

Intraoperative use of mitomycin C in the treatment of recurrent pterygium

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SUMMARY

The prevalence rate of pterygium in Papua New Guinea (PNG) is as high as 15%. Recurrence rates up to 50% are encountered after primary excision. In a country such as PNG where resources in terms of funds and manpower are limited, a simple procedure had to be identified to reduce this alarmingly high rate of pterygium recurrence. This article compares the results of a randomized masked study involving the single intraoperative application of 0.02% mitomycin C solution in 65 eyes undergoing surgery for recurrent pterygium using the bare sclera technique with a similar group of 65 patients in which the drug was not used. The results indicate that a single intraoperative application of mitomycin C solution was enough to reduce the recurrence rate of pterygium to 3% in the treated group as compared to 48% in the untreated group at the end of a 12-month follow-up. In the study it was also seen that, in PNG, pterygia were more common in females and that recurrences tended to occur early and were obvious in the first few weeks following surgery.

Introduction

Pterygium is commonly seen in Papua New Guinea (PNG). In eye clinics within the country (1) 15% of outpatients present with a 'growth' (as it is popularly known) on the nasal aspect of the eye. The coastal areas seem to have a higher incidence of pterygium than the highlands. This is possibly because of the greater exposure to ultraviolet (UV) radiation, wind and small particles of sand and salt on the coast.

The treatment of pterygium is not satisfactory. This is evident by the large number of techniques that have been described in the literature (2-9). The major complication encountered was the recurrence of the lesion to the extent of 35-70%. Our own experience in this regard in PNG is that about 52% of pterygia recurred within 12 weeks of excision using the bare sclera technique (1). Of these patients about half underwent more than two operations for recurrent pterygium. These figures are unacceptably high in a country with limited manpower and resources and a large volume of blind patients. A technique to reduce the recurrence rate of

pterygium needed to be identified which, if successful, would be simple enough to be carried out by paramedical and allied health personnel all over the country.

In the literature many methods to reduce the recurrence rate of pterygium after surgery have been described. These include the use of strontium 90 applications (beta rays) (3), Thiotepa drops (10), mitomycin C (7,11-13) and conjunctival Z-plasty (5). The problems of using antimetabolic agents (7,8) in a population such as in PNG, in which monitoring is poor, hygiene a problem and returning to the hospital for regular supplies of the medication unlikely, are evident. We had to design a procedure which was a one-time formula for handling pterygia. It was decided to use mitomycin C intraoperatively as a single application for recurrent pterygia and compare the results with a series in which the drug was not used.

Patients and Methods

130 patients undergoing pterygium surgery were included in this study. The pterygia were graded according to the amount of cornea covered as outlined in Table 1.

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TABLE 1

GRADING OF PTERYGIUM BY SIZE

Grade	Extent (mm) on to cornea
Grade 1	0-2 mm from limbus
Grade 2	2-4 mm from limbus
Grade 3	more than 4 mm from limbus

Each patient underwent a complete ocular examination pre- and post-operatively with specific reference to visual acuity, tear film morphology evaluation, keratometry, tonometry and ocular movement assessment. Informed consent was obtained before surgery in each case. All surgery was carried out under the microscope as an outpatient procedure under local anaesthesia.

From the 130 patients, 65 were operated on with intraoperative application of mitomycin C and 65 were operated on without it. One of the authors (NV) assigned the patients randomly to each group as indicated in Table 2. All the surgery was carried out by one author (JAG) and the follow-up by the others (AK and RM). The surgical procedure carried out in all cases was essentially the bare sclera technique, which consisted of the following steps:

- 1 topical anaesthesia with amethocaine drops (0.5%)
- 2 infiltration of the pterygium body with 2% lignocaine and 1:200,000 adrenaline injection (1-2 ml)
- 3 superficial keratectomy was performed with a No 15 Bard Parker blade starting from clear cornea adjacent to the pterygium head and moving towards the body of the pterygium so as to leave clear cornea behind
- 4 isolation of the pterygium from the sclera with Wescott scissors
- 5 cutting the conjunctiva with Wescott scissors along the margins of the pterygium towards the medial canthus
- 6 excision of 5 mm of the head of the pterygium along with the associated conjunctiva

- 7 dissection and excision of the body of the pterygium from under the conjunctiva keeping away from the underlying rectus muscle
- 8 cautery of the bleeding episcleral vessels
- 9 subconjunctival injection of gentamicin (0.25 ml of 40 mg/ml) at the conclusion of the procedure, followed by
- 10 patching of the operated eye with a sterile pad for 24 hours.

