# COMPARATIVE EVALUATION OF DIFFERENT CONCENTRATIONS OF MITOMYCIN C AS AN ADJUVANT IN FILTERING SURGERY

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**ABSTRACT**

**BACKGROUND**
Glaucoma, one of the common disorders of the eye, has made enormous and rapid progress. Trabeculectomy first described by Cairns in 1968 is most frequently performed partial thickness filtering surgery nowadays. Recent interest has focused on medical therapy designed to maintain the potency of the fistula and to promote filtering bleb formation by modifying the subsequent wound healing process.

**MATERIALS AND METHODS**
The present study was conducted in the Upgraded Department of Ophthalmology, NSCB Medical College, Jabalpur in which 22 cases were selected from the patients attending the Outpatient Department to compare the ultimate outcome and recurrence rate in the two groups [Getting different concentrations of Mitomycin C intraoperatively (0.2 mg/mL vs. 0.4 mg/mL)].

**RESULT**
IOP was said to be controlled when IOP was <21 mm. It was 75% in 0.2 mg/mL group and 90% in 0.4 mg/mL group. One remained uncontrolled even with topical medications in 0.2 mg/mL group. In our study, most common early post-operative (within one week) complication was hypotony (25% in group I and 30% in group II), followed by shallow AC (8.33% in group I and 10% in group II, SPK (10% in group I only) and hyphema (8.33% in group I only).

**CONCLUSION**
There is no significant difference regarding success rate (75% in group I and 90% in group II), post-operative IOP and complication between these two groups (0.2 mg/mL vs. 0.4 mg/mL)

**KEYWORDS**
POAG, MMC, IOP.

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## BACKGROUND

Glaucoma, one of the common disorders of the eye, has made enormous and rapid progress. Worldwide, it is estimated that 65 million people are affected by glaucoma, which remains cause of blindness. Primary open-angle glaucoma, most common cause and presentation of disease, is estimated to have an incidence of 2.4 million new cases per year.

The current European Glaucoma Society Guidelines describe the aim of glaucoma treatment as "preservation of visual function adequate to individual needs, with minimal or no side effects, for the expected lifetime of the patient, without any disruption of his/her normal activities, at a reasonable cost." Long-term intraocular pressure (IPO) control plays a pivotal role in achieving this goal.

Trabeculectomy first described by Cairns in 1968 is the most frequently performed partial thickness filtering surgery nowadays.

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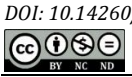

**In particular, surgery may be indicated when**

- Medications are inappropriate due to individual patient circumstances.
- Medication is unavailable or unattainable (due to cost).
- Medication is not sufficiently potent/effective.
- Medical treatment is poorly tolerated, and/or the patient is noncompliant.

Recent interest has focused on medical therapy designed to maintain the potency of the fistula and to promote filtering bleb formation by modifying the subsequent wound healing process.

The antimetabolite mitomycin C has become widely used as an adjunct medication for inhibiting fibroblast proliferation in glaucoma filtering procedure. Mitomycin C is an antibiotic isolated from streptomycin caespitosus. Although excellent results in IOP reduction have been reported with the use of intraoperative mitomycin C (in the eyes at high risk of surgical failure), postoperative complications including persistent hypotony remains a problem. Optimum concentration and exposure time of mitomycin C used during trabeculectomy surgery varies between 0.2–0.5 mg/mL and 1-5 minutes. An effort has been made here to compare the efficacy and safety of different concentrations of mitomycin C (0.2 mg/mL vs. 0.4 mg/mL).

**Aims and Objectives**

- To compare the efficacy of mitomycin C when used in different concentrations (In filtering surgery).
- To compare the ultimate outcome and recurrence rate in the two groups [getting different concentrations of Mitomycin C intraoperatively (0.2 mg/mL vs. 0.4 mg/mL)]

**MATERIALS AND METHODS**

Patients attending upgraded department of Ophthalmology of NSCB Medical College, Jabalpur.

Mitomycin C – It is available as deep blue violet crystals in vials containing 2 mg, 4 mg and 5 mg. It is used in concentrations of 0.2 mg/mL or 0.4 mg/mL. Concentration of 0.2 mg/mL is prepared by mixing the 2 mg of MMC with 10 mL of balanced saline solution, and 0.4 mg/mL concentration is prepared by diluting 4 mg vial with 10 mL of saline solution. A 4×4 mm sized surgical sponge soaked in 0.1 mL of mitomycin C (0.2 mg/mL or 0.4 mg/mL) was applied below the partial thickness scleral flap for 2 minutes.

