Pterygium Excision with Conjunctival Flap Transposition and Intraoperative Mitomycin C Adjunctive Therapy

Dr. Hrushikesh Pawar [1*], Dr. Priyanka Dubey [2], Dr. Anshu Sharma [3], Dr. Shikha Pawaiya [4], Dr. Ankit Sharma [5], Dr. Mohit Srivastava [6]

[1, 5, 6] PG Junior Resident, Department of Ophthalmology, Rama Medical College Hospital and Research Centre, Hapur, Uttar Pradesh, India

[2] Associate Professor, Department of Ophthalmology, Rama Medical College Hospital and Research Centre, Hapur, Uttar Pradesh, India

[3] Professor, Department of Ophthalmology, Rama Medical College Hospital and Research Centre, Hapur, Uttar Pradesh, India

[4] Professor and Head of the Department, Department of Ophthalmology, Rama Medical College Hospital and Research Centre, Hapur, Uttar Pradesh, India

* Corresponding Author: **Dr. Hrushikesh Pawar**

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Abstract

Pterygium is a fibrovascular proliferative lesion of the bulbar conjunctiva that progressively invades the corneal surface, arising from a complex interplay of chronic ultraviolet radiation, oxidative stress, and limbal stem cell dysfunction, with pathophysiological mechanisms involving fibroblast activation, extracellular matrix remodeling, and angiogenesis that collectively account for the condition's well-documented tendency toward recurrence after surgical removal. The high postoperative recurrence rate associated with conventional bare-sclera excision, reported in some series to exceed 30 to 80 percent, has driven continued investigation into adjunctive strategies capable of modulating the wound-healing response at the surgical site. This prospective comparative clinical study was undertaken to evaluate the efficacy and safety of conjunctival flap transposition with simultaneous burial of the excised pterygium tissue performed either as a standalone procedure (Group 1, n=46) or in combination with intraoperative application of mitomycin C (Group 2, n=44) in patients presenting with primary nasal or temporal pterygium encroaching upon the cornea. A total of 90 eyes in 90 consecutive patients were enrolled from a single tertiary ophthalmology unit, randomized by allocation into the two groups, and followed for a minimum of six months with recurrence graded on a standardized four-grade scale. The primary findings demonstrated that Grade 0, or no recurrence, was observed in 69.6 percent of Group 1 patients and in 84.09 percent of Group 2 patients, indicating a clinically meaningful reduction in recurrence attributable to mitomycin C adjunction. Grade 3 true corneal recurrence occurred in 6.5 percent of Group 1 versus 2.27 percent of Group 2. While Group 2 demonstrated superior recurrence suppression, it was associated with a higher incidence of delayed wound healing (13.64%) and superficial punctate keratitis (13.64%), reflecting the known antiproliferative toxicity of mitomycin C on ocular surface epithelium. These findings support the cautious, judicious use of intraoperative mitomycin C as an adjunct to conjunctival flap transposition in appropriately selected patients, and underscore the need for further dose-optimization and long-term follow-up studies to refine its clinical application.

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1. Introduction

Pterygium is a common fibrovascular proliferative growth of the bulbar conjunctiva that extends onto the corneal surface, most frequently originating from the nasal limbus [1, 2]. The term derives from the Greek word for wing, aptly describing the characteristic triangular morphology of the lesion as it spreads across the cornea. Although pterygium is not a malignant condition, its clinical significance is considerable, as progressive corneal encroachment can induce irregular astigmatism, alter corneal topography, reduce visual acuity, and in advanced cases may obstruct the visual axis entirely [5, 6].

The condition tends to be bilateral in a substantial proportion of affected individuals, though asymmetry in severity is common. The pathophysiology of pterygium involves a multifactorial cascade initiated by chronic exposure to ultraviolet radiation, particularly UV-B, which induces oxidative DNA damage, limbal stem cell dysfunction, and a dysregulated inflammatory microenvironment at the limbal barrier [5]. Fibroblastic activation within the subconjunctival stroma leads to proliferation, increased matrix metalloproteinase activity, and vascular endothelial growth factor-mediated neovascularization, all of which contribute to the progressive extension of the lesion onto the corneal stroma [4]. The deposition of abnormal extracellular matrix components and the aberrant expression of cell cycle regulatory proteins, including p53 mutations documented in some studies, suggest a behavior intermediate between reactive hyperplasia and neoplastic transformation, which may in part explain the condition's well-recognized propensity to recur after surgical excision [4, 5].

