SCIENTIFIC REPORT

Deep sclerectomy and low dose mitomycin C: a randomised prospective trial in west Africa

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Aim: To study the efficacy and safety of deep sclerectomy (DS) augmented with intraoperative low dose mitomycin C (MMC) in a west African population.

Methods: Prospective, randomised, controlled trial. Trial participants were Nigerian patients with medically uncontrolled primary open angle glaucoma undergoing primary surgery at Maja Hospital, Lagos, Nigeria. 39 eyes of 39 patients undergoing DS were randomised into receiving intraoperative MMC 0.25 mg/ml for 2 minutes at the end of procedure (DS-MMC) and a control group (DS-noMMC).

Results: There were 21 patients in the DS-noMMC and 18 in the DS-MMC group with no difference in the preoperative characteristics of the groups. Mean follow up was 16.4 (SD 11.3) months. The probability of maintaining an intraocular pressure less than 18 mmHg with or without additional medications (95% confidence intervals) at 1 year was 70% (47–92%, 95%) and 79% (57–100%), and at 18 months was 35% (8–62%) and 38% (7–69%) for the DS-noMMC and DS-MMC groups, respectively, with no difference in success rates ($p=0.6$). An IOP of less than 18 mmHg without additional medication was maintained in 65% (41–89%) and 73% (49–96%) at 1 year and 24% (8–48%) and 13% (13–46%) at 18 months for the DS-noMMC and DS-MMC groups, respectively ($p=0.5$). There were no serious complications related to the procedure.

Conclusions: The success rates of DS in black west African glaucoma patients, as performed in this study, were low. The study did not achieve sufficient power to detect whether low dose intraoperative MMC application can increase success rates of DS.

Primary open angle glaucoma and its treatment remains a difficult problem in people of west African origin. The incidence of the disease is high.^{1–4} The onset is earlier⁵ and it leads to blindness more often than in white people.⁶ In west Africa the problem is probably worse.^{5–7} Medical treatment is far from satisfactory owing to poor compliance and expense and non-availability of glaucoma medications. Trabeculectomy, with or without antimetabolites, is effective in lowering the intraocular pressure (IOP), at least in the short term.^{8–11} It is not a popular procedure with surgeons or patients because of poor understanding of the nature of the procedure among patients, late presentation and a high incidence of cataract progression.^{5–7}

Reports from South Africa suggest that non-penetrating glaucoma surgery procedures (NPGS) like viscocanalostomy (VCT)¹² and deep sclerectomy (DS)¹³ have a low incidence of complications and have a satisfactory IOP lowering effect. Recent studies on European patients indicate that DS augmented by intraoperative mitomycin C (MMC) application is safe and results in significantly lower intraocular

pressures (IOPs)^{10–14} and the IOP outcomes are comparable to those of MMC enhanced trabeculectomy.¹⁵ The aim of this study was to prospectively compare the effectiveness and the safety of primary deep sclerectomy with and without the use of low dose MMC in eyes with open angle glaucoma in west African patients in Lagos, Nigeria.

METHODS

The study was conducted in a private hospital in Lagos, Nigeria. Permission for the trial was taken from the hospital management, in the absence of a research ethics committee. Two surgeons performed the operations—one of them (NA) had done a 100 DS procedures before the trial. The surgeries were done consecutively, between November 2000 and November 2001. Inclusion criteria were patients with primary open angle glaucoma, uncontrolled IOP, and no previous surgery. The nature of the procedure and the trial was explained to the patients and consent was taken. Randomisation was done by computer generated random numbers on an MS Excel spreadsheet. The group allocation (DS-MMC or DS-noMMC) was noted in the patient records. The data collectors were unmasked to group allocation.

The DS procedure has been described elsewhere.¹⁶ After dissection of a fornix based conjunctival flap, the superficial scleral flap, 5 mm×5 mm, a third scleral thickness was dissected. The deep scleral flap was dissected in the plane of the scleral spur, de-roofing the Schlemm's canal, and excised leaving behind the filtration membrane, termed the trabeculo-Descemet's membrane (TDM). The superficial scleral flap was loosely sutured with two 10/0 nylon sutures. In line with our practice in the United Kingdom at that time, 2–4 collagen sponges (Visitec, UK) dipped in MMC 0.25 mg/ml, were applied for 2 minutes in the subconjunctival space posterior to the scleral flap. Postoperatively, patients received a topical steroid antibiotic combination for at least 6 weeks. The local doctors checked visual acuity, IOP, and performed an anterior segment and fundus examination on each visit. In all cases where the IOP was high glaucoma medications were commenced. If the IOP was still high an appointment was made to be reviewed by the visiting ophthalmologists.

