

# Comparative evaluation of outcomes of novel approach of subconjunctival Mitomycin C (MMC) injection at the end of trabeculectomy versus intraTenon injection of MMC prior to the initial conjunctival incision – A pilot study

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**Purpose:** To describe a novel approach of subconjunctival injection of mitomycin C (MMC) at the end of trabeculectomy and compare it with intraTenon MMC injection. **Methods:** This pilot study included 40 eyes of 40 patients with uncontrolled primary and secondary glaucoma. Patients below 18 years and failed trabeculectomy were excluded. Patients were randomly allocated into groups A and B (20 patients each). Group A patients received subconjunctival MMC injection in the superonasal quadrant at the end of standard trabeculectomy. Group B received an intraTenon MMC injection before the initial conjunctival incision. Outcome measures included intra-ocular pressure (IOP) reduction, bleb morphology, and complication rates. The complete success was defined as an IOP of  $\leq 21$  mmHg without antiglaucoma drugs. **Results:** The mean preoperative IOP of  $46.00 \pm 11.2$  mmHg in group A and  $43.05 \pm 10.3$  mmHg in group B reduced to  $12.00 \pm 2.41$  mmHg ( $P \leq 0.001$ ) in group A and  $13.65 \pm 2.76$  mmHg in group B ( $P \leq 0.001$ ) at last follow-up. Complete success was 95% and 75% in groups A and B, respectively, 19 months after surgery. Avascular microcystic blebs (70% of group A and 45% of group B) were more common than avascular white blebs (15% in group A and 35% in group B). No intraoperative complications were seen. Postoperative wound leak, hypotony, choroidal detachment, or endophthalmitis were not encountered in any group. **Conclusion:** A novel approach of subconjunctival MMC application during trabeculectomy is reported. Both approaches appear to be highly effective in reducing IOP in primary and secondary glaucoma with similar safety profiles and bleb morphology. Subconjunctival MMC yielded a greater success rate (95%) compared to the intraTenon MMC group (75%).

**Key words:** IntraTenon, mitomycin C, subconjunctival injection, trabeculectomy

Glaucoma is the leading cause of global irreversible blindness. The number of people with glaucoma worldwide has been estimated to be 76.0–79.6 million in 2020 and 111.8 million in 2040.<sup>[1]</sup> The beneficial effect of lowering IOP in halting the progression of the disease has been conclusively established.<sup>[2]</sup> Although trabeculectomy remains the gold standard surgical procedure, the waning success rate (63% at 1 year, 54% at 2 years, 45% at 3 years, and 40% at 4 years<sup>[3]</sup>) over time is a serious concern. Scarring of the drainage fistula created is considered the major cause for failure of trabeculectomy.<sup>[4]</sup> Therefore, antimetabolites such as MMC have been tried, which affect the wound healing response. Studies have proven that the method of application of MMC during trabeculectomy contributes to the morphology of the drainage bleb and its long term survival.<sup>[5]</sup> The inherent drawback of using MMC are hypotony, shallow/flat anterior chamber (AC), choroidal detachment, cystic blebs, leaking blebs, blebitis, and late-onset endophthalmitis.<sup>[6]</sup>

Various concerns with the use of sponges soaked with MMC are its inability to determine the actual quantity of the drug delivered to the tissues and the lack of standardized sponge

material or size, which leads to inconsistent and unreliable absorption of MMC into the sponge material.<sup>[7,8]</sup> The effect of irrigating the site of MMC application with saline is also variable, and surgeons must use multiple sponges for a more diffuse application, which increases the risk of retained sponge fragments.<sup>[7]</sup>

To circumvent the above mentioned disadvantages, injection methods of MMC application have been tried in intraTenon, subconjunctival, and subTenon spaces prior to the conjunctival incision in trabeculectomy. The literature is scanty regarding the intraoperative use of MMC injection in trabeculectomy.<sup>[7,9-12]</sup>

To the best of our PubMed search, no study has described and evaluated the technique of injecting subconjunctival MMC at the end of trabeculectomy.

The present study, therefore, reports a novel approach of subconjunctival injection of MMC at the end of trabeculectomy

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and compares the results and complications with those of injecting MMC prior to the initial conjunctival incision. We hypothesize that postoperative MMC injection may ensure 100% delivery and diffuse and posterior application of MMC, leading to lower postoperative IOP and diffuse bleb formation.

