The Effect of Reducing the Exposure Time of Mitomycin C in Glaucoma Filtering Surgery

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Background: The use of adjunctive intraoperative mitomycin C has considerably improved the success rate of glaucoma filtering surgery. However, the ideal concentration and exposure time of mitomycin C is unknown. The purpose of this study is to determine whether a satisfactory surgical outcome can be achieved with a lower incidence of adverse side effects by using a shorter exposure time of mitomycin C than has been recommended previously.

Methods: Twenty-five eyes of 25 consecutive patients who were considered to be at high risk for surgical failure because of their age (<55 years), previous failure of trabeculectomy, previous cataract surgery, or traumatic glaucoma received a single intraoperative application of mitomycin C (0.2 mg/ml for 2 minutes). They were case-matched with a group of 48 consecutive patients who received a single intraoperative application of mitomycin C (0.2 mg/ml for 5 minutes) by using age, race, type of refractory glaucoma, and preoperative intraocular pressure (IOP) as variables.

Results: Eighteen months after surgery, 22 (88%) patients in the 2-minute group and 21 (84%) patients in the 5-minute group had an IOP less than 21 mmHg with or without treatment. No significant differences were found in the complication rate: in 2 (8%) of 25 eyes of the 2-minute group, chronic hypotony developed compared with 3 (12%) of 25 eyes in the 5-minute group. Hypotony-related maculopathy developed in one eye in the 5-minute group. A cystic bleb was found in 15 (60%) eyes in the 2-minute group compared with 19 (76%) eyes in the 5-minute group, although this difference was not statistically significant. Two (8%) eyes in the 2-minute group and one eye (4%) in the 5-minute group had a bleb-related infection. In one (4%) patient in each group, late severe endophthalmitis developed.

Conclusion: These results suggest that a 2-minute intraoperative application of 0.2 mg/ml mitomycin C is as effective as a 5-minute exposure, but the complication rate remains unaltered. *Ophthalmology 1995;102:84–90*

The use of antimetabolite therapy has considerably improved the success rate of glaucoma filtering surgery by interfering with wound healing at the site of the filtration bleb.[1] Previous reports have demonstrated the effectiveness of postoperative 5-fluorouracil, but because of a high incidence of corneal epithelial defects in the early postoperative period and the discomfort of repeated subconjunctival injections, there has been a trend toward using a single intraoperative application of antimetabolite at the filtering site before performing trabeculectomy.[2–5]

Mitomycin C, an anticancer antibiotic drug isolated from *Streptomyces caespitosus,* has the ability to significantly suppress fibrosis and vascular ingrowth after exposure to the filtration site.[5,6] Encouraging success rates after the use of this drug are tempered by a number of serious complications directly related to the use of mitomycin C. In particular, a high incidence of cystic filtration blebs may predispose the eye to devastating late infection.[6,7] Ocular hypotony, resulting in chorioretinal folds

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in the macular region and visual loss, is also emerging as a major side effect of mitomycin C.[3,4,8–11] The same complication has been reported after subconjunctival 5-fluorouracil.[12]

The optimum concentration and exposure time of mitomycin C to the filtration site are not known. A wide range of concentrations and exposure times have been reported.[8–11,13] An experimental study reported that a 1-minute exposure of a 0.04% concentration may be as effective as a 5-minute exposure, but these results have not been confirmed in a clinical study.[14]

In this report, we present the results of a case-controlled retrospective study which was undertaken to determine whether a satisfactory surgical outcome could be achieved with a lower incidence of adverse side effects, by using a shorter exposure time of mitomycin C (0.02%) than has been recommended previously.

Table 1. Patient Characteristics

Variable	2 Mins	5 Mins
Age (yrs)		
Mean	51.3	51.7
Range	24–72	23–72
Race		
Mixed	13	13
Black	12	12
Preoperative intraocular pressure (mmHg)		
Mean ± SD	29.7 ± 12.2	30.0 ± 9.9
Diagnosis		
Chronic open-angle glaucoma	15	14
Chronic angle-closure glaucoma	3	3
Traumatic glaucoma	7	8

SD = standard deviation.