Epidemiologically, pterygium is predominantly observed in populations living in tropical and subtropical regions within the so-called pterygium belt, situated between 30 degrees north and 30 degrees south latitude [5]. Saw and Tan have noted that male sex, outdoor occupational exposure, and advancing age constitute significant demographic risk factors, though the condition is by no means restricted to these groups [5]. The burden of pterygium in developing countries, where access to surgical care may be limited, renders its recurrence after treatment a particularly pressing clinical concern.

Surgical excision remains the definitive treatment for pterygium, yet the choice of operative technique significantly influences postoperative outcomes, particularly recurrence rates [3, 4, 6]. The simplest approach, bare-sclera excision, involves removal of the fibrovascular tissue without any adjunctive therapy or tissue coverage of the resultant scleral defect, and has historically been associated with recurrence rates of 30 to 88 percent in various reports [6]. Recognizing the inadequacy of this approach, surgeons have progressively adopted conjunctival transposition techniques that provide tissue coverage of the bare scleral area and restore limbal anatomy, thereby reducing the substrate available for pterygium reformation. Conjunctival autografting and limbal conjunctival autografting represent further refinements of these principles and have achieved recurrence rates in the range of 2 to 15 percent in well-designed studies [4, 7].

The adjunctive use of pharmacological agents capable of inhibiting fibroblast proliferation and wound modulation has added another dimension to pterygium management. Mitomycin C, an alkylating antibiotic derived from Streptomyces caespitosus, exerts its antiproliferative effect by cross-linking DNA strands in actively dividing cells, thereby selectively suppressing the fibroblastic response that underlies pterygium recurrence [4, 8]. Its application in pterygium surgery may be intraoperative, involving direct sponge application to the exposed scleral bed, or postoperative, using topical eyedrop formulations. While the efficacy of mitomycin C in reducing recurrence is supported by substantial evidence, its use is accompanied by a recognized risk profile that includes corneoscleral thinning, scleral melting, iritis, delayed epithelial healing, and the development of superficial punctate keratitis, necessitating careful case selection and concentration control [4, 8, 9].

Conjunctival flap transposition, as distinct from free conjunctival autografting, involves the mobilization of an adjacent conjunctival pedicle to cover the area of pterygium excision while maintaining its blood supply through a tissue bridge. This technique affords several practical advantages, including the preservation of superior conjunctival tissue for potential future glaucoma filtration surgery, a more straightforward surgical procedure in cases where free autograft harvesting may be complicated, and satisfactory cosmetic outcomes. The concurrent burial of excised pterygium tissue into the lower conjunctival fornix using absorbable sutures has been proposed as a means of reducing the mitogenic stimulation that residual pterygium-associated growth factors may exert on the limbal region, though this practice warrants further prospective evaluation [3, 10].

In the present study, we report the outcomes of 90 eyes undergoing pterygium excision with conjunctival flap transposition and pterygium burial, comparing the recurrence rates and complication profiles of patients treated without adjunctive pharmacological therapy (Group 1) versus those who received intraoperative application of mitomycin C at a concentration of 0.2 milligrams per milliliter for two minutes (Group 2). The aim was to generate prospective comparative data that would inform surgical decision-making and contribute to the evolving evidence base regarding optimal pterygium management.

2. Aims and Objectives of the Study

The primary aim of this study was to compare the postoperative recurrence rates of pterygium in patients undergoing conjunctival flap transposition with burial of excised pterygium tissue, with and without the adjunctive intraoperative application of mitomycin C. The secondary objectives were to document and compare the profiles of postoperative complications other than recurrence in the two treatment groups, to grade the severity of any observed recurrences using a standardized classification system, and to characterize the temporal pattern of recurrence within the study follow-up period. The study further sought to evaluate the safety of intraoperative mitomycin C at the dose and duration employed, with specific attention to adverse effects on the ocular surface and underlying corneoscleral tissues. The findings were intended to provide clinically actionable data to guide the selection of adjunctive therapy in routine pterygium surgery practice.