## Methods

This pilot study enrolled 40 eyes of 40 patients with uncontrolled primary and secondary open/closed angle glaucoma from March 2017 to May 2018 after approval from the institutional ethics committee. The study adhered to the tenets of the Declaration of Helsinki. Patients with age <18 years, no light perception vision, combined surgery, follow-up <3 month, dry eyes, failed trabeculectomy, viral keratitis, active uveitis, and pregnant/lactating females were excluded.

After informed consent, the patients were randomly allocated according to a computer-generated block randomization table into group A (20 patients), who underwent trabeculectomy augmented with subconjunctival injection of MMC at the end of the procedure, and group B (20 patients), who underwent trabeculectomy augmented with an intraTenon injection of MMC prior to the initial conjunctival incision.

After a detailed glaucoma workup including IOP measurement by Goldmann applanation tonometry (GAT) or Tonopen (where GAT was not possible), group A patients underwent standard trabeculectomy with limbal-based conjunctival-Tenon flap and 4 mm × 4 mm × 4 mm triangular partial thickness scleral flap at the 12-o'clock position. The scleral flap was closed tightly with seven (10-0 nylon) interrupted sutures [Fig. 1a]. MMC 0.1 mL (0.02 mg) was injected subconjunctival 10 mm above the limbus and 2 mm medial to the superior rectus muscle [Fig. 1b]. In group B patients, MMC 0.1 mL (0.02 mg) was injected intraTenon at the same site as group A before the initial conjunctival incision [Fig. 2a]. After injecting, the area was washed with 10 mL saline followed by spreading of the injected MMC with the help of lens spatula [Fig. 2b]. A conjunctival-Tenon flap as in group A was made. The dissected area was again washed with 15 mL saline. Standard trabeculectomy as in group A was performed.

All surgeries were done by a single surgeon (VPG) at a single institute, and the same postoperative care was given to patients of both groups, that is, they were bandaged with moxifloxacin 0.5% and administered atropine 1% eye ointment daily for 3 days, followed by topical moxifloxacin 0.5%, topical prednisolone acetate 1%, and homatropine 2% four times a day for 3 weeks. The IOP reduction, bleb morphology, success and complication rates were the main outcome measures. Complete success was defined as postoperative IOP ≤21 mmHg without marked loss of visual acuity, prolonged hypotony (IOP <6 mmHg over 3 months), or requirement for additional surgery to control IOP or treat postoperative complications. Qualified success was defined as achieving the above with additional antiglaucoma drugs.

Follow-up was done on postoperative day 1, day 7, and monthly thereafter till the end of the study. At each visit, parameters such as visual acuity, IOP, AC depth (Van Herick's method),<sup>[13]</sup> and bleb assessment (The Indiana Bleb Appearance Grading Scale<sup>[14]</sup>) were determined. Data were analyzed by applying the Mann-Whitney test, Independent

*t* test, Chi-square test, and Fisher's exact test by using SPSS software version 21.0.

## Results

The demographic and clinical details of groups A and B are summarized in Table 1. The two treatment groups were similar in composition ( $P = 0.320$ ); however, group A had a significantly higher proportion of eyes with secondary glaucoma than group B [9 patients (45%) vs. 3 patients (15%), respectively]. The baseline mean IOPs for groups A and B were not significantly different ( $P = 0.392$ ) [Table 1]. The baseline IOP was significantly reduced postoperatively in both group A ( $P \leq 0.001$ ) and group B ( $P \leq 0.001$ ) [Table 1]. All patients in both groups achieved an IOP reduction of  $\geq 2/3^{\text{rd}}$  from the baseline IOP on day 1. At 12 months, an IOP reduction of  $\geq 2/3^{\text{rd}}$  occurred in 15 (75%) patients of group A and 11 (55%) of group B, while  $\geq 30\%$  reduction was noted in 19 (95%) patients of group A and 15 (75%) patients of group B. The mean IOP decrease at last follow-up was higher in group A (74%) than in group B (68%) ( $P = 0.051$ ) [Table 1].

