Role of Post-Operative Topical Corticosteroids in Recurrence Rate after Pterygium Excision with Conjunctival Autograft

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Abstract

Background : Recurrence of pterygium is the most common failure of the pterygium operation. The use of conjunctival autograft after pterygium excision has shown a low recurrence rate. However, it has a board range of variations regarding the recurrence rates, which may be influenced by many factors. From the authors' clinical observation, it was found that the recurrence rate was higher in patients who received inadequate post-operative topical corticosteroid treatment.

Objective : To study the association between adequacy of post-operative topical corticosteroids and recurrence rate in patients with primary pterygium who underwent excision with conjunctival autograft.

Design : Retrospective, case-control study.

Subjects and Method : A total of 142 eyes of 137 patients with primary pterygium who underwent excision with conjunctival autograft between January 1996 and June 2002 were enrolled in this study. These patients were evaluated for recurrence of their pterygia and adequacy of post-operative topical corticosteroids by chart review, re-examination, self-reported questionnaire, and interview. Cases were patients with recurrent pterygium. Controls were from patients without recurrence.

Results : There were 21 recurrences (14.8%) of a total of 142 eyes treated. Five of the 21 recurrences occurred in good compliant patients with adequate post-operative topical corticosteroid therapy. Sixteen recurrences occurred in patients with inadequate post-operative topical corticosteroids. In this group, 6 cases missed their follow-up schedules, 3 cases were lost to follow-up after 1.5-2 months, 1 case had poor compliance with treatment, and 6 cases were steroid responders then the treatment was discontinued or changed to a weaker preparation. The study demonstrates significant association between the adequacy of post-operative topical corticosteroid and pterygium recurrence rate. The odds ratio was 190.4 (95% CI, 36.61-951.84).

Conclusions : A high recurrence rate was found in patients who received inadequate post-operative topical corticosteroid. However, the recurrence rate was much lower from 14.8 per cent to 4

per cent when the patients with inadequate corticosteroid therapy were excluded. The study provides evidence that post-operative topical corticosteroids appear to play a role in reducing the pterygium recurrence rate.

Key word : Pterygium, Conjunctival Autograft, Topical Corticosteroids

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Pterygium is a wing-shaped fibrovascular growth of the conjunctiva which invades onto the cornea. There is a strong suggestion of a causal relationship between exposure to ultraviolet light and the prevalence of pterygium[1-5]. It is commonly found in the periequatorial and tropical regions. Thailand is located at the latitude (parallel) of 15 degrees north of the equator with strong sunlight and hence ultraviolet radiation[6]. Pterygium is a common eye disease in Thailand with a prevalence of 10 per cent [7]. Although pterygium is a benign condition, it causes disfigurement, eye irritation, dry eye, inflammation, irregular corneal astigmatism, and decreased vision when its growth occludes the optical axis. In these cases, surgical removal is recommended[8-11]. There are many options of surgical treatment. The simplest technique is bare sclera excision. However, its result is mostly unsatisfactory because of a high rate of recurrence of between 20-69 per cent[12-15]. To prevent recurrence, adjunctive therapies are usually performed including beta irradiation with strontium 90, application of mitomycin C, conjunctival autograft, limbal autograft, sliding conjunctival flap, lamellar keratoplasty, and amniotic membrane transplantation[16-28].

The use of free conjunctival autograft to cover the bare sclera after pterygium excision has shown satisfactory outcomes without serious complications. The current technique of conjunctival autograft transplantation was described by Kenyon in 1985 with its impressively low rate of recurrence (5.3%) [19]. The technique is now considered the gold standard to which other procedures are benchmarked[29]. However, there is a wide variation of recurrence rates using this technique among different surgeons, ranging from 2 to 39 per cent[30]. The variation of success rates of conjunctival autografting may be contributed to the following factors, namely, personal differences in performing the surgical technique, surgeon's skills, post-operative inflammation, pterygium morphology, patient's age, patient's lifestyle, and geographical variations[31-33].

