

EFFECTIVENESS OF HIGH-DOSAGE MITOMYCIN-C IN TRABECULECTOMY: High risk patients with glaucoma

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ABSTRACT

Objective: To evaluate the effectiveness of high-dosage mitomycin-C (MMC) in patients with glaucoma undergoing trabeculectomy and its use for preventing failure of operation.

Methodology: We used 0.5mg/ml MMC for 5 minutes during trabeculectomy operation for twenty patients with glaucoma (twenty eyes). MMC was applied on episclera without any contact with the wound. Patients were followed-up for twelve months. Success of operation by the use of high-dosage MMC was defined with intraocular pressure (IOP) between 5 and 20mmHg together with decline of snellen visual acuity not more than two lines.

Results: Trabeculectomy together with high-dosage MMC led to decline of IOP on an average of 66%. The mean preoperative IOP was 34.8±5.16 mmHg and the mean postoperative IOP was 12.6±2.93 mmHg. The difference between preoperative and postoperative IOP was statistically significant (p<0.05). Of the twenty patients, 100% had successful operation, 90% had formation of thin avascular bleb, 25% had postoperative leakage, 20% had shallow anterior chamber, 20% had choroids effusion, and 10% had cataract at postoperative evaluation.

Conclusion: High-dosage Mitomycin-C is safe & effective for high risk patients with glaucoma who undergo trabeculectomy and it leads to significant control of IOP if postoperative complications are managed and treated as well.

KEY WORDS: Mitomycin-C, Trabeculectomy, Intraocular, Glaucoma.

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INTRODUCTION

Wound formation is the leading cause of failure in trabeculectomy operation in patients with glaucoma. It seems that fibroblasts of conjunctiva and Tenon's capsule are the main cause of wound formation.¹ That is why ophthalmologists are trying to prevent this

reaction in trabeculectomy to reach more successful operative outcomes. Mitomycin-C (MMC) is an antineoplastic antibiotic produced from fermentation of *Streptomyces caespitosus*.² MMC prevents deoxyribonucleic acid (DNA) synthesis and histological investigations illustrate that it suspends cell growth and fibroblast replication, thus the aim of using this medication during trabeculectomy is to suspend fibroblasts of conjunctiva and Tenon's capsule and therefore, to increase the success of operation and stability of bleb or fistula in surgery.^{2,3} In trabeculectomy, patients with high-risk characteristics are those who have more postoperative risks because of cellular replication and increased inflammation. These patients might have one of these backgrounds in their medical history: intraocular surgery, ocular trauma with angle recess, operation of conjunctiva, failed trabeculectomy operation,

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aphakia, pseudophakia, young age (less than eighteen), long-term use of antiglaucoma medications, uveitis, and neovascular glaucoma.³⁻⁵

METHODS

This research was designed as an experimental study and it was done during 2005 to 2006. During these two years, patients with glaucoma (intraocular pressure more than 20 mmHg together with damage of optic nerve and changes in visual field) were selected from Nikoukari ophthalmology hospital, Tabriz, Iran. Of the entire glaucoma patients during this period, those who had progressive disease and their problem had not been controlled by the use of multiple antiglaucoma medications, were included in the study to undergo trabeculectomy. Finally, twenty patients (twenty eyes) were included in the study of which nineteen (95%) had history of ocular surgery with wound in superior limbus region.

All the trabeculectomies were performed by an identical surgeon using standard surgical procedure for each patient. After administration of regional or general anesthesia, the superior rectus muscle was suspended with a 4-0 silk suture. A superior limbus-based conjunctival flap was created approximately 10 mm posterior to the limbus at 12 o'clock position. Then, conjunctiva and Tenon's capsule were removed from the episcleral surface and after determining the site of scleral flap, 0.5mg/ml MMC solution was applied on episcleral surface by three 4x4mm sponges for 5 minutes. Conjunctiva and Tenon's capsule were transferred to cornea to prevent any contact between MMC and them or between MMC and wound edges. MMC wash-out was done by 30 ml of sterile normal saline and an approximately 4x4mm triangular scleral flap that had width of 1/3 of scleral thickness was formed. A 1x2.5mm scleral block removed and after peripheral iridectomy, the scleral flap was sutures with one or three 10.0 monofilament nylon in apex. The conjunctiva and Tenon's capsule were then closed with 10.0 nylon suture. Postoperative follow-up of subjects was done one week, two weeks, one month, three months, six months, and twelve months after

