Original Article

Trabeculectomy With Topical Application of Mitomycin-C In High Risk Glaucoma Patients

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Purpose: To observe and compare the intraocular pressure (IOP) lowering effect of trabeculectomy with topical application of mitomycin C, using two different concentrations, of 0.2mg/ml and 0.4mg/ml, in high risk glaucoma patients.

Material and Methods: Forty eyes of 26 patients of glaucoma, who were considered to be at high risk for failure because of their young age, previous ocular surgery like cataract extraction and trabeculectomy, inflammatory glaucoma, high myopia and prolonged anti-glaucoma medication, underwent trabeculectomy with topical application of 0.2mg/ml concentration of mitomycin C for three minutes. They were case matched with a group of same number of eyes of 27 high risk glaucoma patients who received 0.4mg/ml concentration of drug for same duration.

Results: The mean pre-operative IOP in the two groups was similar (29.63mmHg in group I and 30.43mmHg in group II). Twelve months after surgery, the mean pre-operative IOP decreased from 29.63mmHg to a post-operative level of 16.15mmHg in group I, with a success rate of 85%, and from 30.43mmHg to 16.88mmHg in group II, with the success rate of 82.5%. This difference in success rate is not significant statistically ($p<0.05$). Also no statistically significant differences were found in the complication rates as regards to development of conjunctival wound gaps, cataract formation, post-operative uveitis, hyphema, vitreous loss and ocular hypotony and its related maculopathy.

Conclusion: The present study supports the conclusion of previous studies that mitomycin C is highly effective drug when used in association with trabeculectomy, and when used in concentration of 0.2mg/ml for three minutes is as effective in controlling post-operative IOP as 0.4mg/ml of the drug for same duration. Higher but not statistically significant frequency of complications was found with the 0.4 mg/ml of mitomycin. We therefore recommend that in all patients with high risk glaucoma Mitomycin in the concentration of 0.2mg/ml should be used.

Trabeculectomy has been a filtering procedure of choice for control of IOP in most cases of glaucoma[1-2]. It is quick, technically easy to perform, has few complications and has high success rate[3-9]. However it has been observed that filtration failures are not infrequent, especially in eyes with risk factors for drainage failure[10-14] e. g congenital and developmental glaucoma, psuedophakic glaucoma, inflammatory glaucoma, trabeculectomy failure, black race, and high myopia etc (High risk glaucoma patients).

The most common cause of failure of glaucoma surgery is fibrosis of conjunctival bleb[15]. So the under standing of wound healing process and pharmacological factors modulating this process are most notable advances in this field. In addition to other drugs, mitomycin-C has been extensively evaluated in search of the most suitable method[16-18], its concentration, and mode of topical application and its complications[19-23].

Purpose of this study was to observe and to compare the IOP lowering effect of trabeculectomy with topical application of mitomycin C, using two different concentrations of 0.2mg/ml and 0.4mg/ml for three minutes in high risk glaucoma patients. The incidence of prolonged hypotony induced maculopathy was also studied.

MATERIAL AND METHODS

Eighty eyes of 53 high risk glaucoma patients were included in the study. Adequate control of diabetes and hypertension, and treatment of ischemic heart disease prior to surgery were confirmed. A written consent was taken, explaining about the anesthesia, surgical procedure, and topical application of mitomycin-C intra-operatively.

Trabeculectomy was performed with fornix-based conjunctival flap, and with per-operative application of mitomycin C under the conjunctivo-tenon membrane on the surface of the sclera before the formation of a scleral flap, which was 4x4mm in size. The procedure was completed by excision of 1.5 x 1.5 mm trabecular tissue, peripheral iridectomy, and then suturing the scleral and conjunctivo-tenon flaps. The lamellar scleral flap was sutured with five 10/0 interrupted sutures, Tenon and conjunctiva with three and two interrupted 10/0 sutures respectively.

Postoperative medications included dexamethasone eye drops 4 times a day, chloramphenicol eye drops 4 times a day and atropine eye drops twice a day. These were continued for four to five weeks except for atropine eye drops, which were usually discontinued after two weeks, depending upon the anterior chamber reaction during the postoperative period.

Suture lysis of the scleral flap was not carried out by any means although conjunctival sutures were removed when required.

RESULTS

Eighty eyes of 53 patients of high risk glaucoma were studied. Thirty patients were operated upon both eyes. The male patients were almost equal to the females with a ratio of 21:19. In all patients, mitomycin C was applied for three minutes. Average age of patients was 35.48 years, with a range of 5 months to 69 years. The patients were divided into following two groups:

Group I: Those who were treated with 0.2mg/ml concentration of mitomycin C. (Table 1).

