

Original Article

Non-penetrating glaucoma surgery augmented with mitomycin C or 5-fluorouracil in eyes at high risk of failure of filtration surgery: long-term results

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ABSTRACT

Purpose: To investigate the long-term efficacy and safety of non-penetrating glaucoma surgery (NPGS) augmented with mitomycin C (MMC) or 5-fluorouracil (5FU) in eyes at high risk of failure of glaucoma filtration surgery.

Methods: Prospective study of all eyes, undergoing NPGS with 0.04% MMC (1 to 2 min topical or 0.04 mL subconjunctival injection into the superior fornix) or 5FU (25 mg/mL topically for 5 min). Complete success was an intraocular pressure (IOP) \leq 21 mmHg on no medication and qualified success an IOP \leq 21 mmHg with topical medication. An additional criterion for success was a \geq 20% drop in IOP or a reduction of at least two medications.

Results: Twenty-three eyes of 22 patients with a mean follow up of 41.4 months were reviewed. Fifteen eyes had failed trabeculectomy and seven had uveitic glaucoma. Mean preoperative IOP reduced from 25.8 ± 7.8 to 15.4 ± 4.9 mmHg at final visit, a mean change of 41%. Median number of preoperative medications decreased from 3 to 0 postoperatively. Cumulative probability of success was 100% at 2 years, 94% at 3 years and 85% at 4 years. No patient developed any long-term complications. Complete success was achieved in 11 eyes and qualified success in 10 eyes. Two eyes failed and required further surgery.

Conclusion: NPGS augmented with small-volume MMC/5FU provides good long-term IOP control in eyes at high risk of failure with a lower incidence of complications com-

pared with augmented trabeculectomy and eliminates the need for postoperative bleb or suture manipulation.

Key words: deep sclerectomy, filtration failure, non-penetrating glaucoma surgery, uveitic glaucoma, visco-canalostomy.

INTRODUCTION

The management of medically uncontrolled intraocular pressure (IOP) in patients with uveitic glaucoma or previously failed trabeculectomy, both known risk factors for filtration failure,^{1–3} is a challenge. Trabeculectomy in these eyes is likely to fail because of an accelerated scarring response at the subconjunctival/episcleral interface with subsequent bleb failure. Previous surgery and release of inflammatory mediators present in glaucomatous aqueous from inside the eye directly into the subconjunctival space is responsible for fibroblast activation.^{2,3} Antiproliferative agents such as mitomycin C (MMC) or 5 fluorouracil (5FU) have hence been used to modify the wound-healing response and prevent bleb scarring.^{4–12} Use of these antiproliferative agents improves bleb survival but can lead to complications such as hypotony, maculopathy, bleb leaks and endophthalmitis.^{13–18} Even with MMC augmentation success rates in such eyes are low.^{1,4–7}

Non-penetrating glaucoma surgery (NPGS) has been shown to provide comparable long-term success rates to trabeculectomy, with reduced postoperative complications,^{19–24} but there is limited information on its success in high-risk eyes. As NPGS does not rely on a sclerostomy for drainage of aqueous from the eye and causes less postoperative intraocular inflammation compared with trabeculectomy,²⁵ it may be a more effective way of managing

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eyes at high risk of failure of trabeculectomy. As NPGS does not produce blebs,^{26,27} the use of 5FU or MMC in such eyes may be safer than in trabeculectomy where blebs are thinner, more avascular, more likely to leak and develop infection when antiproliferative agents have been used.^{13–17}

Our aims were to study the efficacy, safety and long-term outcome of NPGS augmented with small-volume MMC or 5FU in eyes at high risk of failure and to compare it with the long-term success of augmented trabeculectomy in studies of similar high-risk patients.^{7–12}

METHODS

Patient selection

This was a prospective study of all patients undergoing NPGS with MMC or 5FU for medically uncontrolled glaucoma between January 1998 and December 2003 at the Royal Liverpool University Hospital. The indication for augmented NPGS was an IOP of >21 mmHg on maximum tolerated medical treatment (<21 mmHg if patients were on oral carbonic anhydrase inhibitors in addition to maximum tolerated topical treatment) in the presence of glaucomatous damage to the optic nerve and significant risk factors for filtration failure. Exclusion criteria were: any eye with closure of the superior drainage angle by peripheral anterior synechiae (PAS) whether due to primary angle closure, inflammatory, or secondary to conditions such as the iridocorneal endothelial syndrome. We also excluded any uveitic eye that developed acute elevation of IOP that responded to steroids or antivirals, thus excluding eyes with trabeculitis as a cause of glaucoma. All uveitic eyes in this study had prolonged chronic inflammation. The degree of anterior segment inflammation was responsive to topical and/or systemic immunosuppression but the raised IOP was not responsive to suppression of the inflammation.