the operation. We recorded best corrected visual acuity, intraocular pressure, appearance of the bleb, postoperative complications, leakage of the wound site, position and depth of the anterior chamber, and position and fundus of the lens for all of the study patients.

Patient data obtained six and twelve months after operation were analyzed by SPSS 14.0 software. We used Kolmogorov-Smirnov test for confirming normal distribution of data and then we used t-test for comparing the difference between preoperative and postoperative visual acuity. Friedman test was used for comparing preoperative and postoperative intraocular pressures.

RESULTS

Twenty eyes with high risk of failure of operation underwent trabeculectomy by the use of high-dosage mitomycin-C (0.5mg/ml) for 5 minutes during operation. The normal dosage of mitomycin is between 0.1 and 0.4mg/ml in the review of the literatures. Postoperative follow-up of subjects was done one week, two weeks, one month, three months, six months, and twelve months after the operation and finally data for six month and one year follow-up was recorded and used in analysis.

Of the 20 patients, 19 (95%) had history of intraocular surgery together with conjunctival wound in superior region of limbus. Four patients (20%) had the history of failed trabeculectomy and 13 patients (65%) had the history of cataract operation by extracapsular incision of superior limbus. Two patients (10%) had the history of trauma together with surgery of conjunctival surface and angle recess while one patient (5%) had primary open-angle glaucoma. Of the 13 patients with the history of cataract surgery, 4 were aphakic and the rest were pseudophakic.

The entire patients had the history of long-term and chronic use of antiglaucoma medications for an average of 15 months. They used at least three different drugs and the most common ones were beta-blockers, pilocarpins, and diamox. The mean age of patients was 60 years of age (± 14) ranged between 15 and 82 years. The use of mitomycin-C during trabeculectomy

led to a decline of 66% in intraocular pressure. This decline of IOP was statistically significant ($p < 0.05$). Table-I illustrates preoperative and postoperative IOP changes during patients' follow-up. In this study, success of operation was 100% considering IOP and visual acuity. Of the entire patients, nineteen patients reached to IOP less than 20mmHg without medications and one of them reached this threshold by the use of medications.

The best preoperative corrected vision was 20/100 while after twelve months of follow-up, 40% had one more snellen line, 50% had not any change in their visual acuity, and 10% had lost two snellen lines because of opacity of their lenses. Statistical analysis showed that the difference between postoperative and preoperative visual acuity was not significant ($p > 0.05$). Postoperative complications included wound leakage, shallow anterior chamber, choroidal detachment, and cataract. Hypotonic maculopathy and endophthalmitis were seen in none of patients. Table-II shows the rate of various postoperative complications in study subjects. Patients with postoperative cataract were treated by the use of appropriate interventions. In the twelve-month follow-up, thin avascular bleb was seen in 18 patients (90%).

DISCUSSION

The success of trabeculectomy in the absence of high-risk characteristics, from the surgical point of view, has been reported 85% to 90% in the review of the literature.⁵ Glaucoma operation by the use of mitomycin C was done by Chen in 1983 for the first time.⁴ High-risk characteristics include history of long-term use of local antiglaucoma medications, young ages, history of intraocular surgeries, aphakia, and recess angle.^{3-4,6} In the present study, we applied high-dosage MMC for five minutes on

Table-II: Frequencies and percentages of postoperative complications in study subjects

	Frequency	Percentage(%)
Wound leakage	5	25
Shallow anterior chamber	4	20
Choroidal detachment	4	20
Cataract	2	10
Hypotonic maculopathy	0	0
Endophthalmitis	0	0

episcleral surface and we also prevented the contact of MMC with the edges of the wound for reducing postoperative complications. Applying MMC under the scleral flap has the risks of leakage of the drug to the intraocular spaces and damage of ciliary body and cornea. That is why we used episclera for high-dosage MMC to prevent its leakage to the intraocular spaces. Chen et al. declared that the operations which were successful one year after surgery had more chance of five-year successfulness.⁷ We also follow-up our patients for a maximum of twelve months.

