# Mitomycin–C Concentration during Subscleral Trabeculectomy for Treatment of Primary Open Angle Glaucoma

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### ABSTRACT

**Background:** Sub-scleral trabeculectomy is the standard surgical procedure for management of uncontrolled primary open angle glaucoma (OAG). Intraoperative mitomycin–C is frequently used during sub-scleral trabeculectomy to decrease the risk of recurrence.

**Objective:** This study aimed to assess the impact of mitomycin-C levels used during subscleral trabeculectomy on managing intraocular pressure in primary open angle glaucoma cases.

**Patients and methods:** This study is a prospective comparative interventional and non-randomized study. It was conducted on 30 eyes of 30 patients with uncontrolled open angle glaucoma. They were operated upon by sub-scleral trabeculectomy with intraoperative mitomycin–C. Patients were divided into three equal groups according to the mitomycin–C concentration: Group A [10 patient] received 0.2 mg/ml mitomycin-C. Group B [10 patient] received 0.3 mg/ml mitomycin-C.

**Results:** There were statistically non-significant differences between group A, B and C as regards age, sex and preoperative IOP. Statistically highly significant IOP decrease was detected in all groups one day postoperatively and continued till the end of follow-up period at 3 months postoperatively as compared to preoperative level. There were statistically non-significant differences between groups A, B and C as regards the IOP, UCVA and BCVA at the postoperative follow-up visits.

**Conclusion:** Different concentrations of mitomycin-C (0.2, 0.3, 0.4 mg/ml) were clinically equaled in controlling IOP after glaucoma surgery.

Keywords: Mitomycin–C, Glaucoma, Trabeculectomy, Intra ocular pressure, Hypotony.

#### **INTRODUCTION**

Glaucoma is a progressive optic neuropathy leading to irreversible blindness if left untreated <sup>(1)</sup>. Subscleral trabeculectomy is a primary surgical method for managing glaucoma. While there is often a notable decrease in intraocular pressure (IOP) following the surgery, the long-term success can be compromised due to progressive subconjunctival fibrosis, resulting in a subsequent increase in IOP<sup>(2)</sup>.

Subscleral trabeculectomy is a surgical procedure that establishes an alternative pathway for the drainage of aqueous humor from the front part of the eye to the region under the conjunctiva, which is situated beneath a flap of the white outer layer of the eye called the sclera. In order to guarantee the success of this treatment, it is imperative that the lower half of the somewhat thin scleral flap, the borders of the scleral incision, and the area between the episclera and conjunctiva remain devoid of any healing or scarring mechanisms. It is crucial to avoid obstruction of the drainage of the aqueous fluid through the surgically established fistula. <sup>(3)</sup>.

Mitomycin C, an antineoplastic agent, is derived from the soil bacterium Streptomyces caespitosus. Its primary action is as a cross-linker of deoxyribonucleic acid (DNA), which effectively inhibits the proliferation of fibroblasts <sup>(4)</sup>.

The success rate of the surgical management of glaucoma is related to the healing process to achieve long-term results and healthy operating blebs <sup>(5)</sup>. Antimetabolite agents are used to limit fibrosis that

leads to bleb failure. Two agents have been widely used, the mitomycin C (MMC) and the 5-fluorouracil. Vascular endothelial growth factors have been investigated to have an important role in the healing process in glaucoma surgery. It had been found that they induce fibrosis in human tissues <sup>(3)</sup>.

This study focuses on assessing the impact of mitomycin-C concentration used intraoperatively on controlling IOP during subscleral trabeculectomy in the treatment of primary open angle glaucoma.

#### PATIENTS AND METHODS

This study is a prospective, comparative, interventional, and non-randomized study. 2023. It was held at the Ophthalmology Department of Al-Zahraa University Hospital. It included 30 eyes with primary uncontrolled OAG in 30 patients. They were prepared for surgical treatment in the form of subscleral trabeculectomy. Patients were classified as follows: Group A [10 patient]: They were subjected to subscleral trabeculectomy with 0.2 mg/ml mitomycin-C. Group B [10 patient]: They were subjected to subscleral trabeculectomy with 0.3 mg/ml mitomycin-C. Group C [10 patient]: They were subjected to subscleral trabeculectomy with 0.4 mg/ml mitomycin-C.

