Acta Scientific Ophthalmology (ISSN: 2582-3191)

Volume 4 Issue 6 June 2021

Case Report

# Corneal Epithelial Toxicity Following Intraoperative Use of Mitomycin C during Trabeculectomy - A Case Report

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**Received:** May 08, 2021

**Published:** May 19, 2021



## Abstract

We report a case of post-operative corneal epithelial toxicity following intra operative subconjunctival use of Mitomycin C for 1.5 minutes in twin site phacoemulsification and Trabeculectomy. Patient was doing well till 15 days after the surgery with the clear cornea and 20/20 vision. Then he noticed diminution of vision and cornea showed multiple punctate corneal erosion. On persistence of the lesion till five weeks after the surgery corneal scraping was done and sent for histopathological examination which showed Mitomycin related toxicity. With proper diagnosis and treatment patient improved well with a central clear cornea and vision 20/30. With guarded use and keen eye for possible complications in the follow-up visits one can avoid the undesirable and hazardous effects of MMC.

**Keywords:** Corneal Epithelial Toxicity; Mitomycin C; Trabeculectomy

## Introduction

Mitomycin C (MMC), a naturally derived antineoplastic alkylating agent, has been widely used in ophthalmology owing to its anti-fibroblastic activity, which attributes to its modulatory effect on wound healing [1]. MMC, as an adjunct to trabeculectomy, was a major advance in the ability to improve the intraocular pressure (IOP) lowering efficacy of the procedure and to reduce postoperative episcleral fibrosis and bleb failure [2].

## Case History

A 70 year old gentleman, a known case of primary open angle glaucoma (POAG), on topical medications- Brimonidine (0.15%) and Timolol Maleate (0.5%) presented to us with complaints of diminution of vision in both eyes since 6 months. On examination best corrected visual acuity (BCVA) was 20/40 in both eyes. Anterior segment examination revealed immature cataract, with a Goldmann applanation tonometry recording an IOP of 16 mm Hg in both eyes and Open angles on Gonioscopy. Fundus showed a cup disc ratio (CDR) of 0.8 and an inferior neuroretinal rim (NRR) loss in the right eye, while the left eye had a CDR of 0.9, with a bipolar loss of NRR. Pachymetry was 499 microns in the right eye and 511 microns in left eye. Humphrey visual field analysis showed a dense superior arcuate scotoma in the right eye and a dense biarcuate scotoma in the other eye. Considering the moderately advanced stage of glaucoma with a cataract in the left eye, Phacoemulsification with MMC enhanced Trabeculectomy for the left eye with a two site approach was planned. The intraoperative regimen that we followed was the use of MMC (0.2 mg/ml) soaked in a polyvi-

nyl alcohol (PVA) sponge placed in sub-conjunctival space for 1.5 minutes, followed by irrigation with 20 ml balanced salt solution. The intraoperative period was uneventful. Post-operatively an antibiotic-steroid combination (Moxifloxacin and Dexamethasone) was prescribed on a tapering schedule along with a cycloplegic eye drops for 15 days.

The patient was doing well at one week follow up with a BCVA of 20/20, N6 and IOP of 16 mm of Hg. However, in the 2nd week follow-up, his BCVA had dropped to 20/63 and the anterior segment showed multiple punctate epithelial erosions (PEEs) on the cornea and hence Carboxy-methyl-cellulose drops were added. IOP recorded was 16 mm of Hg, He was subjected to a closer follow-up and on the 3rd day owing to the persistence of the unhealthy ocular surface, D-panthenol gel (5%) was added and discontinued steroids. However, at the 5th postoperative week, when the clinical picture persisted, we decided to scrape the unhealthy corneal tissue for a histopathological examination (Figure 1 and 2). The cytological study showed sheets of squamous epithelial cells accompanied by dense mixed inflammation, few of the cells showed mild nucleomegaly with prominent nucleoli which are suggestive of and consistent with MMC related epithelial toxicity (Figure 3). Considering this we re-started the patient on topical steroid, (Chloramphenicol and dexamethasone) on a tapering schedule, lubricant drops and D-Panthenol gel. Following this, the ocular surface started improving. At 2 months follow up, his BCVA was 20/30 with few peripheral corneal opacities and an IOP of 16 mm of Hg (Figure 4).

**Figure 1:** Slit lamp photograph showing diffuse unhealthy corneal epithelium with PEEs

**Figure 2:** Slit lamp photo showing large epithelial defect after scraping the epithelium.

**Figure 3:** Histopathological picture suggestive of MMC toxicity.

## Discussion and Conclusion

Long-term follow-up of primary trabeculectomy without adjunctive MMC indicates that despite successful control of IOP at 1 year, the probability of success decreases with time and stabilizes at 67% by 10 years [3]. This has revolutionized the use of MMC as an adjuvant to trabeculectomy. However, its judicious and cautious use becomes imperative, keeping in mind the deleterious ocular side effects, which, though infrequent, could be functionally debilitating and possibly sight threatening too [4].

**Figure 4:** Two months post-operative Slit lamp photo (Diffuse illumination) showing clear cornea with few peripheral opacities.

With respect to the corneal complications, greater endothelial cell loss has been found to be more common following MMC augmented trabeculectomy as compared to standard trabeculectomy [5]. However, there is a paucity of literature on the possible epithelial toxicity associated with MMC. Coppens., *et al*. [6] reported 2 cases of MMC induced epitheliopathy following trabeculectomy, of which one had a similar clinical picture as our case while the other case progressed to corneal melt. Few others studies that have reported MMC related corneal epithelial toxicity however, were following its use in various other procedures like phototherapeutic keratectomy, Pterygium surgery [7,8].

The probable mechanism of drug toxicity could be due to the apoptotic effect of MMC, inhibiting the proliferation of all cells into which it enters in sufficient concentration, including stromal and epithelial cells [9]. Intra-operative use could similarly also cause limbal stem cell damage leading to epithelial toxicity occurring two to three weeks postoperatively.

Sodium hyaluronate eye drops has been recommended in the post-operative period to prevent the development of postoperative corneal epitheliopathy by washing out the remaining MMC from the ocular surface [6,10]. It also stimulates corneal epithelial migration and accelerates healing of corneal epithelial defects.

This paper highlights the potentially toxic effects of MMC on ocular surface. Though there are several studies on the corneal side effects of MMC, there are only a handful of reports on its epithelial toxicity. In addition, the histopathological confirmation of the same in our study, makes the diagnosis of this MMC related epitheliopathy distinctive. One must be cautious in the use of MMC, with respect to its dose, duration of use, handling of the drug. The presence of underlying risk factors which could pose a threat to the ocular surface must be identified and addressed. With guarded use and keen eye for possible complications in the follow-up visits one can avoid the undesirable and hazardous effects of MMC, and rather reap the benefits of this adjunctive drug.

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**Volume 4 Issue 6 June 2021**