INTRODUCTION

Pterygium is a growth of fibrovascular tissue on the cornea and conjunctiva. Surgical intervention of pterygium is indicated in a number of circumstances including obstruction of visual axis, induced astigmatism, motility restriction, and poor cosmesis.

The goal of surgery is prevention of recurrence. The available methods are varying in the technique of handling the conjunctival defect created and when measures are taken to produce a safe, cosmetically acceptable and recurrence-free procedure. Simple excision of pterygium has a very high recurrence rate of about 30 - 70%; whereas, excision with conjunctival autograft has a recurrence rate which varies from 2% to 39%.

Use of Mitomycin-C (MMC) in pterygium surgery is thought to aid in the procedure by inhibiting growth of episcleral fibroblast proliferation. Previously, MMC was utilised intraoperatively and postoperatively. Preoperative role of MMC as an adjunctive therapy before pterygium excision was first evaluated by Donnenfeld et al in the form of subconjunctival Mitomycin-C (SC-MMC) injection into the pterygium tissue in an uncontrolled trial. After the injection, a one-month waiting time was planned before removal of pterygium. In Pakistan, Dawood et al performed this technique for the first time. Both studies found preoperative SC-MMC injection as an effective form of treatment.

To reduce the exposure time of MMC and postoperative complications, Ghoneim modified the original technique of Donnenfeld and chose to inject SC-MMC just 24-hour before excision and compared the results with intraoperative MMC. He found his technique to be equally effective.

Review of the literature on the efficacy of preoperative SC-MMC shows that either the efficacy has been analysed as an uncontrolled trial or the efficacy of SC-MMC has been compared with intraoperative application of MMC. Therefore, the objective of this study was to compare the effectiveness of subconjunctival injection of Mitomycin-C at 24-hour and at one month before pterygium surgery. The rationale was to determine if patients can benefit with the 24-hour preoperative injection so as to improve patient comfort and compliance without compromising on the efficacy, and avoidance of the 01 month waiting time.

ABSTRACT

Objective: To compare the effectiveness of preoperative subconjunctival injection of Mitomycin-C at 24-hour and at one month before primary pterygium excision.

Study Design: Randomised controlled trial.

Place and Duration of Study: Eye Department, Combined Military Hospital, Sargodha, from January to December 2014.

Methodology: Eyes of 60 patients were randomly allocated into two equal groups (A and B) of 30 each. In group A Mitomycin-C was injected into the pterygium one month before, and in group B Mitomycin-C was injected 24 hours before excision. All pterygia received 0.1 ml of Mitomycin-C in a concentration of 0.15 mg/ml. Primary pterygia greater or equal to 2.5 mm were selected and excised as a bare sclera technique. Postoperatively, all patients were followed-up for 06 months. The recurrence and corneoscleral complications were recorded. Pearson chi-square test was used to compare the recurrence between group A and group B.

Results: The recurrence of pterygium in group A was 3.3%; and in group B, it was 6.7%. Comparison of the recurrences between both the groups was statistically insignificant, (p=0.554). Postoperatively, no serious corneoscleral complications occurred in either group.

Conclusion: The preoperative subconjunctival injection of Mitomycin-C in a dose of 0.15 mg/ml given 24 hours prior to excision is as effective as 01 month preoperative injection for primary pterygium surgery with bare sclera technique.

Key Words: Mitomycin-C. Pterygium surgery. Recurrent pterygium. Subconjunctival injection.
METHODOLOGY

This randomised controlled trial was conducted at the Eye Department of Combined Military Hospital, Sargodha. Sixty eyes of 60 patients attending the eye outpatient department were selected and randomly allocated into two equal groups (Group A and Group B) of 30 each, based on computer generated random numbers table. The sample size was calculated to be 30 (n=30) in each group on the basis of the recurrence rate of pterygium using the WHO calculator. The level of significance was kept at 5% (α=5%) and power of the test (1-β) was kept at 90%; and anticipated population proportion in group A was 4% (n=25) and in group B 8% (n=25). In group A patients, MMC was injected into the pterygium one month before excision; and in group B patients, MMC was injected 24 hours before excision. All the patients underwent a bare sclera excision of the pterygium and all the surgeries were performed by one surgeon only. The duration of study extended over 12 months from January to December 2014. Patients between the ages of 20 to 75 years with primary pterygium size of 2.5 mm or more were enrolled in the study. The exclusion criteria were pseudopterygium, recurrent pterygium, dry eyes syndrome, and ocular cicatrival diseases. The study was approved by the Institutional Review Board.

A written informed consent was obtained from all the patients. After obtaining ocular and systemic history, ocular examination was done which included Snellen visual acuity, manifest refraction, automated keratometry, slit lamp anterior segment examination, measurement of pterygium length from the limbus with slit beam, and intraocular pressure measurement.