The mean postoperative IOP for groups A and B on day 1, day 7, 1 month, 3 months, 6 months, and last follow-up are depicted in Table 2. The mean IOP reductions from baseline were significant in both groups at each follow-up ( $P < 0.05$ ) [Table 2]. Group A had lower IOP than group B at all follow-up visits; however, it was statistically significant only on day 1 ( $P = 0.037$ ) and 1 month postoperatively ( $P = 0.017$ ) [Table 2]. The mean IOP at 3 months, 6 months, and last follow-up for both groups showed a greater absolute decrease in IOP in group A than in group B ( $P > 0.05$ ) [Table 2]. One patient (5%) (PPK with SG) of group A and five (25%) (3 PACG, 2 POAG) of group B required antiglaucoma drugs post-surgery to bring their IOP to  $\leq 21$  mmHg. The complete and qualified success rates were achieved in 19 (95%) patients and one (5%) patient in group A, and 15 (75%) patients and 5 (25%) patients in group B, respectively, at the last follow-up [Table 1]. This difference between the two groups was not statistically significant ( $P = 0.091$ , Fischer's exact test).

At 6 months, avascular microcystic (AM), mostly medium blebs extending 3–6 clock hours were significantly more in group A (70%) [Fig. 1d-f] compared to group B (40%) [Fig. 2c-e], while avascular white blebs (AW) were significantly more in group B (35%) [Fig. 1f-g] compared to group A (15%) [Fig. 1c] [Fig. 1c-h and Fig. 2 c-h; Table 3]. Low blebs with moderate vascularity extending  $>2$  to  $<4$  clock hours were observed in three (15%) [Fig. 1g-h] and four (20%) patients [Fig. 2h] of groups A and B, respectively [Table 3]. The vertical and horizontal extent of blebs in both groups were comparable. Furthermore, 65% blebs of both groups extended  $>4$  clock hours (E3), and 35% in both groups extended  $>2$  to  $<4$  clock hours (E2) [Table 3]. The blebs extended posteriorly 7–12 mm from the limbus with a mean of 10.2 mm in group A and 7–10 mm with a mean of 8.91 mm in group B.

No bleb leaks or encapsulated blebs were encountered in any groups. Peribleb congested vessels were noted in 9 and 12 patients of groups A and B, respectively.

Five patients, including one patient each of AM and AW and three out of four moderately vascular blebs in group B,

**Table 1: Patients' demographics, diagnosis, pre and postoperative IOP, follow up and success rates in groups A and B**

Baseline and postoperative data	Group A (post trab S/C MMC): n=20	Group B (pre trab I/T MMC): n=20	P	
Sex: male/female	13 (65%)/7 (35%)	12 (60% )/8 (40%)	0.519	
Mean Age (range) years	49.75±12.84 (21-70)	53.20±11.23 (36-70)	0.372	
Right eye/Left eye	10 (50%)/10 (50%)	09 (45%)/11 (55%)	>0.05	
Diagnosis: POAG	8	11	>0.05	
PACG	3	6	>0.05	
PPK with SG	4	1	>0.05	
PT SG	2	1	>0.05	
PBK with SG	2	00	>0.05	
ABK with SG	1	00	>0.05	
Post uveitic SG	00	1	>0.05	
Lens status: phakic/pseudophakic/aphakic	12/7/1	19/1/0	-	
Mean Baseline IOP (mmHg) (range)	46.00±11.2 (28-64)	43.05±10.3 (22-58)	0.392	
Mean Post op IOP at 3 months (mmHg) (range)	12.10±3.09 (6-17)	12.70±2.88 (8-18)	0.530	
Mean Post op IOP at last follow-up (mmHg) (range)	12.00±2.41 (10-18)	13.65±2.76 (9-20)	0.051	
Mean % IOP decrease at last follow-up	74 (50-83)	68 (36-82)	0.051	
Complete Success rate: n (%)				
POAG	$\left\{ \begin{array}{l} 8/8 (100) \\ 3/3 (100) \\ 8/9 (88.89) \end{array} \right\}$	$\left\{ \begin{array}{l} 9/11 (81.82) \\ 3/6 (50) \\ 3/3 (100) \end{array} \right\}$		
PACG			19 (95)	15 (75)
Secondary Glaucoma				
Mean Follow-up (months)	19.95±4.96 (15-29)	19.05±3.93 (15-27)	0.193	