The mitomycin C solution (0.02%) was prepared by diluting the solution for injection with distilled water, using sterile techniques. This purple-coloured solution was kept refrigerated and was used for surgical procedures over a 2-week period, after which it was discarded.

In group 2 (Table 2) a cotton swab soaked with mitomycin C solution was applied to the bare sclera for 4-5 minutes after achieving haemostasis. The area was irrigated with normal saline to wash away any remaining mitomycin C. The free edges of the conjunctiva were then approximated with two interrupted 6-0 Dexon or Vicryl sutures.

17 patients (7 in group 1 and 10 in group 2) had preoperative diplopia resulting from a mechanical restriction of movement due to scarring. In these eyes, the conjunctiva was recessed and the large bare area covered with a free conjunctival graft taken from the superotemporal quadrant of the bulbar conjunctiva of the same eye and held in place with 6-0 polyglycolic acid sutures.

Postoperatively, the patients were instructed to instil 0.1% dexamethasone drops twice daily for 3 weeks. Later, they were asked to use an artificial tear substitute twice daily and wear dark glasses when outdoors.

They were followed up weekly for the first month, fortnightly for the second month and then two-monthly for a total period of 12 months.

Results

The results of the study were encouraging. In group 2 (mitomycin C), a recurrence of the

TABLE 2

DISTRIBUTION OF PATIENTS

Group	Treatment	Numbers		
		Male	Female	Total
Group 1	No mitomycin C used	23	42	65
Group 2	0.02% mitomycin C used intraoperatively	19	46	65

TABLE 3

NUMBER OF SURGICAL OPERATIONS PERFORMED PREVIOUSLY

	1 operation			2 operations			3 operations			Total		
	M	F	T	M	F	T	M	F	T	M	F	T
Group 1	12	25	37	10	13	23	1	4	5	23	42	65
Group 2	10	21	31	6	18	24	3	7	10	19	46	65
Total	22	46	68	16	31	47	4	11	15	42	88	130

M = male
 F = female
 T = total/subtotal

pterygium was seen in only 2 patients (3%) within 8 weeks of follow-up. In these cases, the hyperaemia in the region of the excised pterygium was persistent and the final extent of the growth on to the cornea was 2.5 mm (grade 2) at 8 weeks. This was the third excision in both cases. The recurrent growth was less fleshy than the original one and cosmetically more acceptable to the patient. Both patients were female and were satisfied with the outcome and did not want repeat surgery. There was no change in the size of the pterygium in the follow-up period. In contrast, in group 1 (no mitomycin C used), a recurrence was seen in 31 cases (48%). At the 99% confidence level, a significantly lower recurrence rate was observed with the use of mitomycin C. Analysis with respect to the number of surgical operations vs recurrence following use of mitomycin C was not done as the numbers were very small.

The gender distribution of patients is given in

Table 2. A comparison of the number of previous surgical operations in the 65 cases in each group is presented in Table 3.

The features common to both groups were the average age of the patients, which was 23.5 years, and the average intraocular pressure (IOP), which was 13 mmHg. The preoperative sizes of the pterygia are given in Table 4.

The recurrences and their grading are presented in Table 5. In those cases with preoperative restriction of ocular motility, a forced duction test (FDT) is made postoperatively to ensure full mobility of the globe.