Beatty et al. applied 0.2mg/ml MMC under the scleral flap of high risk patients for five minutes which led to a success of 83%.⁵ Tham *et al.* reported the results of trabeculectomy with adjunctive intraoperative MMC in Chinese patients with glaucoma.^{8,9} In the present study, the successful operation was seen in all of the patients (100%) and the mean decline of IOP was 66%. Only one patient was prescribed antiglaucoma medications after the surgery and this patient reached to IOP less than 20mmHg by the use of drug therapy. Considering this patients' preoperative IOP (45mmHg) and also his unchanging correction of visual acuity, we can claim that this operation was also successful. According to the results of our study and also the comparison of these with the review of the literature, it seems

Table-I: Preoperative intraocular pressure (IOP) and postoperative IOP 6 and 12 months after trabeculectomy

	Min (mm Hg)	Max (mm Hg)	Mean (mm Hg)	SD (mm Hg)	Statistical Significance*
Preoperative IOP	25	45	34.8	5.16	
IOP after 6 months	8	16	12.1	2.38	P<0.05
IOP after 12 months	8	20	12.6	2.93	P<0.05

IOP, Intraocular Pressure * Friedman test

that high-dosage mitomycin C acts more effectively than lower dosages in high risk glaucoma patients.

In the study by Beatty et al., visual acuity of patients was improved or was unchanged in 80% of patients at their last follow-up and totally, 91.6% had at most one loss of snellen lines. This loss of visual acuity was the consequent outcome of progressed opacity of the patients' lenses.⁵ One of the main complications of application of MMC in trabeculectomy is the formation of thin avascular blebs.¹⁰ Long-term risks of these blebs have not still been defined completely.¹¹ It has been reported that long-term control of intraocular pressure is done better by the presence of these blebs.¹¹ In a study done by Susanna et al., 0.25mg/ml MMC was applied for three minutes during trabeculectomy by limbal base flap. There was not any contact between MMC and conjunctiva or MMC and Tenon's capsule. Then, the MMP application site was washed-out by 100 ml of sterile normal saline and finally, formation of this avascular bleb was seen in 80% of patients.¹² Mandal et al. applied 0.4 mg/ml MMC for three minutes and they reported thin avascular blebs in all of their patients, but they did not see any infections related to these blebs at a follow-up of nineteen and half months.¹³ In our study, 90% had thin avascular bleb at the follow-up of twelve months. It should be mentioned that 95% of our patients had the history of intraocular surgery at the superior conjunctival region which can be a significant cause of ischemia regarding bleb formation Table-II. In general, it seems that high-dosages of MMC lead to postoperative complications more than lesser dosages, however the rates of postoperative complications have wide ranges: hypotonic maculopathy has been reported 0% to 8%,^{3,5,14,15} choroidal detachment has been reported 3% to 25%,^{5,14,15} shallow anterior chamber has been reported 1% to 11%,^{1,3,5,14} and cataract has been reported 2.5% to 10%.^{1,14}

In conclusion, application of high-dosage mitomycin C for glaucoma patients with high-risk characteristics for five minutes on episclera and without any contact with wound edges can lead to a successful trabeculectomy. It seems

that formation of thin avascular blebs does not have any relationship with dosage and duration of MMC application. It might be related to the procedure of conducting conjunctival flap. High-dosages of MMC lead to more post-operative complications which can be lessened by careful patching of wounds and appropriate management of procedures of adverse consequences.

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