Comparison of Two Methods for the Treatment of Primary Pterygium: Amniotic Membrane Transplantation plus Intraoperative Mitomycin C, versus Conjunctival Rotational Autograft plus Intraoperative Mitomycin C

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Abstract

***Purpose*:** To compare outcomes and recurrence rates of amniotic membrane transplantation (AMT) plus intraoperative mitomycin C (MMC) and conjunctival rotational autograft (CRA) plus intraoperative MMC in pterygium surgery

***Methods*:** Ninety-two eyes of 92 patients with primary nasal pterygium were enrolled. All patients were randomized to undergo either AMT or CRA. Forty-three patients underwent AMT plus intraoperative MMC (AMT group), and 49 patients CRA plus intraoperative MMC (CRA group). Patients were followed-up at 1 day, 1 week, 2 week, 1, 3, 6, and 12 months postoperatively. The main outcome measurement was a recurrence rate after surgery.

***Results*:** A total of 92 eyes of 92 patients were included in the study. In AMT group 22 patients were male and 21 patients were female. In CRA group 25 patients were male and 24 patients were female (p=0.923). Mean age in AMT group was 46.4 and in CRA group was 47.7 years (p=0.634). Mean pterygium size in AMT group was 3.4 mm and in CRA group was 3.3 mm (p=0.320). Mean follow-up time in AMT group was 10.5 months and in CRA group was 10.8 months (p=0.535). Nine of 43 eyes (20.93%) in the AMT group developed recurrence compared with four of 49 eyes (8.16%) in the CRA group (p=0.145).

***Conclusion*:** Although no statistically significant difference was present between the two groups, however the recurrence rate seems to be clinically less in the CRA group.

***Keywords*:** Pterygium, Amniotic Membrane Transplantation, Conjunctival Rotational Autograft, Mitomycin C

Iranian Journal of Ophthalmology 2014;26(4):193-8 © 2014 by the Iranian Society of Ophthalmology

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Received: November 25, 2014
Accepted: January 20, 2015

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Introduction

Pterygium is a wing-shaped interpalpebral fibrovascular tissue that extends across the bulbar conjunctiva and limbus onto the cornea, most commonly in nasal side.[1]

It is a common disease (5-15% prevalence) with higher prevalence along periequatorial regions,[2] "pterygium belt" latitudes of 37 degrees north and south of the equator[3] supporting an etiological association with ultraviolet (UV) exposure.[2]

The exact pathogenesis of pterygium remains uncertain,[4] but it is possibly associated with UV damage,[2,5] viruses,[6] p53 tumor suppressor gene abnormality,[7] or chronic inflammation[8] hot, dry and smoky environments.[9] It is more common in patients with outdoor occupations like farmers, labourers, and soldiers and less common in patients with indoor activity like housewives and teachers.[10]

Several surgical modalities have been devised for the treatment of pterygium with highly variable success rates in general.[3]

Simple pterygium excision is associated with high rates of recurrence, reported to vary between 29.2% and 88.9%.[11-14]

To improve outcome, various adjunctive modalities have been described with the aim to decrease recurrence rates and complications.[4]

Conjunctival graft variations would include methods such as sliding conjunctival flap, free conjunctival autograft, and conjunctival rotational autograft (CRA).[4]

In CRA method, pterygium and underlying fibrovascular tissue was removed, then conjunctival flap from superior fornix prepared and put over the bare sclera defect with a 180-degree rotation.[4] Recurrence rates of pterygium excision with CRA ranged from 3% to 16.6%.[4,15-17]

Human amniotic membrane has been used as a surgical material since the 1940s.[3] Human amniotic membrane is rich in basement membrane material such as laminin and type-IV collagen. It lacks immunogenicity, has anti-bacterial, anti-inflammatory, and anti-scarring effects.[18] The membrane produces various growth factors including basic fibroblast growth factor, keratinocyte growth factor and epidermal growth factor which can stimulate epithelization and act as promoters of epithelization.[19] Amniotic membrane has a thick collagen layer and an overlying basement membrane with a single layer of epithelium.[3]

Recently, amniotic membrane transplantation (AMT) has been exploited as a new ophthalmic tool for the management of many ocular surface diseases including reconstruction of conjunctival defects after pterygium surgery.[20-22] The effects of the amniotic membrane make this procedure an attractive therapy after pterygium excision.[3]

Another established approach is the addition of mitomycin C (MMC), an alkylating agent that reduces recurrence by inhibiting fibrovascular growth in the subconjunctival space.[4]

The best method for the use of MMC is intraoperative application of this drug.

The objective of this study was therefore, to compare the excision of primary pterygium in terms of frequency of recurrence in 12 months follow-up by CRA plus intraoperative mitomycin C technique versus AMT plus intraoperative mitomycin C.

Methods

In this randomized clinical trial study, patients with primary pterygium that came to ophthalmology clinic for treatment and had indication of surgery, were enrolled.

