PRIMARY VISCOCANALOSTOMY VERSUS MITOMYCIN-C AUGMENTED TRABECULECTOMY IN PATIENTS WITH OPEN-ANGLE GLAUCOMA: A RANDOMIZED CLINICAL TRIAL

Susan E.I. Williams

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in Ophthalmology.

Johannesburg, 2009

DECLARATION

I, Susan Williams, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in Ophthalmology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other university.

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11th day of May 2009

The work reported in this dissertation was carried out at the St. John Eye Unit of the Chris Hani Baragwanath Hospital (St. John), Johannesburg, South Africa.

DEDICATION

To my parents, Hugh and Elizabeth, for their love and support.

ETHICS APPROVAL

The project was approved by the Human Research Ethics Committee (Medical) at the University of the Witwatersrand.

Clearance certificate number: 020906

PRESENTATIONS ARISING FROM THIS STUDY

The results of this study were presented at the annual congress of the Ophthalmological Society of South Africa (OSSA) in Cape Town, March 2007.

Title: Primary viscocanalostomy versus mitomycin C augmented trabeculectomy in patients with open-angle glaucoma.

Presenter: Susan Williams

ABSTRACT

Purpose

To compare the outcomes of primary viscocanalostomy with trabeculectomy augmented with mitomycin C (MMC) in black South African patients with primary open-angle glaucoma (POAG).

Method

A prospective, randomized study was conducted over a four year period. Fifteen black South African patients with bilateral open-angle glaucoma requiring surgery that met the inclusion criteria and gave informed consent to participate in the trial were randomized to receive either a viscocanalostomy or a trabeculectomy with MMC in the first eye requiring surgery. The fellow eye then received the alternate procedure. Patients were followed up for two years postoperatively.

Results

There were no significant differences between the two surgical groups preoperatively. Twelve eyes in each group were followed for twenty-four months. In both groups the intraocular pressure (IOP) was significantly reduced post-operatively ($p < 0.01$) and the average number of medications used per eye was significantly reduced ($p < 0.02$). At twenty-four months, complete success (IOP less than or equal to 18mmHg without glaucoma medication and with no evidence of glaucoma progression) was seen in 75% of eyes undergoing trabeculectomy with MMC that completed the follow up, but in only

33% of eyes undergoing viscocanalostomy (p = 0.0498). Survival curves for both success and qualified success (IOP less than or equal to 18mmHg with glaucoma medications) in the two surgical procedures confirmed the superiority of trabeculectomy with MMC over viscocanalostomy.

Conclusion

Viscocanalostomy may offer some advantages because it is less invasive, but intraocular pressure control appears to be superior with trabeculectomy with MMC and this continues to be the filtering procedure of choice for the management of glaucoma in black South African patients.

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PREFACE

I first became interested in viscocanalostomies when Professor Robert Stegmann gave a presentation at a meeting of the Ophthalmological Society of South Africa in Johannesburg. His videos of his surgical technique were inspiring. I was particularly interested in the apparent avoidance of the requirement for mitomycin C (MMC) with his operation. Based on the professor's excellent results I began to think that viscocanalostomy might be a safer alternative procedure to trabeculectomy with MMC in the patients at the St. John Eye hospital.

I subsequently visited Professor Stegmann at Garankua Hospital and observed him operating. Once I had learnt the technique I decided to compare the procedure with trabeculectomy with MMC (the surgical standard in our hospital) because a literature search at the time revealed few randomised controlled trials comparing the two procedures. In particular no such trials had been conducted in black South African patients.

1.0 INTRODUCTION

Trabeculectomy has long been considered the gold standard in the surgical treatment of glaucoma. It is, however, not without its problems: the outcome of the operation may be unpredictable and there are numerous potential complications like visual loss, long functional recovery, hypotony with a shallow anterior chamber, choroidal detachment, choroidal haemorrhage and cataract formation. Because of the often high failure rate in our predominantly black South African patients at the St. John Eye Hospital we routinely augment all our trabeculectomies with mitomycin-C (MMC), which produces its own set of complications. As a result of the problems with trabeculectomy there has been increasing interest in so-called "non-penetrating glaucoma surgery" of which viscocanalostomy is one type. This operation was pioneered by Professor Robert Stegmann and consists of a deep sclerectomy underneath a superficial scleral flap that "deroofs" the canal of Schlemm into which high density viscoelastic is injected. Stegmann's hypothesis is that aqueous leaves the anterior chamber by percolating through Schlemm's canal endothelium and Descemet's membrane into the scleral "lake" created by the deep sclerectomy and from there it enters the widened cut ends of Schlemm's canal and thus the aqueous veins and episcleral venous circulation.[1] If this is the case then subconjunctival antimetabolites should be unnecessary and one could avoid their use, making the surgery safer still.

Thus the rationale for this study was to determine if viscocanalostomy is an effective procedure in our setting at the St. John Eye Hospital, if the outcomes with

viscocanalostomy are equivalent to a trabeculectomy augmented with MMC and if it does indeed have fewer complications than a trabeculectomy with MMC.

2.0 LITERATURE REVIEW

Glaucoma Surgery

Despite the fact that intraocular pressure (IOP) no longer forms part of the diagnosis of glaucoma, it is still recognised as an important risk factor for the presence or progression of glaucoma. The Advanced Glaucoma Intervention Study (AGIS)[2] was a seminal work in highlighting the importance of sufficient pressure lowering in glaucoma. All current treatment modalities for glaucoma lower the IOP and thus reduce the IOP-related threat to vision. Surgery is the most effective way of reducing the IOP,[3] but it is generally reserved for those patients in whom medical therapy has been unsuccessful, because of the morbidity associated with surgery. The challenge in glaucoma surgery is to find a procedure that is effective in lowering the IOP sufficiently without complications.

