Original Article

Comparison of Conjunctival Autograft and Intra-Operative Application of Mitomycin-C in Treatment of Primary Pterygium

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Purpose: The purpose of this study was to evaluate and compare recurrence rate in treating primary pterygium by two different techniques: pterygium excision with intra-operative application of mitomycin C versus pterygium excision and conjunctival autograft.

Material and Methods: The patients were selected from the out-patient department of L.R.B.T Free Base Eye Hospital, Karachi from 1st December 2009 to 30th November 2010. Eighty patients with primary pterygium were included in this study with age ranging between 20-50 years. Patients were randomly allocated into two groups: Group A consisted of 40 patients who were operated on for pterygium excision and conjunctival autograft. Group B consisted of 40 patients who were operated for pterygium excision and intra-operative application of mitomycin C (0.02%). Complications and recurrences were assessed and compared.

Results: In Group A, there were 2 (5%) recurrences noted with minor complications in 6 (15%) of the cases. In Group B, there were 9 (22.5%) recurrences noted along with minor complications in 10 (25%) of the cases.

Conclusion: Pterygium excision with conjunctival autograft is a superior technique in terms of lower rates of recurrences and complications as compared to pterygium excision with intra-operative use of mitomycin C.

Pterygium is a common disorder in many parts of the world, with reported prevalence rate ranging from 0.3 to 29%. Epidemiological studies suggest an association with chronic exposure to sunlight; with an increased geographical prevalence within a peri-equatorial 'pterygium belt' of latitudes of 37 degrees north and south of the equator[1]. Clinically pterygium is a fibrovascular wing-shaped encroachment of conjunctiva onto the cornea[2].

Ptregium is thought to result primarily from ultraviolet light induced damage to connective tissue underlying the conjunctiva. The pathological changes consist of elastoid degeneration of the collagen and appearance of sub-epithelial fibrovascular tissue. The cornea shows destruction of the Bowman's layer by fibrovascular in-growth frequently with mild inflammatory changes. The overlying epithelium maybe normal, thick or thin and may show dysplasia.

Ultraviolet B light in solar radiation has been found to be the most significant environmental factor in pterygium pathogenesis[1]. A recent study has suggested that P-53 and human papilloma virus may also be implicated in pterygium pathogenesis. Ultraviolet radiation can cause mutation in genes such as the P-53 tumor suppressor gene, resulting in its abnormal expression in pterygial epithelium. These findings suggest that pterygium is not just a degenerative lesion, but could be a result of uncontrolled cell proliferation[3]. Tseng et al have also speculated that pterygium may represent an area of localized limbal stem cell deficiency[4].

Indications for surgery include visual impairment, cosmetic disfigurement, motility restriction, recurrent inflammation and interference with contact lens wear[5]. Pterygium is graded on the extent of corneal involvement. Type 1 extends less than 2mm on to the cornea, type 2 involves up to 4 mm of the cornea and type 3 invades more than 4 mm of the cornea and involves the visual axis[6]. Surgical management includes simple excision with bare sclera technique, excision with adjunctive measures like intra-operative and post-operative beta radiation, thiotepa drops, intra-operative mitomycin C and various techniques of conjunctival autografting[7]. The reported recurrence rates of these techniques vary widely, from 5% for pterygium excision with conjunctival autografting, to 89% for simple excision[1,5]. Ablation with erbium or YAG laser,[8] and smoothening the corneal surface with excimer[9]. laser has been tried but the results are not encouraging.

Mitomycin C is an antineoplastic-antibiotic alkylating agent isolated from fermentation filtrate of Streptomyces caespitosus. It selectively inhibits DNA replication by forming covalent linkages with guanosine residues in DNA, inhibits cellular RNA and protein synthesis. Therefore, it prevents mitosis leading to cell death and interferes with collagen synthesis, thus preventing recurrence after pterygium surgery[10,11]. Since its first use in pterygium treatment by Kunitomo and Mori in 1963,[12] different concentrations, administration modes and dosing schedules of mitomycin C have been used in different studies. Although generally proven simple and effective, toxicity remains a concern. Complications reported with intra-operative or post-operative use of mitomycin C are pain, iritis, secondary glaucoma, cataract, punctuate keratitis, chemosis, delayed conjunctival healing, conjunctival granuloma and scleral and corneal melting[11,13]. Many of these reported serious complications involved use of high concentrations (0.04 – 0.1%), prolonged post-operative topical use and/or larger cumulative dosages resulting from poor drug compliance[11,13,14].