**Inclusion Criteria:** Primary open angle glaucoma with uncontrolled IOP in patients of either gender and of different age groups.

# **Exclusion Criteria:**

1. Congenital glaucoma or juvenile glaucoma. 2. Normal-tension glaucoma. 3. Patients controlled by medical treatment. 4. Recurrent glaucoma. 5. Secondary glaucoma. 6. Aphakic and pseudophakic glaucoma. 7. Conjunctival disease as ocular cicatricial pemphigoid. 8. Clinically significant cataract where combined surgery may be indicated. 9. Refractory glaucoma as uveitic glaucoma, neovascular glaucoma, and glaucoma after retinal detachment. 10. Patients with any corneal pathology as corneal dystrophies, corneal opacity, corneal ectatic disorders, previous corneal herpes infection, etc. 11. History of ocular trauma. 12. History of prior intra ocular surgeries.

# **Preoperative Assessment:**

*a) Full history taking:* A thorough medical and surgical history was compiled, encompassing a record of any eye trauma, an inventory and count of glaucoma medications taken, a background of any bleeding conditions or the use of blood-thinning drugs, and past instances of eye inflammation or infection.

# b) Comprehensive ophthalmological examination:

Visual acuity, both uncorrected and best corrected, was assessed using a Landolt's C chart. The data were represented using the Decimal fraction scoring system. A slit-lamp examination was done to assess the anterior segment. Additionally, Goldmann's applanation tonometry was conducted, and gonioscopy was performed using the Goldmann 3-mirrors contact lens. Fundus examination was performed using slit-lamp biomicroscopy and a +90 D lens to evaluate the retina and optic disc.

# c) Investigations including:

- 1. Computerized visual field perimetry using the Zies Humphery Visual Field Analyzer.
- 2. OCT using spectral-domain optical coherence tomography, optical coherence tomography angiography and SD-OCT wide-field imaging system.

*d) General medical evaluation* including laboratory tests (complete blood picture, liver & kidney functions, bleeding profiles, random blood glucose, hepatitis viral markers, and conjunctival swab), and internal medicine consultation.

*Medications:* Topical broad-spectrum antibiotics in the form of moxifloxacine hydrochloride ophthalmic solution 0.5% (3 times daily) were started 3 days prior to surgery. Topical  $\beta$  blockers were stopped one day before surgery, and Acetazolamide tablets three times/day were prescribed a day before surgery.

# **Surgical Techniques**

- 1. All surgeries were performed under peribulbar anesthesia (5 mL lignocaine 2%, 2 mL bupivacaine 0.5%, and Hyaluronidase (150 IU/ 1 mL).
- **2.** Sterilization using 10% betadine for the eye lids and surgical field. Betadine 5% was used for the conjunctival cul-de-sac.
- **3.** Application of sterile drapes.
- **4.** The surgical site was at 12 O'clock in all cases.
- **5.** A corneal traction suture using a 8/0 black silk suture at the upper cornea for exposure of the superior part of the bulbar conjunctiva by keeping the eye in downward position.
- **6.** Fashioning of a fornix based conjunctival flap using a Westcott scissor and a non-toothed forceps.
- 7. Meticulous subconjunctival and episcleral hemostasis using a wet field cautery.
- **8.** Formation of a half-thickness scleral flap using a crescent knife or number 15 blade (Figure 1).
- 9. MMC application: In Group A, thin small pieces of microsponges soaked with MMC (0.2 mg/ml) were applied between the sclera and Tenon capsule and above the scleral flap for 4 minutes. In Group B the concentration of MMC was 0.3 mg/ml, while in group C the concentration was 0.4 mg/ml (Figures 2 & 3). The sponges were then removed, and a copious irrigation using a sterile saline solution to the cornea and conjunctiva was done.
- **10.** Excision of a block (About 1X2 mm) at the deep scleral and corneal layer and centered on the limbus was carried out in all cases. It was done using blade 11 and scissors (Fig. 4).
- **11.** A peripheral iridectomy was then done at 12 O'clock (Fig. 5).
- **12.** Two stitches to the scleral flap were then applied using 10/0 nylon sutures (Fig.6).
- **13.** Suturing the conjunctiva with interrupted watertight 10/0 nylon sutures (Fig. 7).
- 14. An antibiotic eye ointment in the form of tobramycin 0.3% (3 mg) and dexamethasone 0.1 % (1mg) ophthalmic ointment were applied to the fornix.
- **15.** An eye patch was then applied.