Patients and Methods

From October 1992 to June 1993, trabeculectomy was performed with adjunct mitomycin C application in 25 eyes of 25 consecutive patients who were considered to be at high risk for surgical failure. The criteria for inclusion were age (<55 years), previous failure of trabeculectomy, pseudophakia, or traumatic glaucoma. All patients were black or of mixed racial ancestry. In these eyes, a surgical sponge that had been previously soaked in a 0.02% solution of mitomycin C was applied between the sclera and Tenon's capsule for a period of 2 minutes. Informed consent was obtained from all patients, and the use of mitomycin C in association with trabeculectomy was approved by the Ethics Committee of the University of Cape Town.

A control group of 48 eyes of 48 consecutive patients was identified, who had undergone the same surgical procedure with a 0.02% solution of mitomycin C applied in an identical manner for a period of 5 minutes. These patients underwent surgery between April 1991 and October 1992. Twenty-five eyes of 25 patients from the 5-minute group were then case-matched with the patients in the 2-minute group, by using age, race, type of refractory glaucoma, and preoperative intraocular pressure (IOP) as variables. The matching was undertaken, taking great care to mask the surgical outcome and complications (Table 1).

In both groups, the surgery was performed by using a technique similar to that described by Cairns.[15] In all patients, the surgery was performed or directly supervised by the same surgeon (JFS). The conjunctival flap was limbal-based. After hemostasis of the episclera was obtained, mitomycin C was applied between the sclera and Tenon's capsule with a surgical sponge measuring 4.5 × 4.5 mm that had been previously soaked in a 0.2-mg/ml solution of mitomycin C. This solution was prepared preoperatively in the hospital pharmacy by mixing 2 mg mitomycin C with 10 ml balanced saline solution. After 2 or 5 minutes, respectively, the sponge was removed, and the entire area was irrigated thoroughly with balanced saline solution. A 4.0 × 4.0-mm limbal-based scleral flap was dissected into clear cornea. A 1.0 × 2.0-mm deep scleral block was removed, and a peripheral iridectomy was performed. The scleral flap was closed with two to four interrupted 10–0 nylon sutures. Tenon's capsule and the conjunctival layer were sutured in two separate layers using a continuous 10–0 nylon suture. Subconjunctival injections of 20 mg gentamicin and 1.5 mg betamethasone acetate were administrated in the inferior fornix. Postoperatively, topical 1% homatropine was instilled twice daily for the first postoperative week. Topical chloramphenicol was used four times daily for 4 postoperative weeks, and topical 1% prednisolone was used four times daily for 3 months.

All patients in both groups were studied prospectively and were examined 1, 2, 3, 4, and 15 days postoperatively and then 1, 2, 3, 6, 9, 12, 15, and 18 months postoperatively. At each postoperative visit, patients were fully examined at the slit lamp and the visual acuity, IOP, and bleb appearance were documented.

For purposes of comparison, the surgery was considered a "complete" success when the IOP was less than or equal to 21 mmHg without glaucoma medication, a "qualified" success when the IOP was less than or equal to 21 mmHg with glaucoma medication or when ocular hypotony was present without visual loss, a "qualified" failure when the IOP was greater than 21 mmHg with or without glaucoma medication or when hypotony-related maculopathy developed with visual loss, and a "complete" failure when an eye required further glaucoma drainage surgery or lost light perception. For the purpose of this study, ocular hypotony was considered to be present when the IOP was less than 5 mmHg on two separate postoperative visits.

