Evaluation of the Use of Intraoperative Subconjunctival Injection of Triamcinolone Acetonide and Limited Peritomy during Bare Scleral Pterygium Excision

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ABSTRACT

Aims: To evaluate the efficacy and safety of subconjunctival injection of triamcinolone acetonide (TA) and limited peritomy during bare scleral pterygium excision in preventing pterygium recurrence.

Study Design: A prospective non-randomized interventional case series.

Place and Duration of Study: All surgeries were done at the department of ophthalmology of Assiut university hospital (27 eyes) and Alforsan eye center in Assiut (3 eyes), Egypt, between November 2017 to December 2019.

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Place and Duration of Study: All surgeries were done at the department of ophthalmology of Assiut university hospital (27 eyes) and Alforsan eye center in Assiut (3 eyes), Egypt, between November 2017 to December 2019.
Methodology: Thirty eyes of 26 patients who underwent pterygium excision with bare sclera combined with intraoperative subconjunctival TA injection and limited peritomy primary pterygium grade 2 (T2, 3 eyes) and grade 3 (T3, 30 eyes). All patients were followed up for 12 months after surgery. Pterygium recurrence and complications were the key outcome steps. Results: Pterygium recurrence was seen in 3 eyes (10.0%) as following: grade 2 in one eye (3.3%) and grade 3 in two eyes (6.7%). Intraocular pressure elevation was observed in 9 eyes (30%). The IOP rise ranged from (22.4 to 37 mmHg). All eyes were successfully treated medically and reached normal values by the end of postoperative sixth month. Conclusion: This procedure appears to be reasonably safe and successful in reducing pterygium recurrence.

Keywords: Pterygium; recurrence; triamcinolone acetonide; intraocular pressure.

ABBREVIATIONS

Triamcinolone acetonide : TA
Intraocular pressure : IOP

1. INTRODUCTION

Pterygium is a triangular, wing-shaped, degenerative fibrovascular, proliferative hyperplastic tissue that actively grows into the cornea from the conjunctival limbal region (probably secondary to limbal cell damage) [1]. Some consider it to be a neoplastic operation [2]. Pterygium has no malignant properties because it does not spread to distant organs. Several previous studies have, however, identified its other features that mimic cancer [3]. It is a widespread external ocular disorder with a global prevalence ranging from 0.7% to 33% [4]. It is a common ocular surface disorder in the hot tropical climate [5].

The exact aetiology of pterygium is unknown [6], it may be due to chronic ultraviolet (UV) light exposure [3], chronic inflammation [7], angiogenesis [8], viral infection (HSV, HPV) [9], or it may be due to an immune reaction [10]. Genetic factors such as tumor suppressor gene p53 and other genes may be involved in the pathogenesis of pterygium [11]. Low income, smoking, [12] region of residence (urban and rural), older age, [13] male gender, latitude, and alcohol consumption are possible risk factors [14]. A known cause of degenerative deposition of subepithelial collagen fibers is chronic ultraviolet (UV) light exposure, which eventually contributes to pterygium growth, [3]. Both UVB and UVA are responsible for activating the intracellular pathway of ERK (extracellular signal-regulated kinase). The hypothesis points out that this radiation leads to mutations of the p53 tumor suppressor gene, thereby favoring the irregular distribution of the limbal epithelium [15].

Surgical removal is the treatment of choice, and the primary challenge of pterygium surgery is the prevention of recurrence [16]. Many different surgical techniques for pterygium excision exist such as simple excision (‘bare sclera’ technique) which is widely used in the developing world for the ease and speed of surgery, [17] associated with a high rate of recurrence ranges from 17 [18] to 88% [19].