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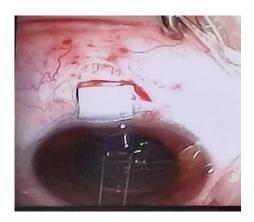


Figure (1): Rectangular shape half scleral flap



Figure (3): Application of MMC



Figure (5): Peripheral iridectomy.



Figure (2): MMC Vial.



**Figure (4):** Excision of a block (About 1X2 mm) at the deep scleral



Figure (6): Suturing scleral flap

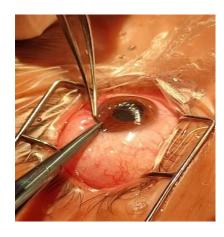


Figure (7): Suturing the conjunctival flap.

**Postoperatively medications:** Topical corticosteroid in the form of 1% prednisolone acetate eye drops was administered 6 times daily, and was then tapered as the clinical course dictates. Topical antibiotics in the form of 0.5% moxifloxacine hydrochloride ophthalmic solution (6 times daily for 2 weeks). Cycloplegic agents in the form of 1% cycolpentolate hydrochloride ophthalmic solution (twice daily).

### **Postoperative follow-up:**

All patients were scheduled to be examined after 1 day, 1 week, 6 weeks and 3 months postoperatively.

# At each follow up visit they were subjected to the following:

- UCVA & BCVA
- Slit-lamp examination
- Goldmann applanation tonometry.
- Autorefractometry using NIDEK Autorefractor Keratometer ARK 501A

Ethical approval: The Ethics Board of AFMG of AL-Azhar University approved the study, and an informed written consent was signed by each participant in the study. The study protocol was in accordance with the tenets of declaration of Helsinki. All procedures were done at Al-Zahraa University Hospital. This study is not financially supported from any organization, society or government.

### Statistical analysis

The analysis of the data was carried out using the Statistical Program for Social Science (SPSS) version 24. For quantitative data, the mean and standard deviation (SD) were calculated, with the mean representing the central value of a set of numbers and the SD indicating the spread of values around this mean. A lower SD suggests that values are closely clustered around the mean, while a higher SD indicates a wider spread. Qualitative data were presented in terms of frequency and percentage. Several statistical tests were employed: the Independent sample t test for comparing two means in normally distributed data, the Mann Whitney U test for comparisons in abnormally distributed data, and the Chi-square test for nonparametric data. In assessing the significance of the findings, a P-value  $\leq 0.05$  was considered significant, less than 0.001 was deemed highly significant, and greater than 0.05 was regarded as insignificant.

#### RESULTS

• **Demographic data:** As regards age, the mean age was  $45.1 \pm 17.14$  years in group A,  $50.9 \pm 14.33$  years in group B, and  $47.8 \pm 12.52$  years in group C. The difference between the three groups was statistically insignificant (p-value = 0.684). As regards sex, in group A there were 2 males (20%) and 8 females (80%). In group B, there were 3 males (30%) and 7 females (70%) & in group C, there were 3 males (30%) and 7 females (70%). The difference between the three

groups was statistically insignificant (p-value = 0.605) (Table 1).