Comparisons between the two groups were performed using repeated-measures analysis of variance, Fisher's exact test, and chi-square analysis for 2 × 2 tables. A finding was considered significant at $P < 0.05$. A correlation coefficient was calculated between the 2-

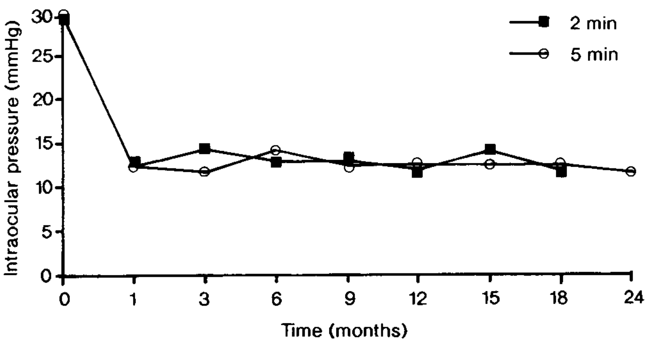

Figure 1. Mean preoperative and postoperative intraocular pressures using a 0.02% concentration of mitomycin C for 2 or 5 minutes. Sample sizes—2-minute group: 25 eyes (preoperative), 23 (1 month), 24 (3 months), 24 (6 months), 18 (9 months), 16 (12 months), 9 (15 months), and 4 (18 months); 5-minute group: 25 eyes (preoperative), 24 (1 month), 22 (3 months), 20 (6 months), 16 (9 months), 22 (12 months), 20 (15 months), 18 (18 months), and 10 (24 months).

minute and 5-minute group at 1, 3, 6, 12, 15, and 18 months postoperatively.

Results

The follow-up was shorter in the 2-minute group (mean, 12.0 months; range, 4–19 months) than in the 5-minute group (mean, 20.2 months; range, 4-35 months) (Fig 1). The mean preoperative IOP in the two groups was similar (29.7 mmHg in the 2-minute group and 30.0 mmHg in the 5-minute group). The mean preoperative IOP decreased from a preoperative level of 29.7 ± 12.2 mmHg (mean ± standard deviation) to a postoperative level of 12.75 ± 5.5 mmHg in the 2-minute group (at a mean time of 12.0 months) and from a preoperative level of 30.0 ± 9.9 mmHg to a postoperative level of 12.2 ± 7.3 mmHg in the 5-minute group (at a mean time of 20.2 months). The mean IOP at 1, 3, 6, 9, 12, 15, 18, and 24 months postoperatively is shown in Table 2. No statistically significant differences were found between the two groups at the 1-, 6-, 9-, 12-, 15-, and 18-month postoperative periods. Although the IOP at the 3-month postoperative visit was higher in the 2-minute group (14.25 mmHg) compared with the 5-minute group (11.7 mmHg), the difference was not statistically significant ($P = 0.07$).

The mean number of medications required to control the IOP in the two groups was similar (1.0 medication in the 2-minute group at a mean time of 8.4 months compared with 1.2 medications in the 5-minute group at a mean time of 14.5 months).

The surgical outcome is shown in Table 3. Of 25 eyes in each group, 18 (72%) were considered a complete surgical success. In the 2-minute group, the surgery in four (16%) eyes was considered a qualified success compared with three (12%) eyes in the 5-minute group. Of the 22 eyes with a successful result in the 2-minute group, three patients had a late reduction of visual acuity of one line of Snellen visual acuity secondary to progressive cataract formation. Of the 21 eyes with a successful result in the 5-minute group, six patients each had a reduction of visual acuity of 1 line of Snellen visual acuity secondary to lens changes.

Of the 25 eyes in each group, 3 (12%) eyes in the 2-minute group and 4 (16%) eyes in the 5-minute group were considered a surgical failure. Of the three eyes in the 2-minute group, one eye was considered a qualified failure and two were considered a complete failure. In the 5-minute group, one eye was considered a qualified failure and three were considered a complete failure. The mean time to surgical failure was 5 months in the 2-minute group and 8 months in the 5-minute group. In the 2-minute group, one failure occurred 12 months postoperatively secondary to endophthalmitis, one patient had an encapsulated bleb 1 month postoperatively, and, despite intensive topical glaucoma therapy and corticosteroids, required a Molteno implant 6 months postoperatively, and one patient, considered a qualified failure, had a flat bleb and uncontrolled IOP 2 months postoperatively. Of the four failures in the 5-minute group, one eye was eviscerated 18 months after surgery because of advanced endophthalmitis, one patient had an encapsulated bleb 3 months after surgery and an uncontrollable IOP but refused further surgery, and one patient had a flat bleb 2 months after surgery and underwent a Molteno implant 4 months later. Hypotonus maculopathy developed in one patient, who was considered a qualified failure, and visual acuity dropped from a preoperative level of 20/40 to 20/300 at the 12-month postoperative visit. The cumulative success probability after trabeculectomy with mitomycin C applied for 2 and 5 minutes using Kaplan–Meier life-table analysis is shown in Figure 2.