Surgical technique

All surgeries were performed by one of the authors (PKW). The technique was similar to that described by Stegmann *et al.*²⁶ and Shaarawy *et al.*,²² except that viscoelastic (Viscoat-Alcon, Fort Worth, TX, USA) was used to fill the deep scleral lake and no collagen or other implants were used. Viscoat was injected at the cut ends of Schlemm's canal, but no attempt was made to intubate the canal. MMC (0.04 mL of 0.4 mg/mL) was injected subconjunctivally into the superior conjunctival fornix prior to dissection of the conjunctival flap or applied topically on a soaked cellulose sponge to the conjunctival bed for 1–2 min. 5FU (25 mg/mL) was applied topically with sponge for 5 min. Both MMC and 5FU topical applications were copiously irrigated with balanced salt solution (BSS). In eyes with previous trabeculectomy the surgical site was adjacent to the previous trabeculectomy site, below the upper lid.

In high-risk eyes, initially we used a 5-min application of topical 5FU 25 mg/mL over the site of the superficial scleral

flap and irrigated it with BSS. Following this we used the technique of topical MMC applied with a cellular sponge to the surface of the superficial scleral flap and irrigated it with BSS. From 2001 following the recommendation of Dr Peter Libre (pers. comm., 2001), we changed our technique to injecting a very small quantity (0.04 mL) of MMC into the superior fornix with a 30-gauge syringe introduced at the limbus and then advanced superiorly into the fornix to create a subtenon's bleb of MMC. The needle was then withdrawn and the entry point was grasped with Moorfields' forceps to prevent exit of the MMC, and a squint hook was used to massage the MMC under the associated tenon's capsule as widely as possible. This technique has the advantage of not contaminating the fornix-based flap wound with MMC and spreads the drug over a wide area. The viscocanalostomy was then performed in the area immediately under the needle track.

Postoperatively all eyes received topical prednisolone 1% four times a day for 2 months and thereafter topical ketorolac four times a day for a further 2 months. All antiglaucoma medications including oral carbonic anhydrase inhibitors (CAI) were discontinued postoperatively. No postoperative interventions such as bleb needling/manipulation or suture lysis were performed.

Data review

For the purpose of this study the preoperative data recorded were: patient demographics, number of years of glaucoma before NPGS, best-corrected visual acuity, number of antiglaucoma medications, IOP and previous antiglaucoma treatments. Postoperative data were recorded for day 1, 1 week, 1 month, 6 months, 1 year, 2 years, 3 years, 4 years, 5 years and final visit and included: IOP, antiglaucoma medications, visual acuity, further procedures and complications. Number of glaucoma medications was calculated as the sum of all topical antiglaucoma medications, irrespective of the type and frequency of medication use. Fixed combinations were assigned a score of 2 as was the use of maximum dose systemic CAI.

Outcome measures

To allow comparison with similar long-term studies of trabeculectomy in high-risk eyes,^{7–12} we used the success criteria of the studies of MMC trabeculectomy in high-risk eyes by Cheung *et al.*,⁹ Perkins *et al.*¹⁰ and Fontana *et al.*¹² They defined complete success as an IOP \leq 21 mmHg on no medication and qualified success an IOP \leq 21 mmHg with topical medication. An additional criterion for success was a \geq 20% drop in IOP from baseline or a reduction of at least two medications from baseline.^{10,12} Failure was an IOP > 21 mmHg, with or without medication or requirement for further glaucoma surgery. Nd:YAG goniopuncture was performed if the IOP was >21 mmHg on any occasion after withdrawing topical steroids. Hypotony was defined as

an IOP ≤ 5 mmHg, measured on two successive occasions occurring after the first postoperative week.

Change in visual acuity was analysed using the Snellen fraction at baseline preoperatively and at final follow up. An improvement of two or more Snellen lines was taken as 'improved vision'.

