Filtration procedures supplemented with mitomycin C in the management of childhood glaucoma

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Abstract

***Aims*—To evaluate the outcome of filtering procedures supplemented with mitomycin C in children with glaucoma.**

***Methods*—All patients aged 17 or younger with glaucoma who underwent filtering surgery supplemented with mitomycin C at a tertiary care centre (n=21) during a 5 year interval (1992 and 1996) were included. One eye for each patient was entered into the analysis. The postoperative intraocular pressure (IOP), use of antiglaucoma medications, clinical stability of glaucoma, complications, and visual acuity were retrospectively evaluated. Kaplan–Meier survival curves were used to estimate the probability of success.**

***Results*—At the time of surgery mean age was 5.7 (SD 5.0) years. The most common diagnoses were trabeculodysgenesis (n=6) and aphakic glaucoma (n=8). Mean IOP before surgery was 35.7 (10.5) mm Hg. Average length of follow up was 18.6 (14.7) months. The probability of having IOP less than 21 mm Hg with no antiglaucoma medications and with clinically stable glaucoma 1 year after surgery was 76.9% in phakic eyes (n=13) and 0% in aphakic eyes (n=8). A phakic patient with Sturge–Weber's syndrome had choroidal effusion after surgery that resolved spontaneously. In the aphakic group one patient had retinal detachment and another developed an encapsulated bleb. Visual acuity deteriorated in one patient.**

***Conclusion*—A guarded filtration procedure with mitomycin C is relatively successful in phakic children with glaucoma, but unsuccessful in aphakic ones.**

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The management of glaucoma in children in whom goniotomy or trabeculotomy has been unsuccessful or is inappropriate is problematic. In these patients filtering surgery without antimetabolites frequently fails, probably related to the greater thickness of Tenon's capsule, the wound healing response in young patients, and the presence of conjunctival scarring from the previous ocular surgery.[1–3] The use of antimetabolites with filtration procedure can reduce the frequency of filtration failure in glaucoma patients with a poor surgical prognosis.[4–6] A guarded filtration procedure (GFP) in conjunction with an antiproliferative agent has recently been shown to be promising in selected patients with refractory paediatric glaucoma. Zalish *et al* reported a successful outcome of trabeculectomy with adjunctive subconjunctival injections of 5-fluorouracil in a small series of patient with congenital and infantile glaucoma.[7] Several series of trabeculectomies with intraoperative mitomycin C to treat children with glaucoma have recently been reported.[8–13] This study describes the outcome of filtering procedures supplemented with intraoperative mitomycin C in a North American paediatric population with glaucoma.

Methods

In a retrospective review, the medical records of all patients under 18 years old who had been treated by a GFP with mitomycin C at the glaucoma service of the Wills Eye Hospital from January 1992 to the end of January 1997 were reviewed.

One eye only from each patient was entered into the analysis. If both eyes underwent a GFP with mitomycin C at the same time, then the right eye was entered into the study. If both eyes underwent a GFP with mitomycin C at different times, then the first operated eye was selected. If an eye had more than one GFP with mitomycin C, then the first procedure was considered to be the surgery of record.

Mitomycin C (Bristol Laboratories, Syracuse, NY, USA) was reconstituted in balanced salt solution to yield a 0.4 mg/ml solution. The surgery was similar in all cases. A superior limbus based conjunctival flap was raised. Haemostasis was achieved with wet field cautery. A cellulose Weck-Cel sponge was soaked with mitomycin C and applied on the episclera, over the site of the planned scleral flap. The conjunctiva Tenon layer was draped over the sponge, avoiding contact of the mitomycin C with the wound edge. The time of exposure varied according to the surgeon's estimation of risk of failure. After 1–5 minutes the sponge was removed and the entire area was irrigated thoroughly with balanced salt solution. A 3×3 mm rectangular scleral flap of one half scleral thickness was dissected. A 2×1 mm tissue block was removed, and a peripheral iridectomy was performed. The scleral flap was closed with single 10-0 nylon interrupted sutures, the number and placement of the sutures designed to allow what was believed to be an adequate amount of filtration. Conjunctiva and Tenon's capsule layers were closed separately with 8-0 or 9-0 polyglactin (Vicryl)