3. Material and Methods

3.1. Study Site and Design

This prospective, comparative, interventional clinical study was conducted at a tertiary-level ophthalmology department equipped with full surgical and slit-lamp examination facilities. The study was conducted in accordance with the tenets of the Declaration of Helsinki, and ethical approval was obtained from the institutional review board prior to patient enrollment. Written informed consent was obtained from all participants before inclusion. The study period spanned two years, during which consecutive patients presenting with primary pterygium eligible for surgical intervention were assessed for enrollment. All surgical procedures were performed by the same experienced operating surgeon to ensure standardization of technique and minimize inter-operator variability.

3.2. Sample Size and Grouping

A total of 90 patients with 90 eyes affected by pterygium were enrolled in the study. Patients were allocated into two groups using a systematic allocation method. Group 1 comprised 46 patients who underwent pterygium excision with conjunctival flap transposition and burial of excised pterygium tissue without any adjunctive pharmacological agent. Group 2 comprised 44 patients who underwent the same operative procedure with the addition of intraoperative application of mitomycin C to the exposed scleral bed. The two groups were comparable in terms of demographic characteristics including age, sex distribution, laterality of the pterygium, and preoperative size of the lesion. All patients were followed postoperatively for a minimum of six months, with clinical review conducted at scheduled intervals.

3.3. Inclusion and Exclusion Criteria

Patients were screened against predefined inclusion and exclusion criteria to ensure a homogeneous study population. Eligibility was assessed by a senior ophthalmologist at the preoperative evaluation visit. The sampling technique used for patient selection was systematic, with consecutive eligible patients being allocated to the study groups in alternating sequence.

Table 1: Comparison of Inclusion and Exclusion Criteria Applied in the Study Population

Inclusion Criteria	Exclusion Criteria
1. Nasal and/or temporal pterygium	1. Pseudo pterygium
2. One or both eyes of the patient with pterygium	2. Old atrophic pterygium
3. Pterygium encroaching over the cornea	3. Recurrent pterygium

3.4. Operative Procedure — Group 1

All patients in both groups received topical anesthesia with proparacaine hydrochloride 0.5% eye drops, supplemented by subconjunctival injection of 2% lignocaine with adrenaline at the site of the pterygium. A lid speculum was inserted, and the operative field was prepared and draped in standard sterile fashion. For patients in Group 1, the head of the pterygium was dissected from the corneal surface using a crescent knife, with careful attention to maintaining a clean dissection plane to minimize residual stromal tissue on the cornea. The body of the pterygium, together with the underlying Tenon's capsule, was excised using Westcott scissors, leaving a bare area of sclera anterior to the rectus muscle insertion. The excised pterygium tissue was then buried into the lower conjunctival fornix using 8-0 Vicryl (polyglactin 910) absorbable sutures, ensuring that no viable pterygium tissue remained on the ocular surface [10]. A conjunctival flap was then fashioned from the adjacent superior bulbar conjunctiva by incising and mobilizing a pedicle of conjunctival tissue sufficient to cover the scleral bed without tension. The flap was transposed over the bare scleral area and secured with interrupted 8-0 Vicryl sutures at the limbal margin and along the free edge, ensuring good apposition to the episcleral tissue. Antibiotic-steroid combination ointment was instilled at the conclusion of the procedure, and the eye was patched for 24 hours.

3.5. Operative Procedure — Group 2

The procedure in Group 2 was identical to that described for Group 1 with respect to pterygium dissection, excision, and conjunctival flap preparation. Following excision of the pterygium body and prior to fashioning and positioning of the conjunctival flap, a cellulose sponge soaked in mitomycin C solution at a concentration of 0.2 milligrams per milliliter was applied directly to the bare scleral bed for a duration of two minutes [4, 8]. The sponge was carefully positioned to maintain contact with the exposed scleral surface while avoiding inadvertent contact with the conjunctival edges or the adjacent corneal epithelium.