From the clinical observations of the authors, despite use of the standard technique of conjunctival autografting in patients with primary pterygium, the recurrence rate is still higher in patients who received inadequate post-operative topical corticosteroid therapy. It seems reasonable to hypothesize that post-operative topical corticosteroids may play a role in reducing the recurrence rate of pterygium. This correlation has never been reported in any previous clinical study. Therefore, this retrospective study was conducted on patients with primary pterygium who underwent excision with conjunctival autograft to study the association between the adequacy of post-operative topical corticosteroid therapy and the pterygium recurrence rate.

SUBJECTS AND METHOD

Using the medical records of 144 consecutive patients with primary pterygium who underwent pterygium excision with conjunctival autograft at the Department of Ophthalmology, King Chulalongkorn Memorial Hospital between January 1996 and June 2002, a case-control study was conducted. All operations were performed by one surgeon (SY) using the

same surgical technique as described below. Patients with less than 6 months of follow-up period were scheduled for re-examination to assess the recurrence. At the same time, the patients were asked to respond to a self-reported questionnaire on their compliance together with in-depth interview. Six of the patients could not attend for re-examination and hence were excluded. One patient was excluded because he had major systemic disease. A total of 142 eyes of 137 patients were enrolled in this study.

Cases were patients with recurrent pterygium. Controls were patients without recurrence. The grading of the post-operative final outcomes was documented during the last visit based on the grading scale of 1 to 4 as previously described by Prabhasawat et al[34]. Only patients with true corneal recurrence (grade 4) were classified as recurrence.

Grade 1 : Normal appearance of the operated site.

Grade 2 : Presence of fine scleral vessels in the excised area, extending to the limbus, but without any fibrous tissue.

Grade 3 : Fibrovascular tissue in the excised area, reaching the limbus but not invading the cornea.

Grade 4 : True corneal recurrence, with fibrovascular tissue invading the cornea.

Surgical technique of pterygium excision with conjunctival autograft

The operations were performed under an operating microscope as outpatient treatment. Topical and subconjunctival anesthesia were applied in all patients. The detailed technique of pterygium excision and conjunctival autograft have been previously described[19]. In brief, a thin, Tenon's free conjunctival graft is obtained from the superior bulbar conjunctiva close to the limbus. The graft is sutured in place with 8-0 Vicryl interrupted sutures. The area of the graft is left with Tenon's capsule exposed. The eye is pressure patched for 24 hours, followed by firm patch with daily changes for 3-5 days. The sutures are removed 2-3 weeks after the operation.

Post-operatively, all patients received a similar regimen of topical corticosteroids (Pred-Forte, 1% prednisolone acetate) and topical antibiotics (chloramphenicol) four times daily for a period of 1 month. They were subsequently replaced with combinations of 0.1 per cent dexamethasone and chloramphenicol eyedrop four times daily for 2 months until the conjunctival graft and the surrounding conjunctiva were no longer injected. The dosage could be slightly adjusted, based on the inflammatory response of the patients. The patients were followed at 1 week, 2-3 weeks for suture removal, 2 months, 3 months, and 6 months after surgery. At each visit, the visual acuity, autorefraction, intraocular pressure, slit lamp examination for the presence or absence of the recurrence, injection, other complications, and patient's compliance with post-operative treatment were noted.

The adequacy of post-operative topical corticosteroids used in each patient was assessed by chart review, re-examination, self-reported questionnaire, and interview. The adequacy of post-operative topical corticosteroids therapy was defined as patients who received topical corticosteroids four times daily for a period of 3 months with good compliance until the conjunctival graft and the surrounding conjunctiva were no longer injected. The inadequacy of the therapy was defined as patients who received topical corticosteroids for 2 months or shorter, since at that time the conjunctiva was still injected.

The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University.

Statistical analysis

The statistical analysis was performed under Stata 6.0 program (Texas, USA). The odds ratio with 95 per cent confidence interval was calculated to estimate the association between the case and the control groups.

