in snellen lines among patients in the study.

<table>
<thead>
<tr>
<th>Item</th>
<th>Preop. Mean ± S.D.</th>
<th>Postop. 3 month Mean ± S.D.</th>
<th>&quot;t&quot; test</th>
<th>P value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>best spectacle corrected visual acuity (BSCVA) in snellen lines</td>
<td>0.84±0.17</td>
<td>0.89±0.2</td>
<td>0.18</td>
<td>&gt; 0.05</td>
<td>Non Significant</td>
</tr>
</tbody>
</table>

Grade 1 haze developed in 5 cases within the first week but disappeared completely by 1 month after surgery by which time topical steroids were discontinued. Pearson correlation test showed a value of 0.41(P=<0.01) denoting a highly significant correlation between preoperative spherical equivalent and the development of Grade 1 corneal haze in the first week after surgery (Table 6).

Table 6: showing the correlation between preoperative spherical equivalent and the development of Grade 1 corneal haze in the first week after surgery.

<table>
<thead>
<tr>
<th>Item</th>
<th>Correlation coefficient &quot;r&quot;</th>
<th>P value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop.Sph.EQ vs Grade 1 corneal haze week-1</td>
<td>0.41</td>
<td>&lt;0.01</td>
<td>Highly significant</td>
</tr>
</tbody>
</table>

Minimal subepithelial infiltrates developed in 3 cases within the first week but disappeared completely by 1 month after surgery by which time topical steroids were discontinued. Pearson correlation test showed a value of 0.28 (P=<0.05) denoting a highly significant correlation between preoperative spherical equivalent and the development of minimal subepithelial infiltrates in the first week after surgery (Table 7).

Table 7: showing the correlation between preoperative spherical equivalent and the development of minimal subepithelial infiltrates in the first week after surgery.

<table>
<thead>
<tr>
<th>Item</th>
<th>Correlation coefficient &quot;r&quot;</th>
<th>P value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop.Sph.EQ vs Subepithelial infiltrates week-1</td>
<td>0.28</td>
<td>&lt;0.05</td>
<td>significant</td>
</tr>
</tbody>
</table>
Discussion:
Laser in situ keratomileusis (LASIK) is becoming increasingly popular for the correction of a wide range of myopia as it preserves the corneal epithelium and Bowman’s layer, significantly reducing the incidence of corneal haze, scarring and regression seen in photorefractive keratectomy (PRK) (Sugar A, Rupano CJ, et al 2002). But insufficient corneal thickness leaving the cornea with an unacceptable residual bed makes LASIK impossible or limits it to smaller ablation zones causing disturbances in night vision when the pupil dilates, or halos and glare (Holladay JT, Dudeja DR, et al 1999). Also cases with previous button holes (Tekwani NH, Chalita MR, et al 2003), Very flat corneas (Slade SG, 1999), Steep corneas (Taneri S, Koch JM, et al 2005) are associated with a higher incidence of flap complications. Excimer laser photorefractive keratectomy was however associated with development of corneal haze and subepithelial infiltrates in a variety of studies (Carson CA, Taylor HR 1995; Teal P, Breslin C, et al 1995, Probst LE, Machat JJ 1996, O’Brart DP, Corbett MC et al 1996, Malondafe MJ, Amal V, et al 1996). The addition of mitomycin C (MMC) as an adjunctive to Excimer laser photorefractive keratectomy (PRK) has recently been used as an alternative to laser in situ keratomileusis (LASIK) for surgical correction of refractive errors with promising results (Gambato C, Ghirlando A., et al 2005, A D Wallau, M Campos 2009).

In this study we will study the safety, efficacy and predictability of PRK with mitomycin 0.02% in moderate to high myopia to find if it can provide a good alternative treatment to cases that are unsuitable for Lasik or are associated with a high risk of Lasik complications.

The age ranged from 20-46 years with a mean of 26.10±5.91 years. The preoperative spherical equivalent refraction (Sph.EQ) ranged from (-2.50 to -9.50 D) with a mean of 5.23 ± 2.09 diopters (D). The preoperative Central pachymetry ranged from 489-581 µ with a mean of 518.11±26.08 µ. The preoperative mean keratometric readings ranged from 39.8-45.9 D with a mean of 43.02±1.63 D.

