Comparison of Outcomes and Predictors of Trabeculectomy Using High-dose or Low-dose Mitomycin C

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Aims: *To compare the outcomes of trabeculectomy using low-dose or high-dose mitomycin C and to determine the factors that predict the postoperative intraocular pressure.*
Patients and Methods: *In a prospective, randomised comparative study, patients undergoing trabeculectomy were randomly assigned to receive either mitomycin C 0.2 mg/mL for 4 minutes or mitomycin C 0.4 mg/mL for 2 minutes. The intraocular pressure, bleb character, and occurrence of complications were compared. Age and sex of the patients, preoperative intraocular pressure, mitomycin C concentration, bleb characteristics, angle status, and age of the surgery were analysed to determine whether they were predictive factors for postoperative intraocular pressure.*
Results: *Seventy four eyes of 68 patients at the Philippine General Hospital underwent trabeculectomy between January and June 1997. Thirty six eyes were treated with mitomycin C 0.2 mg/mL while 38 eyes were treated with mitomycin C 0.4 mg/mL. There were no statistically significant differences in the mean preoperative and postoperative intraocular pressures, and in the mean percent change in intraocular pressures between the 2 groups. Analysis of variance showed that preoperative intraocular pressure and bleb characteristics were significant predictors of postoperative intraocular pressure.*
Conclusions: *There is no apparent difference in the outcomes of trabeculectomies using low-dose and high-dose mitomycin C. Preoperative intraocular pressure and bleb characteristics are predictive factors of postoperative intraocular pressure.*

Key Words: Filtering surgery, Glaucoma, Mitomycin C

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Introduction

The surgical management of glaucoma is an indispensable treatment in developing countries where there are limitations in medical and laser therapy. Glaucoma filtration surgery fails due to the scarring of the filtering bleb, where fibroblast proliferation from the episclera and Tenon's capsule play a significant role.[1] The use of antimetabolites has improved the success rate of glaucoma filtration surgery. Mitomycin C (MMC) is an antibiotic agent with antineoplastic activity that inhibits the proliferation of fibroblasts. At present, there is no consensus as to the ideal concentration and exposure time of MMC.[2-17] The concentrations used in different studies range from 0.02 to 0.5 mg/mL, with the most commonly used concentrations being 0.2 mg/mL and 0.4 mg/mL. Exposure time varies from 30 seconds to 5 minutes, with the latter being the most common.

This study was undertaken to determine the most effective concentration and exposure time of MMC to provide a satisfactory reduction in intraocular pressure (IOP) with the fewest complications such as hypotony, choroidal detachment, scleral necrosis, hyphaema, and cataract formation. The study aimed to compare the outcome of trabeculectomy using MMC 0.4 mg/mL for 2 minutes versus MMC 0.2 mg/mL for 4 minutes in terms of IOP lowering, filtering bleb character, and incidence of complications. The study also aimed to determine the factors that predict the postoperative IOP.

Patients and Methods

Consecutive patients seen between January and June 1997 at the Philippine General Hospital's Glaucoma Clinic and evaluated by the Glaucoma Service as requiring a filtering procedure were classified

as either low risk for surgical failure (e.g., primary glaucomas) or high risk for surgical failure (e.g., congenital and developmental glaucomas, neovascular glaucoma, previous surgeries, failure of previous trabeculectomy, traumatic glaucoma, previous cataract surgery, secondary glaucoma, or inflammatory glaucoma).[18] After classification, each patient was randomly assigned, using a random table of values, to either the 2-minute exposure to MMC 0.4 mg/mL or the 4-minute exposure to MMC 0.2 mg/mL. A trabeculectomy protocol that was previously approved by the consultants of the Glaucoma Service was followed. All surgeries were performed by the glaucoma fellow and the 7 senior residents who were rotating in the Glaucoma Service during that period. The IOPs before surgery and at the most recent follow-up visit were compared. The character of the bleb at the most recent follow-up visit was also described. Complications, if any, were noted.

Univariate analysis was done to determine the effects of other factors such as age and sex of the patient, angle status, preoperative IOP, MMC concentration, bleb characteristics, and age of the surgery on the postoperative IOP, and whether these could be predictive factors.

