EFFICACY OF PRE-OPERATIVE INJECTION MITOMYCIN-C IN PREVENTION OF PTERYGIUM RECURRENCE

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ABSTRACT

Objective: To determine the recurrence rate of pterygium with four weeks pre-operative injection mitomycin-C using bare sclera technique.

Design: An interventional case series.

Place and Duration of Study: This ongoing study was started in November 2005 at eye department of combined military hospital Kharian, Pakistan.

Patients and Methods: Ninety one eyes of 87 patients have been so far enrolled in the study. Cases between 20 to 50 years of age, of either sex, with primary and recurrent pterygia were included. The subjects were first given 0.1 ml injection mitomycin-C 0.15 mg/ml into the body of pterygium. Four weeks later, pterygium surgery was performed using bare-sclera technique. The subjects are being followed up for at least one year to detect any recurrence.

Results: Out of 91 cases, 16 (17.58%) cases have been followed up for 12 months, 19 (20.87%) for 9 months, 21 (23.07%) for 6 months, 17 (18.68%) for 3 months and 18 (19.78%) for less than 3 months. Recurrence has not been encountered in any of these cases so far.

Conclusion: Initial results show that pterygium surgery with pre-operative injection mitomycin-C appears to be an effective form of treatment for prevention of pterygium recurrence. Further follow up and multi-centric studies are required for final conclusion.

Keywords: Pterygium, Mitomycin-C, recurrence

INTRODUCTION

Pterygium is defined as a horizontally oriented triangular fibro-vascular growth of abnormal tissue that invades the cornea from the canthal region of the bulbar conjunctiva [1]. It is a Greek word which means 'wing' and was first described by Hippocrates in 460 BC [2]. Pterygium is more common in tropics and several studies have demonstrated a strong association of ultra violet light exposure in its pathogenesis [3,4]. The major problem in pterygium management is its high recurrence rate. Since the beginning of pterygium surgery, surgeons have been struggling with this challenging clinical problem [5]. The postoperative recurrence rate of pterygium excision alone has been reported to range from 16.04% [6] to 88.9% [7]. To prevent recurrence, various surgical techniques and adjunctive therapies have been devised during the last few decades [1,8]. The surgical techniques include excision with primary closure/ bare sclera, conjunctival autografting and amniotic membrane grafting. Adjunctive therapies include use of thiotepa, 5-fluorouracil (5-FU), B-irradiation, and Mitomycin-C (MMC). These different therapeutic modalities indicate that treatment of choice is yet to be determined.

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Various observers have studied MMC with regard to its efficacy in reducing pterygium recurrence [9-16], as well as its potential to produce sight threatening complications [17-20]. These studies have used MMC as either intra-operative application, or post-operative topical use. Four weeks pre-operative MMC injection into the body of pterygium [21] has been found to produce least recurrence and no serious/sight threatening complications that motivated us to carry out this study in our setting.

PATIENTS AND METHODS

This was an interventional case series. This hospital-based study was conducted at eye department of combined military hospital Kharian, Pakistan. Duration: This ongoing study was started in November 2005. Sample Size: So far 91 eyes of 87 patients have been enrolled in the study. Sampling technique: Non probability convenience sampling technique was used in the study.

Inclusion Criteria

- Pterygium causing visual impairment or cosmetic blemish.
- Age between 20 to 50 years.
- Patients willing for surgery and follow-up.

Exclusion Criteria

- Patients lost for follow up.
- Patients with ocular surface diseases e.g, keratoconjunctivitis sicca, cicatricial conjunctivitis, or history of chemical burns.
- Pregnancy.

Data Collection Procedure

All patients between 20 and 50 years of age with pterygia were evaluated. Informed consent was obtained from willing patients. Detailed history taken and complete ocular examination was performed. After registration case number was allotted and his/her address with telephone number was recorded. For purpose of recurrence evaluation the patients were divided into groups according to age, gender and primary/ recurrent disease. Data was entered in the customized proforma. Patients were then given appointment for injection MMC and operation four weeks later.