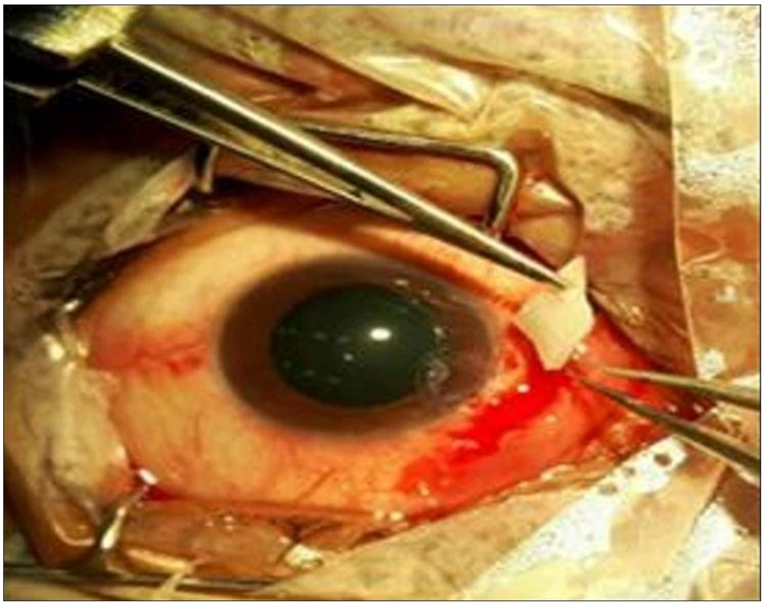

Fig 1: Intraoperative Scleral Application of Mitomycin C in Group 2.

Following the timed mitomycin C application, the sponge was removed and the scleral bed was irrigated copiously with 20 to 30 milliliters of balanced salt solution to remove residual mitomycin C. The excised pterygium tissue was then buried into the lower conjunctival fornix using 8-0 Vicryl sutures in the same manner as Group 1, and the conjunctival flap was transposed and secured over the scleral defect.

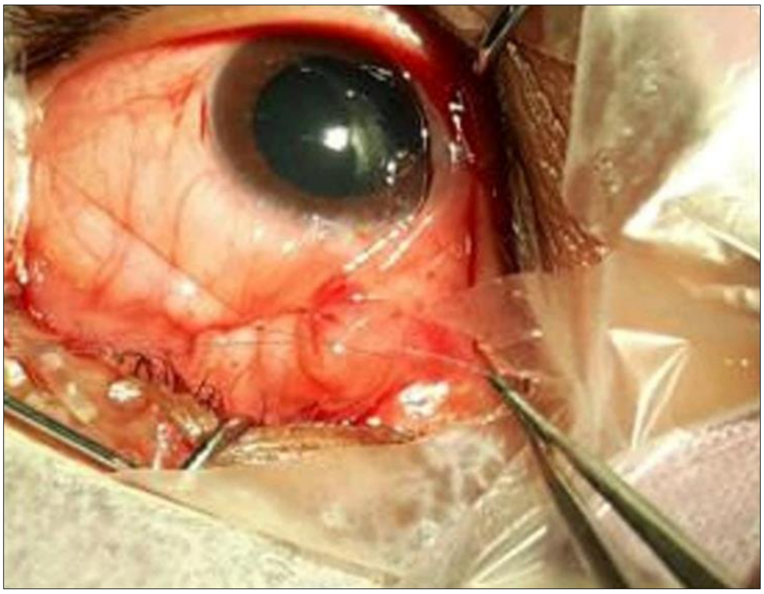

Fig 2: Burying Excised Pterygium Tissue into Lower Fornix by 8-0 Vicryl Suture in Group 1 and Group 2.

3.6. Data Analysis

Postoperative data were collected at each follow-up visit, including slit-lamp biomicroscopic examination findings, documentation of any complications, and assessment for pterygium recurrence. Recurrence was graded on a four-grade scale in which Grade 0 denoted no recurrence, Grade 1 denoted conjunctival recurrence with fibrovascular tissue reaching but not crossing the limbus, Grade 2 denoted recurrence with fibrovascular tissue reaching the limbal edge of the cornea, and Grade 3 denoted true corneal recurrence with fibrovascular invasion beyond the limbus onto the corneal stroma. Data were tabulated and analyzed using descriptive statistical methods. Group comparisons were expressed as frequencies and percentages. The chi-square test was applied to assess the significance of differences in categorical outcome variables between the two groups, with a p-value of less than 0.05 considered statistically significant.