 Table (1): Comparisons of studied groups as regards age and sex

			oup A = 10)		oup B = 10)		oup C = 10)	P-value
Age	Mean	4	45.1		50.9		17.8	0.684
(years)	±SD	1	7.14	14.33		12.52		NS
Corr	Male	2	20%	3	30%	3	30%	0.605
Sex	Female	8	80%	7	70%	7	70%	NS

# A. Clinical data

# **Pre-operative assessment**

1- Uncorrected Visual Acuity (UCVA): In group A, the mean preoperative UCVA was 0.33  $\pm$  0.115. In group B, it was 0.36  $\pm$  0.177. In group C, it was 0.39  $\pm$  0.159. The difference between the three groups was statistically nonsignificant (P = 0.68) (Table 2).

Table (2): Comparison of the studied groups as regards	
the mean preoperative UCVA	

		Group A (N = 10)	В	Group C (N = 10)	P value
Due	Mean	0.33	0.36	0.39	0.69
Pre- UCVA	±SD	0.115	0.177	0.159	0.68 NS

# 2- Best Corrected Visual Acuity (BCVA):

In group A, the mean preoperative BCVA was  $0.82 \pm 0.091$ . In group B, it was  $0.8 \pm 0.133$ . In group C it was  $0.86 \pm 0.084$ . The difference between the 3 groups was statistically non-significant (P = 0.442) (Table 3).

**Table (3):** Comparison of studied groups as regards the mean preoperative BCVA

		Group	Group I	Group	P value
		(N = 10)	(N = 10)	(N = 10)	
Pre-	Mean	0.82	0.8	0.86	0.442
BCVA	±SD	0.091	0.133	0.084	NS

**3-** *IOP*: In group A, the mean preoperative IOP was  $33.7 \pm 3.30$  mmHg. In group B, it was  $32.1 \pm 5.08$  mmHg, while in group C, it was  $31.3 \pm 4.71$  mmHg. The difference between the 3 groups was statistically non-significant (P=0.65) .(Table 4).

		Group A (N = 10)	Group B (N = 10)	Group C (N = 10)	P-value
IOP (mmHg)	Mean	0.31	0.32	0.34	).65 NS
Preoperative	±SD	0.106	0.127	0.149	1.02 INS

**Table (4):** Comparisons of the studied groups as regards the mean preoperative IOP.

#### **Post-operative Assessment:**

*1-Uncorrected Visual Acuity (UCVA):* The difference between the three groups was non-significant (Table 5).

		Group A	-	Group C	P-
		(N = 10)	(N = 10)	(N = 10)	value
UCVA	Mean	0.37	0.41	0.4	
1st day					0.90
post-	±SD	0.2263	0.1449	0.226078	NS
operative					
UCVA	Mean	0.24	0.23	0.31	
1 week					0.432
post-	±SD	0.143	0.1059	0.185293	NS
operative					
UCVA	Mean	0.31	0.35	0.36	
1st month					0.786
post-	$\pm SD$	0.1792	0.1434	0.183787	NS
operative					
UCVA	Mean	0.36	0.39	0.43	
Brd month					0.686
post-	±SD	0.2119	0.1197	0.194651	NS
operative					

**Table (5):** Comparisons of the studied groups as regards the mean UCVA postoperatively at the follow up visits

# 2-Best Corrected Visual Acuity (BCVA):

The difference between the mean changes in BCVA in the 3 groups was a statistically non-significant (P > 0.055) after the first day and 3 months postoperative, while the difference was significant after 1 week and after 1 month postoperative (Table 6).

**Table (6):** Comparison of studied groups as regards the mean postoperative BCVA.

		Group A	Group B	Group C	P-value
		(N = 10)	(N = 10)	(N = 10)	
BCVA	Mean	0.87	0.85	0.95	
1st day post- operative	±SD	0.116	0.108	0.070711	0.0791 NS
BCVA	Mean	0.75	0.71	0.85	
1-week post- operative	±SD	0.1434	0.137	0.070711	0.0438
BCVA	Mean	0.80	0.81	0.93	
1st month post- operative	±SD	0.1155	0.0994	0.105935	0.0196
BCVA	Mean	0.86	0.85	0.95	
3rd month post- operative	±SD	0.1075	0.108	0.070711	0.055 NS

# **3-** Postoperative IOP Assessment

There was a statistically highly significant decrease in mean IOP in the 3 groups. The difference between the decrease in the mean IOP in the 3 groups was a statistically non-significant (P=0.551).