Trabeculectomy with Mitomycin-C (MMC)

Trabeculectomy was first described by Cairns in 1968.[4] The procedure reduces the IOP through the creation of a sclerostomy that bypasses the trabecular meshwork and allows aqueous humour to flow out beneath a scleral flap and collect under the conjunctiva in a filtering bleb where it diffuse into periocular tissues and is subsequently reabsorbed into the vascular system. Trabeculectomy remains the most widely performed incisional surgical procedure for glaucoma worldwide and is considered the gold standard in the surgical treatment of glaucoma. Its effectiveness in lowering IOP has been

established,[5,6,7] but many factors may affect the success rate. One such factor is African ancestry which may be a risk factor for postoperative scar formation and thus filtration failure.[8] Inhibiting wound healing with a single peri-operative application of MMC (a cytotoxic agent that disrupts DNA, induces fibroblast death and inhibits fibroblast proliferation and migration)[9] enhances the success rate of trabeculectomy.[10]

Trabeculectomy is not without complications. In the initial postoperative phase visual loss, hypotony, anterior chamber shallowing, choroidal effusions, suprachoroidal haemorrhages and malignant glaucoma may occur.[5,11] Late complications include prolonged hypotony associated with hypotony maculopathy and bleb-related infections.[5] The use of MMC has led to an increase in the incidence of these complications which may be associated with large avascular blebs.[12,13] Trabeculectomy is also frequently associated with cataract formation.[3,5]

Viscocanalostomy

Viscocanalostomy was developed by Professor Robert Stegmann who perceived the need for a more successful procedure than trabeculectomy in black African patients.[1] The procedure relies on a deep scleral dissection in the plane of the scleral spur and Schlemm's canal to externalize and deroof Schlemm's canal. The cut ends of Schlemm's canal are then cannulated and high-viscosity sodium hyaluronate (Healon GV®) is injected into the canal.[1] Stegmann's hypothesis is that the IOP is lowered by aqueous humour percolating through Schlemm's canal endothelium and Descemet's membrane

into the scleral "lake" (the potential space created by the deep sclerectomy) and from there into Schlemm's canal and thus the aqueous veins and episcleral venous circulation.[1] In theory, the absence of external filtration should obviate the need for inhibition of wound healing with MMC.

Stegmann,[1] in his retrospective review, reported an average IOP reduction of 64% with viscocanalostomy in black South African patients. There were few complications in his series of 214 eyes. Specifically there were no flat chambers or choroidal detachments and there was no cataract development. Only 5% of his patients had subconjunctival bleb formation. The low incidence of complications has been duplicated in prospective studies by Carassa,[14] Sunaric-Mégevand,[15] Luke[16] and Shaarawy[17] with varying success rates.

Comparison of trabeculectomy with MMC with viscocanalostomy in open-angle glaucoma

Several investigators have compared the outcomes of trabeculectomy with viscocanalostomy,[18,19,20,21,22] but there are few randomised prospective trials comparing trabeculectomy with MMC with viscocanalostomy.

Kobayashi et al.[23] compared trabeculectomy with MMC to viscocanalostomy in 50 eyes of 25 patients. After one year's follow-up 88% of the trabeculectomy eyes and 64% of the viscocanalostomy eyes had achieved an IOP under 20mmHg. The mean final IOP was 4.5mmHg lower in the eyes that underwent trabeculectomy with MMC.

O'Brart et al.[24] compared trabeculectomies with antimetabolites (either 5-fluorouracil or MMC based on a risk factor for failure score) with viscocanalostomies in 50 eyes followed for between 12 and 24 months. At 12 months of follow up 100% of the trabeculectomy eyes had an IOP under 21mmHg (with or without medical therapy) whereas only 64% of the viscocanalostomy eyes were successful according to the same criteria. This significant difference held true for complete success (IOP of 15mmHg or less without glaucoma medication). In the trabeculectomy group at one year this was achieved in 76% of the patients whereas it was only achieved in 26% of the viscacanalostomy group. There were more transient complications in the trabeculectomy group and more cataracts developed in this group.

3.0 PATIENTS AND METHODS

This prospective randomized trial enrolled fifteen patients with bilateral open angle glaucoma requiring surgery to both eyes. The diagnosis of glaucoma was based on the appearance of the optic nerve head and the presence of visual field defects. The requirement for surgery was an intraocular pressure (IOP) of greater than 18mmHg on maximum tolerated medical therapy or glaucoma progression on maximum tolerated medical therapy. Written informed consent was obtained from each participant.

Patients were excluded if they had had previous glaucoma surgery or if they had angle closure, neovascular glaucoma, post-traumatic glaucoma or dysgenetic glaucoma.

Preoperatively, the patients were questioned on the use of antiglaucoma medications, coexisting systemic or ocular disease, use of systemic medication, and previous intraocular surgical or laser procedures. The baseline ophthalmological examination consisted of a Snellen best-corrected visual acuity for distance, a visual field test, slit-lamp examination, Goldmann applanation tonometry, gonioscopy and dilated fundoscopy. The type of glaucoma and the lens status were documented.

The patients were randomized into either a trabeculectomy with MMC or a viscocanalostomy in the first eye followed by the other procedure in the second eye. The author performed all the operations.

Surgical Technique

In both procedures the technique involved a fornix based conjunctival flap, vasopressin (POR-8®) was used for haemostasis and a 5mm by 5mm parabolic scleral flap was fashioned which was dissected into clear cornea (see Figure 3.1).

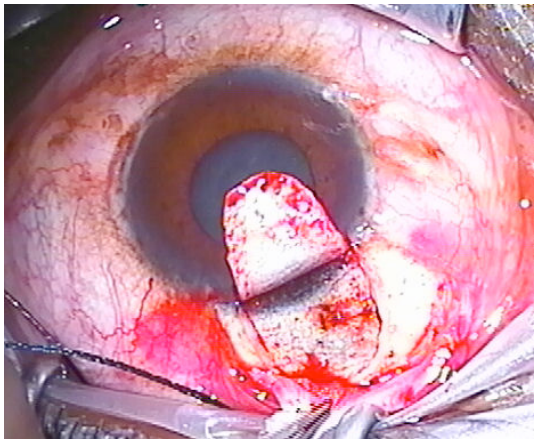

Figure 3.1: Dissection of a parabolic scleral flap

In the trabeculectomies 0,25mg/ml of mitomycin-C was applied with a sponge under the conjunctival flap for one minute before dissecting the scleral flap. This area was then irrigated with balanced salt solution (BSS®). After lifting the flap a 2mm by 2mm sclerostomy was followed by a peripheral iridectomy. The scleral flap was sutured using interrupted 10-0 prolene sutures and the conjunctiva was closed using 8-0 vicryl sutures.

In the viscocanalostomies a 4mm by 4mm deep scleral flap was dissected under the initial parabolic flap to deroof the canal of Schlemm. The dissection was continued anteriorly to form a Descemet's window (see Figure 3.2).

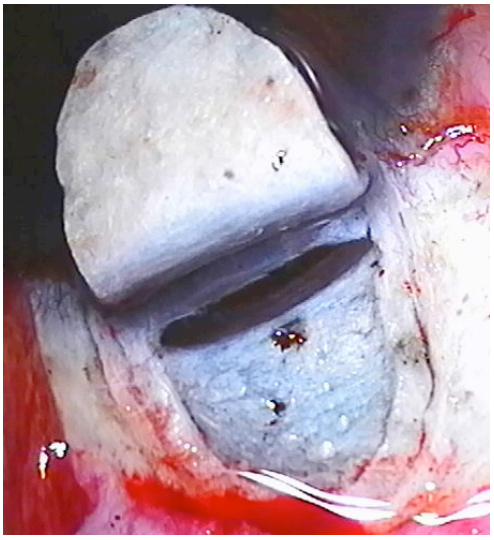

Figure 3.2: Deroofing of the canal of Schlemm with a deep scleral flap

A 150µm cannula (viscocanalostomy cannula) was then inserted into the ostia of Schlemm's canal, both left and right, and Healon GV® was injected into the canal for 4 to 6mm on each side. The scleral flap was sutured using interrupted 10-0 prolene sutures and the conjunctiva was closed using 8-0 vicryl sutures in the same way as with the trabeculectomies.

