Comparison of Standard and Low Dose Intraoperative Mitomycin C in Prevention of Corneal Hazeafter Photorefractive Keratectomy

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ABSTRACT

Background: This study aimed to compare two doses of Mitomycin C in reducing haze formation after photorefractive keratectomy.

Methods: 170 eyes of 85 patients enrolled; in each patient one eye randomly assigned to be treated by low dose intraoperative MMC (LDMMC) and other eye by standard dose MMC (SDMMC). Then the patients were followed up to 6 months and refraction, Uncorrected Distant Visual Acuity (UCDVA), Best Corrected Distant Visual Acuity (BCDVA) and haze formation submitted in each postoperative exam.

Results: The mean preoperative refraction in LDMMC eyes was –3.08 (SD 1.65) sphere and 0.92 (SD 0.88) cylinder. These values for SDMMC eyes were –3.25 (SD 1.80) sphere and 0.81 (SD 0.84) cylinder. Mean postoperative sphere in LDMMC group was –0.132 (SD 0.503) and –0.138 (SD 0.484) in 3 and 6 months after PRK. These results was –0.041 (SD 0.501) and –0.076 (SD 0.489) for SDMMC group. Mean postoperative cylinder 3 and 6 month after PRK was 0.435 (SD 0.218) and 0.423 (SD 0.255). In LDMMC group and 0.435 (SD 0.247) and 0.426 (SD 0.261) in SDMMC group. In third month 14 eyes in LDMMC group presented with grade 1 score of clinical haze. From these eyes only 2 still had this haze after 6 month. 7 eyes in SDMMC group had grade 1 clinical haze at third month- but no clinical haze was seen at the end of 6th month.

Conclusion: The results of the two doses of Mitomycin C were not significant. We suggest to use the lower dose to reduce its side effects.

Keywords: Photorefractive keratectomy, Mitomycin C, corneal haze

INTRODUCTION

Refractive surgery is an evolving ground in recent ophthalmology and photorefractive keratectomy (PRK) is one of the most popular means to correct refractive error of the eye. Many studies have carried to evaluate long-time stability,

complications and causative factors in eyes underwent PRK.[1,2] Kim *et al.,* showed that myopic regression can occur up to 5 years after surgery and pre-PRK refraction is the most important factor.[1]

Alteration in extracellular components after PRK along with generation of myo-fibroblast may reduce corneal transparency which may present as sub-epithelial haze and can be clinically significant in many cases.[3]

Applying intraoperative Mitomycin C (MMC) as an effort to reduce the rate of corneal haze has tried earlier and in numerous studies prophylactic use of MMC 0.02% was associated with lower rates of haze formation and better visual outcomes.[4,5] Majmudar *et al.,* revealed that topical application of MMC (0.02%) may be a successful method of preventing recurrence of subepithelial fibrosis after corneal surgery.[4] Anyway, concerns persist regarding MMC toxicity and long-term complications such as corneal melting and endothelial cell loss.[6,7]

There is one report of corneal edema after phototherapeutic keratectomy (PTK) including intraoperative use of MMC 0.02%. Although evidences of keratocyte apoptosis and myo-fibroblast death which had leaded to reduced corneal cellularity after MMC use is of great concern.[8-11] Effect of Mitomycin C application on endothelial cells has reported in many studies[12] when the ocular surface alteration is also possible.[13]

Because the standard dose of intraoperative MMC (0.02%) has driven empirically based on pterygium removal and glaucoma filtering surgery results many controversies persist in dosing and timing of MMC usage.[14] Because timing of MMC application seems less important than the dosage, this study tries to find the effect of low dose MMC (0.01%) intraoperative use in PRK versus standard dose (0.02%) in preventing corneal haze and promoting desirable visual outcome.

METHODS

All the patients with inclusion criteria were informed of the study and written consent obtained. These patients were myopic patients with ages between 20 and 30 years who will to correct their refractive error by PRK. 170 eyes of 85 patients included. Primary evaluation of refraction, uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), slit-lamp examination with fundus evaluation performed and eyes with any disorder that could influence postoperative outcomes were excluded.

After all, the eyes divided into two arms, in each patient one eye randomly assigned to be treated by low dose intraoperative MMC (LDMMC) and other eye by standard dose MMC (SDMMC). All operations were done by one surgeon. After scrub by povidone-iodine topical anesthetic drop instilled and eyes were treated by Technolas 217z-100 laser ablation and then MMC applied by Weck-cell spongefor 45 seconds. Then the surface irrigated by balanced salt solution.

Postoperative examination done 1 week, 1 month, 3 month and 6 month afterwards, regarding refraction, uncorrected distant visual acuity (UCDVA), best corrected distant visual acuity (BCDVA) and haze formation score, respectively. Haze intensity according to the Frantes scale was graded as no haze, trace, 1, 2, 3 and 4.

Then *t*-test and Mann-Whitney tests were used to analysis the outcome considering 85% power.

RESULTS

170 eyes of 85 patients underwent photorefractive keratectomy between May and November 2011 (23 men and 62 women).

Mean age of the patients in this study was 25.98 years (Range: 20-30 years).

The mean preoperative refraction in LDMMC eyes was –3.08 (SD 1.65) sphere and 0.92 (SD 0.88) cylinder. These values for SDMMC eyes were –3.25 (SD 1.80) sphere and 0.81 (SD 0.84) cylinder.

Mean postoperative sphere in LDMMC group was –0.132 (SD 0.503) and –0.138 (SD 0.484) in 3 and 6 months after PRK. These results was –0.041 (SD 0.501) and –0.076 (SD 0.489) for SDMMC group.