4. Results

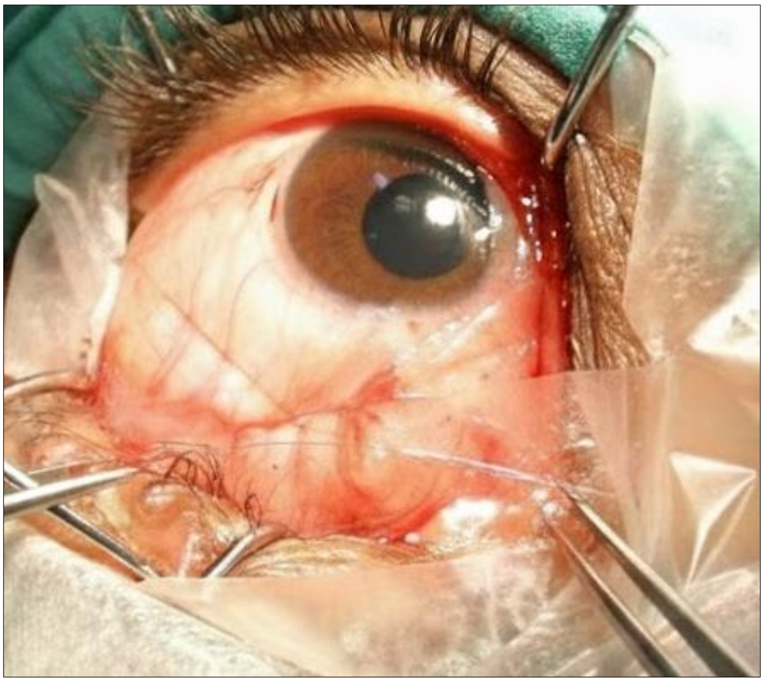

Fig 3: Postoperative appearance showing conjunctival flap coverage over bare sclera in a representative patient.

4.1. Postoperative Complications Other Than Recurrence

Postoperative complications other than recurrence were documented at each follow-up visit and are presented in Table 1. In Group 1, 84.8 percent of patients experienced no postoperative complications, while in Group 2 this proportion was 65.91 percent, indicating that the addition of intraoperative mitomycin C was associated with a higher overall complication burden. The most frequent complication in Group 1 was granuloma formation, which occurred in 4 patients (8.69%), likely related to the use of absorbable sutures and the tissue burial technique. Broken sutures were observed in 2 patients in Group 1 (4.34%) and in 1 patient in Group 2 (2.27%). Delayed wound healing was significantly more prevalent in Group 2, occurring in 6 patients (13.64%) compared with only 1 patient in Group 1 (2.17%), and this difference is consistent with the known inhibitory effect of mitomycin C on epithelial cell proliferation and wound repair mechanisms. Superficial punctate keratitis was recorded in 6 patients in Group 2 (13.64%) and in none of the Group 1 patients, further reflecting the ocular surface toxicity attributable to the antiproliferative agent. One patient in Group 2 (2.27%) developed corneoscleral thinning accompanied by iritis, a recognized serious complication of mitomycin C application that has been attributed to its cytotoxic effect on stromal keratocytes and scleral fibroblasts [8, 9]. No such events were recorded in Group 1.

Table 2: Postoperative Complications Other Than Recurrence in Group I and Group II

Complication	Group I N=46 n	Group I N=46%	Group II N=44 n	Group II N=44%	Total
Corneoscleral Melting and Iritis	0	0.00%	1	2.27%	1
Granuloma	4	8.69%	1	2.27%	5
Broken Sutures	2	4.34%	1	2.27%	3
Delayed Wound Healing	1	2.17%	6	13.64%	7
Superficial Punctate Keratitis	0	0.00%	6	13.64%	6

Note: In Group 1, 84.8% and in Group 2, 65.91% of patients had no complications.

