



STUDY OF PREOPERATIVE INJECTION OF MITOMYCIN-C IN PRIMARY PTERYGIUM SURGERY WITH BARE SCLERA TECHNIQUE.

Ophthalmology

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ABSTRACT

Purpose: To study the efficacy of subconjunctival injection of mitomycin C in primary pterygium surgery with bare sclera technique and compare the results of this method with pterygium excision with conjunctival limbal autografting.

Methods: Prospective, Randomised, interventional, hospital based, comparative study. Sixty eyes of sixty consecutive patients coming to ophthalmology OPD of our tertiary care centre with primary progressive pterygium will be selected. Each patient with primary progressive pterygium were randomly assigned to group A and B and were operated. Group A includes 30 patients with subconjunctival injection of mitomycin C (0.1ml of 0.12 mg/ml), one hour before pterygium excision with bare sclera technique and Group B includes 30 patients with pterygium excision with conjunctival limbal autografting. The patients were followed up postoperatively on days 1,7 and then at months 1,6,12 and 18. The main outcome measures included were recurrence rate and postoperative complications.

Results: By the end of 18 months follow up, the recurrence rate was 6.66% in Mitomycin C group(Group- A) and 3.33% in conjunctival limbal autograft group(Group- B). There were no severe vision threatening complications in either group.

Conclusion: subconjunctival injection of Mitomycin C(0.1ml of 0.12 mg/ml), one hour before pterygium excision with bare sclera technique effectively reduces recurrence rate to an acceptable level without causing any vision threatening complications. It has definite role in patients with recurrent pterygium, large double headed pterygia, patients with glaucoma who may require filtration surgery in future and combined pterygium with cataract patients.

KEYWORDS

Pterygium, Mitomycin-C, Conjunctival Limbal Autograft

INTRODUCTION

Pterygium is a wing shaped, fibrovascular overgrowth arising from subconjunctival tissue extending across the limbus on to the cornea.¹ It is an elastoid degeneration of the subconjunctival tissue which proliferates as a vascularised granulation tissue to invade cornea, destroying superficial layers of stroma and Bowman's membrane, the whole being covered by conjunctival epithelium.² Pterygia also display tumor like features such as propensity to invade normal tissue and high recurrence rate following excision.⁴ Since the pterygia aggressively recur after excision it is also being considered as neoplastic growth disorder and not a simple degeneration.

Conjunctival autografting seems to be an effective method for pterygium treatment that effectively prevents recurrence. Traditionally conjunctival autograft is secured in place with absorbable or non absorbable sutures, however suturing is time consuming and associated with suture related irritation and redness also there can be difficulty in future glaucoma surgery due to conjunctival scarring at donor site. It is technically difficult to treat large double headed pterygium and cannot be done in pterygium and cataract combined surgery. Pterygium excision with bare sclera technique is the simplest technique but is associated with high recurrence rate ranging from 37-91 percent.^{5,6} Various techniques have been evolved to prevent the recurrence of pterygium after surgery. Recurrence is usually more aggressive than primary lesion. The techniques to prevent the recurrence vary from simple excision to ,conjunctival limbal autografting, use of adjunct therapies such as beta irradiation, antimetabolic drugs like 5-FU and Mitomycin- C, cyclosporin A and duanorubicin.

Mitomycin-C is an antineoplastic agent which alkylates and cross links DNA, resulting in inhibition of cellular proliferation for The mechanism of action of mitomycin-C in prevention of pterygium recurrence is attributed to the inhibition of fibroblast proliferation of episclera.^{7,8} Mitomycin-C has a prolonged, if not permanent effect on human fibroblasts. This prevents development of fibrosis and aggressive wound healing that is responsible for recurrence.

Adjunctive mitomycin-c for pterygium surgery was first described by Kunitomo and Mori in japan 1963.⁹ Previous studies show that preoperative use of mitomycin C before bare sclera technique decreases recurrence rate to acceptable levels. These studies were done with inj. Mitomycin C one month prior or one day prior to the surgery.³

Purpose of this study was to find out whether a simpler technique like subconjunctival injection of Mitomycin-c one hour before pterygium excision by bare sclera technique gives results comparable to conjunctival autograft in terms of recurrence rate and other complications.