Of the 25 patients in the 2-minute group, a cystic bleb developed in 15 (60%) eyes, including 1 eye with a conjunctival aqueous leak that developed 12 months postoperatively. A diffuse microcystic bleb developed in six eyes, and an ecapsulated bleb developed in one eye. Of the three eyes with flat blebs, two were described as flat 2 months after surgery but maintained a low IOP and one

Table 2. Mean Postoperative Intraocular Pressure

	Time (mos)							
Exposure Time	*1*	*3*	*6*	*9*	*12*	*15*	*18*	*24*
2 mins	12.3	14.2	12.8	12.7	11.8	13.7	11.7	—
5 mins	12.2	11.7	14.0	12.2	12.3	12.2	12.1	11.3

required glaucoma therapy to lower the IOP. Of the 25 eyes in the 5-minute group, a cystic bleb developed in 19 (76%). One patient with a large cystic bleb had an aqueous leak 6 months postoperatively that resolved spontaneously while receiving treatment with topical chloramphenicol. A diffuse microcystic bleb developed in four eyes, an encapsulated bleb in one eye, and a flat bleb in one eye (Table 4).

Hypotony developed in two patients in the 2-minute group: one that had a persistent IOP of 2 mmHg and one with an IOP of 4 mmHg. The onset of hypotony was 1 and 3 months after surgery, respectively. Neither patient had a loss of visual acuity. In the 5-minute group, hypotony developed in three eyes at 1, 3, and 9 months postoperatively, respectively. Reduced visual acuity secondary to hypotony-related maculopathy subsequently developed in one of these three eyes (Table 5).

A bleb-related infection developed in two eyes in the 2-minute group. Two months postoperatively, a conjunctival leak at the site of the bleb developed in one patient. At the 6-month follow-up visit, the bleb was ischemic and cystic without an aqueous leak and 1 month later conjunctivitis was diagnosed, which responded well to topical antibiotic treatment. Twelve months postoperatively, the patient had a 7-day history of ocular pain and purulent discharge. A severe endophthalmitis was present that was unresponsive to topical and systemic antibiotic therapy and to pars plana vitrectomy. All vision was lost, and an evisceration was performed. An infected bleb with anterior chamber reaction developed three months postoperatively in one patient. The infection was treated successfully with intensive topical antibiotics. In one patient in the 5-minute group, a bleb infection developed. Eighteen months after surgery, the patient had advanced endophthalmitis that did not respond to intensive medical or surgical treatment. All vision was lost, and an evisceration was performed (Table 5).