Trab=Trabeculectomy; S/C=subconjunctival; MMC=mitomycin C; I/T=intraTenon; POAG=Primary open angle glaucoma; PACG=Primary angle closure glaucoma; SG=secondary glaucoma; PPK=post penetrating keratoplasty; PT=Post traumatic; PBK=Pseudophakic bullous keratopathy; ABK=Aphakic bullous keratopathy, Post op=Post operative

**Table 2: Mean postoperative IOP (mmHg) in groups A and B at various time intervals**

Follow-up	Group A	Group B	P
Day 1	9.75±5.32	13.50±5.65	0.037
Day 7	11.85±7.07	14.05±4.72	0.254
1 month	11.00±3.70	15.05±6.20	0.017
3 month	12.10±3.09	12.70±2.88	0.530
6 month	12.82±3.19	15.17±2.48	0.061
12 month	12.00±2.45	16.00	0.191
Last follow-up (Mean)	12.00±2.41	13.65±2.76	0.051
(Group A=19.95±4.96 months)			
Group B=19.05±3.93 months)			

required antiglaucoma treatment. However, only one (5%) (PPK with SG) out of three (15%) moderately vascular blebs of group A required antiglaucoma treatment.

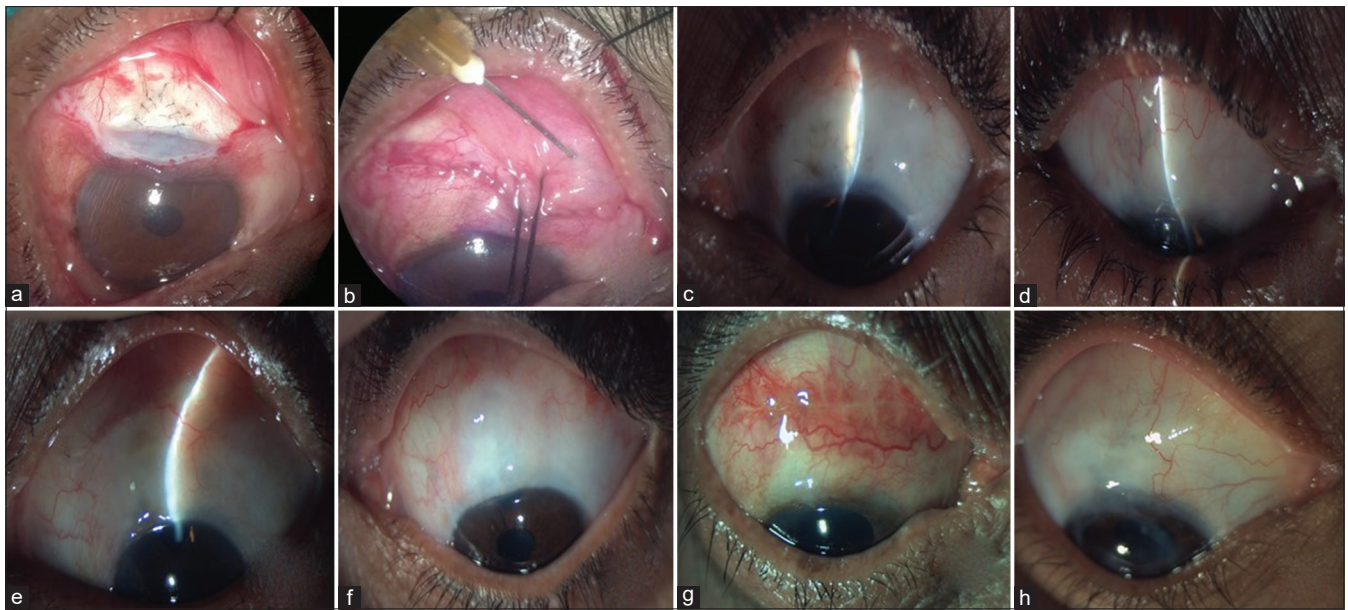
No intraoperative complications were encountered in any group. One patient each had mild hyphema, blebitis, and shallow AC in group A. Hyphema occurred on postoperative day (POD) 1 and resolved spontaneously within 1 week. Shallow AC persisted for 14 days postoperatively and resolved with conservative management. Blebitis was seen 3 months postoperatively and resolved after medical management. No toxic effects related to MMC such as undue congestion, corneal edema, postoperative uveitis, scleral necrosis, or thinning and prolonged hypotony were noted in any patient. In group B, one patient each had hyphema with vitreous hemorrhage and hyphema. Vitreous hemorrhage was seen on POD1

followed by hyphema on POD4 and resolved within 2 weeks on conservative treatment. Hyphema in the other patient was seen on POD1 and resolved spontaneously after 2 weeks. The difference in complications between the two groups was insignificant ( $P = 0.660$ ). None of the patients had marked visual loss, endophthalmitis, hypotony, wound leak, or required additional glaucoma surgery postoperatively.

