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Comparative Study Of Recurrence Rate Between Conjunctival Autograft And Bare Sclera With Intra-Operative Mitomycin-C In Primary And Recurrent Pterygium.

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Abstract:
Objective: *To compare recurrence rate between conjunctival autograft and Mitomycin C after primary pterygium excision in primary and recurrent pterygium .*
Design*: Analytical study on patients of primary and recurrent pterygium from 15 december 2012 to 15 february 2013 and June 2013 to March 2014.*
Setting: *Department of Ophthalmology, M.L. B. Medical College, Jhansi/ U.P.*
Method*: 49 cases of pterygium (including both primary and recurrent) were treated with conjunctival autograft and Mitomycin C (0.02% intra-operatively for 5 minutes at bare sclera under topical proparacaine and local infiltration of lignocaine). Patients were followed postoperatively for 6-12 months to find the recurrence (defined as fibrovascular tissues invading the cornea 1mm or more) of pterygium and complications.*
Results*: Of 49 cases 29 eyes(25 primary ;4 recurrent) received conjunctival autograft and 20 (15 primary ; 5 recurrent) recieved Mitomycin C . There were 6.8% (4% primary ; 25% recurrent) recurrences in group CAG and 15% (6.66% primary; 40% recurrent) recurrences in group MMC. There was no statistically significant difference between two groups. The post operative complications in MMC group were one punctate epithelial keratitis, one scleromalacia while in CAG group we encountered two cases of graft edema and subconjunctival haemorrhage below graft.*
Conclusion*: Excision of pterygium followed by conjunctival autograft has the lowest recurrence rate and minimal incidence of significant complications as compared to intraoperative Mitomycin C.*
Key Words: *Pterygium, autograft, Mitomycin C, recurrence.*

I. Introduction

Pterygium is an ocular surface disorder characterized by fibrovascular, wing shaped encroachment over the cornea [1], with a significant propensity towards recurrence (re-growth attaining the same degree of corneal encroachment as the original lesion, or regrowth exceeding 1 min onto the cornea.) **[9]** after surgical excision. . UV light induced damage to the limbal stem cell barrier with subsequent conjunctivalisation of the cornea is the currently accepted etiology of this condition. It is a common disorder in many parts of the world, with reported pooled prevalence rates about 10.2% (6.3% to 16.1% with 95% CI) [2] . The UV type A and B light in solar radiation [5] has been found to be the most significant environmental factor. It is also more frequent in hot, dry, windy, dusty and smoky environments [3]. Increased prevalence has been found in male gender [4] as compared to their female counterparts which might be related the duration of their outdoor activity. Matrix metalloproteinases (MMPs) [6] and tissue inhibitors of MMF's (TIMPs) at the advancing pterygium edge may be responsible for the inflammation, tissue remodelling, and angiogenesis that characterize pterygia, as well as the destruction of Bowman's layer and pterygium invasion into the cornea. *Tseng et al*. have also speculated that pterygium may represent an area of localized limbal stem cell deficiency. There is also a hereditary factor [7]. The complaints which it may give rise are foreign body feeling, vision loss due to corneal astigmatism or cosmetic problems [8]. Though anti-inflammatory drugs and lubricants have an important role in minimizing the patients discomfort but do not cure the disease. The excision of a pterygium with bare sclera was widely practiced because it was believed to be safe and simple. However, with time it becomes apparent that the recurrence rate was unacceptably high ranging from 24% to 89% [12]. Several methods were implemented with the aim of improving the success rate, among them transplantation of the head of the pterygium, conjunctival flaps, lamellar keratoplasty, mucous membrane grafts, chemotherapy by Thiotepa, radiation therapy by radon bulbs, radium plaques, beta irradiation ablation with erbium YAG laser[15] and smoothening the corneal surface with excimer laser[10] has been tried. Several of them succeeded in lowering the recurrence rates but did so at the price of sight-threatening complications from the tissue damage associated with the treatment [11] .

However, autologous conjunctival grafting seems to be the best method, giving both low recurrence rate and high safety[13,23] . Kenyon et al[14], first described a conjunctival autograft in 1985. They documented a recurrence rate of 5.3% and infrequent minor complications. Since then, the other authors also reported that autologous conjunctival grafting seems to the best method giving both low recurrence rate and high safety . The

primary disadvantage of this technique is prolonged operative time required when compared to the bare sclera technique. These disadvantages are out weighed . Unitomo, and Nori were the first to report the promising effect of Mitomycin C on the recurrence of pterygium. Mitomycin C is an alkylating antineoplastic agent produced by strains of streptomyces caespinosus, which inhibits synthesis of DNA, RNA and proteins. The current regime of Mitomycin C is 0.02 % to the bare sclera for 5 minutes has been found efficient in reducing the recurrence rate to a minimum [16]. In our study, we compared the recurrence rate of two different techniques.