RESULTS

The pre-operative demographic characteristics of the patients are summarized in Table 1. Every patient was followed-up for a minimum of 6 months. The range of the follow-up was from 6 to 83 months, with an average time (SD) of 33.7 (21.05) months.

The grading of the post-operative final outcomes at the last follow-up is listed in Table 2. Overall, 21 out of 142 eyes (14.8%) were found to have true corneal recurrence (grade 4).

Of the 21 recurrences, 5 occurred in good compliant patients who received adequate post-operative topical corticosteroid therapy. Sixteen recurrences occurred in patients wi th inadequate post-operative topical corticosteroid therapy. Among these, 6 cases missed their follow-up appointments after 1-2 bottles of topical corticosteroids were prescribed post-operatively and came back when their recurrences were noted; 3 cases were lost to follow-up after 1.5-2 months; 1 case had poor compliance with treatment;

Table 1. Pre-operative demographic data of 137 patients.

		%
Total number of eyes	142	
Right eye	63	44.4
Left eye	79	55.6
Gender		
Female	96	70
Male	41	30
Age (years)		
Range	17-77	
Mean (SD)	50.6 (13.12)	

Table 2. Grading of the post-operative final outcomes of pterygium excision with conjunctival autograft at the last follow-up.

Grading of the final outcomes	No. of eyes	%
1	63	44.4
2	44	30.9
3	14	9.9
4	21	14.8

and 6 cases had increased intraocular pressure after 1-2 bottles of topical corticosteroids, the medication was then discontinued or changed to a weaker, fluorometholone 0.1 per cent (Table 3). All recurrent pterygia were small, thin, flat, and uninflammed. Only one case required subsequent surgical removal. There was no post-operative complication in this study.

In the nonrecurrence group, 119 cases had evidence of using adequate topical corticosteroids with good compliance. Only two cases had evidence of poor compliance, since they used only one bottle of prednisolone acetate post-operatively and missed their follow-up appointments thereafter.

From these results, the patients can be categorized into 4 groups according to the adequacy of topical corticosteroid used as follows:

Group A : Inadequate topical corticosteroids with recurrence (16 eyes)

Group B : Inadequate topical corticosteroids without recurrence (2 eyes)

Group C : Adequate topical corticosteroids with recurrence (5 eyes)

Group D : Adequate topical corticosteroids without recurrence (119 eyes)

Patients in groups A and C were recurrence group. The age range of these groups was 17 to 77 years, and the mean age (SD) was 44.6 (15.43). Patients in groups B and D were nonrecurrence groups and used as control subjects. The age range of the nonrecurrence group was 23 to 77 years, and the mean age (SD) was 50.8 (12.54).

This study demonstrates significant association between the adequacy of post-operative topical corticosteroid used and the recurrence rate of pterygium. A high recurrence rate was found in patients with inadequate post-operative topical corticosteroid treatment. The odds ratio was 190.4 (95% CI, 36.61-951.84).

If the patients with inadequate post-operative topical corticosteroid treatment were excluded from the study, only 5 of the 124 eyes had pterygium recurrence (recurrence rate, 4%).

DISCUSSION

Pterygium is a common ophthalmic problem affecting people in Thailand. In symptomatic and advanced cases, surgical treatment is indicated. There are numerous techniques available, ranging from simple excision to more complex techniques. The choice of technique depends on the severity of pterygium, patient's age, surgeon's skill, and success rate.

Recurrence of pterygium is the most common and frustrating cause of failure of pterygium surgery. Prevention of recurrence after surgical treatment is still most desirable for surgeons. Many investigators have tried to develop effective and safe techniques to reduce its post-operative recurrence rate.

Many studies have reported a low recurrence rate along with safety using conjunctival autograft as an adjunctive treatment in pterygium surgery. Variation in the results from this technique may be influenced by many factors including variation within techniques, surgeon's skill, the age and location of the patients, length of follow-up and differences in post-operative medications.