Postoperative complications were more common in group 1 (Table 6). The granuloma-like growths seen were interpreted as a misdirected attempt by the free end of the conjunctiva to cover the bare area. Histopathological examination revealed areas

TABLE 4

PREOPERATIVE SIZES OF THE PTERYGIA

	Grade 1	Grade 2	Grade 3
Group 1	3	18	44
Group 2	7	24	34

TABLE 5

POSTOPERATIVE RECURRENCES OF PTERYGIA AND THEIR GRADING

Group	Number			Grade 1	Grade 2	Grade 3
	M	F	T			
Group 1	10	21	31	12	18	1
Group 2	0	2	2	0	2	0

M = male
F = female
T = total

of nonspecific inflammation. These were nodular, pedunculated, 2-3 mm pinkish-red growths. They were treated by simple excision with a pair of Wescott scissors using topical anaesthesia. There were no recurrences of the granulomata.

Persistent hyperaemia in the immediate postoperative period was taken as a warning sign that the pterygium was recurring: application of steroid drops was increased to 4 times a day, the patient was instructed to wear dark glasses and artificial tears were started. These recurrences were apparent within the first 3 to 5 weeks postoperatively, in the sense that patients who ultimately had a recurrence were noted not to really 'settle down' after surgery. Corneal encroachment was fully established by the eighth week. No cases of poliosis or superficial punctate keratitis were seen in group 2 where the mitomycin C was used.

Discussion

Mitomycin C, an antineoplastic antibiotic agent, acts by inhibiting cellular proliferation

which is a basic prerequisite for recurrence of surgically removed pterygia. The present study shows clearly that the intraoperative use of mitomycin C in conjunction with the bare sclera technique seems to be a safe and effective way to reduce the rate of recurrence of pterygia. Care must be taken to minimize the amount of bare sclera as much as possible.

Certain facts regarding pterygia in general in PNG are also apparent. The first is that they seem to be more common in women than men. The reasons for this are not clear although one of the contributing factors is a general reluctance among women to wear eye glasses of any kind, which may result in a larger exposure to UV rays in this population. Also, women in general were more keen to seek medical attention. The second point worthy of note is the pattern of postoperative recurrence of pterygia: those patients in whom the pterygia recurred seemed to have a stormy postoperative course with a swollen, angry-looking conjunctiva and dilated vessels. The pterygium seemed to start growing soon after excision. By the third to fifth week it was

TABLE 6

POSTOPERATIVE COMPLICATIONS

	Group 1	Group 2
Granuloma	14	2
Hyperaemia	31	7
Subconjunctival haematoma	5	3
Severe pain	2	3

apparent that these pterygia were going to recur. The full-blown recurrence was well established by the eighth week. Late recurrences (up to 12 months) were not noted amongst the patients presented in this communication. This pattern of recurrence in the Melanesian population seems to be at variance with that described in the literature, where pterygia may also recur after a period of quiescence. The reason for this is not clear.

The use of mitomycin C as a one-time application intraoperatively did not cause any significant sight-threatening complications. Its use alone is not the answer to the problem of recurrence and additional steps such as advising the patient to use protective sun glasses and artificial tears (9) are also important. However, mitomycin C clearly makes a significant difference to the outcome. We believe that mitomycin C, in fact, should be used intraoperatively for all pterygium surgery, whether it is the first, second or third operation; other authors agree (11-13).

Rarely, complications in the form of corneoscleral melting have been known to occur many years after the use of mitomycin C as drops given postoperatively, but in the current follow-up period of 12 months these were not observed and the results of the study seem to indicate that a one-time application is safe. The advantages of a single intraoperative usage of low-dose mitomycin C far outweigh the risks of repeated surgery for recurrent pterygium. Late complications, however, still remain a distinct but remote possibility. Postoperative use of mitomycin C as drops seems to deliver a higher total dose of the antimetabolite to the eye and may be the cause

of problems such as delayed onset of corneoscleral melting (8).

In Papua New Guinea all the factors which contribute to a high prevalence of pterygium are present in abundance: the sun, the sand and the sea. Manpower is limited and resources scarce: therefore it becomes very important to devise a safe, simple method of preventing recurrences after pterygium surgery, which is often performed by paramedical personnel.

The study was carried out at the Port Moresby General Hospital, which is the tertiary level hospital in PNG. The procedure has now been standardized and is ready to be implemented in other hospitals. A reduction in the recurrence rate of pterygia means that there is more time for eye care personnel to concentrate on tackling other diseases which, if untreated, may lead to blindness.

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