METHODOLOGY

This prospective, randomized, interventional, hospital based and comparative study was conducted at Shri Chattrapati Sarvopchar Rugnalaya, DR. V. M. G.M.C, Solapur during period of December 2017 – July 2019. Data for this study was collected from the subjects fulfilling the inclusion/exclusion criteria. Sixty eyes of sixty consecutive patients coming to Ophthalmology OPD of our tertiary care centre with primary progressive pterygium were selected. Each patient with primary pterygium was randomly assigned to group A and B and operated.

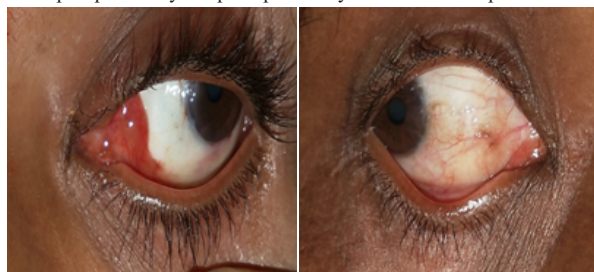
Group A includes cases with subconjunctival injection of mitomycin C(0.1ml of 0.12mg/ml),one hour before pterygium excision with bare sclera technique (30 Patients) and group B includes cases with pterygium excision with conjunctival limbal autografting (30 Patients).

After full preoperative evaluation (complete history and ophthalmological examination), patients underwent the surgical treatment as per the technique of the groups in which they were randomly assigned. Patients in Group A were given subconjunctival injection of Mitomycin C (0.1ml of 0.12mg/ml) in the operation theatre with all aseptic precautions one hour before pterygium excision with bare sclera technique. In case of Group B, each patient was operated for pterygium excision with conjunctival limbal autografting

with suturing for fixation of autograft. Initially, Proparacaine (0.5%) topical anaesthetic was instilled in the involved eye. Commercially available Mitomycin C after reconstitution with distilled water has 2mg/5ml of vial having 0.4mg/ml of Mitomycin C. Beginning with 0.4mg/ml of concentration we added 1 ml of distilled water into it to achieve a concentration of 0.2mg/ml of Mitomycin C. Then took 1ml of the solution containing 0.2mg of Mitomycin C and added 0.7 ml of distilled water giving 0.2mg of Mitomycin C in 1.7ml. So, 1ml of solution contains (0.117 mg) approximately 0.12 mg of Mitomycin C. Then 0.1 ml of Mitomycin C (0.12mg/ml) was taken in an insulin syringe and injected subconjunctivally into the head of pterygium using 30 gauge needle. After injection, the conjunctival sac was irrigated with normal saline to wash out excess of Mitomycin C and the patient received one drop of ofloxacin 0.3% and eyepad applied for one hour. This procedure was carried out with all aseptic precautions.

After one hour, subconjunctival infiltration of xylocaine with adrenaline was given under the body of pterygium. Body of the pterygium was separated from underlying sclera by sharp and blunt dissection using cotton bud and conjunctival scissor. The neck of pterygium was grasped with Saint Martin's forceps and head of pterygium was stripped off the cornea by blunt dissection using cotton bud and forceps. Body of pterygium was then separated from the overlying conjunctiva towards the forniceal end by sharp and blunt dissection using cotton bud and conjunctival scissors. Head and neck of pterygium with overlying conjunctiva and part of the body of pterygium was then excised. Cornea was then polished with no.15 surgical blade on a Barde-Parkar handle to achieve smooth surface at the limbus. Similar procedure was carried out in group B and conjunctival limbal autografting secured with 8-0 vicryl absorbable suture material.