MMC is dispensed as blue coloured powder. It is readily available in Pakistan as "Mitomycin for injection 2 mg potency, Kyowa Hakka Kogyo Co Ltd Tokyo Japan". Price of one vial is Rs 180/-. In our study, we prepared the injection by first adding 2 ml of distilled water to the vial. This made a concentration of 1 mg/ml in the vial. Then 0.15 ml i.e. 0.15 mg of this solution was taken up in a 29 gauge insulin syringe. The remaining volume (0.85 ml) of the insulin syringe was then filled with normal saline to make an exact concentration of 0.15 mg/ml. Only 0.1 ml of this solution was injected into the body of pterygium, rest of the 0.9 ml in syringe was discarded. One vial can thus provide enough MMC for about 12 injections.

After four weeks, pterygium excision was done using standard bare sclera technique. 0.5% proparacaine was used for topical anaesthesia. 0.3- 0.4 ml of 2% lignocaine with 1:100,000 adrenaline was injected sub-conjunctively into the body of pterygium with 29 G needle for conjunctival anesthesia. Pterygium excision was performed under a microscope. Pterygium was grasped with toothed forceps and lamellar dissection was done using number 15 blade to free it from the cornea. Subconjunctival tissue was excised with the help of Westcott scissors. The blade was then used to clear any remnant adherent to the cornea. At the end 2 to 3 mm of sclera was left bare. The eye was padded after instillation of steroid-antibiotic ointment that was continued till healing of the epithelial defect. The patients were followed up at 1, 3, 6 and 12 months for any recurrence.

STATISTICAL ANALYSIS

Data was entered in statistical programme for social sciences software i.e. SPSS 11.0.0. Descriptive statistics i.e frequency

alongwith percentages were used to describe the data.

RESULTS

Out of the 91 cases, 62 (68.1%) were males and 29 (31.9%) were females. Twenty three (25.27%) cases were between 20-29 years of age while 41 (45.05%) cases were between 30-39 years at age and 27 (29.67%) cases were between 40-49 years of age (table-1). Seventy four (81.32%) cases were primary pterygia and 17 (18.68%) cases were recurrent pterygia (fig. 1). In the ongoing follow up process, 16 (17.58%) cases have been followed up for 12 months, 19 (20.88%) cases for 9 months, 21 (23.08%) cases for 6 months, 17 (18.68%) for 3 months and 18 (19.78%) cases have undergone less than 3 months of follow up (fig. 2). Recurrence has not occurred in any of these cases so far. No sight threatening complication was observed. However, mild complications included post-op discomfort and irritation, delayed epithelial healing for upto 2 weeks and conjunctival avascularity (table-2).

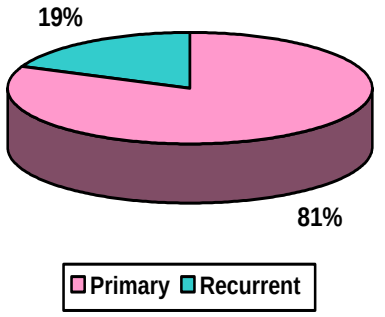

Fig. 1: Nature of pterygia (n=91).

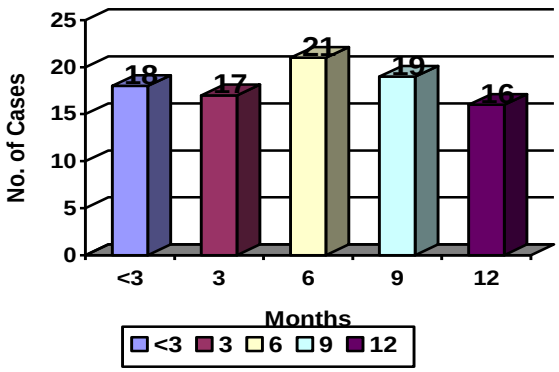

Fig. 2: Followed up cases (n=91).

Table-1: Age wise distribution (n=91).

	20-29 yrs	30-39 yrs	40-50 yrs	Total
No of cases	23	41	27	91
Percentage of total (%)	25.27	45.05	29.67	100

Table-2: Complications (n=91).

	No of cases	Percentage of total (%)
Post-op discomfort	86	94.5
Delayed epithelial healing	62	68.1
Local conjunctival avascularity	4	4.4

DISCUSSION

Regarding pterygium recurrence, it is believed that surgical trauma and subsequent postoperative inflammation activates subconjunctival fibroblastic activity. The proliferation of fibroblasts with deposition of extracellular matrix proteins in turn contribute to the pterygium recurrence [22].