Statistical analysis

Statistical analysis was performed using the SPSS 13 software for windows (SPSS Inc., Chicago, IL, USA). Student's *t*-test was used to determine the significance of any differences in the continuous variables. Wilcoxon's signed rank test was used to compare the pre- and postoperative antiglaucoma medication scores. A *P*-value of <0.05 was taken as statistically significant. The cumulative probability of success was derived using the Kaplan–Meier survival curve.

RESULTS

Patient demographics

Twenty-three eyes of 22 patients with a mean follow up of 41.4 ± 15.6 months were included in the study. Patient demographics and preoperative characteristics are detailed in Table 1. Fifteen eyes had undergone previous trabeculectomy and seven eyes had uveitic glaucoma. The cause of uveitis was juvenile rheumatoid arthritis in one eye, herpes zoster ophthalmicus in one eye, idiopathic in three eyes and heterochromic cyclitis in two eyes. Fourteen eyes had two risk factors, four eyes had three risk factors and one had four risk factors (as detailed in Table 1) for failure of filtration surgery. Three patients had also undergone previous laser interventions in the form of argon laser trabeculoplasty and peripheral iridotomy. All patients had uncontrolled glaucoma with a mean disease duration, prior to augmented NPGS, of 10 ± 5.7 years. MMC was used in 18 eyes (seven topical) and 5FU was used in five eyes.

IOP control

Mean preoperative and postoperative IOP, antiglaucoma medication, outcome and complications are detailed in Table 2. The change in mean IOP with time is detailed in Table 3 and Figure 1. Mean preoperative IOP reduced from 25.8 ± 7.8 to 15.4 ± 4.9 mmHg at final visit, a mean change of 41.4% (range 11–72.5%). The change in IOP was statistically significant at all times postoperatively ($P < 0.001$). Two patients on oral CAI preoperatively had a $<20\%$ change in IOP but a reduction in more than three medications. Their IOP at final visit was ≤ 16 mmHg.

Outcome

Overall success was achieved in 21 eyes (91.3%), complete success in 11 (47.8%) and qualified success in 10 eyes (43.5%) by final follow up. Two eyes (8.6%) failed and required further surgery. Only three eyes (13%) required more than one topical medication to achieve qualified success. One of

Table 1. Patient demographics and characteristics of study population

No. of patients	22
Male	15
Female	7
No. of eyes	23
Race	
Black	1
Caucasian	21
Glaucoma type (eyes)	
Primary open angle	
With PMT	2
Previous trabeculectomy with PMT	11 (3 patients had had ALT as well)
Uveitis	
No other risk factors	2
With PMT	2
Previous trabeculectomy and PMT	2
Previous complicated cataract surgery, trabeculectomy and PMT	1
Stickler's syndrome with PMT	1
Angle recession with previous trabeculectomy and PMT	1
Iridocorneal endothelial syndrome with previous complicated cataract surgery and PMT	1
High-risk factors (as detailed earlier)	
One	4
Two	14
Three	4
Four	1
Age in years, mean \pm SD (range)	67.2 \pm 17.6 (23–88)
Years of glaucoma before NPGS, mean \pm SD (range)	10.3 \pm 5.7 (1–23)
Procedure	
NPGS + MMC (0.04 mL of 0.04%)	
Subconjunctival injection	11 eyes
Sponge application	7 eyes
NPGS + 5FU (25 mg/mL)	5 eyes

ALT, argon laser trabeculoplasty; 5FU, 5-fluorouracil; MMC, mitomycin C; NPGS, non-penetrating glaucoma surgery; PMT, prolonged medical treatment (>7 years).

these had advanced glaucoma with previous trabeculectomy and prolonged medical therapy and one had iridocorneal endothelial syndrome with previous complicated cataract surgery and prolonged medical therapy. Of the two patients who required an Ahmed valve to control IOP, one eye was uveitic glaucoma with previous trabeculectomy and prolonged medical therapy that developed scleritis and raised IOP at 18 months postoperatively that responded to systemic steroids. Sixteen months later the same eye developed intense recurrent iritis that responded to systemic steroids, but IOP control was lost by 36 months. The other failure was an advanced open-angle glaucoma eye with previous trabeculectomy and prolonged medical therapy, which failed at 48 months.