**Cases were Studied under the following Groups**

**Group I-** Intraoperative use of mitomycin C (0.2 mg/mL for 2 minutes).

**Group II-** Intraoperative use of mitomycin C (0.4 mg/mL for 2 minutes).

**Inclusion Criteria**

Adjunctive antimetabolite inhibits the natural healing response that may preclude successful filtering surgery.

They would; however, be used with caution because of serious nature of potential complication and primarily consider in context of known risk factor for failure of trabeculectomy.

**Postoperative Examination**

- Conjunctiva - Bleb Appearance, congestion, sub conjunctival haemorrhage.
- Sclera - Any scleral abnormality.
- Cornea - Any epithelial defect.
- AC - AC depth (Normal or flat).
- Iris - Uveitis, iridodialysis.
- Pupil - size and reaction to light, any synechiae.
- Any opacity, subluxation and dislocation.
- Tension by Schiotz tonometry, then by applanation tonometer, then by NCT (Non-contact tonometer).
- Other investigation – slit-lamp examination and automated perimetry.

**Complication**

- Thin avascular blebs and wound leaks.
- Hypotony and its related complication e.g. Flat AC, maculopathy with vascular tortuosity, macular oedema, retinal folds, disc oedema; additional complications include corneal toxicity and uveitis.
- Cataract.

**Surgical Success is defined as**

1. An IOP level below 21 mm at the end of study period (6 months followup).
2. A failure when IOP is greater than 21 mm of Hg with or without glaucoma medication.
3. Complete failure when the eye required a further glaucoma operation or development of phthisis bulbi or light perception was absent in that eye.

**Indications of Trabeculectomy**

1. It has become the standard operation with excellent results for most forms of open–angle glaucoma.
2. Chronic angle–closure glaucoma.
3. Aphakic, inflammatory and traumatic glaucoma.
4. Secondary forms of uncontrolled glaucoma.
5. Congenital glaucoma after failed goniotomies or trabeculotomies.

**Advantage**

The use of lamellar scleral flap allows a more subtle control of drainage in older operations which created a direct access from the anterior chamber to the sub conjunctival tissues.

**Disadvantage**

- More likelihood of flat anterior chamber.
- Choroidal detachment.
- Cataract development.
- Thin cystic bleb predisposing to endophthalmitis.

**Mitomycin C**

It is antineoplastic, antifibrotic agent isolated from the fermentation filtrate of Streptomyces caespitosus. It markedly inhibits proliferation of cultured fibroblasts by blocking DNA replication, mitosis and protein syntheses. It is cytotoxic to fibroblasts as well as to vascular endothelial cells, in contrast to 5-FU, which is cytotoxic only to fibroblasts.

It is used intraoperatively at the filtering site in eyes with poor surgical prognoses. It was first used by Cher. Bergstrom and co-workers also have demonstrated marked prolongation of bleb function and reduction in IOP with adjunctive use of MMC in a rabbit model of filtering surgery.

A study was done by Bergstrom TJ, Wilkinson WS, Skuta GL et al[1] in (2000), they reviewed 110 eyes of glaucoma which underwent trabeculectomy with adjunct use of mitomycin C (MMC). The series comprised primary open-angle glaucoma 71 eyes, capsular glaucoma 24 eyes and angle-closure glaucoma 15 eyes. Low-concentration MMC of 0.2 mg/mL was used in 42 eyes and high-concentration MMC of 0.4 mg/mL was used in 68 eyes. The intraocular pressure (IOP) averaged 21.4 mmHg in the former group and 21.0 mmHg in the latter. The success rate, which was defined as IOP of 15 mmHg or less without medication 6 months after surgery was 76.2% in the low-concentration group and 88.2% in the high-concentration group.

There was no significant difference between the two groups. No significant differences were present between the two groups regarding postoperative complications including ocular hypotony and cataract. The findings show that similar hypotensive effect results in 6 months after trabeculectomy whether using 0.2 mg/mL or 0.4 mg/mL MMC.

The outcome of trabeculectomy with adjunctive MMC appears to represent a complex interaction of patient and surgical variables. While there is some support for benefit of titrating MMC according to individual patient variables, there is inadequate evidence at the present time to claim superiority for any MMC protocol, with or without titration.

**Observations**

The present study "comparative evaluation of different concentrations of mitomycin C as an adjuvant in filtering surgery" was conducted in the upgraded Department of Ophthalmology, NSCB Medical College, Jabalpur.