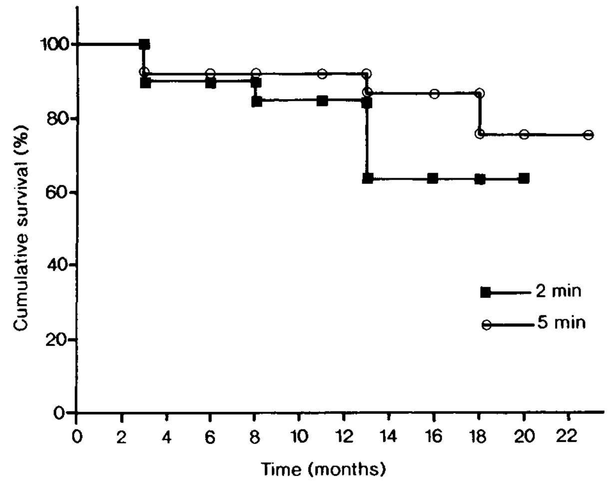

Figure 2. Cumulative success probability after trabeculectomy with mitomycin C applied for 2 and 5 minutes using Kaplan-Meier life-table analysis. Sample sizes—2-minute group: 23 eyes (1 month), 24 (3 months), 24 (6 months), 18 (9 months), 16 (12 months), 9 (15 months), 4 (18 months), and 1 (19 months); 5-minute group: 24 eyes (1 month), 22 (3 months), 20 (6 months), 16 (9 months), 22 (12 months), 20 (15 months), 18 (18 months), and 10 (24 months).

Discussion

The use of a single intraoperative application of mitomycin C at the filtering site has considerably improved the success rate of glaucoma filtering surgery. The ability of mitomycin C to suppress cellular proliferation after a short exposure to the tissue makes the use of this drug simple and effective.[1] However, the optimal concentration of mitomycin C and the time of intraoperative exposure to tissue are still not known (Table 6).

The effect of mitomycin C on the tissue is dose- and time-dependent.[16] Chen et al[8] studied mitomycin C concentrations of 0.01%, 0.02%, and 0.04% exposed to the tissue for 5 minutes and found an improved success rate with a higher concentration. Palmer[13] reported a surgical success rate of 84% (28/33) using a 0.02% concentration for 5 minutes, and Skuta et al[4] described only one surgical failure in a series of 20 eyes using a 0.05% concentration for 5 minutes. Higher concentrations have been reported to be associated with a higher incidence of complications. In a study using 0.05% concentration for 5 minutes, 6 (30%) of 20 eyes had choroidal detachment but in only 1 (5%) of these eyes hypotony-related maculopathy developed.[4] Zacharia et al[9] found a 32.7% (17/52) incidence of hypotony with a concentration of 0.04% applied under a scleral flap in primary procedures: in 9 (17.3%, 9/52) of these 17 eyes hypotony-related maculopathy developed. Kitazawa et al[3] reported a 23.2% (4/17) incidence of hypotony and 5.8% (1/17) incidence of hypotony-related maculopathy after using a concentration of 0.04%. Chen

Table 3. Surgical Outcome*

	Success		Qualified Success		Qualified Failure		Failure	
Variable	No.	(%)	No.	(%)	No.	(%)	No.	(%)
2 mins (n = 25)	18	(72)	4	(16)	1	(4)	2	(8)
5 mins (n = 25)	18	(72)	3	(12)	1	(4)	3	(12)

* See text for definitions of surgical outcome.

Table 4. Bleb Characteristics

	Bleb Characteristics							
	Cystic		*Diffuse*		*Flat*		*Encapsulated*	
Variable	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*
2 mins (n = 25)	15	(60)	6	(24)	3	(12)	1	(4)
5 mins (n = 25)	19	(76)	4	(16)	1	(4)	1	(4)

et al[8] found long-term hypotony in two of three eyes treated with 0.04% mitomycin C, but in none with a 0.02% and 0.01% concentration and suggested that a safe and effective concentration might lie between 0.02% and 0.04%. Palmer[13] found no hypotony in a series of 32 eyes using a mitomycin C concentration of 0.02%, although one patient, excluded from his study because of a short follow-up, had an IOP of 2 mmHg 5 months after surgery and reduced vision secondary to hypotony-related maculopathy.

