Chapter

Recent Advances in the Effects of Various Surgical Methods on Tear Film after Pterygium Surgery

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Abstract

Pterygium is a common ocular disorder with a high prevalence. Surgical resection is the main method of treating pterygium. Recurrence rate of traditional surgical methods such as simple excision of pterygium is high. In recent years, amniotic membrane transplantation, autologous limbal stem cell transplantation, application of mitomycin (MMC) and some other methods become commonly used. Autologous limbal stem cell transplantation is being most widely used. Pterygium has a close relationship with dry eye, and dry eye is one of the important reasons for its recurrence. Different surgical methods have different effects on postoperative tear film. This review will summarize the recent points.

Keywords: pterygium, surgical methods, tear film, dry eye

1. Introduction

Dry eye is a type of disease caused by tear film instability and/or ocular surface damage, which results in eye discomfort and visual dysfunction [1]. The etiology and pathogenesis of dry eye are complicated. Epidemiological studies have shown that there is a positive correlation between pterygium and dry eye [2], and usually accompanied with tear film dysfunction, which is associated with pterygium hyperplasia, irregular, and non-smooth ocular surface. Surgical resection is the main treatment for pterygium which can repair the ocular surface and improve tear film function and reduce dry eye symptoms [3]. It found that different surgical methods of pterygium have different recurrence rates and different tear film function changes [4]. Now, we will summarize the changes of tear film function after different surgical methods of pterygium.

2. Simple excision of pterygium

It reported that the stability of the tear film after pterygium resection is reduced, and dry eye syndrome occurs in severe cases [5]. Compared with preoperative, the tear break-up time (BUT) was significantly prolonged for 1 month after scleral exposure with simple pterygium excision. Tear-ferning test showed a significant increase in normal crystallization ratio, and conjunctival imprint cytology showed a significant increase in goblet cell density. Therefore, they thought that tear function in patients with primary pterygium improves after pterygium excision, which

indicates that pterygium has a close relationship with dry eye [6]. However, there was other studies concluded that pterygium removal may not have any effect on Schirmer's test results and tear BUT 1-month post- surgery [7]. Paton observed that a pterygium is further exacerbated by elevation of the pterygium head, dryness, and delle formation [8]. Pterygium excision can partly restore the tear functions into normal state in patients with pterygium which may be due to the increasing density of the conjunctival goblet cell and the recovery of mucus secretion [9]. Simple excision of pterygium is a traditional surgical method, but the recurrence rate is as high as 24–89% [10], and it is currently less applied.

3. Pterygium excision combined with autologous conjunctival transplantation

Kilic et al. [11] investigated the effects of pterygium excision using the limbal conjunctival autografting technique on the tear function tests in 14 eyes of 13 patients. Since no difference was found in the Schirmer and tear BUT tests at 1 and 6 months postoperative versus preoperative. Shortened BUT and the reduced length of Schirmer test after the removal of pterygium combined with autologous conjunctival transplantation are related to the number of operations, the size of the scleral exposed surface, the thickness of the graft, and the location of the graft. Large removal of the nasal conjunctiva intraoperatively, too large conjunctival graft, and the location too close to the dome or too deep can all lead to shortened BUT, reduced tear secretion test length, and prone to dry eye syndrome [12]. Some authors [13] have found that compared with the opposite healthy eyes, the BUT and mucus fern test (MFT) in the eyes with pterygium were significantly different before the operation ($p < 0.05$). The results of the BUT and MFT in the eyes with pterygium were significantly different before and 4 weeks after the operation ($p < 0.05$). The BUT was prolonged and the ratio of normal crystallization in the MFT increased. Tear functions were abnormal in the eyes with pterygium. Pterygium excision combined with conjunctival autograft transplantation can partially restore the tear film function into normal state, and the tear film function was stable 4 weeks after surgery. Zeng et al. [14] compared the recurrence rates after pterygium excision combined with autologous conjunctiva and amniotic membrane transplantation. After 1 year follow-up, the results showed that the combined autologous conjunctival transplantation group was lower than the amniotic membrane transplantation group, and the difference was statistically significant ($p < 0.05$). No statistically significant difference was observed between the two groups in postoperative tear film BUT ($p > 0.05$).

4. Pterygium excision combined with autologous limbal stem cell transplantation

The lack of stem cells at the neck of pterygium [15] provides a theoretical basis for the treatment of pterygium excision combined with limbal stem cell transplantation. Because of the low recurrence rate after excision of pterygium combined with autologous limbal stem cell transplantation [16], it is widely used. Zhang et al. [17] compared the therapeutic effects of recurrent pterygium treated by limbal stem cell autograft transplantation and amniotic membrane transplantation. After the follow-up of 6–24 months, the recurrence rate was 3.03% in limbal stem cell autograft transplantation group, and 22.86% in amniotic membrane transplantation group. There was statistical significant difference between two groups ($p < 0.05$). The average epithelial recovering time of corneal wound was 4.73 and 6.38 days in two groups,