## Discussion

Intraoperative MMC injection in intraTenon/subconjunctival space at the beginning of trabeculectomy offers several advantages.<sup>[7,9,10,12,15]</sup> However, this is a new evolving technique with limited experience. This prospective, single-surgeon, single-center study compared the IOP reduction, success rate, bleb morphology, and complication rates after subconjunctival MMC injection at the end of trabeculectomy versus intraTenon MMC injection prior to initial conjunctival incision.

IOP reduction of  $\geq 30\%$  and  $\geq 2/3^{\text{rd}}$  of baseline IOP without antiglaucoma treatment on the last follow-up was noted in 95% and 80% of patients, respectively, of group A, which was a greater reduction compared to 75% and 60% of patients of group B. Lee *et al.*<sup>[9]</sup> reported that 70.3% of eyes had an IOP of  $\leq 2/3^{\text{rd}}$  listing IOP without anti-glaucoma medication at 12 months with intraTenon MMC injection at the beginning of trabeculectomy. Lim *et al.*<sup>[15]</sup> noted that the proportion of eyes that achieved  $< 22$ ,  $< 18$ , and  $< 15$  mmHg IOP at 24 months in the intraTenon MMC injection was 70.5%, 69.3%, and 66.8%, respectively. Maheshwari *et al.*<sup>[12]</sup> described that the mean preoperative IOP of 29.00 mmHg reduced to a mean IOP of 12.19 mmHg at 12 months after subconjunctival MMC



**Figure 1:** Intraoperative and postoperative pictures of group A. (a) Intraoperative picture showing seven interrupted sutures at the scleral flap. (b) Subconjunctival MMC injection at the end of trabeculectomy. (c-h) Postoperative blebs seen in group A patients

**Table 3: Bleb morphology**

IBAGS Grading	Group A, n=20 Number (%)	Group B, n=20 Number (%)
Avascular Microcystic Blebs	14/20 (70)	9/20 (45)
V1, H2, E3, S0	10 (50)	5 (25)
V1, H2, E2, S0	2 (10)	4 (20)
V1, H3, E3, S0	1 (5)	
V2, H2, E2, S0	1 (5)	
Avascular White Blebs	3/20 (15)	7/20 (35)
V0, H3, E3, S0	2 (10)	1 (5)
V0, H2, E2, S0	1 (5)	
V0, H2, E3, S0		6 (30)
Moderately vascular/Low blebs	3/20 (15)	4/20 (20)
V3, H1, E2, S0	3 (15)	4 (10)

