Original Article

Clinical Study on Interferon Treatment of Early Scarring in Filtering Bleb

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Abstract

Purpose: To investigate the effectiveness of needle revision combined with subconjuctival injection of interferon α-2b in reversing early scarring of filtering blebs following trabeculectomy surgery.

Methods: Twenty-five glaucoma patients (31 eyes) who presented with scarred or encapsulated filtering bleb after glaucoma surgery underwent needle revision in combination with subconjuctival injection of interferon α-2b, and were followed for 12 months. Intraocular pressure (IOP) and filtering bleb morphology were observed post treatment.

Results: The mean time until scarring occurred was 21.0±7.4 days. The average time between recognition of bleb scarring and completion of needle revision was 2.2±0.8 days. The time interval between surgery and needle revision was inversely correlated with the time until needle revision ($r = -0.694$, $P < 0.001$). The mean IOPs before and after needle revision were 24.2±2.7 mmHg and 19.6±3.8 mmHg, respectively ($t = 5.916$, $P < 0.001$). At the 12-month follow-up visit, 18 eyes (58.1%) achieved complete success in IOP control, and 6 eyes (19.4%) had conditional success. The overall success rate for needling was thus 77.4%. Subconjunctival hemorrhage was observed in 4 eyes during the needle revision procedure. Punctate staining was found in the corneal epithelium of 2 eyes. Shallow anterior chamber (Grade I or II) was identified in 5 eyes.

Conclusion: Slit-lamp needle revision combined with subconjunctival injection of interferon α-2b may be efficacious in the treatment of early scarring of filtering blebs, easy and safe to perform, and may be considered for more widespread application. (***Eye Science 2011; 26:197–200***)

Keywords: glaucoma; surgery; scarring; interferon

Filtering bleb encapsulation and scarring are regarded as causing early surgical failure and elevated IOP following glaucoma filtering surgery. The incidence of postoperative scarring has decreased due to improvements in anti-glaucoma surgery and the administration of anti-metabolism drugs. However, a considerable proportion of patients have experienced filtering bleb encapsulation and scarring postoperatively. Most of these subjects had an undesirable prognosis if they failed to actively take corresponding measures. Conventional clinical therapies include conservative pharmacotherapy, eye massage, needle revision, and bulbar conjunctival injection of anti-metabolism agents. Previous studies[1-3] indicate that needle revision combined with subconjunctival injection of anti-metabolism drugs is efficacious in the early stage after surgery. In this study, we performed needle revision in combination with subconjunctival injection of interferon α-2b (IFN α-2b) for patients with encapsulated or scarred filtering blebs after anti-glaucoma surgery and determined the corresponding efficacy and safety using slit-lamp examinations.

Materials and methods

General information

A total of 25 patients (31 eyes) with encapsulated or scarred filtering blebs after glaucoma surgery at our hospital[1] between July, 2005 and July, 2011 were enrolled in this study. Of these participants, 16 were male (18 eyes) and 9 were female (13 eyes); their average age was 57.8 ± 8.0 years. Eighteen patients (23 eyes) presented with primary open-angle glaucoma, six (7 eyes) had primary closed-angle glaucoma, and one (1 eye) had traumatic glaucoma. Glaucoma surgery consisted of trabeculectomy or trabeculectomy in combination with phacoemulsification cataract extraction and intraocular lens implantation. Mitomycin C (0.2 mg/ml) was used for 2–5

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min intraoperatively; the usage time was determined according to the condition of the conjunctiva and Tenon's capsule.

Inclusion criteria

Early signs of a scarred filtering bleb are: ① the filtering bleb is flattened and confined, with neovascularization; and ② IOP > 21 mmHg after the removal of sutures, in addition to obstructed massage drainage (mainly characterized as unchanged or slightly decreased IOP).

Early signs of an encapsulated filtering bleb are: ①the filtering bleb displays a dome-shaped bulge, confined limits, a relatively thick bleb wall, high tension, vessels growing on the surface of the filtering bleb and surrounding tissues, and angioplerosis; and ②IOP>21 mmHg after the removal of sutures, in addition to poor massage drainage(mainly characterized as unchanged or slightly decreased IOP). These symptoms can occur approximately 2–8 weeks postoperatively.