<b>Table (7): (</b>	Comparisons	of	the	studied	groups	as
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		Group A (N = 10)	Group B (N = 10)	Group C (N = 10)	P- value				
IOD	14	· · · · · · · · · · · · · · · · · · ·			varue				
IOP	Mean	9.5	9.4	9.4					
(mmHg) 1st day post- operative	±SD	1.08012345	1.712697677	1.264911064	0.982 NS				
IOP	Mean	11.00	11.9	11.3					
(mmHg) 1-week post- operative	±SD	1.247219129	2.078995484	1.567021236	0.479 NS				
IOP	Mean	12.8	11.7	12.2					
(mmHg) 1st month post- operative	±SD	1.032795559	1.49	1.316561177	0.1832 NS				
IOP	Mean	12.2	12	12.5					
(mmHg) 3rd month post- operative	±SD	0.788810638	1.054092553	1.178511302	0.551 NS				

# Pre and postoperative assessment of IOP & UCVA and BCVA in group A

# 4- Pre and postoperative assessment of IOP in group A.

At the end of follow up period at 3 months postoperatively, there was a statistically highly significant decrease in IOP at 3 months postoperatively when compared with the preoperative level in group A (P < 0.001).

There were statistically non-significant differences between groups A, B and C as regards the changes in UCVA (P = 0.70) & BCVA (P = 0.28) comparing the preoperative to the 3 months postoperative levels.

**Table (8):** Comparisons between preoperative and postoperative assessment of IOP, UCVA and BCVA in group A

	Group A		Pre- operative (N = 10)	Post- operative (N = 10)	P-value
I	IOP	Mean	33.7	12.2	0.000001<
	(mmHg)	±SD	3.301	0.788	0.001 HS
I	UCVA	Mean	0.33	0.36	0.70
		±SD	0.115	0.211	NS
I	BCVA	Mean	0.82	0.86	0.28
l		±SD	0.091	0.107	NS

# 5- Preoperative and postoperative assessment of IOP & UCVA and BCVA in group B.

At the end of follow up period at 3 months postoperatively, there was a statistically highly significant decrease in IOP at 3 months postoperatively when compared with the preoperative level in group B (p-value< 0.001).

There was a statistically non-significant difference between groups A & B and C as regards the change in UCVA (P = 0.663) & BCVA (P = 0.369) preoperatively and 3months postoperatively respectively.

Preoperative and postoperative assessment of IOP & UCVA and BCVA in group B.

Group B		Pre- operative (N = 10)	Post- operative (N = 10)	P-value
IOP	Mean	32.1	12	0.0009<
(mmHg)	±SD	5.087	1.054	0.001 HS
UCVA	Mean	0.36	0.39	0.663
	±SD	0.177	0.119	NS
BCVA	Mean	0.8	0.85	0.369
	±SD	0.133	0.108	NS

**Table (9):** Comparisons between preoperative and postoperative assessment of IOP, UCVA and BCVA in group B.

Preoperative and postoperative assessment of IOP &UCVA and BCVA in group C

Group	O C	Preoperative $(N = 10)$	Postoperative $(N = 10)$	P-value
IOP	Mean	31.3	12.5	0.0002
(mmHg)				< 0.001
(IIIIIIng)	±SD	4.715	1.178	HS
UCVA	Mean	0.39	0.43	0.62
	±SD	0.15951	0.194651	NS
BCVA	Mean	0.86	0.95	0.19
	±SD	0.08433	0.070	NS