Kaplan–Meier survival curve analysis (Fig. 2) showed a cumulative probability of maintaining an IOP ≤ 21 mmHg

Table 2. Results

Follow up in months, mean \pm SD (range)	41.4 \pm 15.6 (12–72)
Mean IOP in mmHg, mean \pm SD (range)	
Preoperative	25.8 \pm 7.8 (14–47)
Postoperative (final visit)	15.4 \pm 4.9 (9–30)
Outcome, No. of eyes (%)	
Complete success	11 (47.9)
Qualified success	10 (43.5)
Failure	2 (8.6)
Further procedures, No. of eyes (%)	
Ahmed valve	2 (8.6)
YAG GP	6 (21.7)
Medication	
Preoperative	
Score, median (range)	3 (1–5)
Patients on oral acetazolamide	8
Postoperative	
Topical score, median (range)	0 (0–2)
Complications, No. of eyes	
Preoperative	
Perforation of TDM	2 (1 requiring PI)
Early postoperative	
Increased IOP within 1 month	1 (resolved after YAG GP)
Hyphaema	1 (resolved spontaneously)
Temporary hypotony	3 (1 CMO, all resolved by 3 months)
Late postoperative	
Avascular blebs	2

CMO, cystoid macular oedema; IOP, intraocular pressure; PI, peripheral iridotomy; TDM, trabeculo-Descemetic membrane; YAG GP, Nd:YAG goniopuncture.

with or without topical antiglaucoma medication and a $\geq 20\%$ drop in IOP, or a reduction of at least two medications from baseline was 100% at 1 year, 100% at 2 years, 94% at 3 years and 85% at 4 years with a mean survival time of 67.6 months (95% confidence interval 62–73).

Change in medication

Eight patients were on oral CAI preoperatively that could be withdrawn in all patients postoperatively. At final visit 11 patients were on no treatment, seven on one topical medication and five on two topical medications. Median topical medications used decreased significantly from 3 (range 1–5) to 0 (range 0–2) postoperatively, a mean change of 80.5% (Wilcoxon's signed rank test, $P = 0.000$).

Visual acuity

Visual acuity improved in nine eyes, seven of which underwent cataract surgery postoperatively and remained stable in 14 eyes (11 had preoperative visual acuity $\geq 6/12$ and the

other three had visual acuity $\leq 6/36$, which was long standing).

Further procedures

Postoperative Nd:YAG goniopuncture was performed in six eyes (26%). The settings were 5 mJ \times 5 shots. The mean time between NPGS and Nd:YAG goniopuncture was 22 months (range 3–36 months). Mean pre-Nd:YAG goniopuncture IOP changed from 24.2 \pm 6.2 to 12 \pm 5.1 post-Nd:YAG goniopuncture. IOP reduced in all but two eyes that went on to have an Ahmed glaucoma valve. None of the eyes required repeat Nd:YAG goniopuncture.

Complications

Preoperative complications included perforation of the trabeculo-Descemetic membrane in two patients, one of which required a peripheral iridotomy. Both eyes were successful. In the immediate postoperative period two eyes had an IOP > 30 mmHg at week 1, which was diagnosed as a steroid response as the IOP fell to below 21 mmHg following withdrawal of topical steroids. Hyphaema was noted in one patient (resolved spontaneously) and temporary hypotony in three patients, one of whom developed cystoid macular oedema (CMO). The eyes with hypotony all recovered to an IOP of > 7 mmHg by 3 months postoperatively without intervention. No patient had an IOP < 5 mmHg on any occasion after 6 months. Two patients, both with topical MMC application, developed avascular blebs. One of these two eyes had controlled IOP, the other had uncontrolled IOP and later required an Ahmed glaucoma valve at 48 months postoperatively.

DISCUSSION

Control of IOP

The medium and long-term (up to 5 years) success rates of NPGS are comparable to those of trabeculectomy^{23,24,28} with a much lower incidence of early or late complications. Our qualified success rate of 91.7% for NPGS is at least equivalent to that of augmented trabeculectomy for high-risk eyes, with less complications and less need for postoperative interventions than are reported following augmented trabeculectomy.^{7–12}

In eyes at high risk of failure of glaucoma filtration surgery, the use of antifibrotic agents is considered essential as the bleb survival and IOP control have been shown to be improved with their use.⁸ Most glaucoma surgeons now use antifibrotic agents in all eyes undergoing trabeculectomy (whether low or high risk) on the basis of better bleb survival and IOP control with their use.^{29–31} The Fluorouracil Filtering Surgery Study Group (FFSSG) provided long-term (5 years) data on eyes with either prior failed filtering surgery (24%) or prior cataract extraction (80%) eyes⁸ and Rothman *et al.*'s study gave 5-year data on primary trabeculectomy plus 5FU