Post-operatively the treatment regimen was the same in both surgical procedures and consisted of:

- Topical prenisone acetate given two hourly for the first week then four times a day for three weeks, then tapering over the next two months in combination with
- Topical homatropine given twice daily for the first week
- Topical chloromycetin drops given three times daily for the first week.

Follow up

Patients were followed for twenty-four months post-operatively. They were examined at one day, one week, one month, and three months post-operatively and then three monthly thereafter. At each visit Snellen best corrected visual acuity, IOP, anterior chamber activity, appearance of the bleb, lens appearance, optic disc status and number of antiglaucoma agents required to achieve optimal levels of IOP were documented. At months six, twelve, eighteen and twenty four the patients had visual fields, gonioscopy and stereo disc assessments to exclude glaucoma progression. Extra visits were scheduled as clinically warranted. The incidence of any complications and the requirement for any additional procedures was documented.

Outcome measures

The main outcome measure was the intraocular pressure.

Success was defined as an IOP of less than or equal to 18mmHg without glaucoma medication and with no evidence of glaucoma progression whereas a qualified success was an IOP of less than or equal to 18mmHg with glaucoma medication but with no evidence of glaucoma progression.

A qualified failure was defined as an IOP of greater than 18mmHg with glaucoma medication but with no evidence of glaucoma progression and failure was an IOP of

greater than 18mmHg with evidence of glaucoma progression or requiring further glaucoma surgery. Bleb needling procedures and laser goniopunctures were not considered as failures.

A secondary outcome measure was the number of glaucoma medications used per eye.

Statistical testing

Paired *t* tests were used to compare continuous variables between the groups such as IOP.

The Wilcoxon matched pairs signed rank test was used to compare count data that was not normally distributed such as the difference in number of medications.

Fisher's exact test was used to compare categorical data.

Kaplan-Meier survival analyses were carried out using the definitions of success and qualified success as criteria. Comparisons between groups were done by the log-rank test.

A Cox model was used to investigate the effect of certain variables (covariates) on the success of surgery.

All tests were two-tailed and p-values of less than or equal to 0.05 were taken to be significant (95% confidence level) unless otherwise indicated.

4.0 RESULTS

Fifteen South African black patients with bilateral open-angle glaucoma were enrolled in the study. The demographics of the patients are recorded in Table 4.1.

Six of the patients were male, and nine were female. The mean age was 65years (range 49 to 75 years). Six patients had a glaucoma diagnosis of exfoliative glaucoma and nine had primary open-angle glaucoma. Nine of the patients were hypertensive on treatment; four of these patients were also diabetic.

Table 4.1: Patient demographics and study diagnosis (XFG = exfoliative glaucoma; POAG = primary open-angle glaucoma, HT = hypertensive)

Patient	Sex	Age	Diagnosis	Medical history
A	Female	73	XFG	HT, Arthritis
B	Male	68	XFG	HT, Diabetic
C	Female	52	POAG	Nil
D	Female	49	POAG	HT
E	Female	69	XFG	HT
F	Male	63	POAG	Nil
G	Female	71	POAG	HT, Diabetic
H	Male	75	XFG	HT
I	Male	69	XFG	Nil
J	Female	57	POAG	Nil
K	Male	67	POAG	HT
L	Male	61	POAG	Nil
M	Female	62	POAG	HT, Diabetic
N	Female	69	XFG	HT
O	Female	60	POAG	Asthmatic

A trabeculectomy with MMC was performed in fifteen eyes and a viscocanalostomy was performed in the fellow fifteen eyes. The preoperative IOP and the number of medications per eye for these two surgical groups were similar (Table 4.2).

Table 4.2: Preoperative IOP and number of medications in the eyes that underwent trabeculectomy with MMC and viscocanalostomy

Surgery	**Trabeculectomy**	**Viscocanalostomy**
Average IOP (mm Hg) *	23.3 ± 2.3	26.4 ± 3.0
Number of subjects	15	
p-value (paired sample t-test)	0.078 (not significant)	
p-value (Wilcoxon matched pairs test)	0.097 (not significant)	
Average number of medications *	2.1 ± 0.2	2.0 ± 0.2
Median number of medications **	2 (2 – 2)	2 (2 – 2)
Number of subjects	15	
p-value (Wilcoxon matched pairs test)	- (not significant)	

* mean ± 95% confidence intervals
** median (25^{th} – 75^{th} percentile range)

In comparing the preoperative IOP in these two surgical groups both the paired sample t-test and the Wilcoxon matched pairs test were used. The paired sample t-test could be used because the differences between the trabeculectomy and viscocanalostomy values were approximately normally distributed. The results were confirmed using the non-parametric Wilcoxon matched pairs test which required no assumptions about the distribution of the data to be met.

Comparing the number of medications used per eye in each surgical group required the Wilcoxon matched pairs test because the paired differences were not normally distributed. There were only two non-zero differences (most of the eyes were on dual

therapy) therefore it was not possible to calculate a p-value, but the difference is not significant.

Preoperatively (Table 4.3) four eyes in each group had lens opacities (in three instances in the same patients), two of the trabeculectomy eyes were pseudophakic as was one of the viscocanalostomy eyes. One of the pseudophakic eyes in the trabeculectomy group (patient H) had had a complicated extracapsular cataract extraction which had resulted in prolonged post-operative intraocular inflammation – the eye was not active at the time of surgery, but this may have been an additional risk for failure. None of the patients had had previous glaucoma laser procedures.

Table 4.3: Preoperative findings in the eyes that underwent trabeculectomy with MMC and viscocanalostomy. The letters (A-O) refer to the individual patients as recorded in Table 4.1

	Trabeculectomy	**No.**	**%**	**Viscocanalostomy**	**No.**	**%**
Preoperative findings		**15**	**100**		**15**	**100**
Arcus Senilis	F	1	6.7	F	1	6.7
Pingueculum	A,B,C,D,E,I,K	7	46.7	A,B,C,D,E,I,K,O	8	53.3
Lens opacities	A,B,E,M	4	26.7	A,E,H,M	4	26.7
Pseudophakic	H,G	2	13.3	G	1	6.67
Intraocular inflammation	H	1	6.7			0

Two of the patients (patients F and N) defaulted before the completion of the study period and patients B (trabeculectomy first) and I (viscocanalostomy first) defaulted after completing the study period of twenty four months of follow-up after surgery to their first eye, but before completing this period with the fellow eye. Thus twenty-four eyes (twelve eyes that had trabeculectomies with MMC and twelve eyes that had viscocanalostomies) were followed for the complete two year period.

