

Postoperative Subconjunctival Corticosteroid Injection to Prevent Pterygium Recurrence

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Purpose: To report the outcome of postoperative subconjunctival injection of triamcinolone in eyes that underwent pterygium surgery and were at risk for recurrence.

Methods: Twelve eyes of 11 patients with primary (7 eyes) or recurrent (5 eyes) pterygia underwent excision and conjunctival autografting (4 eyes, 33.3%), amniotic membrane grafting (6 eyes, 50%), or both (2 eyes, 16.6%). All of these eyes had signs that were considered to be risk factors for recurrence (conjunctival inflammation, hemorrhage, granuloma, and fibrovascular proliferation); accordingly, they also underwent subconjunctival injection of triamcinolone.

Results: Among the 11 patients, there were 8 (72.7%) men and 3 (27.3%) women; the mean age was 41 years (range, 20–56 years). In 5 (41.7%) eyes, the pterygium was graded as T2 (intermediate) and in 7 (58.3%) eyes was graded as T3 (fleshy). The time between surgery and the first injection ranged from 2 to 5 weeks (mean, 3.4 weeks), and 1–3 injections were necessary (mean, 1.7) to achieve the desired effect. After injection, 1 (8.3%) eye developed inflammation, and 2 (16.7%) eyes from another patient developed intraocular hypertension that was controlled with a topical β -blocker. The follow-up after the last injection ranged from 8 to 36 months (mean, 14.5 months); only 1 recurrence (grade 3) occurred during this period.

Conclusions: The postoperative use of subconjunctival triamcinolone seems to benefit patients at increased risk of pterygium recurrence. It is relatively safe and is accompanied by few complications, but controlled and prospective studies are necessary to confirm its efficacy.

Key Words: pterygium, corticosteroids, subconjunctiva, recurrence (*Cornea* 2008;27:406–410)

Many techniques have been described for pterygium surgery, with the variation of recurrence rates ranging from 0% to 89%. The safest technique, and with better results, is conjunctival autografting, first described by Kenyon and

Tseng in 1989, with a recurrence rate ranging between 2% and 40%.^{1,2}

More recently, antimetabolic substances, such as mitomycin C and 5-fluorouracil, have been successfully used after pterygium excision to prevent its recurrence. Nevertheless, complications have been reported, especially when topical mitomycin C was used.³

Since 1995, amniotic membrane grafting has been used as an option to treat various ocular surface diseases.⁴ Tseng and Tsubota⁵ reported good results by using amniotic membrane for conjunctival surface reconstruction after symblepharon and removal of other conjunctival lesions. In 1997, Prabhasawat et al⁶ compared the results of amniotic membrane grafting, simple excision, and conjunctival autografting for primary pterygium and reported recurrence rates of 10.9%, 45%, and 2.6%, respectively. As for recurrent pterygium, those authors reported a recurrence rate of 37.5% for amniotic membrane grafting and 9.1% for conjunctival autografting. In another article, after a modification of the surgical procedure that included extensive removal of pterygial tissue and subconjunctival depot corticosteroid injections during and after surgery, the same group reported better results in eyes that underwent amniotic membrane grafting, with recurrence rates of 3.0% and 9.5% for primary and recurrent pterygium, respectively.⁷

Corticosteroids, such as prednisolone, dexamethasone and fluorometholone, have been topically used in the postoperative management of pterygium and for halting the progression of impending recurrence. They can also be administered through other means, such as subconjunctival injections. There are two types of injectable corticosteroids: the short-duration ones, such as dexamethasone, and long-lasting depot corticosteroids, such as triamcinolone and hydrocortisone. The latter are water-soluble substances that sustain their action for 15–21 days. The most used drugs are dexamethasone, triamcinolone, and hydrocortisone, and there is no evidence of different efficacy among them in the treatment of external eye diseases, such as vernal keratoconjunctivitis.⁸

In ophthalmology, depot injectable corticosteroids have been used intravitreally in the treatment of bacterial and fungal endophthalmitis, retinal neovascularization, proliferative vitreoretinopathy, and posterior uveitis, and they have been used after vitreoretinal surgery; in the subtenon space, they have been used for the treatment of macular edema, and subconjunctivally, they have been used in the treatment of refractory vernal keratoconjunctivitis and nonnecrotizing anterior scleritis.

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More recently, some authors have reported their use in eyes with endothelial immune reactions after penetrating keratoplasty.⁹⁻¹⁵ Nevertheless, the use of subconjunctival corticosteroids to prevent pterygium recurrence has not been well explored.