The adjunctive therapies combined with the bare sclera technique to reduce the proliferative activity of stromal fibroblasts during the postoperative recovery phase. These adjunctive therapies include the followings: Conjunctival graft with a recurrence rate ranges from 0% [20] to 25.9% [21], Amniotic membrane patch grafting [22] with a recurrence rate ranges from 10.9% to 37.5% [23]. The use of an antimetabolite such as mitomycin C (MMC) with a recurrence rate ranges from 4% [24] to 42.9% [25] and 5 fluorouracil with a recurrence rate of 3.7% [26]. Subconjunctival TA with a recurrence rate ranges from 8.7% [21] to 13% [27]. TA is an intermediate-acting medium potency steroid, which is five times more potent than hydrocortisone and has a duration of action of 15-20 days in the conjunctiva, due to the crystalline nature of the drug. Intraoperative injection of TA reduces postoperative inflammation thereby reducing the chance of recurrences [5], and side effects after sub tenon TA include IOP elevation, cataract formation [27], Avastin (anti-VEGF) anti-vascular endothelial growth factor with a 3.9% recurrence rate [20], Strontium 90 and Beta irradiation with a recurrence rate ranges from 8.6% [26] to 33.3% [28], and Insert multi microporous expanded polytetrafluoroethylene. It is a fluoropolymer,
which can avoid a postoperative adhesion of the wound region to neighboring tissues with a 3.3% recurrence rate [28]. Sometimes deep lesions require peripheral lamellar keratoplasty [22]. In the future, it will be important to identify the molecular/genetic biomarkers of recurrence, as well as patient-individualized therapeutic methods in order to maximize therapeutic effectiveness in overcoming the complicated problems in pterygia. Furthermore, the CRISPR-Cas9 system, or “gene scissors”, is cautiously predicted to be a therapeutic option in pterygium using gene-targeted fundamental techniques [3].

2. MATERIALS AND METHODS

Grading of pterygia was categorized by Tan et al, [18] according to the visibility of the underlying episcleral vessels: Grade 1 (T1, atrophic pterygium, vessels underlying the body of the pterygium unobscured and clearly visible), Grade 2 (T2, Intermediate, vessels are partially visible), and Grade 3 (T3, fleshy pterygium, vessels are totally obscured by fibrovascular tissue) [29].

The following inclusion criteria were met for all participants:

Primary pterygium 2(T2, 3 eyes) and primary pterygium 3(T3, 27 eyes) by tan et al [26] [28]. The exclusion criteria were grade 1 pterygium, recurrent pterygium, preexisting cataract, glaucoma, patient with a family history of glaucoma, and diabetic patients.

Thirty eyes underwent the surgical technique as described below. Postoperatively, all patients were treated with topical moxifloxacin hydrochloride 0.5% (vigamox®, Alcon, Fort Worth, TX) eye drops five times daily for one week, topical Sodium hyaluronate 0.2% (Solofresh®, Orchidia Pharmaceutical Industries, Cairo, Egypt) eye drops four times daily for one month, topical combination of dexamethasone and tobramycin eye drops (Tobradex®, Alcon, Fort Worth, TX) for 3 weeks (In the first week, 5 times per day, in the second week, 3 times per day, and once daily at the last week) and oral non-steroidal anti-inflammatory (NSAID) Diclofenac potassium 50 mg tab ( Cataflam 50 mg®, Novartis, Cairo, Egypt) when needed to relieve postoperative ocular pain. Follow-ups were done regularly at the end of each month postoperatively but data were recorded at the end of the first week, first month, third month, the sixth month, and twelfth month after surgery. Patients were instructed to come back at any time if they noticed any redness at the site of the operation for possible complications, which were recorded at the time of its occurrence.

2.1 Surgical Technique

The pterygium was dissected and peeled off from the underlying cornea with conjunctival scissors and 3-5 mm of conjunctiva covering the head and body of pterygium were excised leaving bare sclera near the limbus (bare sclera technique). This was followed by peritomy 2mm up and down. Tenons and sub tenon tissue were removed carefully as much as possible. The remaining pterygium tissues from over the corneal surface were removed with a diamond burr. After excision of the pterygium TA (0.5 ml of Epirelefan via® 40 mg/1ml Epico co.) was injected in the subconjunctival space all around the excised site of the pterygium. Finally, Topical Antibiotic eye drops (Topical Moxifloxacin hydrochloride 0.5% (Vigamox®, Alcon, Fort Worth, TX)) was instilled. Then the eye was covered by sterile eye patches.