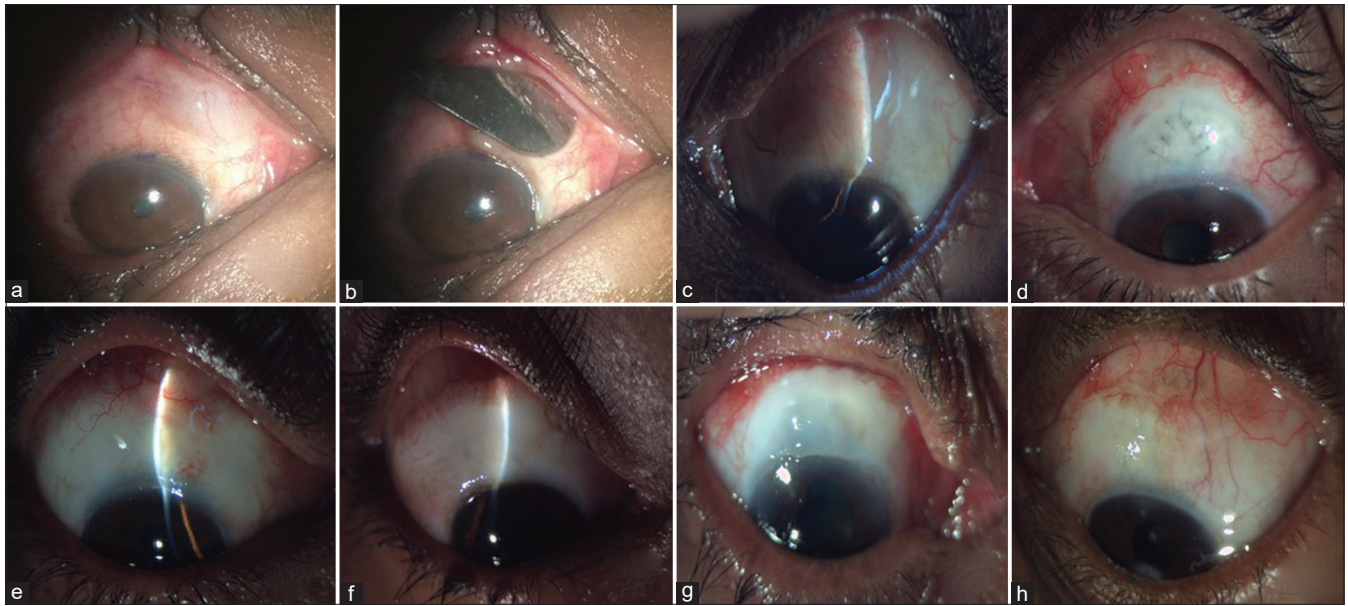
before raising the flap, which is equal to a 57.96% reduction from baseline at 12 months. In our study, IOP <21 mmHg was achieved by 95% and 75% of eyes of groups A and B, respectively. The IOP reduction using various parameters in our study is greater than that in the above mentioned studies in group A, while it is comparable or higher in group B despite higher mean baseline IOP values in our study.

Group A showed a superior complete success rate (95%) and greater absolute IOP reduction compared to group B (75%) despite the higher proportion of secondary glaucoma cases in group A who are known to have a high risk for failure of trabeculectomy. The success rate of intraoperative MMC injection at the beginning of trabeculectomy in previous studies in the literature was 52%–90%.<sup>[7,9,11,12,15]</sup> Lee *et al.*<sup>[9]</sup> in a noncomparative, retrospective study of trabeculectomy surgery augmented with an intraTenon injection of MMC reported a complete success rate (IOP <21 mmHg) of 86% and 90% for the two groups of combined cataract and trabeculectomy surgery

and trabeculectomy alone, respectively. Khouri *et al.*<sup>[7]</sup> reported a success rate of 64% (IOP decrease of >30% from baseline). Quist *et al.*<sup>[16]</sup> reported subTenon MMC application by irrigation method in patients of trabeculectomy with Ex-PRESS shunt, which provided significantly greater IOP lowering effects with a complete success rate of 60.0% and a qualified success rate of 27.5%. However, the irrigation method also resulted in significantly higher rates of hypotony without any significant consequences.<sup>[16]</sup> Maheshwari *et al.*<sup>[12]</sup> reported a low complete success rate of 52.4% in the preoperative injection group despite the exclusion of uveitic, neovascular, postkeratoplasty, and traumatic glaucoma. Lim *et al.*<sup>[15]</sup> found the failure of intraTenon MMC injection group in 21.08% during 24 months follow-up. They concluded that older patient age and limbus-based conjunctival incision were associated with a significantly longer time to fail.<sup>[15]</sup> In our study, group B showed a complete success of 75% and qualified success of 25%. Group A showed a superior complete success rate of 95% and a qualified success rate of 5%.

We hypothesized that postoperative MMC injection may ensure 100% delivery and diffuse and posterior application of MMC, leading to lower IOP and diffuse bleb formation. Our results appear to confirm our hypothesis as AM, diffuse, median blebs extending 3–6 clock hours were significantly more in group A compared to group B. Although the vertical and horizontal extent of blebs in both the groups were comparable, generally, the blebs in group A extended slightly more posteriorly from the limbus (mean: 10.2 mm) compared to group B (mean: 8.91 mm).