22 cases were selected in our study. From the patients attending the Outpatient Department of Upgraded Department of Ophthalmology, NSCB Medical College, Jabalpur.

**Cases were Studied under the following Groups**

Group I: Intraoperative use of mitomycin C (0.2 mg/mL for 2 minutes).

Group II: Intraoperative use of mitomycin C (0.4 mg/mL for 2 minutes).

| Group | No. | % |
|---|---|---|
| Group– I (0.2 mg/mL) | 12 | 54.55% |
| Group– II (0.4 mg/mL) | 10 | 45.45% |
| **Total** | **22** | **100%** |

***Table I. Distribution of Cases in Different Groups***

| Type of Glaucoma | Open Angle Glaucoma | | Chronic Angle Closure Glaucoma | | Total |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Primary | 16 | 72.73 | 3 | 13.64 | 19 (86.37%) |
| Secondary | 3 | 13.64 | 0 | 0 | 3 (13.64%) |
| **Total** | **19** | **86.37** | **3** | **13.64** | **22 (100%)** |

***Table II. Classification of Patients According to the Types of Glaucoma***

Table II shows classification of patients according to the types of glaucoma. 86.37% of the patients with primary glaucoma either open or closed. 13.64% had it secondary to cataract surgery or inflammatory condition of the eye.

| I/o MMC | SPK (Epithelial defect) | Shallow AC | Hypotony | Hyphaema | Total |
|---|---|---|---|---|---|
| Group I (0.2 mg/mL) | 0 | 1 (8.33%) | 3 (25%) | 1 (8.33%) | 4 (33.33%) |
| Group II (0.4 mg/mL) | 1 (10%) | 1 (10%) | 3 (30%) | 0 | 5 (50%) |

***Table III. Early Complications (During First Week)***

Table V shows incidence of complications with I/O use of MMC in different concentrations in early postoperative period (During first week).

| I/o MMC | Uncontrolled IOP | Hypotonic Maculopathy | Cataract | Total |
|---|---|---|---|---|
| Group I (0.2 mg/mL) | 1 (8.33%) | 0 | 1 (8.33%) | 2 (16.66%) |
| Group II (0.4 mg/mL) | 0 | 1 (10%) | 1 (10%) | 2 (20%) |

***Table IV. Late Complications (After Six Months)***

Table IV shows late complications (after six months) with I/O MMC when used in different concentrations (0.2 mg/mL vs. 0.4 mg/mL).

| IOP | I/O MMC | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| In | 0.2 mg/mL | | | | 0.4 mg/mL | | | | 0.2 mg/mL | | 0.4 mg/mL | |
| Mm | Pre-op. | | Post-op. | | Pre-op. | | Post-op. | | C+M | U+M | C+M | U+M |
| | No. | % | No. | % | No. | % | No. | % | | | | |
| <21 | 0 | 0 | 9 | 75 | 0 | 0 | 9 | 90 | 2 | 0 | 1 | 0 |
| 21-30 | 3 | 25 | 3 | 25 | 1 | 10 | 1 | 10 | 0 | 1 | 0 | 0 |
| 31-40 | 8 | 66.66 | 0 | 0 | 5 | 50 | 0 | 0 | 0 | 0 | 0 | 0 |
| 41-50 | 1 | 8.33 | 0 | 0 | 4 | 40 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | | | | | | | | | 2(16.67%) | 1(8.33%) | 1(10%) | 0 |

***Table V. IOP Control with MMC (0.2 mg/mL vs. 0.4 mg/mL) with or without Medications***

Table V shows pre and post-operative mean IOP when MMC was used intraoperatively for 2 minutes in a concentrations of 0.2 mg/mL or 0.4 mg/mL. IOP was said to be controlled when IOP was <21 mm. It was 75% in 0.2 mg/mL group and 90% in 0.4 mg/mL group. One remained uncontrolled even with topical medications in 0.2 mg/mL group.

**DISCUSSION**

The present study consists of 22 cases of glaucoma, primary or secondary in which filtering surgery was planned with the use of wound modulator mitomycin-C in different concentrations (0.2 mg/mL v/s 0.4 mg/mL).

Out of 22 cases, there were 9 males and 13 females. In our series, maximum number of cases belong to more than 50 years of age in both groups of sex. After thorough clinical examination and pre-operative assessment, cases were operated in Eye O.T. under thorough aseptic precautions. All the cases were duly registered.