II. Material And Method-

49 cases of primary+ recurrent pterygium were registered at the M.L.B.Medical college(Department of Ophthalmology) Jhansi, U.P. Patients were randomized in to two groups. Group A received conjuctival autograft and Group B received Mitomycin C. These patients had been questioned and medical data reviewed in details that none had major systemic disease such as hypertension, diabetes mellitus, collagen vascular disorder, etc.. Complete ocular examination including visual acuity, intraocular pressure, extraocular movements, biomicroscopy documentation of pterygeal size and dilated fundus examination was performed to assure that none of them had significant eye conditions such as , glaucoma, cicatrical pemphigoid, pingueculm, dry eye, chronic corneal pathology, chronic conjunctivitis and no other significant ocular surface pathology or vitreoretinal disease. All patients were followed for 6 to 12 months to assess the recurrence rate and complications. The ocular surface was anesthetized in all patients with topical instillation of proparacaine hydrochloride 0.5% in combination with an additional sub conjunctival injection in the bed of pterygium on the bulbar side with 0.5 ml of 2% lignocaine hydrochloride with 0.001% adrenaline. The complete excision of the head of the pterygium from the cornea was done by Bard Parker 15 number blade and the body of pterygium was dissected and excised by conjunctival scissors. In group A (CAG) area of the bare sclera was measured after pterygium excision. A free conjunctival graft was harvested from the superior conjunctiva. Dissection began from fornix to limbus. The graft was flipped over on the cornea and tenons attachment at limbus was meticulously dissected. Them flap was then excised taking care to include the limbal tissue. The graft was then moved on to the scleral bed maintaining limbus to limbus orientation. The four corners were anchored with episcleral bites using 8/0 vicryl suture. In group B (MMC) intraoperative Mitomycin C 0.02% was applied to the bare sclera for 5 minutes by cotton swab. The Mitomycin C was prepared by adding 10 ml of distilled water in 2 mg ampoule of injection. The site of application was then thoroughly irrigated with at least 100 ml of ringer lactate solution. The conjunctiva peripheral to the excised pterygium was undermined and the edges were sutured 2-3 mm from the limbus. Postoperative topical combination of corticosteroid antibiotic ointment was used and pad was applied for 24 hours. Antibiotic and corticosteroid were used 4 times a day for a month and then tapered off during the following 2-3 months. Follow-up visits were scheduled for post operative days 1,7,14, 30 and then every 2 months. The recurrence was defined as post operative fibro-vascular re-growth crossing the corneo-scleral limbus by 1.0 mm or more and this constituted treatment failure. All the information was filled on a proforma. Data were analyzed on SPSS version 10.0.

III. Results

We studied the recurrence rate of two different surgical techniques for primary and recurrent pterygium excision.

Total of 49 eyes of 49 patients underwent surgery with follow up period of 6 to 12 months with mean of 10 months . 85.71% of cases had primary pterygium. There was a male preponderance in cases (61.22%).

Recurrence occurred in 5 eyes. 2 for conjunjunctival autograft and 3 for Mitomycin- C within 6 months of surgery.

Recurrence seen in patients undergoing CAG was 6.8% (overall), 4.00% (primary), 25.0% (recurrent). In cases treated with Mitomycin C it was 15.0%(overall), 6.66% (primary), 40% (recurrent). There was no significant difference between in the recurrence rate among the two groups ,p=0.6404(overall) , p= 1.00(primary) p= 1.00(recurrent). Thus our study shows that CAG was slightly better than Mitomycin C for both primary and recurrent pterygium.

Greater inflammation post-operatively, as seen according to morphological grading of pterygium, led to higher recurrence rates and the two factors appeared to be linked. Also, younger age and male gender was associated with higher propensity to recurrence .

Although it is not uncommon to encounter minor problems such as graft edema, loose graft and epithelial cysts, (in cases of CAG) and mild punctuate superficial keratitis, and scleral granuloma (in Mitomycin C) the overall success of the two procedures, lack of significant complications and independence from adjunctive radiation therapies is especially encouraging. Carefull dissection of Tenon's tissue from the conjunctival graft, minimal manipulation of tisues and accurate orientation of graft to recepient bed are the key factors for an optimal surgical result.

In summary**,** this study has compared recurrence rate of primary and recurrent pterygium removal followed by conjunctival autograft and Mitomycin C Conjunctival autograft showed slightly better results (lower recurrence) as compared to bare sclera with Mitomycin-C and hence effective, safe and simple method of preventing recurrence in pterygium. However Mitomycin C may be preferred for advanced cases with bilateral heads ie. diffuse conjunctival involvement or those who might need glaucoma surgery later (to preserve superior bulbar conjunctiva.)