The IOP results for the study period are summarized in Table 4.4 and illustrated graphically in Figure 4.1. IOP data were included up to twenty-four months after surgery even if patients were placed on antiglaucoma medications or had another procedure to lower IOP. As a result of this, after one month post-operatively the conditions between the matched eyes differ making comparisons difficult.

Table 4.4: IOP results for the study period in the eyes that underwent trabeculectomy with MMC and viscocanalostomy

	Average IOP (mm Hg) ± 95% confidence interval	
Time after surgery	**Trabeculectomy with MMC**	**Viscocanalostomy**
Pre-operative	23.3 ± 2.3	26.4 ± 3.0
1 day	17.3 ± 4.4	10.3 ± 3.5
1 week	12.4 ± 4.5	14.4 ± 4.1
1 month	11.7 ± 4.1	17.8 ± 4.1
3 months	11.4 ± 2.0	15.7 ± 2.5
6 months	9.8 ± 1.7	15.9 ± 2.9
9 months	11.2 ± 1.7	15.0 ± 2.2
12 months	11.6 ± 2.2	14.9 ± 1.9
15 months	12.7 ± 2.3	15.2 ± 1.5
18 months	12.5 ± 2.7	15.8 ± 2.0
21 months	13.5 ± 2.7	15.2 ± 2.0
24 months	14.1 ± 3.8	16.5 ± 2.0

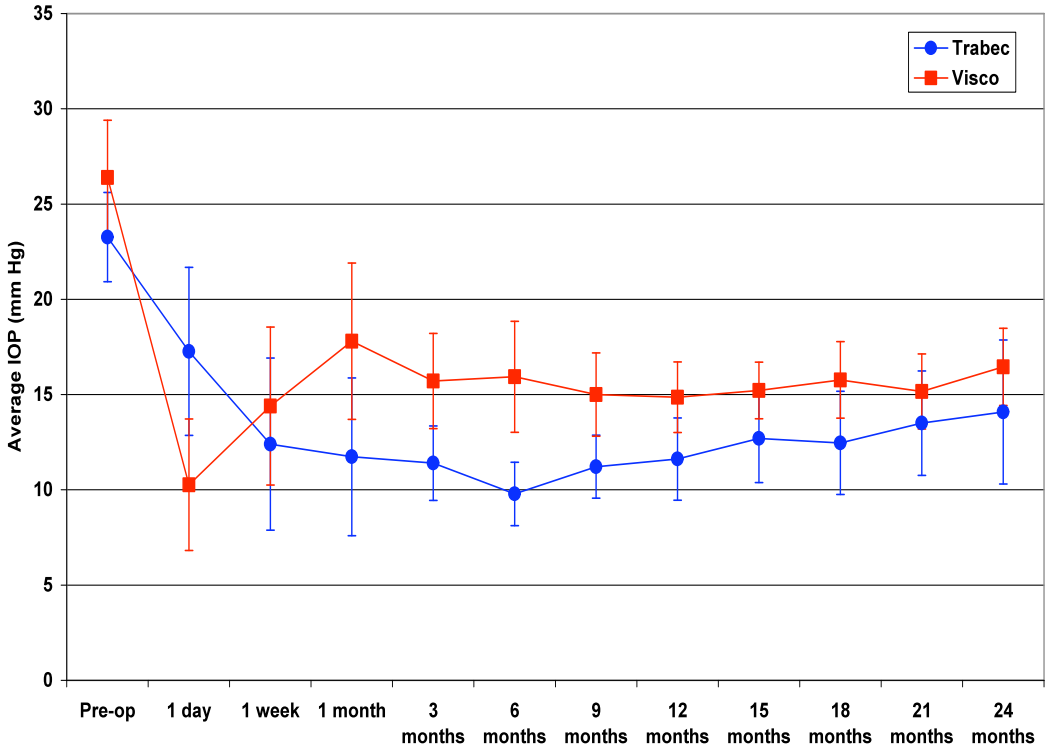

Figure 4.1: Average IOP in mmHg on the y-axis plotted against the time after surgery on the x-axis in the eyes that underwent trabeculectomy with MMC (Trabec) and viscocanalostomy (Visco). Error bars represent 95% confidence intervals for the average IOP

The median number of medications per eye over the study period is recorded in table 4.5 and illustrated graphically in Figure 4.2. The median was used rather than the average because the data are not continuous and are not normally distributed. Medication data were included up to 24 months after surgery even if patients had another procedure to lower IOP.

Table 4.5: Median number of medications per eye for the study period in the eyes that underwent trabeculectomy with MMC and viscocanalostomy

	Median number of medications (25th – 75th percentile)	
Time after surgery	**Trabeculectomy with MMC**	**Viscocanalostomy**
Preoperative	2 (2 – 2)	2 (2 – 2)
1 day	0 (0 – 0)	0 (0 – 0)
1 week	0 (0 – 0)	0 (0 – 0)
1 month	0 (0 – 0)	0 (0 – 0)
3 months	0 (0 – 0)	0 (0 – 0)
6 months	0 (0 – 0)	0 (0 – 0)
9 months	0 (0 – 0)	0 (0 – 0)
12 months	0 (0 – 0)	0 (0 – 0)
15 months	0 (0 – 0)	0 (0 – 1)
18 months	0 (0 – 0)	0 (0 – 1)
21 months	0 (0 – 0.5)	1 (0 – 1.5)
24 months	0 (0 – 0.5)	0.5 (0 – 1)