The mean value for the spherical equivalent decreased from -5.23 ± 2.09 diopters (D) preoperatively to a of -0.26 ±0.49 D at 3 months after surgery with t-test showing a value of 3.35(P=<0.01) denoting a significant difference. The UCVA increased from 0.06±0.03(range 0.017-0.1) preoperatively to 0.76±0.17(range 0.5-1.0) at 3 months postoperatively with t-test showing a value of 3.47 (P=<0.01) denoting a significant difference. The BSCVA increased from 0.84±0.17(range 0.5-1.0) preoperatively to 0.89±0.21(range 0.5-1.2) at 3 months postoperatively with t-test showing a value of 0.18 (P=>0.05) denoting a non significant difference. Three months after surgery, all eyes had uncorrected visual acuity (UCVA) of 20/40 or better, 14 eyes (81.0%) had uncorrected visual acuity of 20/30 and 4 eyes (19.05%) achieved UCVA of 20/20. Regarding the BSCVA 3 months postoperatively, 1 eye (4.76%) gained 4 lines, 5 eyes (23.8%) gained 2 lines, 4 eyes (19.04%) gained 1 line, while 11 eyes (52.36%) showed no change in BSCVA. No eyes had lost any line of BSCVA. Grade 1 corneal haze developed in 5 cases (23.81%) but disappeared completely by 1 month after surgery by which time topical steroid drops was discontinued. Pearson correlation test showed a value of 0.41(P=<0.01) denoting a highly significant correlation between preoperative spherical equivalent and the development of Grade 1 corneal haze in the first week after surgery. Minimal subepithelial infiltrates developed in 3 cases within the first week but disappeared completely by 1 month after surgery by which time topical steroids were discontinued. Pearson correlation test showed a value of 0.28 (P=<0.05) denoting a highly significant correlation between preoperative spherical equivalent and the development of minimal subepithelial infiltrates in the first week after surgery.

Pujara T, Sridhar M et al 2008, presented 12 eyes of 6 patients underwent the PRK with mitomycin C application. All were females with age range of 20 to 45 years. Pre-operative refractive error ranged from -6.75 Ds to -9.25 Ds. Indications for PRK was thin cornea in 8 eyes and forme fruste keratoconus in 4 eyes. The corneal thickness ranged from 457 µ to 502 µ in thin cornea group. In all eyes 10% under correction was planned and Mitomycin C was applied for 30 seconds to 1 minute. 6/12 or better vision was achieved in all except 1 eye (91.6%). Only one had a visual acuity of 6/18 with a spherical equivalent of +2 Ds at one month follow up visit.

Fazel F, Naderiben A., et al., 2008. studied 37 high myopic patients (72 eyes) who had PRK surgery with mitomycin C. The mean follow up period was 27.2 ± 7.9 months. The spherical equivalent error was significantly reduced, from a mean of -9.10 ± 2.12 diopters (D) (range of -7 to -18.25 D) before PRK to a mean of -1.81 ± 1.57 D (range of -8.5 to 0 D) after PRK (P = 0.001). Postoperatively, 34.72% of eyes were within ± 0.5 D of attempted correction and 58.33% within ±1 D and 84.72% within ±2 D. 80.5% of eyes had a vision of 20/40 or better. Best corrected visual acuity (BCVA) was unchanged or improved in 93.05%. Corneal haze formation was seen in 5 patients (6.9%) with grade +1.

Taneri S, MD, Koch M, MD et al., 2005. studied a case report where MMC assisted transepithelial PTK/PRK was successful in removing central haze formation and epithelial ingrowth originating from a buttonhole and in preventing its recurrence and any loss of visual acuity for a follow-up period of 12 months with relatively quick visual rehabilitation.
Conclusion:
PRK with Mitomycin-C provides a promising treatment line for moderate to high myopia in patients that are considered unsuitable for laser in situ keratomileusis (LASIK), due to various causes with no case showing any grade of residual haze by one month postoperative and with increase in BSCVA in most cases and with excellent refractive predictability. However, further research with longer follow-up is suggested.

Financial Disclosure(S):
The authors have no financial interest in any of the materials discussed in this article.

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