Analysis was done on an intent treat basis. From our results with DS in the United Kingdom,¹⁷ it was assumed that the success rates for the eyes not receiving MMC (DS-noMMC group) would be 40% at 1 year and 70% for the eyes receiving MMC (DS-MMC group). The effective sample size was 45 patients in each group ($\alpha=0.05$, $\beta=0.2$). The criteria for success were IOP less than 18 mmHg and a 30% decrease from preoperative IOP—without additional medications to lower IOP; with additional medication to lower IOP. Any

Abbreviations: DS, deep sclerectomy; ECCE, extracapsular cataract extraction; IOP, intraocular pressure; MMC, mitomycin C; NPGS, non-penetrating glaucoma surgery; TDM, trabeculo-Descemet's membrane; VCT, viscocanalostomy

Figure 1 Cumulative proportion surviving (Kaplan-Meier) for success criterion—IOP less than 18 mm Hg with or without medication. Numbers in the graph represent patients left for analyses at each interval.

Figure 2 Cumulative proportion surviving (Kaplan-Meier) for success criterion—IOP less than 18 mm Hg without medication. Numbers in the graph represent patients left for analyses at each interval.

further surgical procedure including needle revision to lower IOP was considered a failure.

Kaplan-Meier plots were constructed for survival data and tested for significance by the log rank test. Cox's proportional hazards regression models were used to determine the effect of various factors on the survival curves. Dichotomous variables were analysed the Fisher exact test. All tests were two tailed and p values less than 0.05 were taken to be significant. Software used for statistical analyses was S Plus-2000 (Mathsoft Inc, USA) and Statistica 6 (Statsoft Inc, USA).

RESULTS

In all, 39 patients were recruited. There were 21 patients in the DS-noMMC and 18 in the DS-MMC group. The mean follow up was 16.4 (SD 11.3) months; 12 patients (31.6%) had follow up less than 6 months. Two patients from the DS-noMMC and one patient from the DS-MMC group had postoperative follow ups of less than 6 weeks. 24 patients (61.5%) had not kept their clinic appointments for the year before database closure in December 2003. No difference was found in the preoperative characteristics of the groups (table 1). Kaplan-Meier survival data are summarised in figures 1 and 2. The probability of maintaining IOP less than 18 mmHg with or without additional medications (95% confidence intervals) at 1 year was 70% (47% to 92%) and 79% (57% to 100%), and at 18 months was 35% (8% to 62%) and 38% (7% to 69%) for the DS-noMMC and DS-MMC groups, respectively and this difference was not statistically significant ($p = 0.61$). IOPs less than 18 mmHg without additional medications were maintained in 65% (41–89%) and 73% (49–96%) at 1 year and 24% (8–48%) and 13% (13–46%) at 18 months for the DS-noMMC and DS-MMC groups

preoperatively, and till 18 months after surgery (log rank test, $p = 0.53$). Cox proportional hazards model for maintaining IOP below 18 mmHg with or without medication showed no significant effect ($p > 0.05$) of age, sex, MMC application, preoperative IOP, and an IOP less than 7 mmHg on the first postoperative day (table 2). During the follow up period 24 eyes (61.5%) were deemed to have failed by the second criterion (IOP < 18 mmHg without medication)—13 (61.9%) from the DS-MMC group and 12 (61.1%) from the DS-noMMC group.

Intraoperative perforations were observed in two eyes (5.1%) of the DS-noMMC group. Immediate postoperative complications were infrequent—a shallow anterior chamber in one eye from each group and a conjunctival edge leak in one eye from the DS-MMC group. Late iris incarceration with consequent pupil peaking and increased IOP was seen in one eye of the DS-noMMC group.

The various glaucoma procedures done to lower IOP after failure of DS and their success rates are summarised in table 2. Nine eyes (42.8%) in the DS-noMMC group and two (11.1%) in the DS-MMC group had subsequent surgical procedures to lower IOP. Extracapsular cataract extraction (ECCE) was done in six eyes (15.4%) after DS, four (19.0%) from the DS-noMMC group, and two (11.1%) from the DS-MMC group. One patient of the DS-noMMC group with advanced glaucomatous optic atrophy had couching of the lens elsewhere.