# **Postoperative complications:**

In our study, hypotony (less than 10 mmHg) was reported 1 day postoperatively in 1 case (10%) in group A, in 3 cases (13%) in group B and in 4 cases (40%) in group C. A11 cases became within the normal IOP without surgical intervention at 1 week postoperatively except 1 case in group C, which became normal at 1 month postoperatively. Hypotony maculopathy was not reported in any of our cases. There was shallow AC in 1 patients (10%) of group A, & in 2 patients (20%) of group B, and in 4 patients (40%) of group C. Over filtration was not reported in group A, B, while it was reported in 2 eyes (20%) in group C. Flat anterior chamber was not reported in any of our cases. There was a statistically non-significant difference between group A & group B and group C as regards postoperative complications.

 Table (10): Comparisons of studied groups as regard

 postoperative complications

	Group A (N = 10)		Group B (N = 10)		Group C (N = 10)		P- value
Hyphemia	1	10%	0	0%	1	10%	0.605 NS
Hypotony	1	10%	3	30%	4	40%	0.304 NS
Shallow AC	1	10%	3	30%	4	40%	0.361 NS
Iritis	3	30%	4	40%	3	30%	0.271 NS

# DISCUSSION

particularly Glaucoma surgery, subscleral trabeculectomy, is often the preferred method for reducing intraocular pressure (IOP) in patients whose glaucoma is not adequately controlled by medication. The fundamental concept of this procedure involves creating a passage for the aqueous humor to flow from the anterior chamber of the eye to the subconjunctival space, resulting in the formation of a filtering bleb. However, a significant challenge of this technique is the potential scarring response at the filtration site, which can hinder the movement of aqueous fluid through the filtering bleb, ultimately diminishing the effectiveness of the surgery in lowering IOP<sup>(6)</sup>.

The utilization of antimetabolites has significantly enhanced the efficacy of trabeculectomy, particularly in cases where there is a heightened likelihood of surgical complications <sup>(5)</sup>. Mitomycin C (MMC), a cytotoxic drug, has been found to be superior than 5fluorouracil in promoting the development of filtering blebs and has the added benefit of not need repeated injections <sup>(5)</sup>. MMC works by inhibiting the growth and proliferation of fibroblast and endothelial cells, thereby reducing the proliferative stage of wound healing, a key factor in the success of trabeculectomy <sup>(7)</sup>.

This study was prospective comparative interventional non-randomized study. It included thirty eyes with uncontrolled primary open angle glaucoma. Patients were prepared for surgical treatment in the form of subscleral trabeculectomy augmented with mitomycin-C application. Patients were divided into three groups: Group A consisted of 10 patients who had sub-scleral trabeculectomy using mitomycin-C at a dosage of 0.2 mg/ml. Group B consisted of 10 patients who had sub-scleral trabeculectomy using mitomycin-C at a dosage of 0.3 mg/ml. Group C consisted of 10 patients who had sub-scleral trabeculectomy using mitomycin-C at a dosage of 0.4 mg/ml. There were statistically non-significant differences between groups A, B and C as regards age, sex or preoperative IOP.

In our study, we observed a statistically highly significant decrease of IOP in all groups, one day postoperatively and continued till the end of follow up period at 3 months postoperatively as compared to the preoperative level. There were statistically non-significant differences between the 3 groups as regards IOP, UCVA, and BCVA during the postoperative follow up visits. In agreement with our findings, **Almobarak** *et al.* <sup>(5)</sup> reported non-statistically significant differences between their groups as regards the baseline IOP, the number of anti-glaucoma medications and the MMC exposure time.