Patients were examined on the 1st post-operative day; then patients were followed up at 1 week, 1 month, 3 months, 6 months and every 6 months thereafter for 1 year. A clinical photograph of every patient was taken preoperatively and postoperatively on each follow up visit



Follow up 12 months- Group A Follow up 12 months- Group B

RESULTS

Maximum number of patients 21 (35%) were from age group 41-50 years. Out of the 60 patients included in this study, 29 (48.33 %) patients were male and 31 (51.67%) patients were female. Out of 60 patients, 44 (73.33%) patients had bilateral pterygium. i.e. pterygium in both the eyes, 11 (18.33%) patients had pterygium only in right eye, 5 (8.33%) patients had pterygium only in left eye. Majority of patients, 34 out of 60 (56.66%) were pursuing outdoor occupations. Majority of patients, 40 out of 60 (66.66%) were residing in rural area.

Average surgery time for conjunctival limbal autografting (26.57minutes) was more compared to subconjunctival injection of Mitomycin C one hour before pterygium excision with bare sclera technique (19.10 minutes).

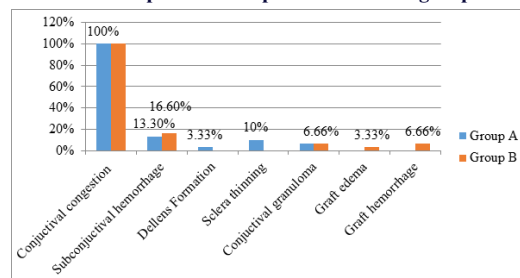
Table no. 1 shows recurrence rate within study period. In group A there were 2 (6.66%) cases of recurrence over a mean follow up period of 12 months and in group B there was 1 (3.33%) case of recurrence over a mean follow up period of 11.47 months. Statistically there is no significant difference between recurrence rates by above two surgical techniques. (z test=0.59, p>0.05).

Table no. 1 : Pterygium recurrence rate of two techniques

Sr. no	Group	Surgical technique	No of eyes operated	No of eyes With recurrence
1.	A	Bare sclera with preop Mitomycin C	30	2 (6.66%)
2.	B	Conjunctival limbal Autograft	30	1 (3.33%)

Chart no.1 shows in the immediate postoperative days all the patients (group A and group B) had conjunctival congestions. In 4 (13.3%) eyes from group A and 5 (16.6%) eyes from group B. Subconjunctival hemorrhage was seen. Dellen formation occurred in 1 (3.33%) eye in group A within one month postoperative day. Scleral thinning was noted in 3 (10%) eyes of group A out of which 2 patients were noted on first week of postoperative day and 1 patient was noted on first month of postoperative day. Conjunctival granuloma was noted in 2 eyes (6.66%) in both group A and group B, graft edema was noted in 1 eye of group B patient and graft hemorrhage was noted in 2 eyes of group B patient. Statistically there is no significance difference in complications that occurred between two groups. (p>0.05).

Chart No. 01: Postoperative complications in both groups



DISCUSSION

In this study, we evaluated two different therapeutic modalities for management of pterygium. We also compared these techniques in terms of recurrence rate and complications. Pterygium excision with bare sclera method is one of the oldest techniques, This is very easy and simple procedure but it is associated with high recurrence rates, between 24-89%. Pterygia also display tumor like features such as propensity to invade normal tissue and high recurrence rate following excision.⁴ So, recently adjunctive such as 5FU and Mitomycin C are being more commonly used antimitotic drugs in preventing pterygium recurrence. Mitomycin C acts by inhibiting DNA synthesis which leads to death of cells caused by inability to repair the genotoxic injury. Inhibition of DNA synthesis leads to reduction in number of mitoses, especially when Mitomycin-C comes in contact with the cells which are in late G1 and early S phase of cell cycle. Its action in prevention of pterygium recurrence occurs by inhibition of fibroblast proliferation in the episcleral region. This prevents the development of fibrosis and aggressive wound healing that are responsible for pterygium recurrence.¹⁰ Several modalities of usage have been described including intra operative application, postoperative topical use and preoperative injection. Intraoperatively Mitomycin C is applied in different concentrations ranging from 0.002% to 0.4% for 3 to 5 minutes.¹¹ The recurrence rate reported in literature for intraoperative use of Mitomycin C varies from 6.7% to 22.5%.¹¹ Mitomycin C before surgery, the concept of use of Mitomycin C preoperatively in pterygium excision was originated from a previous study by Donnenfield¹⁴ and co-workers who reported a case series of subconjunctival injection of Mitomycin C injection one month before surgery in recurrent pterygium. Their results showed that pterygium was less vascular and less inflamed at one month and all pterygia were quiescent at time of surgical excision.¹² The use of subconjunctival injection of Mitomycin C preoperatively is a safer approach for minimising serious vision threatening complications like scleral melting, corneal thinning, ulcer formation, glaucoma, cataract formation¹¹ which occurs due to scleral exposure to excessive dose of Mitomycin C due to increased concentration and exposure time following its intraoperative use. By giving Mitomycin-C subconjunctivally under the head of pterygium exact dose delivery is possible and chances of spill over of Mitomycin C onto adjacent ocular surface is minimised; hence damage to corneal epithelial and limbal stem cell is also prevented. Hence subconjunctival use of low concentration of Mitomycin C in pterygium excision with bare sclera technique can reduce pterygium recurrence effectively and the risk of vision threatening complications can be minimised.