Table 1 Demographics, diagnosis, preoperative data, and surgical outcome of guarded filtration procedure with mitomycin C

Case No, sex race, eye	Age (years)	Diagnosis	Previous antiglaucoma surgeries	IOP	No med	Follow up (months)	Success		Optic cup reversibility	Complications
							Relative	Absolute		
1, m, w, r	0.1	aniridia	G, T	34	0	7	yes	yes	+	
2, m, b, r	8	aphakia, microcornea	–	40	3	5	no	no	–	
3, m, w, r	13	trabeculodysgenesis	G	32	3	13	yes	yes	–	
4, m, b, l	6	Sturge-Weber's	G, T	32	1	17	yes	yes	–	choroidal effusion
5, f, w, r	13	aniridia	–	27	2	8	yes	yes	–	
6, m, w, r	0.4	trabeculodysgenesis	T, GFP	21	0	13	yes	yes	+	
7, f, w, l	7	Rieger's syndrome	–	40	0	6	yes	yes	+	
8, f, w, r	3	aphakia	–	35	2	8	no	no	–	
9, f, w, l	0.1	aphakia	–	47	2	23	yes	no	–	
10, m, w, l	8	aphakia, PHPV	–	36	0	6	yes	no	–	
11, f, b, r	7	aphakia, microphthalmia	–	49	3	7	no	no	–	
12, f, b, l	4	trabeculodysgenesis	G	30	0	53	yes	yes	+	
13, f, w, r	9	Rieger's anomaly	–	31	2	40	yes	yes	+	early hypotony
14, m, w, l	0.8	trabeculodysgenesis	T (×2)	30	0	12	no	no	–	
15, f, b, l	13	trabeculodysgenesis	T	28	3	8	yes	yes	–	
16, m, w, r	8	Peter's anomaly	CCT	70	1	35	yes	no	–	
17, f, w, r	3	aphakia, PHPV	–	32	0	9	no	no	–	
18, m, w, r	5	aphakia	GFP	46	1	7	no	no	–	total RD, PVR
19, m, w, l	4	aphakia	–	31	3	39	yes	no	–	bleb encapsulation
20, m, w, l	3	trabeculodysgenesis	G (×2)	30	1	29	yes	yes	+	
21, f, w, l	5	Sturge-Weber's syndrome	–	29	1	42	yes	yes	+	

IOP = intraocular pressure before filtration surgery; No med = number of antiglaucoma medications before filtration surgery; m = male; f = female; b = black; w = white; r = right; l = left; G = goniotomy; T = trabeculotomy; GFP = guarded filtration procedure; CCT = cyclocryotherapy; RD = retinal detachment; PVR = proliferative vitreoretinopathy.

suture on a tapered needle. After the conjunctival closure, balanced salt solution was again injected into the anterior chamber to test the amount of filtration and to ensure that the conjunctival closure was watertight.

Postoperative treatment was similar in all cases and consisted of corticosteroids (tapered over a 6–10 week period, depending upon the amount of conjunctival injection present), cycloplegics (for approximately 1 month), and antibiotics (for 2 weeks).

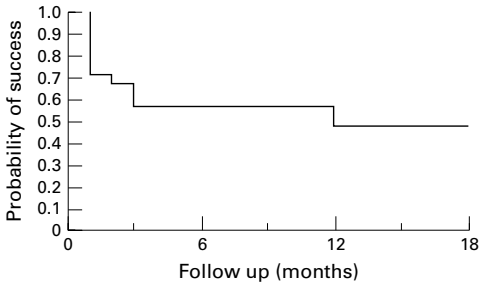

Figure 1 Probability of absolute success at different follow up times. The horizontal axis represents time since surgery (trabeculectomy with mitomycin C) and the vertical axis represents the probability of success, expressed as a percentage. Success was defined as a postoperative IOP less than 21 mm Hg with no antiglaucoma medications, with apparently stable glaucoma, and absence of severe complications.