Table 3. Change in intraocular pressure with time

	Preop	1 day	1 week	1 mth	3 mth	6 mth	12 mth	18 mth	24 mth	30 mth	36 mth	42 mth	48 mth	60 mth
Mean	25.8	10.7	12.2	13.7	13.3	14.6	14.3	15.27	15.4	15.5	16.8	15.9	16	16
SD	7.8	9.2	9.7	9.5	5.4	4.6	4.7	4.3	4.5	5.1	5.8	4.4	4.5	2.8
Range	14–47	0–45	0–38	1–45	4–23	6–23	6–26	6–27	6–25	4–23	9–30	9–23	10–26	14–20
n	23	23	23	23	23	23	23	22	20	19	18	12	10	4

mth, month; n, number of patients; Preop, preoperative.

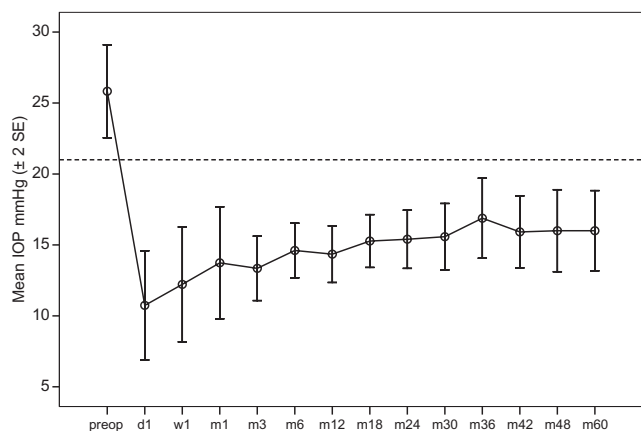


Figure 1. Change in intraocular pressure (IOP) with time. Mean preoperative IOP reduced from 25.8 ± 7.8 to 15.4 ± 4.9 mmHg at final visit, a mean change of 41.4%. The change in IOP was statistically significant at all times postoperatively ($P < 0.001$). d, day; m, month; preop, preoperative; SE, standard error; w, week. Dotted line represents a mean IOP of 21 mmHg.

in normal risk eyes.²⁹ Three-year data on the outcome of MMC trabeculectomy are limited to the studies of Cheung *et al.* that included 70% high-risk eyes, Perkins *et al.* in which most eyes were high risk^{9,10} and 5 years data in the study of Casson *et al.*¹¹ Fontana *et al.* reported the results of MMC trabeculectomy in pseudophakic eyes with open-angle glaucoma and no other risk factors.¹² Towler *et al.* reported that trabeculectomy with 5FU in eyes with glaucoma following uveitis gave a 5-year complete success rate of 67%, which is close to the 72% success rate of 5FU trabeculectomy reported by Rothman *et al.* for low-risk eyes undergoing 5FU trabeculectomy at 5-year follow up.^{7,29}

We used the same definition of success provided by the aforementioned studies of similar populations of high-risk eyes: failure as need for repeat glaucoma surgery or IOP > 21 mmHg with or without medications,⁸ a complete success as IOP < 21 mmHg without medications and qualified success as IOP < 21 mmHg with medications.^{9,10} Fontana *et al.*'s study on the outcome of MMC trabeculectomy in pseudophakic eyes gave a 2-year success rate of 67% defined as qualified success with final IOP ≤ 18 mmHg and $> 20\%$ IOP reduction or a reduction of at least two medications.¹²

Our overall success rate of 91.7% at final follow up is equivalent to the 88.7% Kaplan–Meier success rate of