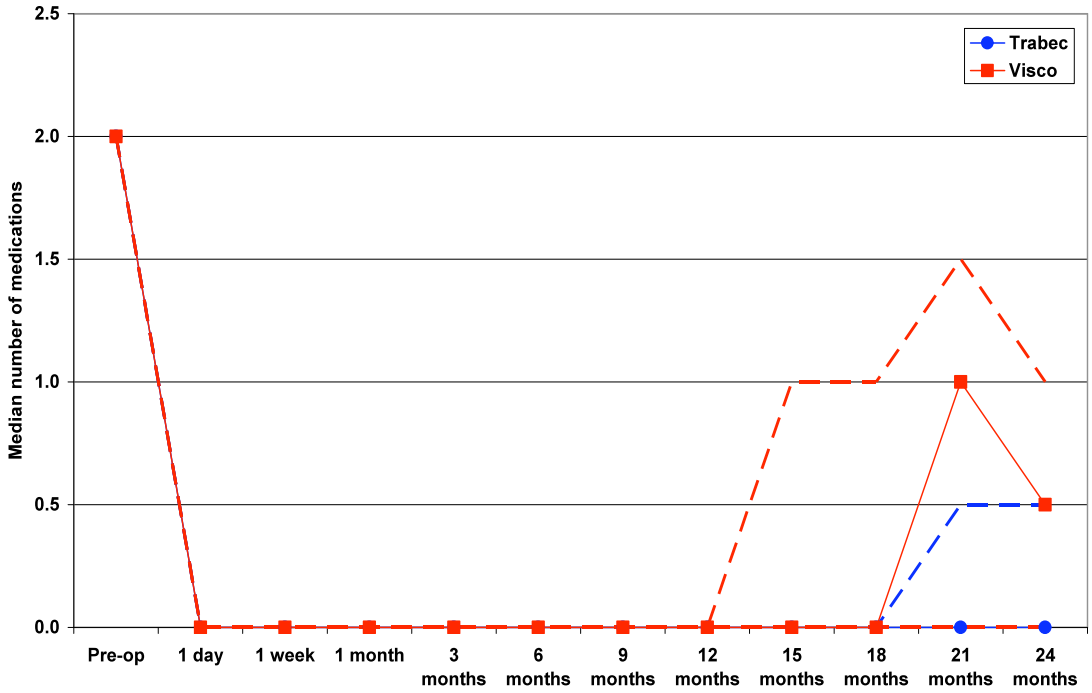

Figure 4.2: Median number of medications used per eye on the y-axis plotted against the time after surgery on the x-axis in the eyes that underwent trabeculectomy with MMC (Trabec) and viscocanalostomy (Visco). The hashed lines represent the 25th and 75th percentiles of the data

In both groups the IOP was significantly reduced post-operatively and the median number of medications used per eye was significantly reduced (Table 4.6).

Table 4.6: Paired sample comparisons of IOP (using parametric and non-parametric paired-sample tests) and number of medications per eye preoperatively (Pre-op) and at the end of the study period (24m) in eyes that had trabeculectomy with MMC and those that had viscocanalostomy

Surgery	**IOP (mmHg)***		**Number of medications ****	
	Pre-op	**24m**	**Pre-op**	**24m**
Trabeculectomy	23.3 ± 2.3	14.1 ± 3.8	2 (2 – 2)	0 (0 – 0.5)
	p = 0.012 *** p = 0.003 (t-test) n =12		p = 0.003 n=12	
Viscocanalostomy	26.4 ± 3.0	16.5 ± 2.0	2 (2 – 2)	0 (0 – 1)
	p = 0.003 p = 0.002 (t-test) n = 12		p = 0.012 n=12	

* mean ± 95% confidence intervals
** median (25^{th} – 75^{th} percentile range)
*** p-value refers to Wilcoxon matched pairs test unless otherwise indicated

Table 4.7 shows the outcome for each patient in the two surgical groups in terms of the defined criteria for success, qualified success, qualified failure and failure. With one exception (H) and the patients where we cannot comment because of dropouts, the trabeculectomy with MMC outcome was the same or better than the viscocanalostomy outcome.

Table 4.8 summarises this data for the group as a whole.

Table 4.7: The surgical outcome for each patient in the eye that had a trabeculectomy with MMC and in the eye that had the viscocanalostomy. S = success, QS = qualified success, F = failure, QF = qualified failure, X = dropped out before completion of the study period

Patient	Trabeculectomy with MMC	Viscocanalostomy
A	S	QS
B	S	X
C	S	QF
D	S	F
E	S	S
F	X	X
G	S	S
H	F	QS
I	X	F
J	QS	F
K	S	QF
L	S	S
M	QS	QS
N	X	X
O	S	S

Table 4.8: The surgical outcome at the end of the study period in the two surgical groups

Surgery	**Trabeculectomy & MMC**	**Viscocanalostomy**
Success	9 (60 %)	4 (26.7%)
Qualified success	2 (13.3%)	3 (20%)
Qualified failure	0 (0%)	2 (13.3%)
Failure	1 (6.7%)	3 (20%)
Dropped out of study	3 (20%)	3 (20%)
Total	**15 (100%)**	**15 (100%)**

Fisher's exact test analysis of the contingency table of complete success versus qualified success, qualified failure or failure (Table 4.9) shows a significant difference between the two surgical procedures ($p = 0.0498$). In this group of patients trabeculectomy with MMC is superior to viscocanalostomy in reducing the IOP to 18mmHg or less without additional glaucoma medication or progression of the glaucoma.

Table 4.9: Contingency table analysis of complete success versus qualified success, qualified failure or failure at the end of the study period in the two surgical groups

Surgery	**Trabeculectomy**	**Viscocanalostomy**	**Total**
Success	9	4	**13**
Qualified success, qualified failure or failure	3	8	**11**
Total	**12**	**12**	**24**

Fisher's exact test, one-tailed: p = 0.0498

Figures 4.5 and 4.6 show the Kaplan-Meier survival curves for complete success (Figure 4.3) and qualified success (Figure 4.4) in the two procedures. The surgical procedures were standardized and performed by a single surgeon, so it was assumed that the probability of survival was the same for early and late recruits into the study. The patients who did not complete the study were assumed to have the same probability of survival as those subjects who completed the study period. The reasons for failure to complete the study are not known (the patients did not return for their follow-up appointments), but it is assumed that it was unrelated to the surgical procedures.