IV. Discussion

Despite the description of more than a 100 medical & surgical techniques, recurrence is the most often observed complication after treatment of pterygium. The recurrence rate varies greately not only among different surgical procedures but also between different groups undergoing same procedure .

It is believed that surgical procedure and subsequent post-operative inflammation activates subconjunctival fibroblasts and proliferation of fibroblasts and vascular cells & deposition of extracellular matrix (ECM) proteins, in turn contribute to the pterygium recurrence.

A recurrent pterygium can be associated with decreased visual acuity due to involvement of visual axis and/or irregular astigmatism, extraocular motility restriction and symblepharon formation [17]. Because of high recurrence rate the bare sclera excision alone proved unsatisfactory. Adjunctive treatment after bare sclera excision with beta irradiation reduced recurrence rate to as low as 0.5%-10% [18], but was associated with significant complications such as scleral necrosis.

In 1985, Kenayn et al published report describing conjunctival autografting as a promising technique in the treatment of pterygium. They documented the recurrence rate of 5.3% in the primary pterygium group. Since then a number of papers on the success of conjunctival grafting have been published with various success rates.

Since studies have indicated that pterygium occurs as a result of localized limbal dysfunction (Dushku , Ried) the success of conjunctival autografting technique that include limbal tissue in the graft in treating primary & recurrent pterygia to provide for the Limbal Stem Cell deficiency has been highlighted (Dua , et al) . This study showed a higher prevalence in males. Previous studies showed similar results. In 1998 Lewallen S [19] published report of a randomized trial of the conjunctival autografting technique for pterygium removal. She documented a lower recurrence rate (21 %) in grafted cases compared with bare sclera technique (37 %). Some studies reported that pterygia occurred in males twice as frequently as in females (Dekaris I) . This observation is probably due to more outdoor activities seen in males.

Age is also important factor in recurrence after conjunctival autografting. The mean age of patients with recurrence in the study by Lewallen was 29 years. While that in the study by Simona was 38 years. These studies showed high recurrence rates of 16% and 35% respectively. In this study, two patients developed recurrence, both were of <40 years age (35 years old male and 40 years old male). This observation is similar to previous findings of Lewallen and Simona. This suggested that lipoid degeneration in the cornea is an inhibiting factor to pterygium growth, based on observation that pterygia do not cross an arcus senilis to any great extent. The presence of lipoid degeneration with age might explain in part the strong association found between age and recurrence. This present study also shows similar high recurrence in males and younger age groups.

On clinical impression, greater inflammation preoperatively led to higher recurrence rate and both the patients in this study who had recurrence had grade III(inflamed, or actively growing pterygia).

Riodan-Eva et al [20] of Moorfields Eye Hospital London supported Lewallen S finding when they reported a statistically significant reduction in recurrence rate following conjunctival autografting for pterygium. They quoted a probability of recurrences of 14 % with this procedure at 36 months after surgery. In 2005 Fahmi et al [21] reported 13.33 % recurrence rate with conjunctival autograft.

Conjunctival grafts including limbal epithelium generally yield better results because it will help to restore its barrier function [22] and the success of conjunctival autografting techniques in treating primary & recurrent pterygia to provide for the limbal stem cell deficiency has been highlighted (Dua,et al) . The recurrence reported by this technique is as low as 5.3% (Kenyon et al, Tan et al). A recurrence rate of 10.9% (Prabhasawat) [13] and 3.8% (David Hui- Kang Ma **)** has been reported for primary pterygium.

The use of Mitomycin-C has been compared with conjunctival autograft and higher recurrence rate after Mitomycin –C (40%) compared to conjunctival autograft (25%) for recurrent pterygium has been noted in our study.

In our study the recurrence rate following Mitomycin-C for primary and recurrent pterygium was 15.0% (primary=6.66%, recurrent=40.0%) and after conjunctival autograft was 6.8% (primary=4.0%, recurrent=25.0%) . Chen et al [23] reported 38% recurrence rate with application of 0.4 mg/ml for 3 minutes (in our study we used 0.2 mg/ml for 5 minutes). While Manning et al [24] reported 10.5%. Sharma et al [25] compared MMC with conjunctival graft and Ma et al [26] postoperative MMC. However these studies failed to show any

difference between MMC and conjunctival autograft. The results of our study reported better results with conjunctival autograft over Mitomycin C.
There was no significant difference between two groups. The results were comparable.

Till date there are no significant sight threatening complications following conjunctival autografting except varying level of discomfort, foreign body sensationtearing and redness for some period in few patients.

Minor complications such as conjunctival epithelial inclusion cysts occurred more frequently in both this and previous studies, which may be caused by embedded conjunctival epithelium underneath the graft or recipient bed. While Mitomycin-C with bare sclera is associated with superficial keratitis.