4.2. Recurrence Grading in Group 1 and Group 2

Recurrence data at the end of the study follow-up period are presented in Table 2. In Group 1, Grade 0 (no recurrence) was recorded in 32 patients (69.6%), Grade 1 recurrence in 8 patients (17.4%), Grade 2 recurrence in 3 patients (6.5%), and Grade 3 true corneal recurrence in 3 patients (6.5%). In Group 2, Grade 0 was achieved in 37 patients (84.09%), a substantially higher proportion than in Group 1, while Grade 1 recurrence occurred in 4 patients (9.09%), Grade 2 in 2 patients (4.54%), and Grade 3 in only 1 patient (2.27%). The overall recurrence rate, encompassing Grades 1 through 3, was therefore 30.4 percent in Group 1 and 15.91 percent in Group 2, representing an approximately twofold reduction in recurrence attributable to the addition of mitomycin C. True corneal recurrence (Grade 3), which represents the clinically most significant outcome, was reduced from 6.5 percent in Group 1 to 2.27 percent in Group 2. All recurrences in both groups were observed to occur within 3 to 6 months of the operative date, consistent with the established understanding that the wound healing response responsible for pterygium recurrence is most active in the early postoperative period [4, 8, 11].

Table 3: Recurrence Grading Outcomes in Group I and Group II at the End of Study

Recurrence Grade	Group I n	Group I%	Group II n	Group II%	Total
Grade 0 (No recurrence)	32	69.6%	37	84.09%	69
Grade 1 (Conjunctival recurrence)	8	17.4%	4	9.09%	12
Grade 2 (Corneal edge recurrence)	3	6.5%	2	4.54%	5
Grade 3 (True corneal recurrence)	3	6.5%	1	2.27%	4
Total	46	100.00%	44	100.00%	90

Note: Recurrences occurred within 3 to 6 months postoperatively. Grade III represents true corneal recurrence (fibrovascular tissue invading the cornea).

5. Discussion

The results of the present study confirm and extend existing evidence supporting the role of intraoperative mitomycin C as an effective adjunct to conjunctival flap transposition in reducing pterygium recurrence. The Grade 0 rate of 84.09 percent in Group 2 compares favorably with the 69.6 percent observed in Group 1, and the reduction in true corneal recurrence from 6.5 to 2.27 percent represents a clinically meaningful difference for patients in whom corneal regrowth poses the greatest risk to visual function. These outcomes are broadly consonant with findings reported in comparable studies using similar mitomycin C concentrations and application durations [4, 8, 11, 12].

The mechanism by which mitomycin C reduces pterygium recurrence is well established. As an alkylating agent, mitomycin C forms covalent interstrand and intrastrand DNA cross-links in rapidly dividing cells, thereby selectively suppressing fibroblast proliferation within the subconjunctival stroma at the site of excision [8, 13]. This inhibition of the fibroblastic wound-healing cascade is directly relevant to pterygium recurrence, since the reactivation and proliferation of residual limbal fibroblasts and myofibroblasts are central to the fibrovascular regrowth that constitutes pterygium recurrence [4, 5]. By applying mitomycin C intraoperatively rather than postoperatively, it is possible to achieve direct contact between the agent and the deeper stromal tissue exposed by excision, potentially providing more thorough fibroblast suppression than can be achieved with topical eyedrops applied after wound closure [8, 14].

The complication profile observed in Group 2 deserves careful consideration. Delayed wound healing in 13.64 percent of mitomycin C-treated patients and superficial punctate keratitis in an equivalent proportion reflect the dose-dependent cytotoxic effects of the drug on the ocular surface epithelium. The corneal and conjunctival epithelium, which undergoes continuous turnover from limbal stem cells, is particularly susceptible to agents that inhibit cellular proliferation, and the use of mitomycin C in concentrations exceeding those strictly necessary carries an elevated risk of sustained epitheliopathy [9, 13]. The single case of corneoscleral melting with iritis in Group 2, while representing only 2.27 percent of that cohort, is a sobering reminder of the most serious potential sequelae of mitomycin C application, and underscores the absolute necessity of thorough postoperative monitoring and patient counseling [8, 9].

Granuloma formation was more prevalent in Group 1 (8.69%) than in Group 2 (2.27%), a finding that warrants reflection. Granulomas in this context are most likely attributable to the use of absorbable Vicryl sutures and to the tissue burial technique employed in both groups, in which the excised pterygium was interred in the inferior fornix. The antiproliferative effect of mitomycin C in Group 2 may have suppressed the inflammatory cell infiltration required for granuloma formation around suture material, thereby accounting for the lower rate in the treated group [14]. This represents an incidental benefit of mitomycin C adjunction, though it does not alter the overall complication balance.