Needle revision procedure

After surface anesthesia, the upper filtering zone was fully exposed under a slit lamp, a 1 ml syringe was used to absorb 0.5 ml IFN α-2b solution (5×10^5 IU/ml), was inserted into the temporal bulbar conjunctiva 10 mm from the filtering bleb and then entered the Tenon's capsule. Blood vessels were avoided. When the needle tip reached the base of the filtering bleb, the needle was inserted into the filtering bleb to incise and separated the base of the filtering bleb from surrounding proliferative tissues. Following needle revision, IFN α-2b solution was directly injected into the filtering bleb and the needle was withdrawn slowly. Signs of successful needle revision included filtering bleb bulge and dispersion, decreased IOP, and a softened eyeball after separating drugs[2]. Special attention should be paid to prevent the syringe head from penetrating the filtering bleb or entering the sclera during surgery. When the needle was withdrawn, it must be noted whether there was aqueous humor leakage. Once the needle was withdrawn, conventional topical antibiotic and anti-inflammatory eye drops were administered. Those patients with well-controlled IOP and normal-shaped filtering blebs were asked to return once a week during the first month after surgery and then once a month for at least one year for follow-ups. Repeated needle revision and IFN α-2b injection were performed when IOP was poorly controlled or the tendency for encapsulated and scarred filtering blebs was noted. However, needle revision was performed less than four times altogether.

Evaluation criteria for treatment efficacy

Complete surgical success meant that patients require neither glaucoma drugs nor subsequent glaucoma surgery and they had an IOP < 21 mmHg. Partial surgical success meant that patients required another type of glaucoma drug and IOP remained below 21 mmHg. Surgical failure meant that patients either required at least two types of glaucoma drugs or underwent glaucoma surgery repeatedly.

Statistical analysis

We used SPSS 11.5 software to perform the data analysis. The IOP of patients was statistically compared using paired *t*-tests before and after needle revision. We used correlation analysis to determine the relationship regarding the time interval between glaucoma surgery and needle revision and the frequency of treatment. $P<0.05$ was considered a significant difference.

Results

The time interval between glaucoma surgery and the first needle revision ranged from 14 to 38 days, 21.0±7.4 days on average. Needle revision was conducted 1–4 times (2.2±0.8 times on average), once for 6 eyes, twice for 15 eyes, three times for 8 eyes, and four times for 2 eyes. The time interval inversely correlated with treatment times ($r=-0.694$, $P<0.001$).

Prior to needle revision, the baseline IOP ranged from 21 to 31 mmHg, with the mean 24.2±2.7 mmHg (23.2–25.1 mmHg; 95% CI). Upon subsequent follow-up, three patients (4 eyes) were transferred to superior hospitals for secondary glaucoma surgery due to poorly-controlled IOP and the remaining 22 patients completed the 12-month follow-up period. All patients showed decreased IOP following needle revision by 5–20 mmHg at the one-week follow-up. The IOP post follow-up was 13–26 mmHg (for partial surgical success and surgical failure cases, the IOP before administering IOP-lowering agents or per-

forming secondary surgery was deemed the final IOP), 19.6 ± 3.8 mmHg on average (18.2 –21.0 mmHg; 95% CI). A significant difference was noted in terms of IOP before and after surgery (t=5.916, P<0.001). At the end of the 12-month follow-up period, 18 eyes (55.1%) completely recovered, 6 eyes (19.4%) partially recovered (using one type of IOP-lowering drug), and the remaining 7 eyes failed to recover. Needle revision positively correlated with IOP at end-point (r=0.779, P<0.001).

During the needle revision procedure, 4 eyes had subconjunctival hemorrhage. Pressure hemostasis was performed with cotton swabs and Chinese patent drugs that could be fully absorbed and digested by two weeks postoperatively were administered to promote blood circulation. Another 2 eyes were administered with corneal nutritional eye drops due to spot staining of the corneal epithelium, which recovered within one week. Three eyes had grade Ⅰ swallow anterior chamber and 2 eyes had grade Ⅱ swallow anterior chamber (which healed after one week of conservative treatment). No severe complications occurred during subsequent follow-up.