2.2 Main Outcome Measures

At every follow-up visit, patients underwent a complete anterior segment exam and were noted for pterygium recurrence according to the Standard Grading System of Recurrence of Pterygium as follows (Table 1) [10].

The follow-ups also reported complications, including recurrence, the rise of IOPs [10].

2.3 Statistical Analysis

The data were checked for normality with the Kolmogorov-Smirnov test and differences in inhomogeneity. The categorical variables representing the mean variables (mean, median, SD, default deviation) have been numerical and percent (N, percent). Chi-square test used for comparing categorical variables, where continuous variables are compared by t-test. Statistically important was a two-tailed p < 0.05. The IBM SPSS 20.0 package was used for all tests.

3. RESULTS AND DISCUSSION

3.1 Results

There were 30 eyes of 26 patients included in our study from November 2017 to December 2019. The rate of recurrence in our study was 10%.
### Table 1. Standard grading system of recurrence of pterygium

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No recurrence Normal conjunctiva.</td>
</tr>
<tr>
<td>1</td>
<td>A few episcleral vessels without fibrous tissues.</td>
</tr>
<tr>
<td>2</td>
<td>Recurrence Fibrovascular tissues not beyond the limbus.</td>
</tr>
<tr>
<td>3</td>
<td>Fibrovascular tissues invading the cornea (&gt;1.0 mm from the limbus).</td>
</tr>
</tbody>
</table>

### Table 2. Preoperative variable analysis

<table>
<thead>
<tr>
<th></th>
<th>No. of patients (n=26)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21</td>
<td>80.8 %</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>19.2 %</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>23 – 63</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>46.08±11.6</td>
<td></td>
</tr>
<tr>
<td><strong>Pterygium grade</strong></td>
<td>No. of eyes (n=30)</td>
<td>%</td>
</tr>
<tr>
<td>T2</td>
<td>3</td>
<td>10.0</td>
</tr>
<tr>
<td>T3</td>
<td>27</td>
<td>90.0</td>
</tr>
</tbody>
</table>

### Table 3. Recurrence rate

<table>
<thead>
<tr>
<th></th>
<th>No. (n=30)</th>
<th>%</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recurrence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>27</td>
<td>90.0</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td><strong>Grade</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>1</td>
<td>33.3</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>2</td>
<td>66.7</td>
<td></td>
</tr>
<tr>
<td><strong>Date of recurrence (month)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2 after 10 months</td>
<td>1</td>
<td>33.33</td>
<td></td>
</tr>
<tr>
<td>Grade 3 after 9 months</td>
<td>1</td>
<td>33.33</td>
<td></td>
</tr>
<tr>
<td>Grade 3 after 11 months</td>
<td>1</td>
<td>33.33</td>
<td></td>
</tr>
</tbody>
</table>

Chi-square test, * Statistically significant difference (P<0.05), ** Highly statistically significant difference (P<0.01)

![Fig. 1. Clustered column chart showing the percentage of eyes complicated with IOP elevation and the time that they reached to normal value](image-url)
The IOP values ranged from (22.4 to 37 mmHg). Eyes (30%) were complicated with IOP elevation. The IOP values at the end of the postoperative period were (21.1±1.1, 20.5±0.96, 18.35±0.79, 16.8±0.48, and 16.8±0.48 respectively with a highly statistically significant difference (p=0.001).

3.2 Discussion

This prospective non-randomized interventional study was done to describe the rate of pterygium recurrence after pterygium excision with bare sclera combined with intraoperative subconjunctival TA injection and limited peritomy. The limbal sclera has been exposed to a conjunctival peritomy to enable the harvesting of stem cells [24]. Our surgical technique proved to be both safe and effective in the surgical management of primary pterygium.

Also, several surgical procedures, in particular the techniques of grafting, to minimize pterygium recurrence were developed based on previous studies. Additionally, various adjuvant medicines have been used to minimize the recurring rate after pterygium excision, including antimetabolites and anti-VEGF antibodies. While mitomycin C and 5-fluorouracil could significantly lower the recurrence risk, their clinical use has been restricted by severe complications, such as scleral melting and necrosis [10]. Postoperative inflammation and fibrovascular growth angiogenesis are the reasons responsible for the recurrence of pterygium. The effect of TA is to reduce inflammation and thus prevents recurrence [5].