Results

Seventy four eyes of 68 patients underwent filtering surgery between January and June 1997. Forty six patients (67.6%) were women and 22 (32.4%) were men. The mean age was 51.0 ± 2.2 years. Thirty nine eyes were classified as low risk and 35 eyes were diagnosed as high risk (Table 1). Thirty six eyes underwent filtering surgery with MMC 0.2 mg/mL while 38 eyes were treated with MMC 0.4 mg/mL. The mean preoperative IOP was 35.90 ± 1.47 mm Hg, while the postoperative IOP was 14.80 ± 0.94 mm Hg (Table 2). The mean follow-up period was 19.7 ± 1.5 weeks. The average percent change in IOP was -53.80% ± 3.31% suggestive of a drop in IOP. Table 3 shows the mean percent change in IOP between the 2 treatment groups. Using analysis of variance (ANOVA), it was found that preoperative IOP and bleb characteristics after surgery were significant predictors of IOP after filtering surgery. The postoperative IOP decreases by 1 mm Hg for every preoperative increase of 1 mm Hg. Compared with a flat bleb, eyes with diffuse blebs were noted to have a lower mean IOP, by 12.75 mm Hg. Eyes with vascular blebs and cystic blebs had a lower mean IOP, by 11.8 and 14.6 mm Hg, respectively, compared with eyes with flat blebs. Eyes with flat blebs, however, had an IOP of 7.4 mm Hg lower than the preoperative IOP. There is no evidence that the following factors are predictors of IOP after filtering surgery: MMC concentration (either 0.2 mg/mL or 0.4 mg/mL), angle configuration, age, sex, and age of the surgery in weeks (Table 4). The sample size power is to detect a difference in IOP according to the respective independent variables. The model from which this analysis is derived, however, has an R^2 value of 82%. This value means that the variability of the IOP after filtering surgery is explained

Table 1. Diagnosis of patients undergoing filtering surgery.

Low-risk diagnosis	Number of eyes (n = 39)	High-risk diagnosis	Number of eyes (n = 35)
Chronic angle closure glaucoma	32	Failed trabeculectomy	8
Primary open angle glaucoma	7	Congenital glaucoma	7
		Neovascular glaucoma	7
		Previous intraocular surgery (other than cataract extraction)	5
		Axenfeld-Rieger syndrome	4
		Post-cataract extraction	2
		Combined cataract and glaucoma surgery	2

Table 2. Comparison of mean intraocular pressures between eyes treated with mitomycin C 0.2 mg/mL and 0.4 mg/mL.*

Treatment group	Preoperative intraocular pressure (mm Hg)		Postoperative intraocular pressure (mm Hg)	
	Mean	Standard deviation	Mean	Standard deviation
Mitomycin C 0.2 mg/mL	37.5	13.2	14.0	7.9
Mitomycin C 0.4 mg/mL	34.4	12.0	15.6	8.4

* The apparent differences are not statistically significant.

Table 3. Comparison of mean percent change in intraocular pressure between eyes treated with mitomycin C 0.2 mg/mL and 0.4 mg/mL.*

Treatment group	Mean percent change	Standard error	Mean intraocular pressure reduction (mm Hg)
Mitomycin C 0.2 mg/mL	-49.4	6.6	18.1
Mitomycin C 0.4 mg/mL	-42.9	6.6	17.4

* The differences are not statistically significant.

Table 4. Factors that are non-predictors of intraocular pressure after filtering surgery.

Factors	Sample size power to detect a difference in intraocular pressure
Mitomycin C concentration	7.3%
Angle closure	12.3%
Age of the patient	24.8%
Sex of the patient	14.1%
Age of the surgery (weeks)	25.5%

by the identified independent variables 82% of the time.

Success of ocular filtering surgery can be defined in 3 ways. The concept of target intraocular pressure is one definition. This is given by the expression:

$$TP = IP (1 - IP/100) - Z \pm 2$$

where TP is the target pressure, IP is the pressure when damage has occurred, and Z is the degree of damage.