Topical corticosteroid and antibiotic medications were used routinely after surgery. The duration of the application varied from 1-3 months[30]. In the present study, topical corticosteroids were used for a period of 3 months continuously until the graft and the adjacent conjunctiva were no longer injected. Corticosteroids are frequently used agents for the treatment of ocular inflammation[35]. After pterygium excision, surgical trauma and post-operative inflammation activate subconjunctival fibroblasts with

Table 3. Clinical data on 21 eyes in 20 patients with recurrence.

Patient No.	Age/gender/ laterality	Recurrent time (months)	Follow-up time (months)	Duration of post-opeprative topical corticosteroids used (months)	Adequacy of post-opeprative topical corticosteroids	Comments
1	77/F/RE	Unknown (after 2 mos)	64	2	No	Lost to FU after 2 mos Attend re-examination
2	45/M/RE	Unknown (after 2 mos)	52	2	No	Lost to FU after 2 mos Attend re-examination
3	42/F/LE	3	6	1	No	Missed FU schedule
4	31/M/BE	2.5, RE 4, LE	15	2, BE	No	Steroid responder, BE
5	55/F/LE	4	8	2	No	Steroid responder
6	60/F/LE	3.5	6	2	No	Missed FU schedule
7	27/M/LE	3	9	2	No	Poor compliance
8	31/F/RE	7	11	1	No	Steroid responder
9	52/F/LE	1.5	13	1.5	No	Lost to FU after 1.5 mos Attend re-examination
10	26/F/LE	2.5	9	2	No	Steroid responder
11	39/F/LE	2	7	1	No	Missed FU schedule
12	45/F/LE	4	16	2	No	Missed FU schedule
13	17/M/LE	1.5	6	1	No	Steroid responder
14	49/F/RE	Between 1-8	24	1	No	Missed FU schedule
15	29/M/RE	2	8	1	No	Missed FU schedule
16	54/M/RE	Unknown (after 3 mos)	83	3	Yes	
17	68/F/LE	Unknown (after 3 mos)	56	3	Yes	
18	60/M/RE	3	83	3	Yes	
19	35/F/LE	3.75	6	3	Yes	
20	49/F/RE	6	6	3	Yes	

M = male, F = female, RE = right eye, LE = left eye, BE = both eyes, FU = follow-up.

proliferation of fibroblasts and vascular cells, which may lead to recurrence(36). Corticosteroids suppress fibroblast and capillary proliferation and collagen deposition, thereby, contributing to reduction of pterygium recurrence. Many authors suggested that post-operative corticosteroids may have an influence in reducing the recurrence rate(25,37).

The recurrence rate in the present study was 14.8 per cent. The recurrence rate decreased to 4 per cent if patients with inadequate corticosteroid therapy were excluded. With a significant odds ratio of (190.4; 95% CI, 36.61-951.84), this study provides evidence that post-operative topical corticosteroids appear to play a role in reducing the rate of pterygium recurrence. However, according to the small number of recurrent cases, the confidence interval of the odds ratio is rather large.

Pterygium excision with conjunctival autograft is generally accepted as the standard procedure because of its safety and low recurrence rate. The conjunctival autograft transplantation has been originally used for the treatment of several ocular surface disorders with successful outcomes. In 1985, Kenyon et al modified it and presented the technique for cases of pterygium, both primary and secondary(19). Post-operatively, topical steroid and antibiotic ointments were applied frequently and continued for about 2 months or longer if the inflammation persisted. They reported 5.3 per cent (3 from 57 eyes) recurrence rate. Lewallen conducted a randomized trial in the tropics where the risk of pterygium recurrence is high(33). She reported a recurrence rate of 21 per cent in 19 cases after conjunctival autograft compared to 37 per cent of 16 cases in the control group treated with the bare sclera technique. Both groups were treated with a combination of steroid/antibiotic ointment three times daily after surgery for 3-4 weeks. The author suggested that the relatively high recurrence rate could

be attributed to climate, race, or age. She found that younger age was a risk factor in recurrence.

