

# Treatment of Encapsulated Blebs with Slit-Lamp Needling and Subconjunctival Interferon Injection

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## Abstract

**Purpose:** To investigate the efficacy and safety of slit-lamp needle revision with subconjunctival interferon injection in eyes with encapsulated blebs.

**Methods:** We reviewed a series of 25 cases (27 eyes) in which primary needling with  $5 \times 10^5$  IFN  $\alpha$ -2b injection was performed for bleb encapsulation and analysed the results over a follow-up period of at least 12 months.

**Results:** The mean time to development of encapsulated blebs after the surgery was  $23.85 \pm 10.66$  days (9 to 60 days). The mean IOP decreased significantly from  $22.51 \pm 5.30$  mm Hg at diagnosis of encapsulated blebs to  $17.26 \pm 7.72$  mm Hg at the last visit ( $P=0.009$ ). Of the 27 eyes, 15 (55.56%) achieved a successful result, 10 (37.04%) were qualified for success and the remaining 2 (7.4%) were considered as failure. The qualified success group took  $1.70 \pm 0.67$  antiglaucoma medications. No serious complications were detected.

**Conclusion:** The needling procedure associated with subconjunctival injection of IFN  $\alpha$ -2b is a safe and effective method in treating encapsulated blebs. (*Eye Science 2011; 26:138-142*)

**Keywords:** encapsulated blebs; needling bleb; interferon  $\alpha$ -2b

Encapsulated filtering blebs, also known as Tenon's capsule cysts, are a common cause of drainage failure in the early post-operative period. The intraocular pressure (IOP) frequently is elevated and may lead to additional vision damage in vulnerable eyes. Many forms of treatment have been advocated, which consist of medical treatment, digital massage maneuvers, and needling revision, but optimal management still is not well-defined. Ocular hypotensive medications, steroid eyedrops and ocu-

lar massage were frequently used as the primary therapy and could achieve an acceptable IOP control in many cases. However, 46% ~ 74% cases required prolonged topical antiglaucoma medication<sup>1-3</sup>, and in resistant cases surgical interventions needed to be performed. Transconjunctival needling revision of encapsulated bleb under slit-lamp magnification accompanied with 5-fluorouracil (5-FU) injection has been reported to be a safe and efficient method of re-establishing bleb function. But the use of 5-FU may cause corneal epithelial defects, bleb leaks and serious intraocular complications if it gains access to the anterior chamber via the bleb. Interferon (IFN)  $\alpha$ -2b was proved to be able to inhibit proliferation of fibroblasts and production of collagen with less toxicity to conjunctival and corneal epithelial<sup>4</sup>. Thus we performed this study to investigate the efficacy and safety of slit-lamp needle revision with subconjunctival IFN injection.

## Patients and methods

All consecutive patients who developed encapsulated blebs after trabeculectomy and underwent needle revision with subconjunctival IFN  $\alpha$ -2b injection between September 2008 and June 2010 were included in this study. Twenty-seven eyes of 25 patients with a minimum of 12 months follow-up since the last needle revision were enrolled.

All filtration surgeries were performed by the same surgeon (Professor Liu), using similar surgical techniques. A limbus-based conjunctival flap was performed approximately 8 to 10 mm posterior to the limbus without tenonectomy. A rectangular  $4 \times 4$  mm scleral flap of one third to one half scleral thickness was dissected, and a sponge soaked with 0.25 mg/ml to 0.33 mg/ml solution of mitomycin C (MMC) was placed in contact with the deep scleral bed for 3

to 5 minutes if needed. Then the sponge was removed and the area was irrigated copiously with 60 to 100 ml balanced salt solution. The corneoscleral block of tissue was excised and a peripheral iridectomy was performed consequently. The scleral flap was closed with four single 10-0 monofilament nylon sutures, two of which were at the corners and the other two were releasable sutures. Tenon's capsule was closed with interrupted 10-0 nylon sutures. Then the conjunctival wound was closed with running 8-0 Vicryl sutures. After surgery, tobramycin and dexamethasone were injected subconjunctivally 180° away from the operation site. All eyes were routinely examined on the first day after surgery, and all received topical antibiotic and topical steroids drops for 1 month in the absence of complications.

Encapsulated blebs were diagnosed on the basis of the appearance of the blebs by the same observer (Liu), disregarding the IOP. Encapsulation of a bleb is defined as a localized, elevated, dome-shaped, thick-walled bleb, with prominent surface vessels. Conjunctival microcysts were absent and the sclerostomy was patent on gonioscopy. Conservative treatments consisted of removing releasable sutures and digital ocular massage, but no antiglaucoma medications were added. If bleb encapsulation did not resolve, bleb needle revision was performed no matter the IOP was higher than 21 mm Hg or not.