Group II: Those who were treated with 0.4mg/ml concentration of mitomycin C. (Table 1).

Table 1: Intraocular pressure comparison for all cases

	Pre operative mmHg	Post operative mmHg
IOP	30.02	16.51
SD	± 9.11	± 7.72
Range	11-58	6-40

Follow up time, for all patients, was 12 months.

For the purpose of comparison, the surgery was considered a "success" when post-operative IOP≤ 21mmHg without anti-glaucoma medication. Comparison between the two groups was performed using Fisher exact test and chi-square analysis. A finding was considered significance at P value< 0.05.

Mean pre-operative IOP for all eyes was 30.02 ± 9.11 mmHg with a range of 11 to 58 mmHg, and mean post-operative IOP for all eyes was 16.5 ± 7.72mmHg having a range of 06mmHg to 40mmHg, as measured on last follow up visit. The average reduction in IOP was 13.52 mmHg. Over all success rate (Table 2) was 83.75 %. The mean pre-operative IOP in the two groups was similar (29.63mmHg in group I and 30.43mmHg in group II). The mean pre-operative IOP decreased from 29.6 mmHg to a post-operative level of 16.15 mmHg in group I, with a success rate of 85%, and from 30.43 mm Hg to 16.88mmHg in group II, with the success rate of 82.5%. This difference in success rate is not significant statistically.($p < 0.05$).

Complications and their incidence (Table 3)

No statistically significant differences were found in the complication rate as regards development of conjunctival wound gaps, cataract formation, post-operative uveitis, hyphema and vitreous loss. Ocular hypotony developed in 7 eyes (17.5%) in group II. Out of these 3 cases (7.5%) were due to wound leakage, only one required surgical intervention and others were cured with conservative measures. In two of these 7 patients hypotony was due to choroidal detachment, which improved spontaneously. The remaining two patients (5%) developed prolonged hypotony along with maculopathy. In group I, no case of hypotony was observed and so no patient developed hypotony related maculopathy in this group. The difference between the two groups regarding development of ocular hypotony was statistically significant, ($p < 0.05$). Although the incidence of maculopathy related to prolonged hypotony was higher in Group II but it was not statistically significant ($p > 0.05$). The complications like hyphema, post-operative uveitis, and conjunctival wound leakage were managed conservatively.

DISCUSSION

The first report of glaucoma surgery with adjuvant mitomycin-C was by Chen[21]. Mitomycin C is an anti-cancer anti-biotic drug isolated from Streptomyces caespitosus. The mechanism by which mitomycin-C influences, ocular tissues in filtration surgery is not fully understood. Tissue culture studies of rabbit's subconjunctival fibroblasts by Yamamoto[22] and Khaw[23] and human subconjunctival fibroblasts by Jampel[24] suggest that mitomycin C has its affects primarily on cell proliferation. This effect is not only concentration dependent, but also exposure time dependent in rabbits[25]. Studying the effects of

Table 2: Group I and group II outcome comparison

	Group I		Group II	
	Pre operative	Post operative	Pre operative	Post operative
Mean IOP	29.63	16.15	30.43	16.88
Success rate	85 (%)		82.5 (%)	

Table 3: Incidence of complications of trabeculectomy with mitomycin-c during present study

Complication	Group II No. of eyes n (%)	Group I No. of eyes n (%)	Total No. of eyes n (%)
Conjunctival wound gap	4 (10)	2 (5)	6 (7.5)
Wound leakage with shallow AC, surgery required	3 (7.5) 1 (2.5)	Nil	3 (3.75) 1 (1.25)
Choroidal detachment	2 (5)	Nil	2 (2.5)
Cataract formation	4 (10)	2 (5)	6 (7.5)
Postoperative Uveitis	2 (2.5)	Nil	2 (2.5)
Hyphema	3 (7.5)	2 (5)	5 (6.25)
Hypotony maculopathy	2 (5)	Nil	2 (2.5)
Vitreous loss	Nil	Nil	Nil

*All cases of Aphakic glaucoma and pseudophakic glaucoma, in which vitreous was found in AC, planned anterior vitrectomy was performed along with filtration.