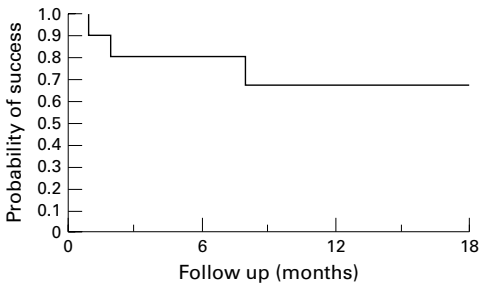

Figure 2 Probability of relative success at different follow up times. The horizontal axis represents time since surgery (trabeculectomy with mitomycin C) and the vertical axis represents the probability of success, expressed as a percentage. Success was defined as no performance of or recommendation of further glaucoma surgery, and absence of severe complications associated with the filtering surgery.

The available data varied among patients depending on their age. Visual acuities were not available in the youngest patients. An estimation of visual function was obtained by clinical methods which involve evaluation of fixating and following behaviour. Visual acuity (VA) in older children was evaluated by preferential looking tests and/or by the Snellen chart at 6 metres. Low vision was defined for this study as best corrected distance VA worse than 6/120. Worsening of VA was defined for older patients as a decrease in best corrected distance VA of two or more lines compared with baseline visual acuity. In younger children, worsening of vision was considered as absence of previous ability to fixate and follow objects.

Data on corneal diameters and axial length were available only in younger age groups. Visual fields were available only in older patients. In addition, some children who had advanced glaucoma before surgery had media opacities that were responsible for at least some of the visual impairment and which limited or prevented satisfactory visualisation of the optic discs. Because intraocular pressure (IOP) was the only variable evaluated consistently in all patients in this study, this variable was used as the principal criterion for assessment of surgical intervention.

Preoperative and postoperative IOPs were measured by applanation tonometry. In infants the IOP was measured under anaesthesia in the operating theatre. Tonometry was performed during the early moments after induction with inhaled anaesthetics and before endotracheal intubation. Intraocular pressure was measured with a Perkins applanation tonometer. In older children the IOP was measured in the clinic. The "preoperative IOP" was the ocular tension measured at the time of the decision to perform the surgical procedure. Postoperative measurements were recorded during follow up visits.

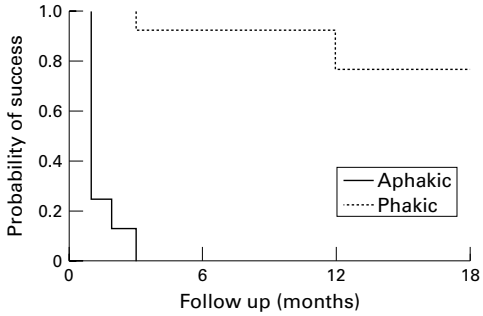

Figure 3 Probability of absolute success at different follow up times according to lens status. The horizontal axis represents time since surgery (trabeculectomy with mitomycin C) and the vertical axis represents the probability of success, expressed as a percentage. Success was defined as a postoperative IOP less than 21 mm Hg with no antiglaucoma medications, with apparently stable glaucoma, and absence of severe complications.

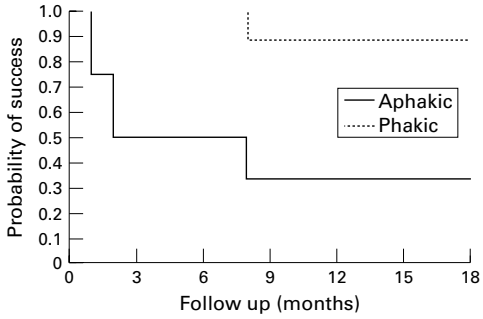

Figure 4 Probability of relative success at different follow up times according to lens status. The horizontal axis represents time since surgery (trabeculectomy with mitomycin C) and the vertical axis represents the probability of success, expressed as a percentage. Success was defined as no performance of or recommendation of further glaucoma surgery, and absence of severe complications associated with the filtering surgery.