Patients were excluded if they had more than one head of pterygium, recurrent pterygium, ocular infection and inflammation, glaucoma, previous ocular surgery in the study eye, pregnant and breastmilk women, or systemic diseases such as rheumatoid arthritis or other collagen vascular diseases.

After informed consent, the patients underwent detailed examination including visual acuity with and without correction, intraocular pressure measurement with Goldman tonometer, slit-lamp biomicroscopy, documentation of pterygial size and morphological classification (ie, atrophic, fleshy, or intermediate), and dilated fundoscopy. Morphology was graded according to the relative degree of fibrovascular tissue present in the body of pterygium, obscuring underlying episcleral vasculature under slit-lamp biomicroscopic examination (atrophic-translucent tissue with clear visualization of underlying episcleral vessels; fleshy-the least translucent with

complete obscuration of episcleral vessels; and intermediate-partial episcleral vessel obscuration).

The patients were randomized with block randomization in two groups: 1) AMT+MMC (amniotic membrane transplantation plus intraoperative mitomycin C) 2) CRA+MMC (conjunctival rotational autograft plus intraoperative mitomycin C)

In AMT group 43 eyes from 43 patients and in CRA group 49 eyes from 49 patients were enrolled. All surgeries were performed in Khalili Hospital under topical and subconjunctival anesthesia.

For surgery; in AMT group the head and body of pterygium first were removed by a similar technique in all patients, with resection of the body in front of plica semilunaris. This was followed by removal of subconjunctival fibrovascular tissue beyond the conjunctival edges and polishing of the cornea with a crescent knife. After minimal cauterization of bleeding vessels, 0.02% MMC was applied both on the bare sclera and under the conjunctival edges by using pieces of Weck-Cel surgical sponge soaked in 0.02% MMC solution. Duration of MMC application was one minute for all cases. After the eye surface was washed with 30 mL balanced salt solution, an amniotic membrane was used as a single layer with the stromal side down, attached with 10-0 nylon interrupted sutures with minimal tension to the conjunctival edges to cover the bare sclera.

In CRA group the head and body of pterygium first were removed by a similar technique in all patients, with resection of the body in front of plica semilunaris. This was followed by removal of subconjunctival fibrovascular tissue beyond the conjunctival edges and polishing of the cornea with a crescent knife. After minimal cauterization of bleeding vessels, 0.02% MMC was applied both on the bare sclera and under the conjunctival edges by using pieces of Weck-Cel surgical sponge soaked in 0.02% MMC solution. Duration of MMC application was one minute for all cases. After the eye surface was washed with 30 mL balanced salt solution, superior nasal conjunctiva (1 mm larger than the bare scleral area and adjacent to the bare sclera) was bluntly dissected from the fornix to 1 mm from the limbus. The flap was completed by cutting the limbal area and preserving the inferior limbal anchoring point (1 mm). The flap was rotated and sutured to the bare sclera and conjunctival edges using multiple interrupted 10-0 nylon sutures.

After surgery, all patients received an identical regimen of topical antibiotics (chloramphenicol eye drop) four times daily for two weeks, topical preservative free artificial tear for six weeks and tapering topical steroids for 1.5 months. The latter included 0.1% betamethasone four times daily for three weeks followed by 0.1% fluorometholone thrice daily for one week, twice daily for one week, and once daily for one week. Postoperative follow-up examinations were performed at 1 day, 1 week, 2 week, 1 month, and 3, 6, and 12 months after surgery. Sutures were removed after two weeks in two groups.

Postoperative recurrence of pterygium was reported using a below grading system: this grading included: grade 1 as the presence of fibrovascular tissue in the surgical area but without invasion onto the cornea, grade 2 as the invasion of the fibrovascular tissue on the cornea <1.5 mm and grade 3 as the invasion of the fibrovascular tissue on the cornea >1.5 mm.

Statistical analysis was performed using SPSS software version 15 (SPSS, Inc, Chicago, Illinois, USA). The χ^2 test and Student *t*-test were used to compare qualitative and continuous quantitative variables, respectively, between the AMT and CRA groups. p-values of 0.05 or less were considered to be statistically significant.

Results

A total of 92 eyes of 92 patients were included in the study (43 eyes from 43 patient in AMT group and 49 eyes from 49 patients in CRA group).

The demographic data of patients in both groups are compared in table 1.

There was no significant difference in sex, age, pterygium size and characteristics, follow-up period, and recurrence rate between the AMT group and CRA group.

In AMT group 22 patients were male and 21 patients were female. In CRA group 25 patients were male and 24 patients were female (p=0.923).

Mean age in AMT group was 46.4 and in CRA group was 47.7 years (p=0.634).

Mean pterygium size in AMT group was 3.4 mm and in CRA group was 3.3 mm (p=0.320).

In AMT group 25.6%, 46.5% and 27.9% of all pterygia were atrophic type, intermediate type and fleshy type, respectively and in CRA group 24.5%, 46.9% and 28.6% of all pterygia were atrophic type, intermediate type and fleshy type, respectively.