In our study, success rate (IOP <21 mmHg) was 75% in group I and 90% in group II. The mean post-operative IOP was 16.20 mmHg in group I and 15.70 mmHg in group II. In our study, most common early post-operative (within one week) complication was hypotony (25% in group I and 30% in group II), followed by shallow AC (8.33% in group I and 10% in group II), SPK (10% in group I only) and hyphema (8.33% in group I only).

So, there is no significant difference regarding success rate (75% in group I and 90% in group II), post-operative IOP and complication between these two groups (0.2 mg/mL vs. 0.4 mg/mL). Our study corresponded with the study done by Shin IU, Greenfield DS, Schiffman J et al[2] They also used MMC in

concentration of 0.2 mg/mL and 0.4 mg/mL in 110 eyes which underwent trabeculectomy. The success rates in their study were 76.2% in low concentration group (0.2 mg/mL) and 88.2% in high concentration group. So like our study, no significant differences were present between the two groups regarding success rate-post operative complications including ocular hypotony and cataract.

Our study also corresponds with the study done by Ichien K, Yamamoto T, Kitazawa Y, Oguri A, Ando H, Kondo Y.[3] They reviewed 26 patients (36 eyes) who underwent trabeculectomy in which MMC was applied intraoperatively. MMC was applied in 3 concentrations; 0.1 mg/mL, 0.2 mg/mL and 0.4 mg/mL. They showed that there were no significant differences present between the two groups (0.2 mg/mL and 0.4 mg/mL) regarding success rate (success rate 100% in 0.4 mg/mL group, 70% in 0.2 mg/mL group) and post-operative complications.

Scott IU, Greenfield DS, Schiffman J et al worked on lower concentration of MMC (0.2 mg/mL) during filtering surgery. They found that 86.5% of patients showed controlled IOP postoperatively without any medication (Mean IOP 16.20 mmHg). In our study (in 0.2 mg/mL group), 75% patients showed controlled IOP postoperatively without any medication (mean IOP 12.98 mmHg). In this study, early post-operative complication included hypotony (21.22%), hyphaema (13.5%), epithelial defects (5.76%). In our study, most common early post-operative complication was also hypotony (25%), followed by shallow AC (8.33%), hyphema (8.33%) in low concentration group (0.2 mg/mL). In their study, most common late post-operative complications were cataract (40%) followed by uncontrolled IOP (3.84%), hypotonic maculopathy (1.9%) whereas in our study most common late complication was also cataract (8.33% cases), other complications were uncontrolled IOP, hypotony, and maculopathy.

Alwitry A, Moodie J, Rotchford A, Abedin A, Patel V, King AJ[4] et al work on higher concentration on MMC (0.4 mg/mL). In their study, 12 out of 15 eyes were classified as surgical success and mean IOP was 15.6±1.3 postoperatively (80%). It was also similar to our study in which success rate was 90% in higher concentration group (0.4 mg/mL) with mean IOP 15.70 mmHg. In their study, none of the patients developed hypotonic maculopathy, but in our study 1 case (10%) developed hypotonic maculopathy after 6 months. Visual acuity decreased in 3 cases. 1 case belonged to group I, and 2 cases belonged to group II. This was again due to cataract changes, corneal complications or hypotony.

Mietz H, Addicks K, Bloch W et al[5] et al in their similar study found that visual acuity decreased in 3 cases (6%) of low concentration group (0.2 mg/mL), in 8 cases of high concentration group 0.4 mg/mL. This was again due to hypotony and cataractous changes.

In our study, fundus and field changes were progressive in 2 cases. 1 belonged to group I and other belonged to group II. In these cases, IOP was not controlled with medical therapy.

In our study, out of 22 eyes, 18 had diffuse, vascularised, microcystic blebs (81.82%), 3 had shallow blebs (13.64%) and 1 had thin avascular bleb (4.54%). In a study done by Cheung JC, Wright MM, Murali S, Pederson JE et al[6] of 45 eyes with complete success, 28 (62.2%) had diffuse microcystic bleb, 12 had shallow bleb (26.7%) and 5 had cystic bleb. In our study, one thin anaemic bleb belonged to group II (0.4 mg/mL group).

Our study also corresponded with the study done by Ozkiris A, Tamcelik M.[7] In this study, MMC was used in concentration of 0.2 mg/mL (Group I) and 0.4 mg/mL (Group II) during trabeculectomy. Like our study, they also found that there were no significant differences between the groups for IOP success rate and complications. In this study, the most common early post-operative complication was also shallow AC (22.9%) whereas in our study, the most common early post-operative complication was hypotony (27.27%).