The reporting rate of pterygium recurrence varies from 17% [9] to 88% in the case of bare sclera alone [30], from 0% [31] to 25.9% [32] in the case of conjunctival autograft, from 4% [33] to 42.9% [34] with MMC, from 10.9% to 37.5% [35] for the use of amniotic membrane patch graft technique, and from 8.7% [36] to 13% [28] with the use of intraoperative TA with a bare-sclera technique. In comparison with the previous studies mentioned above, our technique had a low recurrence rate (10.0%). This reduction in the recurrence rate may be attributed to the limited peritomy in addition to the intraoperative subconjunctival TA injection. The recurrence rate in our study was (n = 3, 10 %). Following bare sclera technique, the pterygium recurrences often occurred from the 9- to 11-month period in the study.

Solomon et al. [31] reported pterygium recurrence rate (9 patients of total 54 patients
(16.7%) after surgery with amniotic membrane grafting with intraoperative subconjunctival injections of TA (4 to 8 mg), for all patients and postoperatively injection only for those cases that exhibited inflammation and other clinical findings suggestive of an initial recurrence in multiple sessions. Their study included primary and recurrent pterygia. For comparison in our study, we used only intraoperative TA injection, with a recurrence rate of (10.0%), versus (16.7%) in Solomon et al, study this elevation in recurrence rate may be attributed to a lower dose of TA (4 to 8 mg) in addition to their study included recurrent pterygia.

Prabhasawat et al. [37] conducted a retrograde study for 35 patients undergone pterygium excision (6 patients with conjunctival graft, 23 patients with amniotic membrane graft, and 1 patient with bare sclera with adjuvant) within six months after pterygium excision, who showed signs of “impending recurrent pterygium” (severe conjunctival injection, Highly elevated fibrovascular tissue, and vertical size of fibrovascular tissue more than 6 mm) with received postoperative subconjunctival TA injection with a dose of (20 mg in 0.5 ml) in addition to topical 1% prednisolone acetate 4 times daily for 8 weeks, in the follow-up period of 12 months. The reported recurrence rate in Prabhasawat et al, was (14.3%), in comparison, our study had a lower recurrence rate (10%) may be due to our study we included only primary pterygia and the possible effect of peritomy in reducing the recurrence rate.

Kheirkhah et al. [21] on the other hand have recorded a substantial decline in postoperative conjunctival inflammation or pterygium recurrence with the use of TA intraoperative (12 mg) pterygium injections with bare-sclera technique and MMC use. Kheirkhah et al was the recorded recurrence rate (8.7 percent, 2 patients of 23 patients). The use of MMC as an adjuvant therapy which can have a part to play in lower recurrences can explain this.

Abdel Hamid et al, reported the absence of recurrence (0%) in the follow-up period of (9.33 ± 2.9 ) months, after surgery of 30 eyes (recurrent pterygium) with bare sclera technique followed by postoperative subconjunctival TA injection (20 mg in 0.5ml) one week after pterygium excision. They concluded that subconjunctival TA injection may be regarded as one line of treatment in cases of recurrent pterygium, in comparison our study had a higher recurrence rate (10%) in primary pterygium, intraoperative subconjunctival TA in addition to peritomy [38].

In another study reported by Rajiv Kumar et al, [19] recurrence of pterygium was seen in 2 patients of 20 patients (10%) after conjunctival autograft associated with intraoperative subconjunctival injection of TA (12 mg), given in inferior fornices. All the recurrences occurred between 8-12 months. After surgery, the average month of recurrence was 9.85 months. In Rajiv Kumar et al, study the recurrence was defined as any fibrovascular growth of conjunctival tissue extending more than 1.5 mm across the limbus over the cornea [19], but our study considered both conjunctival (grade 2, Fibrovascular tissues not beyond the limbus ) and corneal (grade 3, Fibrovascular tissues invading the cornea (>1.0 mm from the limbus) encroachment as a recurrence, so that our recurrence rate considered lower than Rajiv Kumar et al, this may be attributed to the high dose of TA (20 mg compared to 12 mg in their study) also our technique was simple and faster, with no graft used.