Mean follow-up time in AMT group was 10.5 months and in CRA group was 10.8 months (p=0.535).

Nine of 43 eyes (20.93%) in the AMT group developed recurrence compared with 4 of 49 eyes (8.16%) in the CRA group (p=0.145).

In follow-up period, in AMT group the most common complication was hemorrhage under AMT that were seen in 16 (37.2%) of all cases. In one case in AMT group retraction of AMT and dehiscence of sutures was seen that in follow-up of this patient no recurrence was detected.

In CRA group the most common complication was graft edema and congestion that were seen in 24.4% of all cases (12 eyes).

Other complications of pterygium surgery and postoperative medication such as pyogenic granuloma formation, rise in intraocular pressure and etc. was not seen in any of our cases.

Table 1. Patients' demographic data and recurrence rate

	AMT group	CRA group	p-value
No. of patients (eyes)	43	49	-
Sex (M:F)	(22:21)	(25:24)	0.923
Mean age (SD)	46.4 (13.5)	47.7 (11.5)	0.634
Range	21-78	22-75	-
Pterygium size (mm)			
Mean (SD)	3.4 mm	3.3 mm	0.320
Range	2-5.2	2-5	-
Pterygium type			
Atrophic	11 (25.6%)	12 (24.5%)	0.904
Intermediate	20 (46.5%)	23 (46.9%)	0.864
Fleshy	12 (27.9%)	14 (28.6%)	0.874
F/U time (month)			
Mean (SD)	10.5	10.8	0.535
Range	(6-12)	(6-12)	-
Overall recurrence	9 (20.93%)	4 (8.16%)	0.145

AMT: Amniotic membrane transplantation, CRA: conjunctival rotational autograft, M: Male, F: Female, F/U: Follow-up, SD: Standard deviation

Discussion

To prevent pterygium recurrence and other complications, various surgical techniques for pterygium have been developed and are continuously being revised.[23] Pterygium surgery should ideally have a low or no recurrence, minimal adverse events, and be cosmetically acceptable.[24]

Recurrence of pterygium onto the cornea after surgical excision is still the most important and frustrating cause of pterygium surgery failure for both surgeon and patient. Therefore, it is still an ongoing debate regarding the "ideal" pterygium surgery technique.[3]

In this prospective randomized study, we compared two techniques for pterygium surgery. In one group AMT+MMC and in other group CRA+MMC, and we compared recurrence rate between two groups. The recurrence rate was 20.93% in AMT group and 8.16% in CRA group.

Higher recurrence rate was found clinically in AMT group compared to CRA group but this difference was statistically insignificant (p=0.145).

Luanratanakorn et al compared the recurrence rate after excision of primary pterygium combined with AMT (148 cases) and conjunctival autograft (106 cases). In the conjunctival autograft group, the recurrence rate was 12.3% and in the amniotic membrane group, the recurrence rate was 25.0%.[6] Recurrence rate in amniotic

membrane group was comparable to our study (20.93%).[25]

Tananuvat et al compared primary pterygium excision and amniotic membrane versus conjunctival autograft transplantation. They reported higher recurrence rate (40.9%) in amniotic membarane transplantation technique compared to conjunctival autograft technique (4.76%).[3]

Prabhasawat et al carried out AMT on 46 patients of primary pterygium and reported recurrence rate of 10.9% that is lower recurrence rate compared to our study result.[20]

Huang et al reported very low recurrence rate (0.79%) in combining application of mitomycin and amniotic membrane transplantation after pterygium resection in 127 cases.[26]

Alvin L Young et al carried out combined CRA and intraoperative 0.02% MMC in the treatment of primary pterygium. They reported less recurrences rate (3%) than our study which is 8.16%.[4]

Kim et al compared conjunctival autograft and anchored conjunctival rotation flap techniques and reported recurrence rate 8.0% in the conjunctival autograft group and 8.6% in the anchored conjunctival rotational flap group (p=0.659)[23] which is similar to our CRA group.

The difference is recurrence rate of our study with some of the above studies may originate from different demographic and racial factor of our patients, difference in geographic region and sunlight exposure, different definition for recurrence and grading system, length of follow-up, and also time or concentration of MMC applied.

In our study we applied the MMC for one minute, maybe if we increase the time of MMC to two minutes, we may achieve even lower recurrence rates. This can be the aim of our future studies.

Conclusion

No statistically difference was found in recurrence rate between the two group of CRA and AMT in our study.

Although recurrence rate was higher in the AMT group clinically, however it has superiority to CRA method in special circumstances. For example when preparation of conjunctival flap is difficult due to conjunctival atrophy and shrinkage, or when dealing with dual head pterygium and ipsibilateral pterygium. Also in cases which may need a future filtering glaucoma surgery, AMT is the superior technique.

Acknowledgement

The authors are grateful to Mrs Narges Rousta (Statistics), for assisting in the statistical analysis.

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