In our study, it was found that MMC when used in different concentrations (0.2 mg/mL v/s 0.4 mg/mL), there were no significant differences in IOP success rate and complications between 2 groups.

**CONCLUSIONS**

In present study, 22 cases of trabeculectomy with MMC were considered from patients attending outpatient department of eye wards of NSCB Medical College, Jabalpur.

**The cases were divided into following groups:**

**Group I-** Intraoperative use of MMC for 2 minutes in a concentration of 0.2 mg/mL.

**Group II-** Intraoperative use of MMC for 2 minutes in a concentration of 0.4 mg/mL.

In our study, male-female ratio is 0.69: 1 and out of 22 cases, maximum patients were greater than 50 yrs. of age. 16 (86.36%) patients had primary glaucoma either open angle or closed and 6 (13.64%) had it secondary to cataract surgery or inflammatory condition of eye.

In our study, maximum cases 13 (59.1%) had IOP in the range of 31-40 mmHg, 5 (22.73%) patients had IOP in the range of 41-50 mmHg and 4 patients had IOP in the range of 21-30 mmHg preoperatively.

Out of 12 cases in group I (0.2 mg/mL), 9 cases had controlled IOP (<21 mmHg) postoperatively.

Mean IOP postoperatively was 16.20 mmHg in group I and 15.70 mmHg in group II

3 required medications postoperatively. 1 required timolol 0.5% eye drop and another required timolol 0.5% + brimonidine to control the IOP.

In 1 case, IOP was not controlled even with medication postoperatively.

So it was concluded that IOP was uncontrolled in 1 case of group I (0.2 mg/mL).

Out of 10 cases in group II, (0.4 mg/mL) 9 had controlled IOP (<21 mmHg), 1 required timolol 0.5% postoperatively to control IOP.

- So, success rate was 75% in group I (0.2 mg/mL).
- Success rate was 90% in group II (0.4 mg/mL).

Visual acuity decreased in 3 cases. 1 case belonged to group I and 2 cases belonged to group II. This was again due to cataractous changes, hypotony and corneal complications.

In our study, out of 22 eyes, 18 had diffuse, vascularised, microcystic blebs (81.82%), 3 had shallow blebs (13.64%) and 1 had thin avascular bleb (4.54%).

Early postoperative complications included hypotony [3 cases (25%) in group I, 3 cases (30%) in group II], shallow AC [1 case (8.33%) in group I and 1 case (10%) in group II], SPK

[1 case (10%) in group II only], hyphema [1 case (8.33%) in group I only].

Late postoperative complications included cataract [1 case (8.33%) in group I, 1 case (10%) in group II], uncontrolled IOP [1 case (8.33%) in group I only], hypotonic maculopathy [1 case (10%) in group II only].

Hence, in our study, it was concluded that MMC when used in different concentrations (0.2 mg/mL vs. 0.4 mg/mL), there were no significant differences in mean IOP, success rate, and complications between 2 groups.

**REFERENCES**

1. Bergstrom TJ, Wilkinson WS, Skuta GL, et al. The effects of subconjunctival mitomycin-C on glaucoma filtration surgery in rabbits. Arch Ophthalmol 1991;109(12): 1725-30.
2. Scott IU, Greenfield DS, Schiffman J, et al. Outcomes of primary trabeculectomy with the use of adjunctive mitomycin. Arch Ophthalmol 1998;116(3):286-91.
3. Ichien K, Yamamoto T, Kitazawa Y, et al. Mitomycin-C dissolved in a reversible thermosetting gel: target tissue concentrations in the rabbit eye. British Journal of Ophthalmology 1997;81(1):72-5.
4. Alwitry A, Moodie J, Rotchford A, et al. Predictive value of early IOP in Mitomycin-C augmented trabeculectomy. J Glaucoma 2007;16(7):616-21.
5. Mietz H, Addicks K, Bloch W, et al. Long-term intraocular toxic effects o topical mitomycin C in rabbits. J Glaucoma 1996;5(5)325-33.
6. Cheung JC, Wright MM, Murali S, et al. Intermediate-term outcome of variable dose mitomycin-C filtering surgery. Ophthalmology 1997;104(1):143-9.
7. Ozkiris A, Tamcelik N. Long-term results of trabeculectomy with different concentrations of mitomycin-C in refractory developmental glaucoma. Journal of Pediatric Ophthalmology and Strabismus 2005;42(2):97-102.