The purpose of the study described herein was to evaluate the effectiveness of the use of subconjunctival triamcinolone to prevent or treat initial recurrences in eyes that underwent pterygium excision combined with conjunctival autografting and/or amniotic membrane grafting.

MATERIALS AND METHODS

Patients

This prospective consecutive interventional case series study was approved by the ethics committee of the Federal University of São Paulo, Brazil. Twelve eyes of 11 patients with pterygium were subjected to a complete ophthalmologic evaluation; this included visual acuity and intraocular pressure measurements, as well as slit-lamp and fundus examinations. All patients had a preoperative clinical evaluation and signed an informed consent about the treatment that they were going to receive. The pterygia were graded according to the classification reported by Tan et al¹⁶ (Table 1): T1 (atrophic), a lesion with unobscured and clearly distinguishable episcleral vessels underlying its body; T2 (intermediate); T3 (fleshy), a thick pterygium in which episcleral vessels underlie its body and are obscured totally by fibrovascular tissue.

Inclusion criteria included patients who had undergone pterygium excision and whose lesion was graded as T2 or T3. Exclusion criteria included corneal epitheliopathy, persistent corneal epithelial defect, bullous keratopathy, limbal deficiency, preexisting glaucoma, and noncompliance with the study regimen. All patients were informed regarding the potential side effects of the medications.

Preparation and Preservation of Amniotic Membrane

Human amniotic membrane was prepared and preserved by using the method proposed by Kim and Tseng,¹⁷ with some modifications. The human placenta was harvested at the time of cesarean delivery after obtaining informed consent from the donors, each of whom had serology tests that were negative for hepatitis B and C viruses, syphilis, and human immuno-

deficiency virus. Under sterile conditions, the amnion was separated from the chorion by blunt dissection and washed with a phosphate-buffered saline solution containing penicillin (1000 U/mL), streptomycin (20 µg/mL), and amphotericin B (2.5 µg/mL). The membrane was stored at -80°C in a sterile vial containing glycerol and modified Dulbecco Modified Eagle Medium (1:1; Ophthalmos, São Paulo, Brazil).

Surgical Techniques

The surgeries were performed by 1 surgeon (J.A.P.G.). All patients underwent regional anesthesia with a peribulbar injection of 4 mL of Marcaine 0.5% (Marcaína 0.5%; Astra Química, São Paulo, Brazil) and 4 mL of 2% lidocaine without vasoconstrictor (Xilocaína 2%; Astra Química). Two drops of an adrenaline dilution of 1:10,000 were instilled in the eye before surgery to induce conjunctival vasoconstriction. A corneal traction suture at the 12 o'clock limbus was placed to provide good control of positioning of the globe during the procedure. With the use of a forceps and a no. 15 blade, a cleavage plane was dissected between the head of the pterygium and the cornea. From this plane, the pterygium was dissected toward its body, up to the limbus. With a Westcott scissors and a 0.25-mm forceps, the subconjunctival fibrovascular tissue underlying the pterygium was dissected from the pterygium body and scleral bed; it was resected by exerting gentle traction with the forceps to improve its exposure. Finally, the pterygium body was resected, as was a thin strip of normal conjunctiva above and below the pterygium. The excised fragments were fixed in 10% formaldehyde and submitted for histopathologic analysis.

Grafts

Amniotic Membrane

After being thawed, the amniotic membrane was placed over the exposed area, maintaining the initial orientation, with the epithelium facing upward. The tissue was fixed to the episclera and adjacent conjunctiva by using interrupted or continuous 10-0 nylon sutures.

Conjunctival Autografting

The globe was rotated inferiorly to expose the superior bulbar conjunctiva. With the use of a 0.12 forceps and a Westcott scissors, a thin, tenon-free conjunctival graft was obtained starting 1 mm from limbus. This tissue was transferred to the recipient area and fixed to the episclera

TABLE 1. Grading Primary and Outcome After Pterygium Excision

Pterygium	Grade	Characteristic
Primary	T1 (atrophic)	Lesion with unobscured and clearly distinguished episcleral vessels underlying its body
	T2 (intermediate)	
	T3 (fleshy)	Thick pterygium in which episcleral vessels underlying its body were totally obscured by fibrovascular tissue
Recurrent	1	Normal appearance of the operated site
	2	Presence of fine episcleral vessels in the excised area, extending to the limbus but without any fibrous tissue
	3	Fibrovascular tissue in the excised area, reaching the limbus but not the cornea; it means conjunctival recurrence
	4	True corneal recurrence with fibrovascular tissue on the cornea

and conjunctiva with 10-0 nylon continuous or interrupted sutures. Determination of the graft size was from the measurement of the scleral bed after pterygium excision. We usually oversized the graft by 1 mm for a better fit on the scleral recipient bed.