Young AL et al have recommended intra-operative use[15]. The concentrations of intra-operative mitomycin C application used in most of the studies range from 0.01% to 0.04% with 0.02% applied for three months being the commonest dosage used[16]. Applying mitomycin C at the time of surgery provides clear advantage, such that the surgeon has control over the medication delivery and, moreover, single, direct scleral bed application does not expose the entire ocular, nasal, nasolacrimal or oropharyngeal surfaces to the drug[17].

Conjunctival autograft placed at the limbus acts as a barrier to re-growth of the pterygium. The graft taken from the supero-temporal bulbar conjunctiva contains limbal stem cells which result in rapid healing, smooth and lustrous surface without corneal neovascularizatoin and restoration of ocular integrity in a short term.

The aim of study was to find a treatment option for primary pterygium which would result in lower recurrence rate.

MATERIALS AND METHOD

This experimental clinical study was conducted at LRBT Free Base Eye Hospital, Karachi from 1st December 2009 to 30th November 2010. Eighty patients were included in this study with age ranging between 20 and 50 years. Inclusion and exclusion criteria are shown in table 1. Informed consent was taken from the patients. A performa was used to record information. The patients included in this study had pterygium of primary nature. The diagnosis of primary pterygium was made on the basis of clinical examination and history of any surgical treatment. Patients were inquired specially about their occupation, duration of exposure, onset of pterygium, ocular symptoms and history of glaucoma, diabetes and hypertension. Best corrected visual acuity was recorded after refraction, and retinoscopy was performed to assess pre-operative astigmatism. The local examination on slit lamp included examination of the area around the orbit, eyelids (for infection, deformities, entropion and trichiasis), examination of conjunctiva for presence of symblephron, active inflammation, nature of pterygium, extent of pterygium, degree of vascularization observed as well as tear film abnormality, fluorescein staining of cornea and corneal scarring. Intraocular pressure was checked by applanation tonometer. Fundus examination was carried out to see the macula and optic disc. After examination patients were randomly divided into two groups i.e. Group A (40 cases) to undergo surgical excision followed by conjunctival autograft transplantation and Group B (40 cases) to undergo simple surgical excision using bare sclera technique with intra-operative application of mitomycin C 0.02% for three minutes.

All the surgeries were performed under the microscope using topical and local sub-conjunctival

anaesthesia. In Group A patients, the pterygium head was detached from the cornea, and the pathological conjunctiva with the underlying Tenon's tissue was excised with scissors. No extended excision of the Tenon's tissue under the remaining conjunctiva was performed. The cornea was scraped clear, the sclera cleared from the connective tissue and any bleeding vessels were cauterized. The autologous conjunctival graft was harvested at the supero-temporal bulbar conjunctiva and shifted to the recipient site with all precautions. The graft was secured in position with 10/0 nylon interrupted sutures. The donor area was simply left to regenerate. In Group B patients, pterygium excision was done with bare sclera technique in the same manner as in Group A patients. Haemostasis was achieved by minimal cautery. Standardized piece of round filter paper of 4 mm diameter was soaked with freshly prepared mitomycin C 0.02% and applied on the bare sclera for 3 minutes. The area was then gently rinsed with balanced salt solution. In both the groups' post-operative treatment was started on the first post-operative day with steroid-antibiotic combination eye drops, four times daily and ointment at night. All the patients were examined on follow-ups on the first post-operative day, 4th day and then at weekly intervals for up to 1 month and thereafter every month for up to 3 months. Total duration of follow up in this study was three months.

RESULTS

Eighty patients with age ranging between 20-50 years were included in this study. Most of the patients in this study were between 20-35 years (67.5%). Mean age was 32.57 years. Men were more common in this study over the women by 65%. Outdoor workers were seen to be greatly affected by the pterygium (75.5%). Pterygium, 3 mm or more in size, encroaching the cornea were included in this study. Greater number of patients 65 (81.2%) had pterygium of 3-5 mm in size. Refraction and retinoscopy were done for all the patients. All the patients had with-the-rule astigmatism. In Group A recurrence was observed in 2 (5%) cases between 4th and 8th week after surgery. No per-operative complications were seen. There were no untoward effect was observed at the supero-temporal limbal region (graft dissected area), which was subsequently replaced by growth of adjacent tissue during the follow up period. Following complications were observed and subsequently managed: Graft edema 4 (10%) cases and conjunctival cyst 2 (5%) cases. On the other hand, in Group B, pterygium recurred in 9 (22.5%) cases within 8 weeks of surgery. Post-operative complications were ocular irritability in 5 (12.5%) cases, which settled with instillation of topical steroids within 4 days. Mild scleral thinning was observed in 2 (5%) cases, conjunctival granuloma in 3 (7.5%) cases which was excised after 2 months.