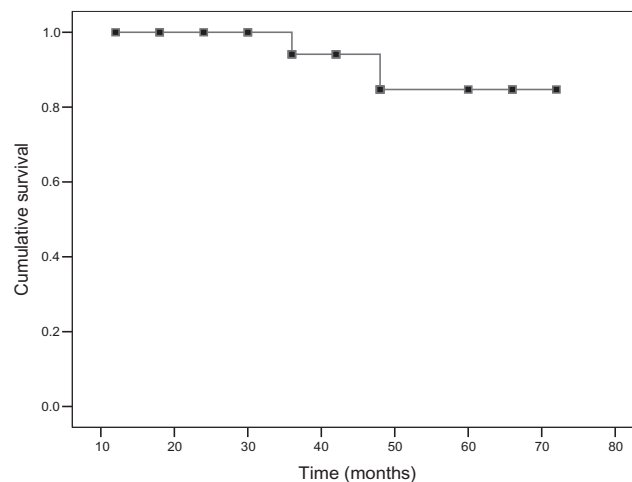


Figure 2. Kaplan–Meier survival curve. Kaplan–Meier survival curve analysis showed a cumulative probability of maintaining an intraocular pressure (IOP) ≤ 21 mmHg with or without topical antiglaucoma medication and a $\geq 20\%$ drop in IOP or a reduction of at least two medications from baseline was 100% at 1 year, 100% at 2 years, 94% at 3 years, 85% at 4 years and 85% at 5 years with a mean survival time of 67.6 months (95% confidence interval 62–73).

Cheung's study where failure was need for repeat surgery.⁹ Our 5-year complete success rate was 48% and equivalent to the complete success rate in Perkins *et al.*'s study at 3 years of 47%.¹⁰ The cumulative 5-year survival in the FFSSG showed the success rate to be 47% in eyes with previous failed filtration surgery.⁸ Our study population had similar or worse risk factors for failure (65% of eyes prior failed trabeculectomy, 30.4% uveitic glaucoma and pseudophakia in 13%) than the aforementioned three studies. In our study one patient (5%) was of black race, which is similar to the 1.3% black race of Cheung *et al.*'s study, 8% black in Fontana *et al.*'s study and Perkins *et al.*'s study where 10% of patients were black.^{9,10,12}

Failure rates (i.e. need for repeat surgery, less than two medications or $< 20\%$ IOP reduction) were also similar in our study to those of augmented trabeculectomy in high-risk eyes. Two eyes (8.6%) in our study required repeat glaucoma surgery compared with 11–15% of high-risk trabeculectomy eyes.^{9,10,12} The FFSSG found at 5 years that 29.5% of eyes required additional surgery for IOP control.⁸ Rothman *et al.*'s study of primary trabeculectomy plus 5FU

at 5 years reported 23% of eyes had failure of IOP control.²⁹

Complications

In our study two eyes in the first postoperative month developed CMO. One case of CMO occurred in an eye with uveitis that had previous uveitic CMO, and the other was in an amblyopic eye that developed temporary postoperative hypotony in the first month and recovered spontaneously. In studies of trabeculectomy augmented with 5FU or MMC, bleb leaks are reported in 9–14.6% of eyes by 5 years,^{8,15,18} hypotony maculopathy in 3.2–9%^{5,9,15} and blebitis/endophthalmitis in 3.2–11%.^{9,18,29} In Rothman *et al.*'s study of primary trabeculectomy, trans-conjunctival needle revision was necessary in 13.5% eyes and Fontana *et al.* reported a 34% requirement for laser suture lysis.^{12,29} Routine MMC trabeculectomy management now includes suture release or manipulation, laser suture lysis, bleb needling or revision and 5FU injections in up to 50% of cases.^{29,32} In our study, the only postoperative intervention that was required was Nd:YAG laser goniopuncture in 26% of eyes and of the seven eyes (30.4%) that underwent cataract extraction, none lost IOP control. Ceballos *et al.* reported a 51.6% incidence of cataract formation after MMC/5FU-augmented trabeculectomy for uveitic glaucoma, of which 25% failed following cataract surgery.⁶

Risk factors and outcome

Previously failed trabeculectomy and uveitis are known risk factors for failure of filtration surgery^{1–3} as are pseudophakia and prolonged topical medication.^{1,33} The inflammatory response is a potent stimulator of subconjunctival fibroblasts and the resultant scarring limits the success of glaucoma filtering surgery.^{2,3} Previous cataract surgery increases the chemotactic activity of aqueous humour that acts as a stimulus to wound healing.³⁴ Agarwal *et al.* noted that the presence of more than one preoperative 'high-risk factor' significantly lowers the success rate of MMC-augmented trabeculectomy.¹ They analysed the odds ratio for individual risk factors and found it to be 3.67 for previously failed trabeculectomy, 1.69 for postuveitic glaucoma and 1.71 for prolonged medical therapy. Sturmer *et al.* had similar findings.³³ Moreover, after NPGS the duration and intensity of anterior chamber inflammation is significantly reduced in comparison with trabeculectomy, which may be important in uveitic eyes.²⁵ Prata Jr *et al.* noted an exacerbation of uveitis in 12.5% patients after trabeculectomy.⁵