Table 2 Visual acuity of the cases studied

	No (%)
Change in VA (preoperative *v* last follow up)	
Worsening of VA	1 (4.1)
VA unchanged or improved	20 (95.2)
VA at last follow up	
Infants	
FF	2 (9.5)
Not able to fixate	2 (9.5)
Cooperative children	
≥6/12	7 (33.3)
<6/12–6/60	6 (28.5)
<6/60–LP	4 (19.8)

In this study success of GFP with mitomycin C was defined before data collection as follows: (1) "absolute success" was defined as a postoperative IOP less than 21 mm Hg with no antiglaucoma medications, with apparently stable glaucoma (see below) and absence of severe complications (see below). "Apparently stable glaucoma" was defined as absence of symptoms such as photophobia, tearing and blepharospasm, absence of corneal oedema, lack of enlargement of the optic disc cupping (if able to be examined), lack of enlargement of corneal diameter (when measured), and lack of increase in axial length (when measured). "Severe complications" were conditions that could compromise the visual prognosis such as retinal detachment, endophthalmitis, corneal oedema, and cataract. (2) "Relative success" was defined as no performance of or recommendation of further glaucoma surgery, and absence of severe complications (see definition above) associated with the filtering surgery.

The total length of follow up for each patient was considered to be the interval between the most recent follow up before the survey date and the date of surgery. For purposes of actuarial data analysis, the length of follow up was regarded as the length of follow up until the date of the detection of that failure (if either absolute or partial failure occurred).

The phakic and aphakic patients were evaluated separately. The influence of previous conjunctival incision and age (splitting the total population by the median age) was also analysed. The Kaplan–Meier survival curves were calculated for each of the failure categories.

Results

Twenty one patients were identified; 11 right eyes and 10 left eyes were analysed. The demographics of the patients are summarised in Table 1. The mean age was 5.7 (SD 5.0) years (median 6 years, range 1 month–17 years). The most common diagnoses were isolated trabeculodysgenesis (n=6) and aphakic glaucoma (n=8). One of the patients (case No 1) underwent bilateral and simultaneous GFP with mitomycin C.

In the aphakic patients cataract surgery was done within the first 6 months of age. Five patients underwent lensectomy, posterior capsulotomy, and anterior vitrectomy with automated vitrectomy instruments (cases 2, 8, 10, 11, and 17). A limbal approach was used in all patients but one (case 17) who underwent a pars plana vitrectomy and lens extraction. Three cases (cases 9, 18, and 19) underwent lens extraction and posterior capsulotomy, and later required secondary pupillary lens membrane removal with anterior vitrectomy. After cataract surgery there was no evidence of chronic inflammation. One patient (case 17) underwent surgical repair of retinal dialysis. After recognition of glaucoma, no signs of active inflammation were present. All cases but one (case 18) had an open angle. Before filtration surgery (Table 1) the average IOP was 35.7 (SD 10.5) mm Hg and the median number of antiglaucoma medications was one. Previous glaucoma surgery had been performed on most phakic eyes (nine, 69.2%) but on only one aphakic eye in this series. The median number of prior intraocular procedures was also one.

The mean time of application of mitomycin C was 2.7 (1.0) minutes (median 3.0 minutes, range 1–5 minutes). In the phakic group the time of application of mitomycin C was 3.1 (1.0) minutes, and in the aphakic group 2.2 (0.9) minutes. At the time of GFP with mitomycin C an anterior vitrectomy was done in two aphakic patients (cases 11 (anterior approach) and 18 (through pars plana)).

Average follow up after surgery was 18.6 (14.7) months (median 14.0 months). In the total population, the probability of having a

Table 3 Summary of studies evaluating the outcome of guarded filtration procedures with mitomycin C in children

Author	*No of patients/eyes*	*Type of glaucoma*	*Procedure*	*Criteria of success*	*% of successful cases (months of follow up)*
Mandal *et al*	13/19	Congenital and developmental	GFP with mm C 3 min, 0.4 mg/ml	IOP <21 mm Hg at slit lamp or <16 mm Hg under anaesthesia	94% (19)
Susanna *et al*	68/98	Congenital and developmental	GFP with mm C 5 min, 0.2 mg/ml	IOP <22 mm Hg	67% (17)
Agarwal *et al*	16/30	Congenital and developmental	GFP with mm C*	IOP <21 mm Hg without meds	
			4 min, 0.2 mg/ml		60% (18)
			4 min, 0.4 mg/ml		86% (18)
Asrani and Wilensky	(?)/14				
	7	Aphakic	GFP with mm C	IOP <22 mm Hg	85% (?)
	5	Aphakic	GFP		60% (?)
Wallace *et al*	(?)/13	Aphakic	GFP with mm C 4 min, 0.2–0.4 mg/ml	IOP <26 mm Hg without meds or IOP <21 mm Hg with meds	61% (?)
Walton	(?)/14	Aphakic	GFP with mm C (?)	(?)	64% (?)
Azuara-Blanco *et al*	21/21				
	13	Congenital, developmental	GFP with mm C,	IOP <21 mm Hg without meds	76% (18)
	8	Aphakic	1–5 min, 0.4 mg/ml		0% (18)