Other definitions of a successful filtering surgery are 30% and 40% reduction in preoperative IOP. Cox proportional hazards modelling was employed to determine the success rate of the surgeries using the 2 MMC concentrations. This analysis revealed the same deductions as the univariate analysis, i.e., preoperative IOP and the type of bleb are the identified determinants of filtering surgery success.

In the model, it was seen that eyes with diffuse blebs had a 6.89-fold increase in probability of success when compared with a flat-bleb eye. Eyes with vascular blebs and eyes with cystic blebs had a 1.73-fold and a 24.40-fold increase in probability of success, respectively, when compared with a flat-bleb eye. Furthermore, the Cox proportional hazards analysis showed that for every 10 mm Hg reduction in preoperative IOP, the probability of successful surgery was increased 3.35-fold. All these findings reached a statistical significance of <0.020. These observations were true for all 3 definitions of a successful filtering surgery.

Figure 1 shows the success rate of the surgical intervention with respect to the MMC concentration used. There were very few complications, as shown in Table 5.

Figure 1. Comparison of the success rate for mitomycin C 0.2 mg/mL and 0.4 mg/mL.

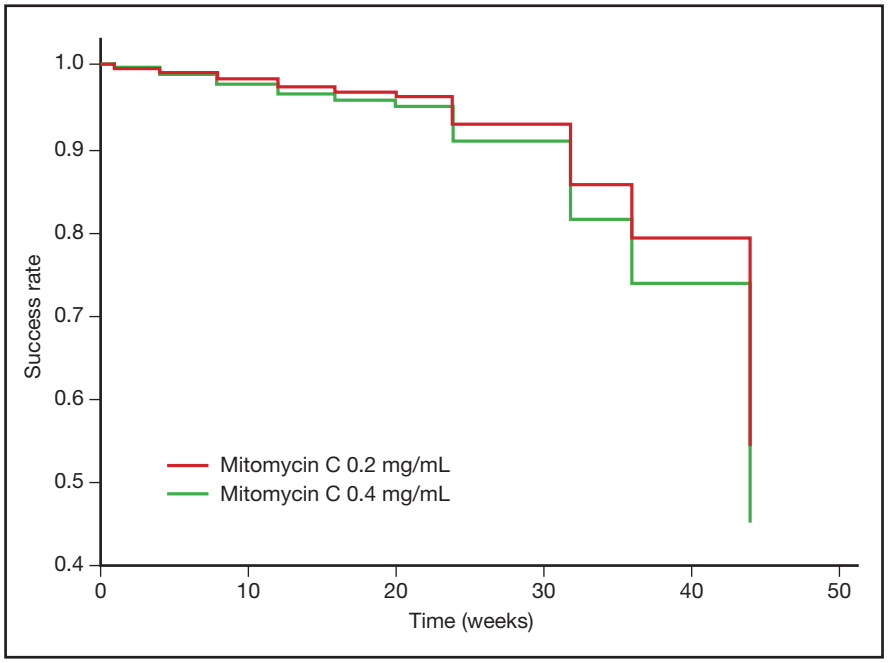

Table 5. Distribution of complications between eyes treated with mitomycin C 0.2 mg/mL and 0.4 mg/mL.

Complication	Mitomycin C 0.2 mg/mL	Mitomycin C 0.4 mg/mL
Hypotony	2	1
Hyphaema	1	3
Flat anterior chamber	0	1
Choroidal effusion	2	0
Bleb leaks	0	0
Scleral melting	0	0

Discussion

There was no difference in the characteristics of the eyes in the 2 treatment groups in terms of preoperative IOP. This finding would have a bearing on the comparability of characteristics between the treatment groups prior to the introduction of the intervention. There was no evidence of a difference in the success rate of the 2 MMC concentrations employed in this study. Angle closure, age, and sex were not found to be predictors of the success of filtering surgery. Although most of the variability of the success rate is explained by the enumerated variables, there is still room for the determination of other factors that could affect the success rate of filtering surgery. Inter-surgeon variability can be a very important factor and could be addressed in future studies.

Conclusion

There were no apparent differences observed in the outcomes of trabeculectomies using MMC 0.2 mg/mL for 4 minutes versus MMC 0.4 mg/mL for 2 minutes in terms of visual acuity, postoperative IOP, bleb character, and complication rate.

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