Table 1:

Inclusion Criteria
• Age between 20 to 50 years • Pterygium size 3 mm or more • Pterygium interfering with vision either by occluding visual axis or inducing astigmatism • Cosmetic disfigurement
Inclusion Criteria
• One eyed patients • Glaucoma • Ocular surface abnormalities • Chronic ocular infection and chronic dacryocystitis • Recurrent pterygium

Table 2: Comparing recurrence rates in Group A and Group B

Group A n = 40	**Group B n = 40**
2 (5%)	9 (22.5%)

Table 3: Post-operative complications in Group A and Group B

Group A n = 40	**Group B n = 40**
Graft edema 4 (10%)	Ocular irritability 5 (12.5%)
Conjunctival cyst 2 (5%)	Mild sclera thinning 2 (5%)
–	Conjunctival granuloma 3 (7%)
Total: 6 (15%)	Total: 10 (25%)

Higher recurrence rate was seen in patients undergoing pterygium excision with intra operative

mitomycin C as compared to pterygium excision with conjunctival autograft (p=0.048).

Recurrence rates and post-operative complications in the two groups are summarized in table 2 and table 3 respectively.

DISCUSSION

Pterygium is an excessive proliferation of fibrovascular tissue over the exposed ocular surface and frequently leads to almost irreversible visual loss. It is a worldwide disease which is particularly common in tropical and sub-tropical regions such as Pakistan. Exposure of ultraviolet light is the most important risk factor in its development. [18] The definitive management of pterygium is surgical but bare sclera technique carries a recurrence rate, which varies from 55.9% to 89%[13]. Thus, the ideal adjunctive procedure is still to be determined. The purpose of this study is, therefore, to find the most ideal procedure in terms of minimal recurrence rates. In the current study the recurrence rate in Group A (patients who underwent pterygium excision followed by conjunctival autograft) was 5%. Baig et al showed a similar result recurrence rate of 9.09% in their study[19]. Narsani et al showed that there was 7.69% recurrence with conjunctival autograft technique[20]. Quraishy MM documented 6.6% recurrence for primary pterygium[21]. Khan et al showed 8.8% recurrence rate in their study[22]. Massaoutis in his study documented 5.25% recurrence rate in conjunctival autografting for primary pterygium[23]. Post-operative complications in this group were mild which were well managed. In Group B (patients who underwent simple surgical excision using bare sclera technique with intra-operative mitomycin C 0.02%), recurrence rate was 22.5% with post-operative complications in 25% of the cases. Koranyi G et al showed 38% recurrence rate with intra-operative mitomycin C application in their study in 2010[23]. Ma et al used post-operative mitomycin C and Sharma et al compared mitomycin C with conjunctival autograft, but neither showed any statistical difference in the recurrence rates,[25,26] whereas Young et al also compared intra-operative mitomycin C with conjunctival autograft but they found a statistically significant difference in recurrence rates between the two groups[15]. Narsani also compared conjunctival autograft with intra-operative mitomycin C and he also found statistically significant difference in the recurrence rates between the two groups.

In this study, we compared pterygium excision and conjunctival autograft, and pterygium excision with intra-operative mitomycin C (0.02%) and found significant higher in recurrence rate in Group B as compared to Group A (p=0.048).

CONCLUSION

This study was carried out to find a treatment option for primary pterygium which would result in lower recurrence rate. Group A, which consisted of patients undergoing pterygium excision with conjunctival autograft, showed a lower recurrence rate of 5% as compared to Group B which consisted of patients undergoing pterygium excision with intra-operative 0.02% mitomycin C (22.5%). Based on the above findings we conclude that pterygium excision with conjuctival autograft is a superior technique for the treatment of primary pterygium, in terms of lower recurrence rate and minor post-operative complications. Larger controlled studies are required.

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