Postoperative Period

Postoperatively, all patients were treated with 0.1% dexamethasone acetate and 0.3% tobramycin (Tobradex; Alcon, São Paulo, Brazil) every 4 hours. This regimen was tapered beginning 7 days after surgery and was stopped by 60 days after surgery.

Recurrence Evaluation

We followed the grading system of Prabhasawat et al,⁶ which classifies pterygium excision outcome from grades 1 to 4 (Table 1): Grade 1 indicates a normal appearance of the operated site; grade 2 indicates the presence of fine episcleral vessels in the excised area, extending to the limbus but without any fibrous tissue; grade 3 indicates fibrovascular tissue in the excised area, reaching to the limbus but not invading the cornea and significant conjunctival recurrence; and grade 4 indicates a true corneal recurrence with fibrovascular tissue invading the cornea.

Subconjunctival Injection

Patients who manifested a pterygium excision outcome of grade 2 or more underwent subconjunctival corticosteroid injections to control the recurrent pterygium (Figs. 1 and 2).

At the slit lamp, a drop of topical anesthetic (Proxymetacaine 1%–Anestalcon 1%; Allergan, São Paulo, Brazil) was instilled. By using a 5-mL syringe with a 30-gauge needle, we performed 6–8 applications of subconjunctival corticosteroid around the graft site for a total of 0.2–0.4 mL. Risk factors, including subconjunctival hemorrhage, hyperemia, granuloma, fibrosis, neovascularization, inflammation, and further recurrence, were evaluated; if needed, treatment was repeated 3 times, with an interval between applications of at least 2 weeks. The endpoint was the absence of recurrence

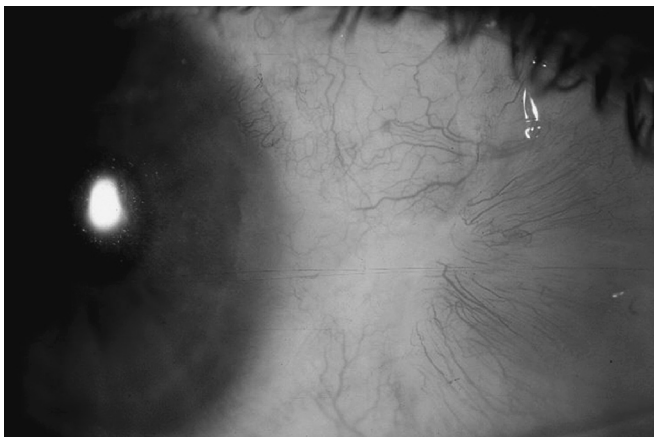


FIGURE 1. Right eye of patient 3 showing pterygium recurrence of grades 2–3. Note the presence of fine episcleral vessels in the excised area, which reach the limbus but do not invade the cornea.

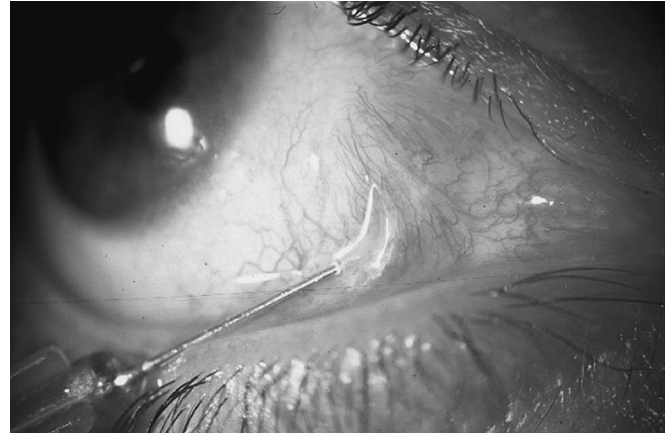


FIGURE 2. Technique of application of the corticosteroid injection to prevent pterygium recurrence. Four to 6 applications, each containing ~0.3 mL of the corticosteroid, are made subconjunctivally around the amniotic membrane graft. The injections can be performed under topical anesthesia at the slit lamp.

and control of inflammation. The corticosteroid used was 20 mg/mL triamcinolone acetonide (Theracort; TheraSkin, São Paulo, Brazil) and, when triamcinolone was not available, 40 mg/mL methylprednisolone acetate (Depo-Medrol; Pharmacia, São Paulo, Brazil) or 8 mg/mL dexamethasone acetate with 8 mg/mL dexamethasone phosphate 2 mg/mL (Duo-decadron; Aché, Guarulhos, Brazil) was used.