In concordance with our findings, Almobarak et al.  $^{(5)}$  reported no difference between 0.2, 0.3 and 0.4 mg/ml MMC in in treatment of primary open angle glaucoma. According to their report, increasing the concentration of MMC did not have any additional impact on the survival and success of sub-scleral trabeculectomy compared to a lesser concentration. Furthermore, they indicated that there was no discernible disparity in the immediate postoperative problems associated with hypotony when comparing various amounts of mitomycin-C. Additionally, they stated that increased levels and prolonged exposure to MMC can inhibit the process of wound healing and lead to the formation of thin blebs and delayed leakage of blebs. Robin and colleagues (8) conducted a study in 1997 where they assessed three separate groups, each administered a unique dosage of mitomycin C (MMC): 0.2 mg/mL, 0.3 mg/mL, and 0.4 mg/mL. The study, which incorporated a one-year follow-up period, sought to investigate the correlation between the concentration and duration of MMC exposure and its efficacy. The researchers determined that there is a dose-response connection, suggesting that the effectiveness of MMC may alter depending on the concentration and duration of exposure. In addition, the study observed no substantial variations in the management of intraocular pressure (IOP) and postoperative complications across the various groups with varied concentrations of MMC<sup>(8)</sup>.

The study conducted by **Lee** *et al.* <sup>(9)</sup> investigated the impact of three distinct MMC concentration (0.2 mg/mL, 0.3 mg/mL, and 0.4 mg/mL) on a total of 36 eyes. They found no statistically significant disparity in the reduction of intraocular pressure (IOP) across these concentrations. Postoperative hypotony occurred in only two subjects, both were in the 0.4 mg/mL group <sup>(9)</sup>.

In 999, **Sanders** *et al.* <sup>(10)</sup> discovered that subscleral trabeculectomy had the same level of effectiveness in eyes at higher risk while using a lower dosage (0.2 mg/mL) of mitomycin C (MMC) compared to a higher dosage (0.4 mg/mL). In addition, they noted a higher frequency of hypotony-related problems in the group that received the higher concentration of 0.4 mg/mL of MMC <sup>(10)</sup>. In 2003, **Laube** *et al.* <sup>(7)</sup> assessed the effectiveness of three concentrations of MMC 0.2, 0.3 and 0.4 mg/ml, each applied for 2.5 minutes in their study. They concluded that 0.2 mg/mL was the most effective dose for their purposes <sup>(7)</sup>. Following this, *Maquet et al.* <sup>(11)</sup> in 2005, also studied the three MMC concentrations (0.2 mg/mL, 0.3 mg/mL, and 0.4 mg/mL). Their findings revealed nonsignificant differences in the control of intraocular pressure (IOP) and postoperative complications across these varying concentrations of MMC <sup>(11)</sup>.

Simsek *et al.* <sup>(12)</sup> reported that severe complications including, thin bleb, overhanging bleb, hypotony, choroidal detachment with subsequent leakage blebitis, and endophthalmitis may be aggravated by MMC application. These complications are highly correlated to MMC concentration and its duration time <sup>(12)</sup>. *Kitazawa et al.* <sup>(13)</sup> in their 1993 study, found that lower concentrations of MMC with shorter duration times were as effective in reducing intraocular pressures (IOPs) as higher concentrations and longer durations. They also observed that higher concentrations and prolonged application of MMC could be related to complications <sup>(13)</sup>.

In our study, no anti-glaucoma medications were needed in any of our patients in the 3 groups till the end of the follow up at 3 months postoperatively. This result is in agreement with Liao et al. (14) who reported a significant drop in the use of anti-glaucoma medications. In 2005, Simsek and colleagues (12) discovered that using MMC during sub-scleral trabeculectomy frequently led to the development of thin-walled, avascular blebs that had reduced outflow resistance. Frequently, this situation resulted in excessive filtration and hypotony, which is defined by an unusually low pressure inside the eye. In addition, they observed that these thin blebs were more prone to leakage, which heightens the likelihood of developing blebitis, endophthalmitis and severe eye infections. Therefore, they determined that employing releasable sutures or tighter suturing of the scleral flap, along with postoperative laser suture-lysis, is necessary to prevent excessive filtration and the resulting development of hypotony maculopathy.