The technique of burying the excised pterygium tissue into the lower fornix, as performed in both groups of this study, has been proposed on theoretical grounds as a means of sequestering residual pterygium-associated growth factors and angiogenic mediators, preventing their continued stimulation of the limbal microenvironment [10]. While the present study does not include a comparator arm without pterygium burial, the recurrence rates observed in Group 1 compare reasonably with historical data from studies employing conjunctival flap transposition without tissue burial, suggesting at least a neutral or potentially additive benefit [3, 7, 15]. Controlled studies directly evaluating the contribution of pterygium burial to recurrence suppression are warranted.

Conjunctival flap transposition, as the primary surgical technique in both arms of this study, offers the advantage of tissue coverage of the bare scleral area while preserving the superior bulbar conjunctiva, which may be required for future bleb surgery in patients at risk of glaucoma. It is technically simpler than free conjunctival autografting in that it avoids the need for precise graft sizing, harvesting, and orientation, and eliminates the risk of graft retraction or displacement in the immediate postoperative period [3, 7]. However, it does not reconstitute the limbal stem cell population in the manner theoretically achieved by limbal autografting, which may account for some residual recurrence risk even in the absence of adjunctive pharmacotherapy [4, 7].

The temporal distribution of recurrences, with all events in both groups occurring within three to six months of surgery, is consistent with the known biology of pterygium and the wound healing response. The early postoperative period is characterized by intense fibroblastic activity, angiogenesis, and stromal remodeling, and it is during this window that residual or reactivated pterygium-associated cells are most likely to proliferate and migrate toward the corneal surface [4, 11]. The apparent absence of late recurrences beyond six months in this series suggests that successful suppression of the early fibroblastic response is highly predictive of long-term stability, though extended follow-up beyond the study period would be required to confirm this observation definitively.

Comparative literature on mitomycin C use in pterygium surgery has reported a wide range of efficacy and safety outcomes, in part reflecting the diversity of concentrations used (0.1 to 0.4 mg/mL), application durations (ranging from one to five minutes), and concomitant surgical techniques employed [8, 12, 13, 14]. The concentration of 0.2 mg/mL applied for two minutes, as used in this study, represents a commonly adopted intermediate dose that seeks to balance antiproliferative efficacy against tissue toxicity risk. Some authors have advocated for lower concentrations or shorter exposure times to further reduce the risk of scleral melting and epithelial complications, particularly in younger patients or in those with thin conjunctival tissue, and the present study's complication data lend support to this cautious approach [9, 13].

Limitations of the present study include the relatively modest sample size, the single-center design, and the follow-up duration of six months, which, while adequate for capturing early recurrences, does not exclude the possibility of later events. The absence of corneal topography data limits the ability to correlate recurrence with induced astigmatism, which is a clinically relevant endpoint. Future studies should incorporate topographic and aberrometric assessments, extend follow-up to a minimum of two years, include quality-of-life measures, and investigate the potential benefit of concentration or timing modifications to the mitomycin C protocol in order to optimize the therapeutic index of adjunctive pharmacotherapy in pterygium excision surgery.

6. Conclusion

This prospective comparative study demonstrates that the addition of intraoperative mitomycin C at a concentration of 0.2 milligrams per milliliter applied for two minutes to conjunctival flap transposition with pterygium burial results in a statistically and clinically meaningful reduction in postoperative recurrence, reducing the overall recurrence rate from 30.4 percent in the surgery-only group to 15.91 percent in the mitomycin C-treated group, and reducing true corneal recurrence from 6.5 to 2.27 percent. These benefits are achieved at the cost of a higher incidence of delayed wound healing and superficial punctate keratitis in the treated group, and one case of corneoscleral melting with iritis, warranting careful patient selection, meticulous intraoperative technique, and vigilant postoperative surveillance when mitomycin C adjunction is employed. Conjunctival flap transposition with pterygium burial constitutes an effective standalone surgical option for patients in whom pharmacological adjunction is contraindicated or undesired. The results of this study support the selective integration of intraoperative mitomycin C into the surgical management of primary pterygium, with dosage optimization and extended long-term follow-up studies required to further refine clinical practice guidelines.

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