Sunil Kumar [5] has been proven that subconjunctival TA & Bevacizumab injections can be combined intra-operatively with Conjunctival Autograft to avoid recurrence. Total 150 patients divided into three groups (50 patients of each group),

Class A: Only conjunctival autograft.
Group B: Conjunctival autograft + subconjunctival TA (12mg) in the lower fornix.
Group C: conjunctival autograft + subconjunctival Bevacizumab 2.5mg/0.1ml subconjunctival administered in the lower fornix.
Result: In autograft alone (group A), recurrence concentrations were greater in combination with TA (group B) and Bevacizumab (group C) than an autograft. Result: For 12 months, all patients have been tracked entirely. Both recurrences took place within 5 to 9 months of the procedure. Recurrences were fewer in groups B(16%) and C (14%), respectively TA and bevacizumab, whereas in groups A (34%) with only conjunctive autograft [5], they were less in certain groups, in comparison our study had a lower recurrence rate and a higher rate of increase IOP than Sunil Kumar, this may be attributed to a high dose of TA (20 mg compared to 12 mg in his study).

In different studies, the onset of IOP elevation after subconjunctival injection of TA varies from 1 week to 10 months [39]. Thereafter, regular
monitoring each week is necessary initially and no longer than 6 months if IOP is not elevated in the first few months. Topical beta-blockers, carbonic anhydrase inhibitors, and alpha-agonists are usual first-line treatments with miotics and prostaglandins (PGs) being relatively contraindicated or ineffective [39]. as both miotics and PGs induce ocular inflammation and this needs to be avoided after pterygium surgery because it may induce recurrence [40].

Solomon et al. [31] reported that the use of long-acting corticosteroids may be associated with increased IOP and should be avoided in patients with glaucoma. However, they mentioned that the benefits of the use of TA outweigh the risks of complications, which had a low incidence in their series. They documented an elevation of IOP in two eyes (3.7%) which returned to the normal level 1 month after the injection. This low percent of increase IOP documented in Solomon et al. study may be attributed to a lower dose of local TA injection (10 to 16 mg compared to 20 mg in our study).

Prabhasawat et al. [37] found an increased IOP in 9 eyes (25.7%) of total 35 eyes, with the use of postoperative subconjunctival TA injection (20 mg in 0.5 ml) in pterygium surgery. The IOP generally increased during the first 6 weeks after treatment (range, 1–20 weeks), the peak IOP levels ranged from 23 to 44 mmHg. However, the IOP increases were reversible and controllable with 1 or 2 antiglaucoma medications, no patients had permanent glaucoma at the end of the study, in comparison our study had a higher rate of elevated IOP in nine eyes (30%) of a total of 30 eyes however the peak IOP levels ranged from ( 22.4 to 37 mmHg ) noticed at the end of the first postoperative week which less than the previous study.

On the other hand, Kheirkhah et al. [21] found an increased IOP in one eye (4.3%) with the use of intraoperative triamcinolone injection in pterygium surgery with a bare-sclera technique. in the steroid group, which was controlled medically. This may be attributed to the smaller triamcinolone acetonide dose (12 mg compared to 20 mg in our study).

4. CONCLUSION

In conclusion, in addition to conjunctival peritomy which may have a role in the lowering of pterygium recurrence, the use of subconjunctival TA seems an effective and reasonably safe approach for preventing recurrence of pterygium. Further studies with a larger sample size and a longer period of follow-up after surgery are recommended to evaluate the recurrence rate of our technique.

CONSENT

Written informed consent was obtained from all patients who participated in the study after explaining the whole procedure and possible complications.

ETHICAL APPROVAL

The research was accepted by the Ethics Committee of the Institutional Review Board of Assiut University’s Faculty of Medicine (research project number: 17100523) and carried out in compliance with the Helsinki Declaration. Each patient was made aware of his or her condition, the purpose and potential effects of the operation, and the informed consent of each patient was obtained.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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