Other complications, such as scleromalacia and corneal ulceration, were reported after the surgical excision of pterygia when mitomycin C was used at a concentration of 0.04%.[17] A concentration of 0.02% was reported to be associated with a significantly reduced complication rate when used after pterygium surgery.[18]

Jampel[14] varied the exposure of 0.04% mitomycin C to human Tenon's capsule fibroblasts experimentally and found a 90% inhibition of fibroblast proliferation with a 5-minute exposure compared with a 77% inhibition with a 1-minute exposure at the same concentration. Zacharia et al[9] reported a 20% (2/10) incidence of hypotony in eyes exposed for 3½ minutes compared with 35.7% (15/42) in eyes exposed for 7 minutes. A 94.8% (37/39) success rate was reported in primary trabeculectomy using a 0.04% concentration of mitomycin C for 1.5 to 2.5 minutes, but included three (5.9%) eyes with hypotony-related maculopathy.[10] In a recent study, the time of exposure of mitomycin C to the tissue was varied in every patient according to the presumed risk for surgical failure (youth, black race, previous failed filtering procedure, aphakia or pseudophakia, active anterior uveitis).[11] Mitomycin C was exposed to the tissue for 2 minutes in elderly patients with no previous surgery and no secondary glaucoma, and 1 additional minute was added for each risk factor. Hypotony-related maculopathy developed in 4 (7.7%) of 52 eyes exposed for 2 or 3 minutes, whereas none of the eyes receiving mitomycin C for 4 or 5 minutes had hypotony. This suggests that factors other than concentration and time of exposure of mitomycin C may play a role in hypotony-related maculopathy.

These studies demonstrate that a low concentration and short exposure time of mitomycin C to the tissue may still result in successful filtration surgery. Our study supports this, because it clearly shows that a 2-minute application of 0.02% of mitomycin C is as effective as a 5-minute application of the same concentration. Twenty-two (88%) eyes in the 2-minute group and 21 (84%) eyes in the 5-minute group had IOPs of less than 21 mmHg and the mean IOPs were similar at the 6-, 9-, 12-, 15-, and 18-month postoperative visits. These results are similar to the 84% (28/33) of eyes reported by Palmer.[13] Three (12%) eyes in the 2-minute group and four (16%) in the 5-minute group were considered failures, with a mean onset of IOP rise at 5 months in the 2-minute group and 8 months in the 5-minute group. This earlier onset of failure in the 2-minute group may explain why the mean IOP was higher in the 2-minute group than in the 5-minute group at the 3-month follow-up visit.

No statistically significant differences were found in the complication rate. Ocular hypotony developed in two (8%) eyes in the 2-minute group and three (12%) in the 5-minute group. This incidence is similar to that found by Chen et al[8] and Palmer[13] but lower than that reported in previous studies using a higher concentration of mitomycin C.[4,9,10] An incidence of hypotony as high as 21.1% and 32.7% may be related to the fact that mitomycin C was used during a primary procedure in patients with little or no risk for failure and not only to the use of higher

Table 5. Complications

	Hypotony* related Maculopathy		Infection		Endophthalmitis		Conjunctival Leak	
Variable	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*
2 mins (n = 25)	0	(0)	2	(8)	1	(4)	1	(4)
5 mins (n = 25)	1	(4)	1	(4)	1	(4)	1	(4)

* Hypotony = an intraocular pressure of <5 mmHg on 2 separate postoperative visits.

Table 6. Concentrates, Exposure Times, and Complications of Mitomycin C Reported by Previous Studies

References	No.	Mitomycin C Concentration (%)	Exposure Time (mins)	Success Rate (%)	Success Criteria (mmHg)	Hypotony*		Hypotony-related Maculopathy		Choroidal Detachment or Shallow AC	
						No.	(%)	No.	(%)	No.	(%)
Chen et al[8]	45	0.01–0.04	5	78–100	≤20†	2	(4)	2	(4)	NR	
Palmer[13]	33	0.02	5	84	≤17‡	1	(3)	1	(3)§	NR	
Kitazawa et al[3]	17	0.04	5	88–100¶	≤20†	4	(23.2)	1	(5.8)	12	(71)
Skuta et al[4]	20	0.05	5	NR	≤20†	NR		1	(5)	6	(25)
Zacharia et al[9]	52	0.04	3.5–7.0	NR	NR	17	(32.7)	9	(17.3)	NR	
Costa et al[10]	54	0.04	1.5–3.5	93.3–97.4	≤21‖	8	(14.8)	3	(5.9)	24	(33.8)
Shields et al[11]	59	0.04	2–5	70–94	NR	6	(10.1)	6	(10.1)	NR	

AC = anterior chamber; NR = not reported.