Except for elderly patients, both primary and recurrent pterygia require some form of special surgical technique or adjunctive medical therapy to minimize recurrence. Among the popular surgical techniques in vogue, conjunctival autografting and amniotic membrane grafting are both tedious and time consuming procedures. In addition, recurrence rates of 31.3% with conjunctival autografting and 26.7% with amniotic membrane grafting have been observed [23]. Among the adjunctive therapies, thiotepa has been used topically in postoperative period, after bare sclera excision. It causes severe allergic reactions and has a recurrence rate of upto 38% [24]. 5-fluorouracil is applied intra-operatively and has a recurrence rate of upto 32.5% [25]. Beta-irradiation requires specialized equipment and radiotherapist. It has an observed recurrence rate of upto 23% [26] and it frequently leads to complications like cataract and corneoscleral necrosis. Due to these reasons, none of the above mentioned modalities has come up to the mark for combating the problem of recurrence.

MMC is an antibiotic isolated from bacterium Streptomyces caespitosus. It

undergoes metabolic activation through a cytochrome P-450 reductase mediated reaction to create an alkylating agent. MMC affects proliferating fibroblasts and vascular cells by inhibiting the synthesis of DNA, RNA and protein, and is radiomimetic in many of its actions [27,28].

Kunitomo and Mori in Japan first used MMC in pterygium surgery in 1963 [9]. In 1988, Singh et al introduced it to the western world. They used it topically in the form of eye drops (1 mg/ml in one group and 0.4 mg/ml in another) after pterygium excision. They reported a lower recurrence rate (2.3%) as compared to no MMC group (88.9%) at 23 weeks of follow-up, with minimal adverse effects [7]. Later studies, although confirming the reduced recurrence rate with topical MMC [8,14] also reported various sight threatening complications [17,18]. These complications included corneal oedema / perforation, scleral necrosis/calcification, incapacitating pain, glaucoma, and cataract.

To avoid these complications, single intra-operative application of MMC was studied. Although a few studies have reported higher recurrence rate compared to postoperative topical regimen [29], in majority of these studies intra-operative MMC application has shown better results regarding recurrence rate, and fewer complications compared to its topical use [13-16].

Four weeks preoperative MMC injection is a newer and safer approach for reducing recurrence rate and minimizing above-mentioned complications. In our study we planned follow-up period for 12 months, since most recurrences have been reported to occur within one year [1,30]. Age group that is prone to develop recurrence [1] (20-50 years) was selected. We used MMC in a concentration of 0.015% (0.15 mg/ml). This concentration is quite less than that used previously in topical/intra-op applications. In addition, the chances of spillover of MMC onto adjacent structures is minimized, hence corneal epithelial and limbal stem cell damage is also prevented. This may explain the absence of any serious/vision threatening complication in our patients.

This form of treatment has been tried by a very few eye surgeons. Therefore, very few studies are available on its efficacy and complications. Carrasco [31] reported local scleral necrosis in a patient who received subconjunctival MMC according to a protocol similar to that of our study. However that patient had severe dry eyes and had already received cautery for both lower puncta. As ocular surface disorders including dry eyes can predispose to such complications, such cases were excluded from our study.

Anduz, using the same method, reported a recurrence rate of 1.5% at 3 years of follow-up [21]. Recurrence occurred in only those eyes that had undergone prior pterygium surgery (recurrent pterygia). Donnenfeld et al have observed a recurrence rate of 6% over a mean follow-up of 24.4 months [32]. Avisar observed that no recurrence occurred at 12 to 23 months of followup [33]. We also did not observe any recurrence so far.

We did observe some mild and self-limiting complications, which are worth mentioning. Post-operative pain/discomfort were more than usual. It was observed in 94.5% cases and it persisted for 2-4 weeks. Delayed epithelial healing (for up to 2 weeks) was also observed in many (68.1%) cases. Four (4.4%) cases developed local conjunctival avascularity, the conjunctival epithelium remained intact over it. This peculiar finding which did not produce any long term complication was also observed by Raiskup [8]. No scleral thinning was noticed in any case.

CONCLUSION

Pterygium surgery with four weeks pre-operative injection of MMC relieves surgeon's headache about the menace of recurrence, for which no satisfactory treatment was available so far. This promising treatment appears as a ray of hope for these cases. Further/ multicentric studies are recommended to see

the long term effects of this method of MMC delivery in prevention of pterygium recurrence.

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