In our study, hypotony was reported 1 day postoperatively in 1 case (10%) in group A, in 3 cases (30%) in group B and in 4 cases (40%) in group C. All cases were become within the normal IOP without surgical intervention at 1 week postoperatively except 1 case in group C, which became normal at 1 month postoperatively. Hypotony maculopathy was not reported in any of our cases. Shallow AC was reported in 1 patients (10%) of group A, in 2 patients (20%) of group B, and in 4 patients (40%) in group C. Over filtration was not reported in group A and B, while it was reported in 2 eyes (20%) in group C. Flat anterior chamber was not reported in any of our cases. Differences between groups A, B and C were statistically non-significant as regards postoperative complications.

# CONCLUSIONS

Subscleral trabeculectomy augmented with mitomycin-C application was an effective glaucoma surgery for IOP control. There were statistically nonsignificant differences between the different concentrations of mitomycin-C application (0.2, 0.3 and 0.4 mg/ml) for IOP control after glaucoma surgery.

# RECOMMENDATIONS

It is advisable to conduct a comprehensive study on a large scale, with an extended time of observation, in order to assess the effectiveness of using mitomycin-C during subscleral trabeculectomy for patients with uncontrolled open angle glaucoma. Further research is advised to assess the optimal length of time for applying mitomycin-C during subscleral trabeculectomy.

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### REFERENCES

- 1. Flaxman S, Bourne R, Resnikoff S *et al.* (2020): Global causes of blindness and distance vision impairment 1990-2020: a systematic review and meta-analysis. Lancet Glob Health, 5 (12): 1221–1234.
- 2. Vera V, Sheybani A, Lindfield D *et al.* (2019): Recommendations for the management of elevated intraocular pressure due to bleb fibrosis after XEN gel stent implantation. Clin Ophthalmol., 13: 685–694.
- **3.** Khaw M, Richard L, Cynthia Y *et al.* (2019): Antifibrotic agents in glaucoma surgery. Ophthalmology. Maryland Heights, MO, USA, Pp: 687– 697.
- 4. Singh P, Singh A (2019): Mitomycin-C use in ophthalmology. J Pharm., 3 (1): 12–14.

- **5.** Almobarak F, Alharbi A, Morales J *et al.* (2018): Glaucoma filtration surgery: indications, techniques, and complications. Int Ophthalmol., 38 (6): 2371-2379.
- **6. Huang C, Tseng H, Wu K (2013):** The effect of lowand high-dose adjunctive mitomycin C in trabeculectomy. Taiwan J Ophthalmol., 3: 31-36.
- 7. Laube T, Ritters B, Selbach M et al. (2003): Clinical experiences and results of mitomycin C in trabeculectomy. Klin Monbl Augenheilkd., 220 (9): 618–624.
- 8. Robin A, Ramakrishnan R, Krishnadas R *et al.* (1997): A long-term dose–response study of mitomycin in glaucoma filtration surgery. Arch Ophthalmol., 115 (8): 969–974.
- **9.** Lee J, Park K, Youn D (1996): The effect of low- and high-dose adjunctive mitomycin C in trabeculectomy. Korean J Ophthalmol., 10 (1): 42–47.
- **10.** Sanders S, Cantor L, Dobler A *et al.* (1999): Mitomycin C in higher risk trabeculectomy: a prospective comparison of 0.2- to 0.4-mg/cc doses. J Glaucoma, 8 (3): 193–198.
- **11.** Maquet J, Dios E, Aragón J *et al.* (2005): Protocol for mitomycin C use in glaucoma surgery. Acta Ophthalmol Scand., 83 (2): 196–200.
- 12. Simsek M, Citirik A, Batman A *et al.* (2005): Efficacy and complications of releasable suture trabeculectomy and standard trabeculectomy. Int Ophthalmol., 26: 9-16.
- **13.** Kitazawa Y, Suemori-Matsushita H, Yamamoto T *et al.* (1993): Low-dose and high-dose mitomycin trabeculectomy as an initial surgery in primary openangle glaucoma. Ophthalmology, 100 (11):1624–1628.
- 14. Liao, Liu Y, Gao X *et al.* (2023): Noncontact Conjunctiva: A Better Mitomycin C Application Site for Trabeculectomy. Ophthalmol Ther., 12:1723–1735.