the difference was significant ($p < 0.05$). Limbal stem cells autograft transplantation can decrease the recurrent rate and improve epithelial recovering time of corneal wound. It is an ideal method of recurrent pterygium surgery. It was shown that pterygium excision combined with limbal stem cell transplantation has less effect on tear film function than traditional pterygium excision, and the incidence of dry eye is lower [18]. Other authors [19] compared the incidence of dry eye after the operation of pterygium excision combined with autologous limbal stem cell transplantation and amniotic membrane transplantation. They showed that patients with primary pterygium treated with autologous limbal stem cell transplantation can improve the tear film stability in the early postoperative period and reduce the incidence of dry eye. However, the long-term effects of the two surgical methods and the dry eye are not obvious. Clinically, the surgical method should be reasonably selected according to the actual situation of the patient. Tear film stability of pterygium excision combined with limbal stem cell transplantation is better compared with pterygium excision combined with amniotic membrane transplantation at early postoperative. Patients bear mild symptoms of dry eye [20]. Deng et al. [21] observed the situations of different surgical methods on dry eyes in patients with pterygium excision combined transplantation. Group A underwent pterygium excision combined large autologous conjunctival flap transplantation; group B underwent pterygium excision combined with small conjunctival flap; and group C underwent pterygium excision combined with small conjunctival flap with autologous limbal stem cell. Repair of postoperative corneal epithelium, tear film BUT, and questionnaire of ocular surface disease index (OSDl) preoperation and 1, 3 months postoperation were observed among three groups, which caused the situation of dry eyes by pterygium and pterygium excision were evaluated. They concluded that pterygium excision combined with small conjunctival flap and autologous limbal stem cell shows quickly corneal epithelium recover and low dry eye ratio. Jin et al. [22] investigated the effect of pterygium excision combined with autologous corneal limbus stem cells transplantation on lacrimal film recovery between primary and recurrent pterygium. About 1 week after operation, both groups appeared dryness and shortened BUT, which was more serious in recurrent pterygium group ($p < 0.05$); there was no significant difference in Schirmer I test between two groups. One month after operation only recurrent pterygium group appeared dryness and shortened BUT compared with primary pterygium group, which was nearly recovered ($p < 0.05$). Results showed that the recovery of tear stability and lacrimal secretion was poorer in recurrent pterygium than in primary pterygium, which partly explains high recurrence rate of recurrent pterygium. A study [23] suggested that pterygium excision combined with limbal stem cell transplantation can provide a healthy source of epithelial cells. The damaged corneal epithelial surface is repaired, and the limbal anatomy and physiological reconstruction are obtained by the proliferation and differentiation of stem cells and the centripetal repair of cells. Flatter graft makes smoother surface, and the tear film stability is better. In contrast, other authors [24] suggest corneal limbal conjunctival autograft combined with pterygium excision yields sound long-term efficacy and a low recurrence rate than pterygium excision with exposed sclera, and induces only mild damage on the ocular surface. No statistically significant differences are observed between the two groups regarding postoperative tear film BUT.

5. Pterygium excision combined with amniotic membrane transplantation

Amniotic membrane is a thin and transparent membrane in the placenta. It has no blood vessels and lymphatic vessels. It contains a variety of cytokines, which can

effectively reduce inflammation, promote wound healing, and anti-fibrosis [25]. The recurrence rate of pterygium excision combined with amniotic membrane transplantation was significantly lower than that of single pterygium excision group [26]. Pterygium excision combined with amniotic membrane transplantation mainly inhibits fibroplasia in the operation area, inhibits leukocyte activation, reduces inflammatory reaction, reduces scar formation, inhibits vascularization, and prevents recurrence of pterygium [27]. Yao [28] compared tear BUT and Schirmer I test at preoperatively, 1, 3 months postoperatively between simple pterygium excision group and pterygium excision combined with amniotic membrane transplantation group, and ocular surface temperature and dry eye symptom score were taken at 2 months after operation. Pterygium excision combined with amniotic membrane transplantation can effectively improve the dry eye, which is conducive to the stability of tear film function. Some authors [29] compared two surgical methods (pterygium excision combined with conjunctival flap transplantation and pterygium excision combined with amniotic membrane transplantation) on tear function. BUT and Schirmer I were shortened on both groups at 1 and 3 months postoperation, and the differences were significant ($p < 0.05$). Pterygium excision affects tear film function at the early postoperative stage. Tear film function returns to preoperative levels 3 months after surgery. Influence of pterygium excision combined with amniotic membrane transplantation on function of the tear film is less than that of pterygium excision combined with conjunctival flap transplantation at early postoperative stage. Amniotic membrane transplantation can limit fibrosis of the sub-conjunctival tissue, improve the success rate of surgery, and reduce the incidence of postoperative dry eye. The reason is the basement membrane surface of the amniotic membrane and the fibroblasts of the conjunctiva stimulate the differentiation of conjunctival goblet cells, keeping the conjunctiva and cornea of the postoperative patients moist, reducing the incidence of dry eye [30].