The MMC injection at the end of trabeculectomy provided significantly greater IOP lowering effects so that only one (5%) patient of post-PPK secondary glaucoma of group A required additional antiglaucoma treatment compared to 25% of patients of group B. No bleb leaks and encapsulated blebs were encountered in either group in our study. Diffuse application of MMC results in a very low-profile diffuse bleb and avoids



**Figure 2:** Intraoperative and postoperative pictures of group B. (a) Intraoperative intraTenon injection of MMC before initial conjunctival incision. (b) Intraoperative spreading of MMC after 10 mL wash post MMC injection. (c-h) Postoperative blebs seen in group B patients

focal, thin, ischemic (V0), and cystic blebs, which are more prone to leakage and infection.<sup>[10,12,17,18]</sup>

Pakravan *et al.*<sup>[10]</sup> described low lying, less vascularized, more diffuse, and larger extent blebs in the subTenon MMC group compared to the sponge group. Cystic blebs were observed in three (7.5%) cases in the subTenon MMC group.<sup>[10]</sup> Lee *et al.*<sup>[9]</sup> reported thin, avascular cystic blebs in 19.4% and Tenon's cysts in 4.6% after intraTenon MMC injection. Lim *et al.*<sup>[15]</sup> reported tense, vascularized, or encapsulated bleb in 15% in the early postoperative period and 3% in the late postoperative period after intraTenon MMC injection. Postoperative office procedures in the intraTenon group included bleb needling (5.4%), postoperative 5-fluorouracil injection (19.5%), and flap suture lysis (58.9%).<sup>[15]</sup> Interestingly, our study did not require postoperative office procedures in either group.

Various complications reported in previous studies include hypotony (11%–26%), bleb leak (5%–26%), shallow anterior chamber (27%), choroidal detachment (15.7%), hyphema (14.8%), need for postoperative bleb needling with 5FU (10%–26.9%), and cataract progression (7.4%).<sup>[7,9–11,15]</sup> Following trabeculectomy with intraTenon MMC injection, Lee *et al.*<sup>[9]</sup> reported hypotony in 21.3% and choroidal detachment in 15.7%, while Lim *et al.*<sup>[15]</sup> reported hypotony maculopathy (3%), blebitis (1%), bleb leak (4%–8%), over filtration (1%–4%), and bleb dysesthesia (3.24%).<sup>[15]</sup> Pakravan *et al.*<sup>[10]</sup> and Khouri *et al.*<sup>[7]</sup> observed no difference in the rates of hypotony. Quist *et al.*<sup>[16]</sup> described significantly higher rates of hypotony without maculopathy in the MMC irrigation method.

In our study, no patient in any of the groups had hypotony. One (5%) patient in group A and two (10%) patients in group B had hyphema. None of the patients had bleb leak, choroidal detachment, endophthalmitis, or needed additional antiglaucoma surgery in any of the two groups. The complications between the two groups of our study were comparable and not statistically significant. However, the

complications encountered in both the groups of our study were minimal compared to those described in the literature.<sup>[9]</sup>

As the number of patients is small in our study, it is possible that there are no complications. However, MMC is a potentially toxic drug and MMC injection has several potential complications. The use of MMC is known to cause late bleb leaks, bleb infections, endophthalmitis, thin-walled cystic blebs, corneal epithelial toxicity, regional bullous keratopathy, corneal or scleral ulceration and perforation, hypotony and hypotonic maculopathy, necrotizing scleritis, iridocyclitis, cataract, and symblepharon.<sup>[19–22]</sup> There is a risk of subconjunctival hemorrhage with a subconjunctival injection, which reduces the effective MMC concentration and may cause inflammation and fibrosis.<sup>[23]</sup>

Subconjunctival MMC injection may cause limbal stem cell deficiency.<sup>[24]</sup> Three out of seven eyes developed marked ocular surface problems, including corneal thinning (n = 1) and scleral melting (n = 2) during follow-up of 2–5 years as a late complication of 20–40 mcg MMC subconjunctival injection at 12 o'clock before making the conjunctival flap for trabeculectomy.<sup>[25]</sup> However, one recent study did not encounter any limbal stem cell-related corneal complications as also in our study as MMC was injected 8–10 mm above the limbus.<sup>[18]</sup> In addition, there was no difference between the subTenon injection versus the soaked sponge group in terms of complication rates and endothelial cell count.<sup>[18]</sup> Nuyts *et al.*<sup>[26]</sup> concluded that the dose and method of application used in practice should not result in significant corneal complications unless there has been inadvertent exposure to the anterior chamber.