RESULTS

Data are presented in Table 2. Twelve eyes of 11 patients (8 men and 3 women), with a mean age of 41 years (range, 20–56 years), were included in this study. Seven eyes had a primary pterygium, among which 1 eye had a double-headed pterygium. The other 5 eyes had recurrent pterygium. Eleven eyes had a nasal pterygium, and 1 eye had a temporal pterygium. Seven eyes were graded as T3 (fleshy), 5 as T2 (intermediate), and none as T1 (atrophic).

The surgical technique used was pterygium removal with conjunctival autografting in 4 eyes, amniotic membrane grafting in 6 eyes, and conjunctival autografting combined with amniotic membrane grafting in 2 eyes.

At the time of the first treatment, 6 eyes had a pterygium excision outcome of a grade 2, and 5 eyes had conjunctival recurrence (grade 3). One eye had fibrosis that required resection at the slit lamp. Other complications encountered before the injections were subconjunctival hemorrhage (3 eyes), hyperemia (3 eyes), granuloma (3 eyes), fibrosis (2 eyes), neovascularization (4 eyes), and inflammation (4 eyes).

Follow-up I (time between surgery and the first subconjunctival injection of corticosteroid) ranged from 2 to 5 weeks (mean, 3.4 ± 0.8 [SD] weeks). At the time of initial injection, a recurrence or a risk of recurrence was noted. It took 1–3 injections (mean, 1.7 ± 0.9 injections) until control of the recurrence. All patients received at least 1 injection of triamcinolone. Patient 2 also received 2 injections of methylprednisolone, and patient 4 also received 2 injections of

TABLE 2. Clinical Description and Outcome of the Use of Subconjunctival Corticosteroid Injection to Prevent Pterygium Recurrence

Case	Sex	Age (y)	Eye	Pterygium Characteristics	Surgical Technique	Recurrence and PO Complications	Type of Depot Steroid Used	Time Between Surgery and First Injection (wks)	Time Between Last Injection and Last Examination (mo)	Complications	G4 – Corneal Recurrence
1	Male	20	OD	Iry, N, S, T3	ACT	SC. Hemor., Granuloma, G2	Triamcinolone 1×	5	18	—	No
2	Female	26	OS	Rec., N, L, T3	AMT	Hyperemia, G2	First methylprednisolone 3 weeks Second methylprednisolone 5 weeks Third triamcinolone 24 weeks	3	12	—	No
3	Female	49	OS	Rec., N, M, T3	ACT	Fibrosis, G2	First triamcinolone 3 weeks Second triamcinolone 22 weeks + fibrosis resection	3	18	—	No
4	Male	44	OD	Iry, N and T, M, T2	AMT	Neovasc., Hyperemia, G3	First dexamethasone 2 weeks Second dexamethasone 4 weeks Third triamcinolone 9 weeks	2	10	—	No
5	Male	40	OS	Iry, T, M, T3	AMT	Granuloma, Infl., Neovasc., G2	One triamcinolone injection	3	36	—	No
6	Female	49	OS	Rec., N, M, T2	ACT	Granuloma, Neovasc., G2	One triamcinolone injection	4	11	Infl.	No
7	Male	52	OD	Rec., N, M, T2	ACT + AMT	Fibrosis, Infl., Neovasc., G2	One triamcinolone injection	3	8	—	No
8	Male	46	OS	Rec., N, L, T2	ACT + AMT	Infl., SC Hemor., Hyperemia, G2	One triamcinolone injection	3	12	—	No
9	Male	35	OD	Iry, N, L, T2	AMT	Infl., SC Hemor., G3	First triamcinolone 1 week Second triamcinolone 8 weeks Third triamcinolone 14 weeks	4	15	—	No
10	Male	38	OD	Iry, N, L, T3	AMT	G3	One triamcinolone injection	4	14	↑ IOP	No
11	Male	38	OS	Iry, T, M, T2	AMT	G3	First triamcinolone 3 weeks Second triamcinolone 8 weeks	3	11	↑ IOP	No
12	Male	55	OD	Iry, N, M, T3	ACT	Infl., G3	One triamcinolone injection	4	9	—	No