Using a 30-G insulin needle, 0.1 ml of 0.15 mg/ml of MMC was injected into the tissue of pterygium after instilling a drop of proparacaine under the operating microscope. The needle was inserted approximately 1.5 mm away from the limbus into the pterygium under aseptic condition. A drop of 0.3% Ofloxacin eye drop was placed after the injection. The patients had a slit lamp examination at 01 day and then 01 month after excision and there was mild bleeding intraoperatively. In pterygia in group A were quiescent at the time of excision and there was mild bleeding intraoperatively. In group B, 2 patients out of 30 (6.7%) had recurrence at the fourth and sixth month of postoperative period. Statistical comparison of the recurrence of both groups was insignificant (p=0.55, Table I).

There was not a single case of any serious corneoscleral complication in either group. Preoperatively, all the pterygia in group A were quiescent at the time of excision and there was mild bleeding intraoperatively. In group B, the majority of pterygia were hyperaemic at the time of excision with few pterygia developing subconjunctival haemorrhages and during surgery there was more bleeding as compared to the group A. Postoperatively no patient developed scleral melting, persistent epithelial defect or dellen. Minor complications like conjunctival avascularity, or conjunctival irritation occurred in 13 eyes in group A and 15 eyes in group B.

RESULTS

Average age of the patients was 56.6 ±13.4 years in group A and 51.7 ±11.1 years in group B. There was no statistically significant difference of age between group A and group B (p=0.12). Eighteen (60%) out of 30 patients in each group were males and 12 (40%) were females in each group. One patient out of 30 (3.3%) developed a recurrence of pterygium in group A at 3 months while in group B, 2 patients out of 30 (6.7%) had recurrence at the fourth and sixth month of postoperative period.

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Table I: Comparison of the recurrence of pterygium of group A and group B patients.

<table>
<thead>
<tr>
<th>Recurrence</th>
<th>Group A * (n=30)</th>
<th>Group B** (n=30)</th>
<th>Pearson Chi-square test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>1 (3.3%)</td>
<td>2 (6.7%)</td>
<td>p=0.554</td>
</tr>
<tr>
<td>No</td>
<td>29 (96.7%)</td>
<td>28 (93.3%)</td>
<td></td>
</tr>
</tbody>
</table>

* Group of patients receiving subconjunctival injection of MMC 01 month before excision.
** Group of patients receiving subconjunctival injection of MMC 24 hours before excision.
DISCUSSION

Recurrence of pterygium is the most enigmatic complication of pterygium surgery. Recurrence of pterygium, following SC-MMC injection, varies widely. In one study, this was 4.2% for primary pterygium with 01 month prior injection of SC-MMC during a follow-up of 24 months.7 At the other end, Avisar et al. had no recurrence of primary pterygium excision in a follow-up of 12 to 23 months.8 Similarly, Khaskoor after giving SC-MMC injection at one month and following-up his patients for at least 12 months, did not detect clinically significant recurrence in any of his primary pterygium cases.9 In another study in Pakistan, the recurrence was 2.9% with a limited follow-up of 03 months.10 In this study, among the group of patients who received SC-MMC injection at 01 month, their recurrence was 3.3% in 06 months of follow-up. This recurrence is in agreement with the previously published data.

The recurrence for patients who have undergone surgery for recurrent pterygium with 01 month of SC-MMC injection also has a wide variation. Dawood et al. reported no recurrence in a follow-up ranging from 12 to 23 months among his patients comprising both primary and recurrent pterygium.9 On the other hand, Donnenfeld et al. recorded a 6% recurrence in his cases of recurrent and primary pterygium after a mean follow-up of 24.4 months.4 Here, the authors did not operate upon recurrent pterygium with the purpose of solely determining the recurrence rates following primary pterygium excision only.

The failure rate of pterygium surgery in patients who are given SC-MMC just 24 hours before removal and therefore, with 24 hours of exposure of MMC to the corneoscleral bed and pterygium tissue, has been reported to be 5.7% for primary pterygium at 01 year postoperative time and 4% in recurrent cases at 12 months follow-up.5,11 The 6.7% recurrence in the presently reported group of patients, which is similar to the scarce data that exist in literature with 24 hours of preoperative SC-MMC injection.