Tan et al found association between pterygium morphology and its recurrence rate[32]. According to the study, pterygium fleshiness was a significant risk factor in recurrence, but not the age of the patient. Chen et al had a impression that the greater the pre-operative inflammation, the higher the recurrence rates, although it was not significantly proved [38]. They also found that increase of the patient's age was significantly associated with the less risk of recurrence. The post-operative regimen in their study consisted of prednisolone acetate 1 per cent eight times daily tapered over two months and topical antibiotic four times daily for one month. The reported recurrence rate after conjunctival autograft was 39 per cent.

Ti et al analyzed the success rates of conjunctival autografting in primary and recurrent pterygium performed by 12 surgeons[31]. The study had a similar patient source and the patient age was not significantly different. The post-operative regime was also similar between different surgeons and consisted of topical chloramphenicol 0.5 per cent and betamethasone 0.1 per cent four times daily for a period of 4-8 weeks, depending on the degree of edema and redness of the graft. They found that the recurrence rate varied widely among surgeons, ranging from 5-82 per cent. This might be related to a learning curve or differing surgical techniques employed in the operations. In the present series, the operations were performed by the same surgeon in order to avoid personal variation.

The patients in the present study came from the same educational and socioeconomic backgrounds. Most of them were strict to the post-operative management and their follow-up schedules. The mean age of the patients in the recurrence group (44.6 years) was lower than those in the nonrecurrence group (50.8 years). Age, therefore, may also be an important factor contributing to pterygium recurrence. The present study has the limitation that the patient's age, which might affect the likelihood of recurrence, was not pre-stratified. Further studies on a larger number of patients with stratification for patient age and other important risk factors are therefore recommended to obtain a more precise and valid comparison.

Six eyes of 5 patients in the present series had increased intraocular pressure caused by topical corticosteroids. All of these steroid responders had recurrence of pterygium after discontinuing or changing to a weaker corticosteroid. The elevation in intraocular pressure was reversible in all cases with topical glaucoma medications. To reduce the risk of pterygium recurrence, the authors suggest continued use of topical prednisolone or dexamethasone together with glaucoma medications in spite of the side effects.

In conclusion, conjunctival autografting after pterygium excision is an effective and safe technique. The reported recurrence rates were generally low, but variation in recurrence rates still exist. There are many risk factors contributing to pterygium recurrences.

The anti-inflammatory effects of corticosteroids may prevent vascularization and re-growth of pterygium, thereby preventing recurrences. The present study supports that the adequate use of post-operative topical corticosteroids results in reduction of pterygium recurrence rates. Along with appropriate post-operative management, the conjunctival autografting after pterygium excision can yield a better outcome to the patients.

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ผลของยาหยอดตาคอร์ติโคสเตียรอยด์ต่ออัตราการกลับเป็นซ้ำในผู้ป่วยหลังผ่าตัดต้อเนื้อแบบที่มีการปลูกถ่ายเยื่อบุตา

สุดารัตน์ ใหญ่สว่าง, พบ, พิทยา ปิยพัฒนากร, พบ**

ที่มา : การกลับเป็นซ้ำของต้อเนื้อหลังการผ่าตัดพบได้บ่อยมาก การผ่าตัดต้อเนื้อแบบที่มีการปลูกถ่ายเยื่อบุตาร่วมด้วยพบว่ามีอัตราการกลับเป็นซ้ำต่ำ อย่างไรก็ตามยังมีความแตกต่างในอัตราการกลับเป็นซ้ำทั้งที่ใช้วิธีการผ่าตัดเดียวกันนี้ ซึ่งอาจเกิดได้จากปัจจัยหลายอย่าง จากการสังเกตทางคลินิกพบว่า อัตราการกลับเป็นซ้ำของต้อเนื้อพบได้สูงในผู้ที่ได้รับยาหยอดตาคอร์ติโคสเตียรอยด์ในระยะหลังผ่าตัดไม่เพียงพอ

วัตถุประสงค์ : เพื่อศึกษาความสัมพันธ์ระหว่างการใช้ยาหยอดตาคอร์ติโคสเตียรอยด์ในระยะหลังผ่าตัดและอัตราการกลับเป็นซ้ำ ในผู้ป่วยที่ได้รับการผ่าตัดต้อเนื้อโดยวิธีที่มีการปลูกถ่ายเยื่อบุตาร่วมด้วย