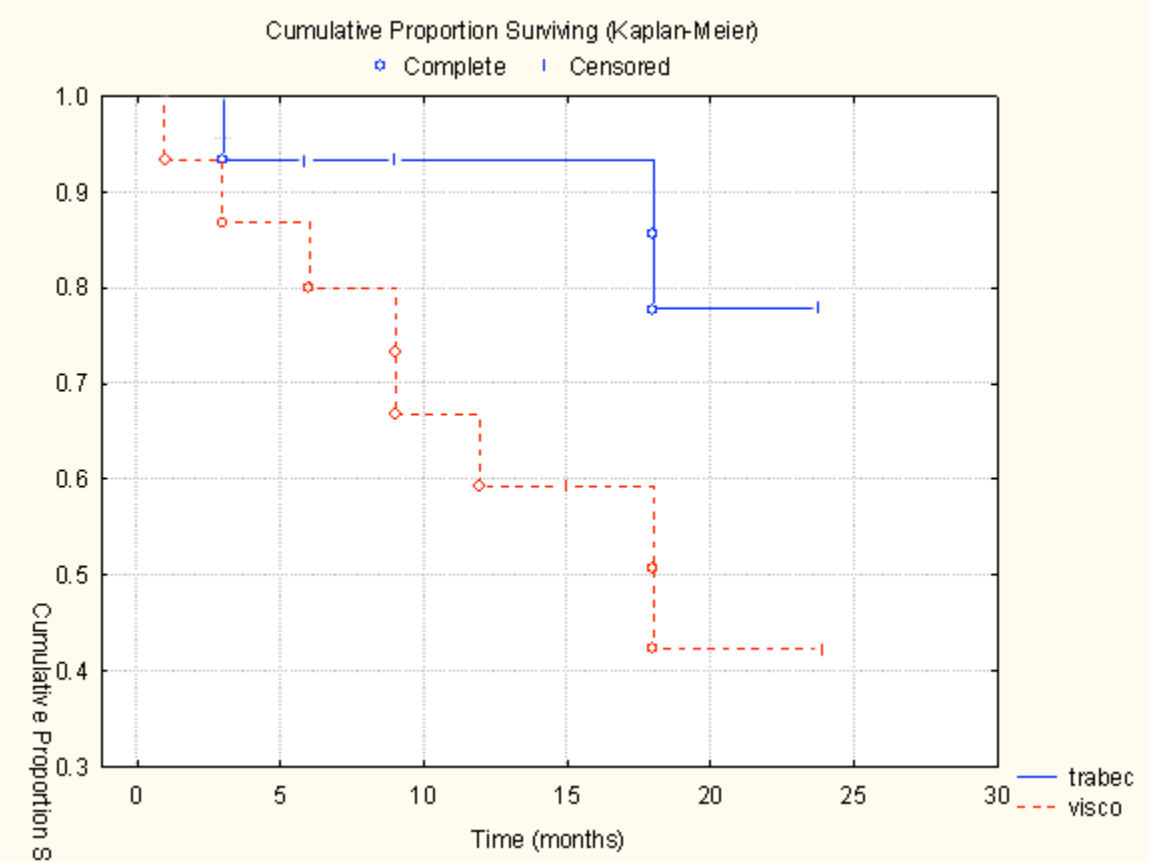

Figure 4.3: Comparing trabeculectomy with MMC (trabec) and viscocanalostomy (visco) outcomes. Kaplan-Meier survival curves for maintaining IOP at 18mmHg or less without medication. Complete = patient's eye required medical therapy; Censored = dropped out or end of study. **Log rank test, p = 0.044**

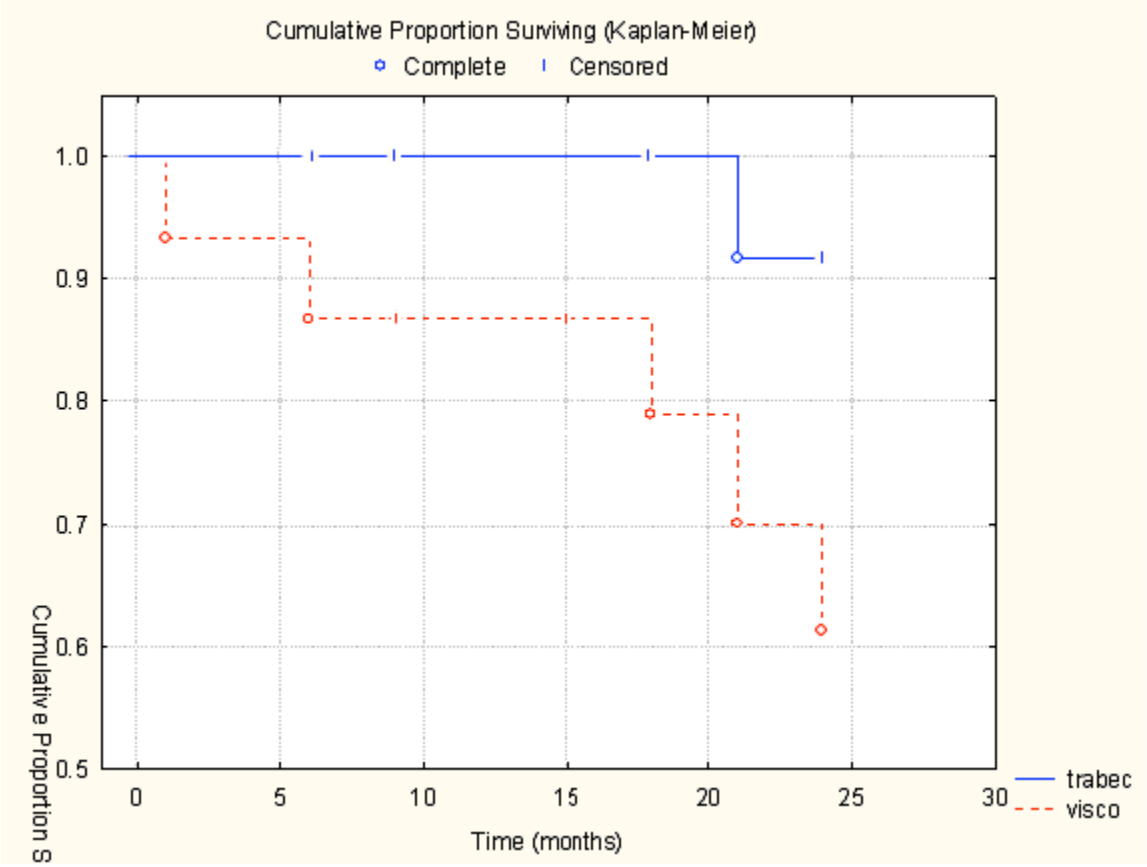

Figure 4.4: Comparing trabeculectomy with MMC (trabec) and viscocanalostomy (visco) outcomes. Kaplan-Meier survival curves for maintaining IOP at 18mmHg or less with additional glaucoma medication. Complete = patient's eye required medical therapy; Censored = dropped out or end of study. **Log rank test, p = 0.059**

The logrank test on the Kaplan-Meier survival curves shows that the two surgical procedures are significantly different for complete success at the 95% confidence level (p = 0.044) and for qualified success at the 90% confidence level (p = 0.059).

A Cox model was used to investigate the effect of certain variables (covariates) on the success of surgery. The result of this proportional hazard analysis is given in Table 4.10.

Univariate analyses were first conducted for each factor with the intention of including those covariates having an effect with statistical significance of $p<0.1$ in a multiple regression model.

Table 4.10: Results of Cox's regression analysis for the two success criteria. Complete success = IOP ≤ 18mmHg without medication; Qualified success = IOP ≤ 18mmHg with medication

Variable	Complete Success		Qualified Success	
	Hazard Ratio	**p-value**	**Hazard Ratio**	**p-value**
First Surgery	0.84	0.77	0.82	0.80
Pseudophakia	0.94	0.95	1.47	0.73
Gender	0.95	0.93	0.50	0.40
Age	1.00	0.92	0.96	0.45
Diagnosis	0.84	0.78	1.07	0.94
Surgery	**3.48**	**0.067**	**6.06**	**0.10**

Despite the small numbers (reflected in the p-values), the analysis confirms the significance of the type of surgical procedure on the success rates. The order of surgery, the presence of preoperative pseudophakia, gender, age and glaucoma diagnosis did not have a significant influence on the outcome of the surgery, however with a larger sample size this might change.