Table 4: Comparison of reported series of filtering surgery with mitomycin-c

	Megavand GS and other (1995)	Beaty S and others (1998)	Ishioka and others (2000)	Casson R and others (2001)	Brart DPSO and others (2004)
MMC Concentration	0.2 mg/ml	0.2 mg/ml	0.2 mg/ml	0.2 mg/ml	0.2mg to 0.4mg/ml
Hypotony maculopathy (% age)	10% (5/50)	1.4% (1/72)	Nil	5% (1/21)	Nil
Success rate	72%	72%	68.4%	81%	91%

mitomycin C on human Tenon's capsule fibroblasts, Jampel[26] only examined the effects on proliferation of cells and not on fibroblast migration, collagen production or local vasculature. Reduced vascularity of filtration bleb in trabeculectomy with topical application of mitomycin C, may enhance the other actions of the drug because it has been observed that mitomycin C is selectively toxic to hypoxic cells[27].

The ability of mitomycin to prevent proliferation of fibroblasts of sub-conjunctival tissue and those of Tenon's capsule after single application at filtration site, has significantly improved the success rate of glaucoma filtering surgery. Many studies has since confirmed the enhanced IOP lowering effect of trabeculectomy, augumented by mitomycin C[16-21, 26-32]. However, the optimal concentration of mitomycin C, and the duration of its exposure to the tissues, is still not known. The purpose of this study was to determine whether adequate post-operative control of IOP and a lower incidence of post-operative complications, can be achieved by using mitomycin-C in a lesser concentration during trabeculectomy, performed in high risk glaucoma patients.

In most of the studies, mitomycin C was applied in variable concentrations. Chen et al[21]used 0.2mg/ml in majority of their cases (32/45). Palmer used 0.2mg/ml in his 33 patients[20]. Kitazawa used 0.4 mg/ml[33]Skuta et al[17] used 0.5mg/ml and Shields[19] used 0.4 mg/ml. Yamamoto et al[27] in their study of titrating the dose of mitomycin-C demonstrated that 0.2mg/ml and 0.1mg/ml of mitomycin-C applied for 5 minutes at the time of trabeculectomy resulted in adequate control of post-operative IOP.

The results of present study, regarding success rate for post-operative control of IOP and incidence of post-operative hypotony related maculopathy, are similar to the results of recently reported studies (Table 4). Shields MB et al[19] titrated the duration of exposure of eyes to mitomycin C according to the risk factors for failure of filtration from excessive fibrosis. Patients with relatively no risk were treated for 2 minutes, while an additional minute was added for each risk factor, e.g young age, black race, repeat surgery etc, up to a maximum of 5 minutes. The reported success rate was 72%. The incidence of hypotony maculopathy was 10% (6/59) and it was mostly observed in patients treated with 0.4mg/ml concentration of mitomycin C for 5 minutes. Megavand[28] reported a success rate (IOP ≤ 21mmHg without anti-glaucoma medication) of 72%,while prolonged hypotony developed in 10% (5/50 eyes). Beaty[29] and Misaki Ishioka[30] reported 72% and 68.4% success rates respectively, both using 0.2mg/ml concentration of mitomycin C. The incidence of hypotony maculopathy was only 1.4% and zero percent respectively. Casser[31] reported 81% success rate and 5% incidence of hypotony maculopathy (1/21 eyes), using 0.02% mitomycin C for only 2 minutes. Similarly Brart[32] using 0.2mg/ml to 0.4mg/ml concentration of mitomycin C for 2 minutes, reported a relatively higher success rate (91%), without any case of hypotony related maculopathy.

In the present study, two concentrations of the drug, 0.2mg/ml and 0.4mg/ml, were used, so that effects of different concentrations of the drug on post-operative control of IOP may be studied. There was, statistically no difference in the success rate ($p>0.05$). The incidence of prolonged hypotony related maculopathy was more i.e. 5% (2 patients) with 0.4 mg/ml concentration of the drug, compared with no case of hypotony related maculopathy with 0.2 mg/ml concentration of the drug. This indicates that this vision threatening complication was considerably less with lesser concentration, even though this difference in the incidence of maculopathy was still statistically insignificant ($p>0.05$). These results are similar to the recently reported studies, all indicating that the success rate of surgery remains the same by reducing concentration of mitomycin C, although the incidence of vision threatening complications, like maculopathy, is reduced.

CONCLUSION

The present study supports the conclusion of previous studies that mitomycin C is highly effective drug when used in association with trabeculectomy, and when used in concentration of 0.2mg/ml for three minutes is as effective in controlling post-operative IOP as 0.4mg/ml of the drug for same duration. Higher but not statistically significant frequency of complications was found with the 0.4 mg/ml of mitomycin. We therefore recommend that in all patients with high risk glaucoma Mitomycin in the concentration of 0.2 mg/ml should be used.

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