รูปแบบการศึกษา : การวิจัยเชิงวิเคราะห์แบบย้อนหลัง

วิธีการศึกษา : การศึกษาทำในผู้ป่วยที่เป็นต้อเนื้อจำนวน 137 ราย ประกอบด้วย 142 ตา ซึ่งได้รับการผ่าตัดลอกต้อเนื้อร่วมกับการปลูกถ่ายเยื่อบุตา ในระหว่างเดือนมกราคม พ.ศ. 2539 ถึงเดือนมิถุนายน พ.ศ. 2545 โดยการประเมินหาข้อมูลเกี่ยวกับการกลับเป็นซ้ำของต้อเนื้อและการได้รับยาหยอดตาคอร์ติโคสเตียรอยด์ในระยะหลังผ่าตัดว่าเพียงพอหรือไม่ โดยดูจากประวัติการรักษา การเรียกผู้ป่วยกลับมาตรวจตาซ้ำ การตอบแบบสอบถาม และการสัมภาษณ์ กลุ่มประชากรศึกษาคือผู้ป่วยที่มีการกลับเป็นซ้ำของต้อเนื้อ ส่วนกลุ่มเปรียบเทียบคือผู้ป่วยที่ไม่มีการกลับเป็นซ้ำ

ผลของการศึกษา : จากจำนวนตาที่ได้รับการผ่าตัดรักษาทั้งหมด 142 ตา พบว่า 21 ตา (14.8%) มีการกลับเป็นซ้ำของต้อเนื้อ โดยใน 5 ตาที่ต้อเนื้อกลับเป็นซ้ำพบในผู้ป่วยที่ได้รับยาหยอดตาในช่วงหลังผ่าตัดอย่างพอเพียง ส่วนอีก 16 ตาพบในผู้ป่วยที่ใช้ยาไม่เพียงพอเนื่องจากสาเหตุต่าง ๆ ดังนี้คือ 6 ตาเกิดจากผู้ป่วยไม่ได้มาตรวจตรงตามเวลาที่แพทย์นัด, 3 ตาเกิดจากผู้ป่วยไม่ได้มาพบแพทย์อีกเลยหลัง 1.5–2 เดือน, 1 ตาเกิดจากผู้ป่วยหยอดยาไม่ครบตามที่แพทย์สั่ง, และอีก 6 ตาเกิดจากผู้ป่วยมีความดันตาสูงซึ่งเป็นผลข้างเคียงที่เกิดจากยาคอร์ติโคสเตียรอยด์ จึงต้องหยุดยาก่อนกำหนดหรือเปลี่ยนมาใช้ยาชนิดที่มีฤทธิ์อ่อนกว่า จากการศึกษานี้พบว่ามีความสัมพันธ์ระหว่างการใช้ยาหยอดตาคอร์ติโคสเตียรอยด์อย่างพอเพียงในระยะหลังผ่าตัด และอัตราการกลับเป็นซ้ำ โดยมี odds ratio เท่ากับ 190.4 (95% CI, 36.61–951.84)

สรุป : อัตราการกลับเป็นซ้ำของต้อเนื้อพบได้สูงในผู้ป่วยที่ใช้ยาหยอดตาคอร์ติโคสเตียรอยด์ไม่เพียงพอ อัตรานี้จะลดลงจาก 14.8% เหลือเพียง 4% ถ้าตัดผู้ป่วยที่ใช้ยาหยอดไม่เพียงพอออกไป การศึกษานี้แสดงให้เห็นว่ายาหยอดตา คอร์ติโคสเตียรอยด์ที่ใช้หลังการผ่าตัดอย่างพอเพียง มีผลทำให้การกลับเป็นซ้ำของต้อเนื้อลดลง

คำสำคัญ : ต้อเนื้อ, การปลูกถ่ายเยื่อบุตา, ยาหยอดตาคอร์ติโคสเตียรอยด์

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