Mean postoperative cylinder 3 and 6 month after PRK was 0.435 (SD 0.218) and 0.423 (SD 0.255) in LDMMC group and 0.435 (SD 0.247) and 0.426 (SD 0.261) in SDMMC group.

In third month 14 eyes in LDMMC group presented with grade 1 score of clinical haze. From these eyes only 2 still had this haze after 6 month. 7 eyes in SDMMC group had grade 1 clinical haze

at third month - but no clinical haze was seen at the end of 6th month.

Comparison of two arms of this study did not disclose any significant difference in preoperative parameters including refraction, UCDVA and BCDVA. *t*-test study also reveals no meaningful difference in these parameters in postoperative measurements.

Comparison of haze formation rate in these two groups by Mann-Whitney test demonstrated no significant difference in results (P = 0.104 3rd month and P = 0.156 6th month after operation).

DISCUSSION

Application of intraoperative MMC is a valuable mean to prevent corneal haze especially in high myopic patients but concerns about its side effects lead us to determine if a lower dose of MMC may be as effective as the standard dose. Midena *et al*. demonstrated that 0.02% topical MMC has no significant adverse effect on corneal keratocytes.[15] Goldsberry *et al*. also remarks no side effect of MMC on endothelial quantitative and qualitative parameters.[16] Although Netto *et al*. reported that MMC may cause keratocyte and myo-fibroblast apoptosis and decrease in anterior stromakeratocyte density may lead to future complications.[17]

According to our study there was no significant difference in visual outcome or haze formation by use of lower dose of MMC (0.01%) compared with standard dose (0.02%).

CONCLUSION

Our findings shows that low dose intraoperative MMC has the same effect as standard dose in prevention of corneal haze and visual outcomes have no meaningful difference while it promises lower side effects and long-term complications.

REFERENCES

1. Kim JH, Kim MS, Hahn TW, Lee YC, Sah WJ, Park CK. Five years results of photorefractive keratectomy for myopia. J Cataract Refract Surg 1997;23:731-5.
2. Haviv D, Hefetz L, Krakowsky D, Abrahami S, Kibarski U, Nemet P. For how long can regression continue after photorefractive keratectomy for myopia? Ophthalmology 1997;104:1948-50; discussion 1950-1.
3. Moller-Pedersen T, Cavanagh HD, Petroll WM, Jester JV. Stromal wound healing explains refractive instability and haze development after photorefractive keratectomy: A 1-year confocal microscopic study. Ophthalmology 2000;107:1235-45.
4. Majmudar PA, Forstot SL, Dennis RF, Nirankari VS, Damiano RE, Brenart R, *et al*. Topical mitomycin-C for subepithelial fibrosis after refractive corneal surgery. Ophthalmology 2000;107:89-94.
5. Xu H, Liu S, Xia X, Huang P, Wang P, Wu X. Mitomycin C reduces haze formation in rabbits after excimer laser photorefractive keratectomy. J Refract Surg 2001;17:342-9.
6. Alió JL, Artola A, Claramonte PJ, Ayala MJ, Sánchez SP. Complications of photorefractive keratectomy for myopia: Two year follow-up of 3000 cases. J Cataract Refract Surg 1998;24:619-26.
7. Chabner BA, Ryan DP, Paz-Ares L, Garcia-Carbonero R. Anti-Neoplastic agent. In: Hardman JG, limbira LE, editors. Goodman and Gillman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: MC Graw Hill; 2001. p. 1389-459.
8. Kim TI, Tchah H, Lee SA, Sung K, Cho BJ, Kook MS. Apoptosis in keratocytes caused by mitomycin C. Invest Ophthalmol Vis Sci 2003;44:1912-7.
9. Smith S, D'Amore PA, Dreyer EB. Comparative toxicity of mitomycin C and 5-fluorouracil *in vitro*. Am J Ophthalmol 1994;118:332-7.
10. McDermott ML, Wang J, Shin DH. Mitomycin and the human corneal endothelium. Arch Ophthalmol 1994;112:533-7.
11. McKelvie PA, Daniell M. Impression cytology following mitomycin C therapy for ocular surface squamous neoplasia. Br J Ophthalmol 2001;85:1115-9.
12. Nassiri N, Farahangiz S, Rahnavardi M, Rahmani L, Nassiri N. Corneal endothelial cell injury induced by mitomycin-C in photorefractive keratectomy: Nonrandomized controlled trial. J Cataract Refract Surg 2008;34:902-8.
13. Dogru M, Erturk H, Shimazaki J, Tsubota K, Gul M. Tear function and ocular surface changes with topical mitomycin (MMC) treatment for primary corneal intraepithelial neoplasia. Cornea 2003;22:627-39.
14. Virasch VV, Majmudar PA, Epstein RJ, Vaidya NS, Dennis RF. Reduced application time for prophylactic mitomycin C in photorefractive keratectomy. Ophthalmology 2010;117:885-9.
15. Midena E, Gambato C, Miotto S, Cortese M, Salvi R, Ghirlando A. Long-term effects on corneal keratocytes of mitomycin C during photorefractive keratectomy:

A randomized contralateral eye confocal microscopy study. J Refract Surg 2007;23:S1011-4.
16. Goldsberry DH, Epstein RJ, Majmudar PA, Epstein RH, Dennis RF, Holley G, *et al*. Effect of mitomycin C on the corneal endothelium when used for corneal subepithelial haze prophylaxis following photorefractive keratectomy. J Refract Surg 2007;23:724-7.
17. Netto MV, Mohan RR, Sinha S, Sharma A, Gupta PC, Wilson SE. Effect of prophylactic and therapeutic mitomycin C on corneal apoptosis, cellular proliferation, haze, and long-term keratocyte density in rabbits. J Refract Surg 2006;22:562-74.

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