6. Application of MMC in the treatment of pterygium excision

MMC is an anti-tumor antibiotic isolated from the filtrate of Streptomyces cephalosporin. It inhibits the synthesis of DNA, RNA, and protein and is radiomimetic in many of its actions [31]. It could reduce tissue adhesions and scar formation that has been widely adopted in pterygium surgery to lower the recurrence rate [32]. The purpose of the use of MMC as an adjunctive treatment is to prevent the recurrence of pterygium after the surgery [33]. It has been reported that the wound tissue has not been completely repaired within 2 weeks after pterygium resection. Local use of MMC is prone to lead to ischemic necrosis of wound tissue, especially for patients with bulbar conjunctival flap transplantation [34]. Research [35] has shown that pterygium excision with a free conjunctival autograft combined with intraoperative low-dose MMC is a safe and effective technique in pterygium surgery. MMC can prevent vascular regeneration in the surgical field, prevent fibroblast proliferation and scar formation, and reduce the recurrence rate after pterygium surgery. Intraoperative administration of mitomycin C at 0.05% is safe and effective in preventing pterygium recurrences [36]. Gao et al. [37] compared the clinical efficacy of treatment on recurrent pterygium using different concentration MMC in the pterygium excision operation combined with the corneal limbal stem cell autografting. In their study, complications are corneal edema, corneal ulcer, and conjunctival flap infection. Scleral necrosis occurs in 0.2–4.5% of patients, and higher risk is linked to adjunctive use of MMC, especially more concentrated or repeated doses [38]. It was reported that a case of corneoscleral melt that occurred 50 years after resection of pterygium with postoperative administration of MMC [39]. The application

of 0.2 mg/ml MMC during operation for 3 minutes could effectively control fiber hyperplasia of conjunctivas and there are no complications on cornea and sclera [40]. Study [41] shows that the dry eye symptoms, basic tear secretion and BUT values of the MMC group are significantly better than the simple pterygium excision group. The difference between the two groups is statistically significant ($p < 0.05$). Therefore, it is believed that the treatment of pterygium excision combined with MMC has little effect on the stability of tear film and the secretion of basic tears, and the cure rate is high, which is an effective method for treating pterygium [42]. There is no significant difference in the cure rate and recurrence rate between pterygium excision combined with MMC and pterygium excision combined with autologous limbal stem cell transplantation ($p > 0.05$), both of which can effectively treat primary pterygium, but pterygium excision combined with MMC treatment will not destroy the ocular surface microenvironment, and the operation is easy to master, which is worthy of clinical promotion [43]. However, some studies have shown that the use of 0.2 g/L MMC in the treatment of simple pterygium excision showed signs of significant improvement in ocular surface environment early after surgery, and patients who use 0.29/L MMC are observed obvious ocular surface damage, keratinization of epithelial cells, loss of normal cuboid morphology, loose connection between cells, increased cell gap, increased nuclear-to-plasma ratio, and marked decrease in goblet cell density in analyzed area 3 months after surgery [44].

7. Other surgical methods

By combining autologous corneal limbal stem cell transplantation with conjunctival flap and amnion transplantation, the barrier between corneal epithelium and conjunctival epithelium is maintained and the invasion of foreign conjunctival tissue is prevented, so that the recurrence of pterygium and relevant complications are reduced [45]. The operation of transplantation of amniotic membrane and limbal stem cells can further reduce the postoperative recurrence rate [46]. Tear function is abnormal in patients with recurrent pterygium. The tear functions in patients with recurrent pterygium can improve significantly after combined surgery, restore the cornea stem cells and cohesion margin health conjunctival, and promote the ocular surface reconstruction perfect [47]. Tear film stability of pterygium excision combined with limbal stem cell and amniotic membrane transplantation is better than that of pterygium excision combined with limbal stem cell transplantation or amniotic membrane transplantation in early postoperative stage, but the forward performance and severity of xerophthalmia after surgical treatment of pterygium are about the same. Operation method should be chosen according to the patient's condition [48].

8. Summary

Pterygium is a common ocular surface disease, and the prevalence rate is high. The main treatment method is surgical resection. The recurrence rate and incidence of postoperative dry eye after traditional simple pterygium resection is high. The recurrence rate and the incidence of dry eye of pterygium excision combined with autologous limbal stem cell transplantation is low, so it is most widely used currently. The healthy conjunctival tissue will not be damaged in combined amniotic membrane transplantation which provides conditions for glaucoma filtration surgery. Combined use of low concentration of MMC can effectively reduce the recurrence rate of pterygium, easy to operate, but there are risks of long-term

complications such as scleral lysis. Amniotic membrane transplantation combined with autologous limbal stem cell transplantation can reduce the recurrence rate of pterygium and recurrent pterygium, and has little effect on the tear film. The surgical method can be selected according to the actual situation of pterygium patients.

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