Complications

The intra-operative, early and late postoperative complications in each surgical group are recorded in table 4.11.

Table 4.11: Intra-operative, early and late complications and additional procedures required in the eyes that had trabeculectomy with MMC tabulated with those that underwent viscocanalostomy. The letters (A-O) refer to the individual patients as recorded in table 4.1

	Trabeculectomy	No.	%	Viscocanalostomy	No.	%
Intraoperative complications						
▪ Microperforation of canal of Schlemm		0	0	E,F,N	3	20
Early complications						
▪ Hypotony (IOP<6 mmHg)	G,J	2	13.3	E,F,I	3	20
▪ Anterior chamber shallowing	G,J	2	13.3		0	0
▪ Choroidal detachments		0	0		0	0
▪ Overlarge blebs	K	1	6.7		0	0
▪ IOP spike	D,L	2	13.3		0	0
Late complications						
▪ Avascular blebs	A,C,D	3	20		0	0
▪ Overlarge/overhanging blebs	C,K,L	3	20		0	0
▪ Hypotony (IOP<6 mmHg)	A,F	2	13.3		0	0
▪ Late bleb leak		0	0		0	0
▪ Eyes requiring cataract surgery	A,B,F,I,K	5	33.3	A,H	2	13.3
Additional procedures						
▪ Ocular Massage	C,D,E,K,L,M,O	7	46.7	G	1	6.7
▪ Cataract surgery	A,B,F,I,K	5	33.3	A,H	2	13.3
▪ YAG goniotomy		0	0	A,B,C,D,G,J,K,L,M	9	60
▪ Bleb needling	M	1	6.7	B,K	2	13.3
▪ Suturelysis	G,H,O	3	20		0	0
▪ Flap revision	G,J	3	20		0	0
▪ Repeat glaucoma surgery for failure	H	1	6.7	D,I,J	3	20

Intra-operatively the surgery was uneventful in both groups. In three of the viscocanalostomy eyes a diagnosis of microperforation of the canal of Schlemm was made based on the observation of loss of convexity and an increase in the egress of fluid through the Descemet's window.

Two of the trabeculectomy eyes (13.3%) were hypotonous on day one with shallow anterior chambers which required flap resuturing. Three of the viscocanalostomy eyes (20%) had IOPs less than 5mmHg on day one, but the anterior chambers were well formed, there were no choroidal detachments and the hypotony resolved without intervention or consequences. On the first post-operative day, seven of the trabeculectomy eyes (46.7%) required ocular massage to bring the IOP to acceptable levels. Two of these patients had a post-operative IOP spike which was controlled with ocular massage. Only one (13.3%) of the viscocanalostomy eyes required ocular massage.

Before the one month follow up visit three of the trabeculectomy eyes required suturelysis to bring the IOP down to below 18mmHg (only one of these eyes had required ocular massage on day one).

Over the study period five eyes in the trabeculectomy group (33.3%) and two in the viscocanalostomy group (13.3%) required cataract surgery for deteriorating visual acuity. Both of the eyes requiring cataract surgery in the viscocanalostomy group had cataracts preoperatively that worsened during the study period. In contrast three of the

trabeculectomy eyes had clear lenses preoperatively but developed cataracts after the glaucoma surgery – presumably as a result of it. Patients E and M had bilateral lens opacities preoperatively, but the cataracts did not progress during the study period in either the viscocanalostomy or the trabeculectomy eyes.

Three eyes in the trabeculectomy group had symptomatic blebs compared to none in the viscocanalostomy group. All the functioning viscocanalostomy eyes had conjunctival blebs, but the blebs were more diffuse and shallower than those seen in the trabeculectomy eyes. Nine (60%) of the viscocanalostomy eyes required Nd:YAG laser goniopuncture. Two of the complete successes (50%) in the viscocanalostomy group had had YAG goniotomy procedures. One eye in the trabeculectomy group and two in the viscocanalostomy group underwent a bleb needling procedure.

5.0 DISCUSSION

The results of this prospective, randomized study indicate that both trabeculectomy with MMC and viscocanalostomy are effective procedures (they both significantly lower the IOP and reduce the requirement for antiglaucoma medications) for the control of IOP in open angle glaucoma in black South African patients. The results further indicate that trabeculectomy with MMC is superior to viscocanalostomy in controlling IOP in this group. The mean IOP levels were lower in the trabeculectomy group from month one postoperatively, however it is difficult to comment accurately on these findings because some eyes were being treated medically with antiglaucoma medication. Complete success rates (IOP less than or equal to18 mm Hg with no glaucoma medications) at 24 months were significantly better with trabeculectomy augmented with MMC. In addition, the number of eyes receiving antiglaucoma medications and the average number of medications per eye required postoperatively in order to maintain an IOP at 18 mm Hg or lower were less with trabeculectomy with MMC. Kaplan-Meier survival analysis with log rank to compare and Cox proportional hazard method confirmed the superiority of trabeculectomy with MMC in achieving a successful outcome.

A review of the current literature supports these findings. Prospective, randomized studies comparing trabeculectomy without antifibrosis with viscocanalostomy demonstrated higher success rates in the trabeculectomy treatment group.[18,19,20,21,22] Two further prospective randomized trials compared trabeculectomy augmented with

antimetabolites with viscocanalostomy and, in common with my study, found the trabeculectomy treatment arm to be more successful in lowering IOP. [23,24]

The mechanism of viscocanalostomy in its ability to reduce IOP is uncertain. Stegmann [1] postulated that IOP was lowered by aqueous humour percolating through Schlemm's canal endothelium and Descemet's membrane into the scleral "lake" (the potential space created by the deep sclerectomy) and from there into previously non-functional sectors of Schlemm's canal and to collector chanels. Tamm et al.[25] performed viscocanalostomies on rhesus monkeys and they, in contrast, suggest that the most likely cause of the reduction in outflow resistance after this type of surgery is a focal disruption of the inner wall endothelium and opening of the juxtacanalicular or cribriform region of the trabecular meshwork which they found on electron microscopy. Injection of viscoelastic into Schlemm's canal may not only dilate the canal, but it may also disrupt the walls of the canal and the adjacent trabecular layers. This procedure may thus act as a trabeculotomy. Other possible mechanisms that have been proposed are external filtration from the scleral "lake" to the subconjunctival space and uveoscleral absorption directly from the scleral "lake".[23,24] In all the viscocanalostomy eyes in this report with successful drainage, there was evidence of subconjunctival drainage of aqueous, confirmed by the presence of conjunctival drainage blebs (Figure 5.1). In eyes without successful drainage these changes were not evident. This is in contrast to Stegmann,[1] who reported bleb formation in only five percent of his patients, but is supported by O'Brart's findings.[24]