Trabeculectomy works by allowing aqueous to escape from the eye into the subconjunctival space and drain into the episcleral venous system. Trabeculectomy fails when there is scarring at the conjunctival/episcleral interface and such wound healing is more likely to occur in the presence of increased levels of mediators of ocular inflammation such as are present in eyes with previous filtering surgery, uveitis or cataract surgery. With NPGS, after removing the juxtacanalicular

tissue and the inner endothelial lining of the Schlemm's canal, the aqueous crosses the remaining corneo/uveoscleral meshwork and may enter the cut ends of the Schlemm's canal or leave the eye via transcleral flow or uveoscleral outflow.³⁵ Whichever way the aqueous leaves is as yet unknown, but the aforementioned three routes are adapted to aqueous egress and therefore should not incite a healing reaction such as occurs at the episcleral interface when it comes into contact with aqueous. Miserocchi *et al.* noted good results with viscocanalostomy in eyes with uveitic glaucoma and a 4-year follow up.³⁶ Souissi *et al.* reported long-term IOP control in all eight eyes of a series with uveitic glaucoma using deep sclerectomy with no augmentation.³⁷

Most surgeons performing deep sclerectomy place a collagen or other implant^{19,21,22,38–41} under the remaining superficial scleral flap to encourage subconjunctival drainage. With viscocanalostomy, on the other hand, Stegmann *et al.* recommend tight closure of the superficial scleral flap to avoid any bleb formation.²⁶ Our previous results for deep sclerectomy without implant and viscocanalostomy have been almost identical.²³

A single 5-min exposure of 0.4-mg/mL MMC can almost completely inhibit the proliferation of fibroblasts *in vitro*⁴² and has long-term effects on conjunctival and scleral fibroblasts *in vivo*.⁴³ Anterior chamber fluorophotometry has shown a decreased aqueous humour production in eyes undergoing trabeculectomy with MMC compared with eyes undergoing trabeculectomy without MMC, suggesting a role of MMC-induced ciliary body toxicity in postoperative hypotony.⁴⁴ Agarwal *et al.* in a comparative study of subconjunctival versus intrascleral application of MMC in trabeculectomies found an increased incidence of hypotony, hypotony maculopathy and choroidal detachment with the latter, which may be explained by the higher concentration reaching the ciliary body.⁴⁵ Rebolleda and Munoz-Negerte in a study of deep sclerectomy with MMC in eyes with failed trabeculectomy (90% of which were pseudophakic) achieved a qualified success rate of 100% at 1-year follow up without complications. They applied MMC under the conjunctival and superficial scleral flaps.⁴⁶

From our study we do not know if the use of antifibrotics aided the success in these eyes with high risk of failure. Only a randomized controlled trial could answer this question but to randomize patients with multiple risk factors to two equal treatment arms would be very difficult. Our long-term results are satisfying in this group of difficult eyes as the majority of our patients have well-controlled IOP, none have developed a bleb-related complication and only two eyes have required further surgery. It may be that we would have achieved the same results had we not used antifibrotic agents. A single dose of topical 5FU preoperatively has been shown not to be of benefit in primary trabeculectomy and therefore would not be regarded as sufficient antifibrotic treatment in a high-risk eye undergoing trabeculectomy.⁴⁷ It is also debatable as to whether our superior fornix injection of MMC made any difference as these patients did not develop blebs and therefore the bleb survival effect that MMC normally produces

may not have had any significant effect on the outcome of viscocanalostomy.

There was no difference in the success between those eyes that had 5FU, topically applied MMC or superior fornix injection of MMC and the patient groups were roughly comparable containing an equal number of eyes with uveitis or failed trabeculectomy. Because of the small numbers of high-risk eyes in this study, we cannot make strong recommendations as to the use of 5FU or MMC in such cases. As no blebs are produced with NPGS, factors that give rise to bleb failure namely inflammatory mediators causing scarring at the subconjunctival episcleral interface may not worsen outcome in NPGS. Lack of blebs and good IOP control represents a major quality of life advantage to NPGS patients compared with those undergoing trabeculectomy where blebs are a potential source of sight-threatening complications¹⁸ and also a cause of significant ocular discomfort.⁴⁸

Our results show that augmented NPGS is a successful procedure in the management of high-risk eyes with a lower incidence of complications than reported by studies of augmented trabeculectomy. The lack of bleb formation and the lack of need for postoperative bleb manipulation make NPGS a safer and more acceptable treatment for patients.

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