The concentration of MMC for subconjunctival injection that has been chosen in the majority of previous studies is 0.15 mg/ml. This dose was first used by Donnenfeld in 1998, based on the findings by Chen et al. who reported that MMC in a dose of 0.10 mg/ml inhibits fibroblast replication and higher dose of 0.3 mg/ml causes death of fibroblast.4,12 Later on, it was demonstrated through electron microscopy that SC-MMC injection of 0.1 ml in a concentration of 0.15 mg/ml inhibits fibrovascular activity in the pterygial stroma, leading to degeneration of the extracellular matrix and nerve axons and therefore, effective in decreasing the recurrence of pterygium.13 Studies in the past that have utilised SC-MMC 01 month prior to excision in a concentration of 0.015% have not reported any of the serious side effects like persistent epithelial defects, scleral melting or dellen formation during their postoperative follow-up.4,7,8,10 Khaskoor, using a slightly higher concentration of 0.02% MMC, found that only two out his 36 cases developed mild side effects comprising of hypovascularity and scleral whitening.9

Similarly, the few studies that have been carried out to evaluate the efficacy of 24 hours preoperative SC-MMC in a concentration of 0.015% have also not faced any serious complications. Among these studies, Ghoneim reported a single case of scleral thinning in a total of 35 eyes that he operated and Zaky found 8% of his cases presenting with delayed epithelialisation of more than 02 weeks’ duration in the postoperative period.5,11 Based on the results of previous studies, we chose to inject the same concentration of 0.15 mg/ml. With this dose, there was not a single case of serious corneoscleral complication at any time during the 06 months follow-up in both groups which further proves that SC-MMC injection given at 24-hour before excision is safe.

The follow-up period for the detection of corneoscleral complications and recurrence of pterygium in this study, comprising of primary pterygium only, was selected to be 6 months as majority of recurrences following primary pterygium surgery occur in the first 6 months.2 However, the safety profile of SC-MMC injection increases the longer follow-up period as suggested by Donnenfeld where he followed his patients for 24.4 months which is the longest series published.4 Avisar in his study of 143 eyes concluded that 01 year of follow-up is the optimal time for detection of recurrence.14 The follow-up period that was selected in studies in the past evaluating SC-MMC injection varies from as low as 03 months to 24.4 months.4,7,8,10 But inspite of this wide range of follow-up, all the recurrences have occurred within 03 and 07 months of postoperative period. To date, there are no published studies that have specifically analysed the influence of follow-up duration on the recurrence rate with respect to SC-MMC injection prior to pterygium removal. Based on the clinical data, the authors believe that 6-month follow-up is not inadequate in detecting the majority of recurrences as far as the influence on the recurrence rate is concerned. However, longer follow-up is desired for analysing the safety profile of SC-MMC.

Among the demographics, studies report that young age (< 50 years) correlates significantly with recurrence of pterygium whether a graft is sutured or intraoperative MMC is applied.15-17 However, Ti Seng-Ei et al. found that patient age is not an independent risk factor that should be accounted for higher recurrences rather the pterygia are more fleshy and aggressive in young patients,18 and there is a statistically significant higher recurrence rate in fleshy, non-translucent pterygia.19 The authors did not record the morphology of the pterygia and therefore, did not study its effect on the recurrence.
Regarding the age group in this study, the mean age in group A and group B was 56.6 ±13.4 and 57.7 ±11.1 years, respectively. These values were statistically insignificant when compared. Keeping in view the objective of this study which was to compare the efficacy of preoperative SC-MMC with two different techniques, the age of the patients did not influence our recurrence.

The pterygium size selected for surgery in this study was greater or equal to 2.5 mm from the limbus. Yamada found that large pterygia (within pupillary area) had greater recurrences than small pterygia. But, Anguria found that large pterygia were protective against recurrence as an independent risk factor irrespective of patients’ age. This contradiction may be explained on the basis of the difference in the conjunctival treatment applied, as Yamada applied beta-irradiation and Anguria performed a conjunctival graft. In this study although all the pterygia were greater than 2.5 mm, but here the authors did not record the exact size and hence could not perform statistical analysis to see the effect of size on recurrence with the presently used technique of adjunctive treatment. Since recurrence depends heavily on the type of adjunctive treatment for prevention of recurrence therefore, the authors believe it is the technique rather than size that would have greater influence on recurrence which needs to be proved with future studies employing SC-MMC injection.

The present study compared the efficacy of preoperative SC-MMC injection at one month and 24-hour before surgery with recurrence as the scale for measuring the efficacy. The authors suggest that the 24-hour preoperative injection is effective, makes it a one, stage procedure compared to the two-stage procedure of one month preoperative injection and waiting time. It is therefore, more patient-friendly. To further clarify its effectiveness and safety profile, it is suggested that influence of factors like young age, pterygium size, its morphology, longer follow-up period on the recurrence, and corneoscleral complications be evaluated in future research work.

CONCLUSION

The preoperative subconjunctival injection of Mitomycin-C in a dose of 0.15 mg/ml given 24-hour prior to excision was as effective as one month preoperative injection for pterygium surgery with bare sclera technique.

REFERENCES