Snellen visual acuity (VA) was less than 20/40 in 21 eyes (53.9%) before surgery. There was little change in the average visual acuity over time ($p = 0.64$, Friedman ANOVA). No significant difference was seen in the VA between the two groups preoperatively, and till 18 months after surgery ($p > 0.05$ Mann-Whitney U test). Six patients (15.4%) lost

Table 1 Patient demographics and preoperative characteristics

	DS-noMMC	DS-MMC	p Value
No patients (eyes)	21	18	
Mean age (SD)	60.0 (14.1)	57.5 (13.7)	0.91
Sex (male/female)	15/6	14/4	0.81
Mean number of preoperative medication (SD)	1.47 (1.12)	2.05 (0.64)	0.14
Follow up (months) (SD)	18.3 (13.1)	14.3 (8.7)	0.09
Preoperative IOP (SD)	29.5 (8.0)	26.4 (5.88)	0.19
Intraoperative perforations	2 (9.5%)	0	

Table 2 Subsequent procedures to lower IOP after DS. Some eyes had more than one procedure

	DS-noMMC		MMC-DS	
	Number	Successful*	Number	Successful*
Needling with 5-FU	1 (4.8%)	0		
Needling with MMC	7 (33.3%)	4†		
DS revision with MMC	1 (5.6%)	0		
Conversion to trabeculectomy with 5-FU	1 (4.8%)	1		
Conversion to trabeculectomy with MMC	3 (14.3%)	3	2 (11.1%)	2

*Success defined as IOP less than 18 mm Hg after at least 6 months follow up.

†Follow up less than 2 months in two cases.

more than two lines of VA after surgery—three (14.2%) from the DS-noMMC, and three (16.7%) from the DS-MMC group.

DISCUSSION

This is the first report on DS from west Africa. There are two previous reports from South Africa on NPGS. Stegmann *et al* reported that an IOP of 22 mmHg or less was achieved without medical therapy in 82.7% of eyes with an average follow up of 35 months after VCT.¹² Dahan *et al* reported that after DS in a racially mixed group, the filtration site was revised in 48 eyes (56%) to maintain the IOP below 21 mmHg without medication. This was after a mean period of successful filtration of 29.9 months. The revision rate was however higher in black patients (78%).¹³ The survival rates for DS in this study are poorer than our reported results for both MMC augmented and non-augmented DS in a predominantly white population.¹⁷ The reasons may be multifactorial. Failure in some cases may have been due to inadequate dissection of the inner scleral flap. Shaarawy *et al* have pointed out that studies showing poor results with NPGS had high first postoperative day IOPs.¹⁸ In this study 14 eyes (36%) had a first postoperative day IOP of less than 7 mmHg. However, regression analyses did not show any significant effect of a low first day IOP on the success rates.

Progressive resistance to outflow at the level of the TDM is believed to be the cause of increasing IOP and a significant proportion of patients undergoing non-augmented DS will require Nd:YAG laser goniopuncture to maintain IOP control.^{17 19 20} A prospective study reported that laser goniopuncture was needed in 43% of patients and the mean time for performing the procedure was about 10 months. Pressures fell from a pre-treatment level of 22 mmHg to about 12.5 mmHg and remained stable for at least the following year.²⁰ This clearly illustrates the importance of laser goniopuncture in sustaining IOP success after DS. Therefore, the inability to perform Nd:YAG laser goniopuncture of the TDM when the IOP was increasing was probably a major factor contributing to failure after the first year. In eyes where surgical revision was performed, extensive subconjunctival and episcleral fibrosis were observed.

Previous reports on trabeculectomy outcomes in Africa are limited by short follow up periods or their retrospective nature.^{8 10 11 21–27} Irregular follow ups with a high percentage (61.5%) of patients not attending for the year before database closure also limit the value of this study. However, we were still able to document failure in 61% of the subjects. The trial was stopped before recruitment was completed because of the high rates of failure observed after the first year.

How do these results compare with those for trabeculectomy from the same region? A prospective report with a mean follow up of 10 months from Ghana showed that IOPs less than 18 mmHg with or without additional glaucoma medications are achieved in 29% of eyes with non-augmented trabeculectomy and 67% of eyes receiving intraoperative 5-FU.⁸ In another prospective randomised trial by the same

authors and with similar follow up, 70.5% of eyes receiving intraoperative MMC and 56.8% of eyes with 5-FU augmentation achieved a final IOP of less than 18 mmHg.⁹ Retrospective results from our centre in Nigeria show that the probability of maintaining an IOP of 14 mmHg or less at 18 months was 64% in eyes with 5-FU augmented trabeculectomy and 39% in the controls ($p = 0.018$).¹¹ Hence, it would appear that DS is not effective as trabeculectomy in lowering IOP in this population.

In conclusion, low dose MMC as applied in this study, while safe, did not appear to increase success rates of DS in a black, west African population. The success rates of deep sclerectomy in both groups were disappointingly low and IOP control was attained only by adding medications or further procedures in majority of the eyes. The DS procedure, without facilities for Nd:YAG laser goniopuncture and regular follow up has poor success rates in this population.

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