Discussion

Complex trabeculectomy is a commonly used treatment for glaucoma. A morphology profile of filtering blebs is the best way to evaluate the postoperative filtering function. The occurrence of scarred and encapsulated filtering blebs during the early postoperative stage potentially leads to repeated IOP elevation and surgical failure. A scarred filtering bleb is pathologically characterized as the migration and proliferation of fibroblasts in addition to the adhesion healing among scleral flap, Tenon's capsule and conjunctiva, which collectively block aqueous outflow. In order to reduce the incidence of scarred filtering blebs and improve the surgical success rate, many clinicians administer anti-metabolism drugs intraoperatively, such as mitomyein C (MMC) and 5-fluorouraeil (5-FU), in an attempt to inhibit the proliferation of fibroblasts. However, glaucoma surgery does not always correct scarred filtering blebs. Previous studies[4,5] indicate a substantial proportion of subjects still present scarred or encapsulated filtering blebs during the early postoperative stage (especially during the 2–4 week period). Thirty-one eyes in this study formed a scarred or encapsulated filtering bleb within 14–38 days (21 days on average) postoperatively. Although multiple glaucoma treatments, including drug therapy and eyeball massage, are available in clinics, few desirable curative effects have been obtained. Feldman et al[2]. found that needle revision combined with subconjunctival injection of 5-FU and interferon plays a role in decreasing the recurrence of scarred filtering blebs and stimulating the formation of functional filtering blebs. Hodge et al. used needle revision in combination with subconjunctival injection of 5-FU to treat glaucoma and then conducted subsequent follow-ups, yielding a 47% complete success rate and a 41% conditional success rate. A study in China[6] reported similar results, with a complete success rate of 75% and an effective rate of 87.5% . Different studies produce various outcomes depending upon treatment time and the duration of follow-up. In general, the formation of filtering bleb scarring was controlled or alleviated to various degrees following the combined treatment of needle revision and subconjunctival injection of 5-FU in more than half the cases studied previously. These studies[2,5,6], however, indicated that 5-FU resulted in relatively intense corneal epithelium toxicity. In addition, severe intraocular toxicity might be provoked when 5-FU accidentally enters the anterior chamber. IFNα-2b is able to suppress the proliferation of fibroblasts and has been used as an anti-metabolism drug in the treatment of systemic diseases, such as malignant tumors. Some researchers[4,7] have employed needle revision combined with subconjunctival injection under a slit-lamp microscope to treat scarred filtering blebs after glaucoma filtration surgery. A previous study[4] confirmed that the complete success rate of this treatment was more than 50% and the conditional success rate was more than 90% at the end of 12-month follow-up. These studies also revealed that IFNα-2b results in less aggressive toxicity compared with 5-FU. Commonly observed complications include subconjunctival hemorrhage and mild injuries to the corneal epithelium. The administration of IFNα-2b was safer than that of 5-FU. In this study, a total of 18 eyes (58.1%) fully recovered and 77.4% partially recovered after 12-

month follow-up, which was slightly lower compared with other relevant domestic studies in terms of the treatment effective rate.

A previous study[4] revealed that the more times needle revision was performed, the lower the success rate, suggesting that the time of the first treatment was negatively related to treatment frequency. In addition, the frequency of needle revision positively correlated with the final IOP, indicating that the early occurrence of scarring led to a greater degree of scarring, decreased sensitivity to IFNα-2b, and a worse curative effectiveness. In the current investigation, the IOP of 2 eyes was poorly controlled even after receiving needle revision 4 times and were eventually treated by a second glaucoma surgery. Another 8 eyes received a combined therapy of needle revision and drug administration 3 times. Of those, 4 eyes required at least 2 types of drugs to bring IOP under 21 mmHg. Another 2 eyes were subjected to surgical treatment. We therefore suggest that the vigorous proliferation of fibroblasts in the Tenon's capsule is possibly associated with the poor response of some patients to the chosen treatment. Although corresponding needle revision and anti-scarring therapy were performed repeatedly, the tendency toward scarring was irreversible. The trauma induced by repeated needle revision might stimulate the proliferation of fibroblasts and aggravate the scarring of filtering blebs. We recommend needle revision should not be performed more than twice for those patients receiving a combination of needle revision and subconjunctival injection of IFNα-2b because excessive needle revision would have no effect and may worsen filtering bleb scarring. More clinical trials and experimental findings are required to validate this hypothesis due to the limited sample size of cases that repeatedly received needle revision in this study.

In conclusion, the combined therapy of needle revision under a slit-lamp microscope with subconjunctival injection of IFNα-2b is a relatively effective and safe method of treating encapsulated and scarred filtering blebs during the early postoperative stage.

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