GFP = guarded filtration procedure; mm C = mitomycin C; IOP = intraocular pressure; meds = antiglaucoma medications; (?) = not mentioned in the study; *filtration surgery was associated with trabeculotomy.

postoperative IOP less than 21 mm Hg without antiglaucoma medications and with stable glaucoma (that is, absolute success) after 18 months of follow up was 47.6 % (Fig 1). The probability of having relative success (no further surgery or severe complications) was 67.4% after 18 months of follow up (Fig 2).

Phakic cases appeared to have a better outcome than did aphakic ones (Figs 3 and 4). After 18 months of follow up, the cumulative proportion of eyes with absolute success was 76.9% in the phakic group but 0% in the aphakic group. Similarly, the cumulative actuarial probability of relative success was 88.8% in the phakic group and 33.3% in the aphakic group after 18 months of follow up. Primary failure (high IOP and no evidence of filtration in the early postoperative period) occurred in two aphakic cases (patients 2 and 17). No vitreous was observed in the anterior chamber and the cause of failure of these cases was unknown. Eyes without previous conjunctival incision (n=8) had higher actuarial probability of absolute and relative success than did eyes with previous conjunctival incision. Regarding age, children 5 years old or younger and those 6–18 years old had similar actuarial rates in both absolute and relative success.

During the early postoperative period hypotony (defined as IOP <6 mm Hg) occurred in one case (see Table 1) and resolved spontaneously. One patient with Sturge–Weber's syndrome had moderate choroidal effusions and shallow anterior chamber that resolved with medical treatment. One child developed a total retinal detachment and severe proliferative vitreoretinopathy (not treated because of the poor visual prognosis). In successful cases the filtering blebs were avascular while failed cases had a flat and thick bleb. One case had an encapsulated bleb that resolved with medical treatment (Table 1). Seven successful cases had an improvement of the optic disc appearance (that is, decreased optic disc cupping, see Table 1).

Visual acuity information is summarised in Table 2. Visual acuity worsened after surgery in one patient (the aphakic patient who developed a total retinal detachment in the study eye, see above).

Discussion

Many children with glaucoma respond adequately to one or more surgical procedures, usually goniotomy or trabeculotomy.[14 15] When such surgery is unsuccessful or inappropriate, however, filtration surgery may become necessary. Filtration surgery in children gives less satisfactory results than in adults, and the outcome may be worse depending upon the type of glaucoma and whether or not there had been previous surgery. In children with complicated secondary glaucomas or with previously failed goniotomy, Beauchamp and Parks reported a high rate of complications and a success of 50% at 18 months.[1] The use of β irradiation in children was associated with a better surgical outcome than a control group.[3] The use of 5-fluorouracil and mitomycin C in children with glaucoma undergoing filtration surgery has been reported recently.[7–9] The need for several postoperative subconjunctival injections makes the use of postoperative 5-fluorouracil in children difficult. Mitomycin C may be a better alternative to 5-fluorouracil in complicated glaucomas because there is no need of postoperative injections (difficult to administer in children) and mitomycin C results in a lower postoperative IOP. Intraoperative mitomycin C is more potent than 5-fluorouracil and increases the success rate of filtration surgery in adults.[16] Mitomycin C supplemented trabeculectomy had a high success rate (94.7%) in phakic Asian children with glaucoma with previously failed surgery (see Table 3).[9] Susanna *et al* reported a moderately successful outcome of guarded filtration procedures supplemented with mitomycin C in a phakic South American paediatric population; in their study, younger patients (0–1 year old) showed a lower success rate than the older ones, but number of previous surgeries was not associated with a reduced success.[8]