Iry, primary; Rec., recurrent; N, nasal; T, temporal; S, small; N, medium; L, large; T1, atrophic; T2, intermediate; T3, fleshy; ACT, autologous conjunctival transplantation; AMT, amniotic membrane transplantation; G1, normal appearance of the operated site; G2, fine episcleral vessels in the excised area, extending to the limbus, but without fibrosis; G3, fibrovascular tissue in the excised area, reaching to the limbus, but not invading the cornea; G4, true corneal recurrence with fibrovascular tissue invading the cornea; SC Hemor., subconjunctival hemorrhage; Infl., inflammation; Neovasc., neovascularization; IOP, intraocular pressure.

dexamethasone. After the injection, 1 patient displayed local inflammation and another had ocular hypertension in both operated eyes; the ocular hypertension was controlled with topical medication, and there was no progression to glaucoma after >1 year of follow-up.

Follow-up II (time after the last corticosteroid injection) ranged from 8 to 36 months (mean, 14.5 ± 7.5 months), and a recurrence of fibrovascular tissue in the cornea (grade 4, corneal recurrence) was not observed in any case. Nevertheless, we had 1 case of recurrence of fibrovascular tissue that extended to the limbus (grade 3, conjunctival recurrence).

DISCUSSION

The etiopathology of the pterygium is multifactorial and may be related to a chronic injury of the limbus by ultraviolet radiation, actinic keratoconjunctivitis, limbal deficiency, human papillomavirus, or genetic factors. Solomon et al showed that fibroblasts isolated from the pterygium body exhibit a phenotype identical to that of transformed or neoplastic cells. These cells can proliferate and contribute to pterygium progression or pterygium recurrence if they are stimulated by proinflammatory cytokines, dryness, or environmental insults, such as exposure to ultraviolet radiation.^{18,19}

Options for the treatment of pterygium remain under study. Although many approaches for definitive treatment have been described, such as excision with bare sclera, sliding conjunctival flaps, excision with adjunctive therapies (β irradiation, mitomycin C administered intraoperatively and postoperatively), conjunctival or limbus-conjunctival grafting, amniotic membrane grafting, lamellar keratoplasty, buccal mucous membrane grafting, phototherapeutic keratectomy with excimer laser, and the use of angiostatic steroid components, no technique has been reported to be completely safe or completely effective.²⁰

The recurrence of a pterygium is a difficult complication to avoid, especially in cases in which the pterygium is already recurrent or if the lesion is large and inflamed.²¹ Often, the recurrence cannot be controlled with the use of topical corticosteroids alone. In this study, we included a series of patients who underwent pterygium removal and conjunctiva and/or amniotic membrane grafting and who underwent 1 or more subconjunctival injections of a depot corticosteroid to prevent recurrence of the pterygium.

The risk of recurrence is increased by factors such as inflammation, vascularization, fibrosis, and edema,¹⁷ although other intraoperative and postoperative complications also contribute to an increased risk of recurrence. In our study, the more prevalent postoperative complications were neovascularization and inflammation.

Solomon et al⁷ reported a decreased incidence of pterygium recurrence after surgery and amniotic membrane grafting, after a few modifications were made to their technique. These modifications included extensive surgical removal of the lesion and corticosteroid injections given both intraoperatively and postoperatively. In this study, the corticosteroid injection was performed in those cases that exhibited inflammation and other clinical findings suggestive of an initial recurrence (grade 2 or 3). The injection was repeated in those cases in which inflammation persisted, but always within the first 6 months after surgery. No patient developed a corneal recurrence, suggesting that the treatment was effective. The first injections were performed at a mean of 3.4 weeks after surgery. This early injection seems to be important in the control of inflammation at the initial stages, thereby preventing pterygium recurrence. Two eyes that underwent corticosteroid injections developed ocular hypertension, although this was controlled with the use of a topical β -blocker and did not progress to glaucoma.

In a recently reported study, 5-fluorouracil was superior to triamcinolone in precluding pterygium recurrence.²² In that study, the authors injected the substance in the area of the lesion. In our study, we performed the injection in the area surrounding the graft, where the feeder vessels were most prominent; this change might explain the difference in the results.

In conclusion, the use of subconjunctival corticosteroids seems to be an efficient and relatively safe method to prevent the recurrence of a pterygium. Controlled and prospective studies, however, are necessary to better evaluate this treatment.

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