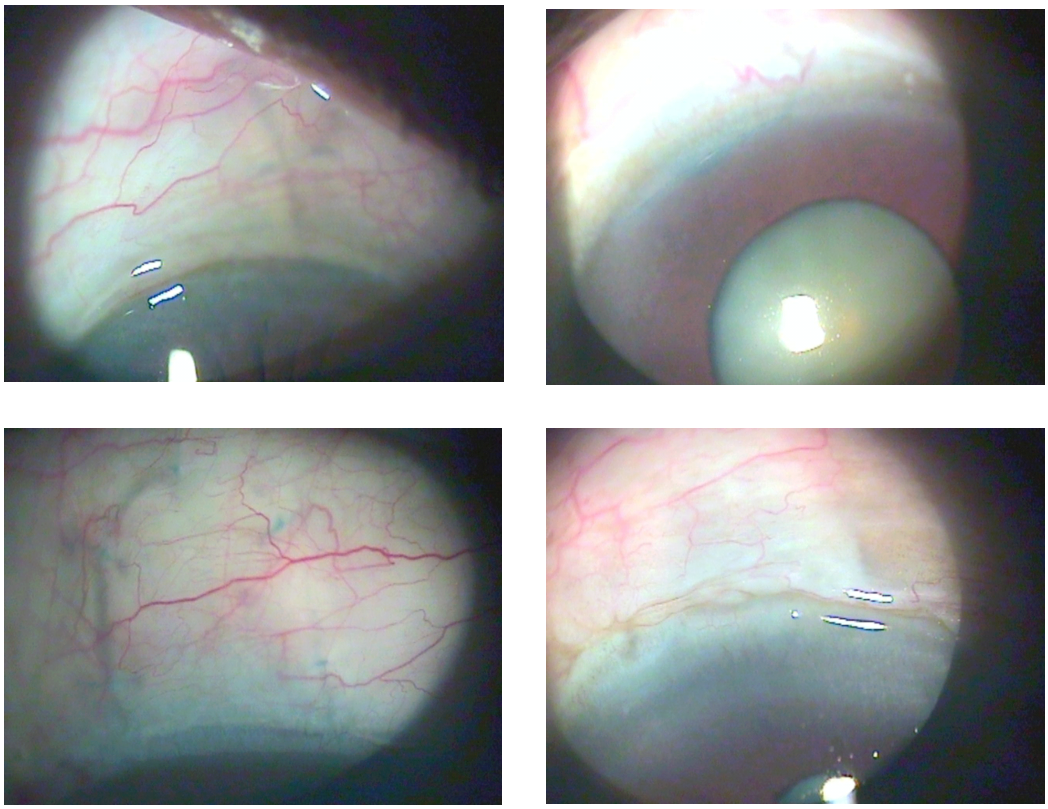

Figure 5.1: Subconjunctival blebs following viscocanalostomies

Such findings suggest that in the viscocanalostomy technique used in this study (which although based on Stegmann's technique was not identical to his technique – the operations were not under general anaesthetic and the author was not as rigorous as he in making the sutured scleral flaps water-tight), the subconjunctival route is the main drainage pathway. This may be one of the reasons for the higher success rate in the trabeculectomy eyes. Black patients are at higher risk for failure of trabeculectomies without antifibrosis;[8] if this viscocanalostomy technique relies on subconjunctival drainage it follows that this technique should also be augmented with MMC. O'Brart et al.[24] came to a similar conclusion and they went on to perform a second prospective, randomized trial where antimetabolites were used as an adjunct in both operative

groups.[26] Disappointingly they still found that trabeculectomy was the superior procedure for IOP lowering.

Viscocanalostomy has the theoretical advantage of being less invasive than trabeculectomy. This advantage is borne out in this group by fewer early complications such as anterior chamber shallowing associated with hypotony and, at the other end of the spectrum, IOP spikes. There was also a reduced incidence of postoperative cataract formation with viscocanalostomy. This is a common finding in other studies comparing these two procedures.[24,26] The early complications were managed with effective intervention. Cataract surgery returned the visual acuity to preoperative levels and had no impact on bleb survival.

In this study the viscocanalostomy eyes generally had shallower and more diffuse blebs than the trabeculectomy eyes where there was a higher incidence of avascular and overlarge blebs. This may be related to the use of MMC in the trabeculectomy eyes.

O'Brart et al.[26] found that encysted blebs and the requirement for bleb needling was more common in trabeculectomy eyes. This was not the case in this series. Many of the viscocanalostomy eyes, however, required and responded to Nd:YAG laser goniopuncture for additional IOP lowering during the study period. Stegmann[1] did not perform goniopunctures in his series, but many other investigators do with varying frequency. In this study 60% of the viscocanalostomy eyes had a goniopuncture

procedure. This is similar to the findings of Kobayashi et al.[23] where 56% of the viscocanalostomy group received a goniopuncture at an average of four weeks postoperatively, but is more than the incidence reported by O'Brart,[24,26] Sunaric-Mégevand,[15] and Shaarawy.[17] This reliance on Nd:YAG laser technology may limit the appropriateness of this intervention to patients from urban areas with easy access to tertiary health care.

6.0 CONCLUSION

Viscocanalostomy was first described in a population of predominantly black South African patients, the same as this study population; however the procedure was not compared with the gold standard of trabeculectomy with antimetabolites.[1] This prospective randomized study sought to compare these two procedures in this population group over a two year time period. The study is limited by a small sample size, but the results indicate that viscocanalostomy is an effective way of decreasing the IOP in patients with open angle glaucoma; however a trabeculectomy augmented with mitomycin C was the more successful procedure in this sample.

Viscocanalostomy tends to have fewer postoperative complications and less symptomatic blebs, but many of the patients require laser goniopuncture during the postoperative period and may require more follow-up visits. Viscocanalostomy is associated with less cataract formation, but significant problems permanently impairing vision did not occur with either technique.

On examination of the eyes in this study in which successful viscocanalostomy was performed, it was found that they all had shallow subconjunctival blebs. Subconjunctival drainage of aqueous may be the main mechanism of aqueous drainage in these eyes, so the procedure should probably also be augmented with mitomycin C in a population such as this one that has such a high failure rate for glaucoma drainage procedures.

Although viscocanalostomy offers some advantages because it is less invasive, intraocular pressure control appears to be far superior with trabeculectomy with MMC and this continues to be the filtering procedure of choice for the management of glaucoma in black South African patients.

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