Cataracts in children can be treated by lens aspiration, aspiration, and discission of the posterior capsule, and automated capsulotomy and anterior vitrectomy. Glaucoma after cataract surgery in children is a frequent and severe complication. The use of vitreous cutting instruments is associated with more complete removal of lens tissue and probably with a

decreased incidence of secondary glaucoma.[13] However, Mills and Rob found a similar frequency of glaucoma after childhood cataract surgery of 240 eyes among various surgical methods of cataract removal.[17] The cause of glaucoma in children is not known. Pupillary block and angle closure is now an infrequent cause and most patients have an open anterior chamber angle.[17–22] It is possible that the trabecular meshwork is damaged by lens remnants and inflammation. In this series only one aphakic patient had angle closure glaucoma.

In this study, the outcome of GFP supplemented with mitomycin C in North American children with glaucoma was evaluated. Most patients had previous intraocular surgery. Overall, phakic patients had an excellent outcome without complications, while aphakic cases had poor postoperative control of IOP. The success rate of phakic filtration surgery with mitomycin C appears to be similar to that reported in the literature (Table 3). However, aphakic patients had worse outcome when compared with previous studies.[11–13] Two of eight aphakic cases had primary failure; vitreous incarceration, which has been associated with primary failure in aphakic patients, did not occur, and the cause of primary failure was unknown. Because the surgical technique was similar in phakic and aphakic patients the worse outcome observed in aphakic children may be related to the presence of pre-existing conjunctival scarring or to an increased postoperative inflammation. Other unknown factors cannot be excluded.

In the phakic group the time of application of mitomycin C was 3.1 (1.0) minutes, and in the aphakic group 2.2 (0.9) minutes. Mitomycin C appears to have its greatest effect during its initial exposure. Jampel suggested that the largest effect of mitomycin C occurs during the first minute of drug exposure.[23] Several studies have failed to show an influence of different exposure time to mitomycin C on surgical outcome. Megevand *et al* found no decrease in final IOP while using mitomycin C exposure times of 2 minutes versus 5 minutes.[24] Stone *et al* found a similar success rate and percentage of IOP reduction after trabeculectomy with mitomycin C between groups with different exposure time to mitomycin C. The exposure times ranged from 1 to 5 minutes.[25] Similarly, Shin *et al* did not observe any significant difference in the success rate among the mitomycin C applications for 1, 3, and 5 minutes in primary glaucoma triple procedures. In this study the difference in time of sponge exposure does not explain the different outcome of aphakic and phakic patients.[26]

It is generally believed that the younger children experience more pronounced scarring after filtration surgery than do older children and that younger children therefore have a worse outcome following the surgery.[1 8] However, in this study of guarded filtration surgery supplemented by intraoperative mitomycin C age seemed to have no influence on postoperative outcome. This suggests a favourable impact of the mitomycin C on the outcome of surgery, but bias between the subgroups is at least as likely an explanation.

Reversibility or decrease of the optic disc cupping is common in young patients after glaucoma surgery,[27 28] but it can be also observed in adult patients.[29 30] In this study reversibility of the optic disc cupping was noted in seven cases. The topographic changes of the optic disc were not quantified.[31] All cases with reversible cupping had successful surgery.

No major complications that could be attributed to the mitomycin C occurred in any children in this group through the available follow up. One patient developed early hypotony, and a patient with Sturge–Weber developed temporary choroidal effusions, probably related to elevated episcleral venous pressure. Long term hypotony was not observed. In spite of this, the long term effects of antimetabolites in children are unknown. Furthermore, the use of antimetabolites probably increases the late risk of bleb related endophthalmitis.[32–34] Endophthalmitis after trabeculectomy with mitomycin C in children has been recently reported by several authors.[12 34 35] Long term follow up is mandatory on all children treated with such drugs. Aqueous shunts could be an alternative but they are also associated with severe complications and modest success.[36–39]

In conclusion, trabeculectomy with mitomycin C produced a satisfactory outcome in most phakic children with glaucoma but had limited success in aphakic childhood glaucoma. An alternative approach to aphakic childhood glaucoma may be needed.

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