The concentration of Mitomycin C for preoperative subconjunctival injection that has been chosen in majority of previous studies is 0.15mg/ml. This dose was first used by Donnenfield in 1998, based on the findings by Chen et al. who reported that Mitomycin in a dose of 0.10mg/ml inhibits fibroblast proliferation and higher dose of 0.3 mg/ml causes death of fibroblast.⁸ Studies in the past have utilised subconjunctival Mitomycin C one month and one day prior to

pterygium excision in a concentration of 0.1ml of 0.15mg/ml and have not reported any of the serious side effects like persistent epithelial defects, scleral melting or any vision threatening complications during their followup.⁸ Also all previous Mitomycin C related studies were carried out at one month or one day prior to pterygium excision surgery.^{13,16} The drawbacks associated with these studies are double hospitalisation and twice visits to operation theatre is required which may decrease compliance of patients.

So a study of low effective dose of Mitomycin C (0.10-0.15mg/ml) through subconjunctival injection with shorter duration of exposure before pterygium excision seemed to maintain the efficacy of drug and avoid long unnecessary exposure with subsequent penetration of Mitomycin C.¹³ Therefore we used subconjunctival Mitomycin C injection of 0.1ml in a concentration of 0.12mg/ml one hour before pterygium excision. The rationale behind this was to determine if patients can benefit with one hour preoperative injection so as to improve patient comfort and compliance with single visit to operation theatre. From the above mentioned studies recurrence rates after **pterygium excision with bare sclera technique without Mitomycin C varies from 20% to 72%, and recurrence rate with use of Mitomycin C varies between norecurrence to 7%.^{15,16} In our study the recurrence rate with use of Mitomycin C is 6.66% which shows significant reduction in the rate of recurrence, and is comparable with those found in literature.**

Dellen formation occurred in one case which resolved on conservative treatment of lubricating eye drops. Scleral thinning was seen in 3 cases in Group A which occurred in 2 cases (case no. 15,22) within first week and in one case (case no. 20) within one month follow up period. All 3 cases resolved within 4-6 weeks under conservative treatment with topical lubricant therapy. No other serious postoperative complications were reported.

CONCLUSION

Both the methods i.e. subconjunctival injection of Mitomycin C one hour before pterygium excision with bare sclera technique and pterygium excision with conjunctival limbal autografting are effective and safe treatments of pterygium. Therefore, both the techniques can be considered as very good options for treatment of primary progressive pterygium.

Thus from the present study it is concluded that, subconjunctival injection of Mitomycin C one hour before pterygium excision with bare sclera technique is simple, safe, economical, less time consuming. It also effectively reduces recurrence rate to an acceptable level. It has definite role in patients with recurrent pterygium, large double headed pterygia, patients with glaucoma who may require filtration surgery in future and combined pterygium with cataract patients. As Mitomycin C can produce deleterious effects years after its use, longer follow up is required in these cases. So larger study with large number of patients with longer follow up is needed.