* Hypotony = intraocular pressure < 5 mmHg.

† Intraocular pressure ≤ 20 mmHg with or without antiglaucoma medication.

‡ Intraocular pressure ≤ 17 mmHg with or without antiglaucoma medication.

§ Patients excluded from the study because of short follow-up (5 mos).

¶ 88% success "category 1": intraocular pressure ≤ 20 mmHg without antiglaucoma medication; 100% success "category 2": intraocular pressure ≤ 20 mmHg with antiglaucoma medication.

‖ Intraocular pressure ≤ 21 mmHg without antiglaucoma medication.

concentrations for prolonged periods of exposure.[9,10] Zacharia et al[9] found a threefold greater rate of hypotony among eyes undergoing primary filtering procedures than among eyes with previously failed filtering procedures. In our study, hypotony-related maculopathy and reduced visual acuity developed in only one (4%) eye in the 5-minute group and none in the 2-minute group. It also has been suggested that youth and myopia may be risk factors for the development of hypotony-related maculopathy.[12] In our series, four of the five patients with hypotony were young (<44 years), three had traumatic glaucoma, two had chronic open-angle glaucoma, and none was myopic. The only patient to have hypotony-related maculopathy was a 28-year-old patient with emmetropia and primary open-angle glaucoma. Although progressive cataract change developed in six patients in the 5-minute group, this complication was unrelated to ocular hypotony.

Bleb-related infection occurred in two eyes in the 2-minute group and in one eye in the 5-minute group. One patient in each group lost all vision in the eye that underwent surgery because of late severe endophthalmitis. Wolner et al[19] reported a 5.7% (13/229) incidence of late bleb-related endophthalmitis after the use of postoperative injections of 5-fluorouracil. This occurred an average of 26 months after surgery, and all eyes had a cystic bleb. A previous study from our department reported an 8% (3/39) incidence of late bleb-related endophthalmitis after using 5-fluorouracil associated with trabeculectomy.[7] All three patients had post-traumatic angle-recession glaucoma and a thin-walled cystic bleb. Although the creation of a cystic bleb is associated with good IOP control and therefore could be considered a desirable surgical result, the incidence of late endophthalmitis seems to correlate with the presence of a thin-walled, cystic bleb.[20] Although a statistical difference was not shown in our current study, a cystic, thin-walled bleb developed in 76% (19/25) of eyes in the 5-minute group compared with 60% (15/25) in the 2-minute group. Histopathologic studies in rabbits, monkeys, and humans have shown that mitomycin C creates a filtration site with hypocellular or acellular bleb cavities by inhibiting the subconjunctival fibroblast proliferation.[6,11,21] This effect is dose- and time-dependent, which suggests that longer exposure of mitomycin C to the tissue at higher concentrations will tend to result in a higher incidence of cystic blebs, with a subsequent risk of hypotony or bleb-related endophthalmitis.

Our study supports the conclusions of previous studies that mitomycin C is a highly effective drug when used in association with trabeculectomy, particularly in patients with risk factors for failure. A 2-minute exposure of a 0.02% concentration of mitomycin C is as effective as a 5-minute exposure of the same concentration. However, hypotony and devastating late intraocular infections are complications that remain a potential danger when this antimetabolite is used as adjunctive therapy. Although the incidence of cystic bleb formation is slightly less after 2 minutes of exposure to the tissue compared with 5 minutes, the incidence of complications is not diminished by a reduction in the time of exposure. As a recent study has suggested that concentration and exposure time of mitomycin C to the tissues may not be the only factors which influence the incidence of late complications, further clinical studies are required to determine the optimal dosage and application time of mitomycin C, as well as the ocular and demographic factors that may predispose to late complications.

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