In summary, we have compared the surgical results of primary and recurrent pterygium removal followed by conjunctuval autograft and Mitomycin-C . We have shown that both these techniques are almost effective (conjunctival autograft, slightly better) in preventing the recurrence of pterygium with no major complications.

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TABLE –I (Original): CLINICAL DATA OF PATIENTS IN BOTH THE STUDY GROUPS

Types			Subtypes			Sex distribution		Site			Extent			Condition of fellow eye			Vascularisation			Surgical procedure	
primary	recurrent	total	Atrophic (grade-I)	Non-atrophic (grade-II)	Inflammed/actively growing (grade-III)	male	female	Nasal	Temporal	Both sides of limbus	Across limbus	Midway between limbus and pupil	Across pupil	pterygium	pingueula	normal	mild	moderate	severe	Conjunctival autograft	Bare sclera with MMC
40 (81.63%)	09 (18.36%)	49 (100%)	13 (26.53%)	28 (57.14%)	08 (16.32%)	30 (61.22%)	19 (38.77%)	44	03	02	17	31	01	36	07	06	14 (28.57%)	27 (55.10%)	08 (16.32%)	29	20

MMC= Mitomycin C

TABLE- II(Original) : AGE DISTRIBUTION

Age {Year}	No. of Cases			Total	%
	g-I	g-II	g-III		
<45 year	0	0	4	4	08.16
46-50 year	0	7	4	11	22.44
51-55 year	0	8	0	8	16.32
56-60 year	7	13	0	20	40.81
>60 year	6	0	0	6	12.24
Total	**13**	**28**	**08**	**49**	**100**

CHART- I(Original) : AGE DISTRIBUTION OF PTERYGIUM

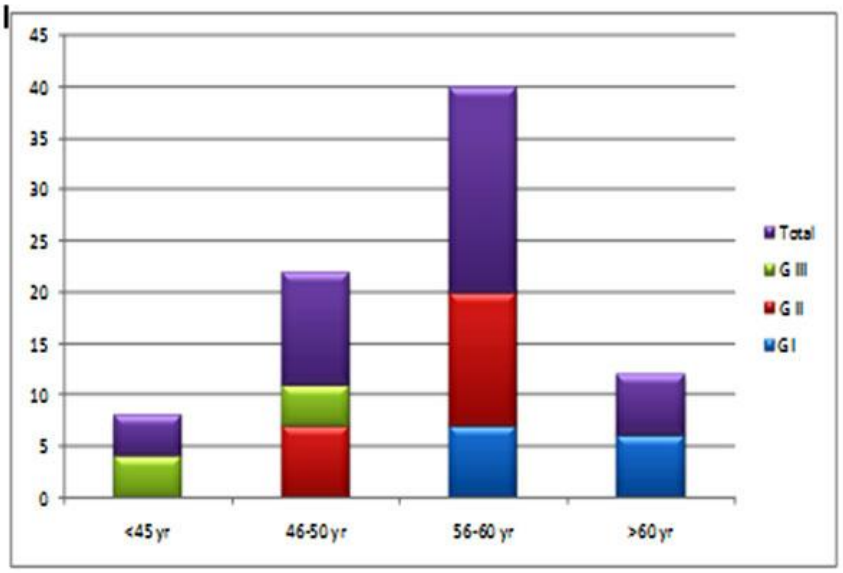

TABLE- III(Original) :RECURRENCE AFTER SURGERY

	Total Cases			Recurrence	% Recurrence	
		P	R			
Conjuctival autograft	29	25	4	02	6.8	P=4.00 R=25.00
Bare sclera with Mitomycin C	20	15	5	03	15.00	P=6.66 R=40.00
TOTAL	49			05		

P= Primary
R=Recurrent

TABLE-IV (Original) : **COMPLICATIONS OF PTERYGIUM SURGERY**

CONJUNCTIVAL AUTOGRAFT			BARE SCLERA WITH MITOMYCIN C	
COMPLICATIONS	NO. OF CASES		COMPLICATIONS	NO. OF CASES
Graft oedema	02		Scleromalacia	01
Loose autograft	00		Scleral ulcer	00
Graft necrosis	00		Perforation	00
Graft retraction	00		Cataract	00
Corneoscleral dellen	00		Neuroscleritis	00
Epithelial cyst	00		Iridocyclitis	00
Sub-conjunctival haemorrhage below graft	02		Glaucoma	00
symblepharon	00		Scleral calcification	00
Muscular disinsertion	00		Lower lacrimal punctual occlusion	00
Corneal thinning	00		Punctuate epithelial keratitis	01
Tenon's granuloma	00			

Photograph –I (Original) **: Ist day post-operative appearance after pterygium excision with conunctival autograft**

Photograph-II (Original) **: one month post-operative appearance of the same patient(pterygium excision with CAG)**

CAG= conjunctival autograft

Photograph-III (Original) **: One month post-operative appearance after bare sclera with mitomycin C**