Even topical application of a sponge soaked with MMC on the bare sclera of rabbits showed toxic effects on the ciliary epithelium in the case of eyes treated with 0.4%, while 0.04% MMC showed no evident toxic effects.<sup>[27]</sup> Chiew *et al.*<sup>[28]</sup> reported a higher incidence of hypotony and shallow AC in the sponge-applied MMC group compared to the subconjunctival injection group. However, the incidence of shallow AC and

hypotony was equal in intraoperative injection and soaked sponge groups in two recent studies.<sup>[7,18]</sup>

It is established that significant amounts of MMC can be detected intraocularly after topical application.<sup>[29,30]</sup> In both rabbit and human eyes, a reduction in the normal and elevated IOP can be achieved with subconjunctival injections of MMC without filtering procedures. Diffuse toxic changes in the two layers of the ciliary epithelium have been demonstrated in the human eye shortly after surgery with MMC.<sup>[29,30]</sup> Many other studies suggest that ciliary body toxicity caused by MMC plays a role in the higher incidence of postoperative hypotony.<sup>[29,30]</sup> One study concluded that 20 mcg of subconjunctival MMC seems to be comparatively nontoxic to the ciliary body of the rabbit eye.<sup>[31]</sup> Furthermore, the rabbit eyes that received lower doses of MMC ranging from 5 to 80 mcg and balanced salt solution showed normal ciliary body epithelium at the injection site and 180° away.<sup>[32]</sup> These studies amply emphasize the high toxic potential of MMC in higher doses, whereas we injected only 20 mcg of MMC, which has been found to be safe in animal studies.<sup>[31,32]</sup>

MMC delivery by injection offers the advantage of delivering a known amount of medication to the surgical site as the concentration of prepared drug and the volume injected can be used to calculate the exact amount of drug delivered to the target tissues. However, it is not known how much MMC gets washed away during irrigation and how much is available to the operation site in group B. In contrast, in the postop injection technique in group A, the actual dose of MMC delivered to ocular tissues is known, and its consistency, uniformity, and repeatability is ensured in all patients.

Hence, our technique of augmenting trabeculectomy with subconjunctival injection of MMC at the end of the surgery appears to be superior in terms of increased success rate with minimal complications. The increased success rate in group A may be attributed to the calculated dose of MMC consistently being available at the trabeculectomy site, whereas in group B after injecting the same amount of MMC, the site was irrigated with saline, which may remove a certain amount of MMC. Finally, we believe that the amount of MMC available for wound modulation appears to be less in group B than in group A, giving rise to superior results in group A. Lee *et al.*,<sup>[9]</sup> Lim *et al.*,<sup>[15]</sup> and Pakravan *et al.*<sup>[10]</sup> in their technique washed the site with saline after MMC injection; thus, it appears that the actual dose retained cannot be calculated. In contrast, in our study, we injected the exact dose at the end of surgery which can be given with consistency to all patients. In addition, injecting MMC at the end is more time-saving as compared to injecting MMC prior to the conjunctival incision as the time required in milking and washing the injected MMC is saved.

In addition, we believe that tight closure of the scleral flap by using seven sutures might have contributed to decreased chances of hypotony and persistently shallow AC. Tight suturing of the scleral flap did not adversely affect the functioning of the bleb till the last follow-up. In previous studies with MMC injection before trabeculectomy, they applied two interrupted sutures<sup>[7,10]</sup> or 1–3 releasable sutures on the scleral flap.<sup>[9,12]</sup>

The limitations of our study include that the study was not masked and had a smaller number of cases with lack of long term follow up. Further studies with a larger sample size and

longer duration of follow-up are required to assess the safety and efficacy of this modality in other populations.

## Conclusion

Thus, it is finally concluded that this is the first study in the literature to describe a novel approach of subconjunctival MMC application at the end of trabeculectomy. Both approaches appear to be highly effective in reducing IOP in primary and secondary glaucoma with similar safety profiles and bleb morphology. Subconjunctival MMC yielded a greater success rate (95%) compared to the intraTenon MMC group (75%).

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## Conflicts of interest

There are no conflicts of interest.

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