### Needling Procedure

Informed consent was obtained from all patients before the procedure was performed. The surgeon drew up 0.5 ml with a concentration of  $5 \times 10^5$  IFN  $\alpha$ -2b into a TB syringe attached to a 30-gauge needle. After 0.4% oxybuprocaine was delivered three times to induce topical anaesthesia, the patient was seated at the slit-lamp and was instructed to look downward while an assistant retracted the upper lid to have superior conjunctiva and the encapsulated bleb exposed adequately. A fraction of the solution was injected about 5 mm from the bleb superotemporally into the subconjunctival space to cause the conjunctiva surrounding the bleb balloon and then provide a tract for the needle. The needle was advanced in the subconjunctival space and the needle point was used to perforate the wall of the cyst. A gentle

sweeping motion was used to enlarge the perforation and lyse fibrotic strands until the bleb became much flatter and softer. Great care should be taken not to desterilise the needle on the lid margins or lashes and not to button-hole the conjunctiva overlying the drainage site. Then all IFN  $\alpha$ -2b solution in the syringe was injected subconjunctivally to form a bubble. The needle was then withdrawn slowly and the minute conjunctival entry wound be closed automatically without aqueous leak most of the time. If Seidel test was positive, the puncture point was tamponaded for several minutes with a sterile cotton bud. At the end of the procedure, a drop of 0.3% tobramycin was instilled.

The patients were instructed to use topical antibiotic and steroid drops four times a day and were all reviewed 1 day after bleb needling. Then if the IOP was well controlled and no complications happened, they would be reviewed weekly for one month and monthly for half a year. At each review, the IOP was determined carefully. The appearance of the bleb and the presence of needling complications were also noted. Repeated needle revision was performed if there were signs of recurrent encapsulation and the IOP was above 21 mm Hg. When the bleb tended to be scarred or flattened, it would not be reneedled. Needling procedures should not be performed more than 4 times.

The procedure was considered a complete success if the long-term IOP was equal to or lower than 21 mm Hg without glaucoma medications or further filtration surgery, a qualified success if the IOP less than 21 mm Hg was obtained with adjunctive medications, and a failure if the IOP was greater than 21 mm Hg with medications or when further surgery was required.

Statistical analyses were performed with SPSS software (version 15.0, SPSS Inc., Chicago, IL). We used paired, two-tailed Student's *t*-test to compare pre-operative and post-operative data, an unpaired, two-tailed Student's *t*-test for continuous variables. Probability values of  $<0.05$  were considered significance.

### Results

A total of 27 eyes from 25 patients (14 males, 11

females) were recruited. Mean age was  $59.64 \pm 14.01$  years (27 to 79 years). Demographic information was summarized in Table 1. Twelve cases had bilateral trabeculectomy, and two developed EB in both eyes. Eight patients had prior medication therapy before filtering surgery for one month to one year.

The mean time to development of EB after the surgery was  $23.85 \pm 10.66$  days (9 to 60 days) for all eyes and  $26.13 \pm 12.94$  days (12 to 60 days) for the 15 eyes that had undergone trabeculectomy with adjunctive MMC. There was no significant difference between the identification time of EB in eyes with regard to preoperative application of MMC.

Needling procedure was performed once in 15 (55.6%) eyes, twice in 5 (18.5%) eyes (mean interval between first and second needling:  $7.6 \pm 1.1$  days), three times in 4 (14.8%) eyes (mean interval between second and third needling:  $10.4 \pm 4.7$  days) and four times in 3 (11.1%) eyes (interval between third and fourth needling: 17.5 days). The mean follow-up was  $16.37 \pm 6.34$  months (12 to 36 months) after the last needle revision.

The mean IOP at diagnosis of EB without antiglaucomatous medications was  $22.51 \pm 5.30$  mm Hg (10 to 32 mm Hg) with an IOP over 30 mmHg in two eyes. After needling procedure, all patients showed an important IOP decrease. The mean IOP on the second day after needling was  $11.57 \pm 4.82$  mmHg (4 to 21 mmHg) and was significantly lower compared with IOP at baseline ( $t=9.413, P=0.000$ ). Twelve eyes had recurrence of EB and required repeated bleb needling. At the last visit, the overall mean IOP was  $17.26 \pm 7.72$  mmHg (7 to 20 mmHg), and there was significant difference between the baseline and the final IOP level ( $t=2.832, P=0.009$ ).

Of the 27 eyes, 15 (55.56%) achieved a successful result, 10 (37.04%) were qualified successes and the remaining 2 (7.4%) were considered failures. The qualified success group used an average of medication of  $1.70 \pm 0.67$  glaucomatous medications. In the two failure cases post-needling, one had 3 needling procedures and the other had 4. But the IOPs were still above 30 mm Hg with glaucomatous medications, therefore one case underwent tube shunt implantation and the other had a repeat trabeculectomy, and the IOP was controlled well after 6 months

postoperative follow-up period.

The needling procedure was generally well tolerated and no severe complications were detected. Two eyes had a self-limited bleb leak at the piercing site and responded well to pressure patching. Three eyes developed hypotony without choroidal detachment and resolved within 3 days. No corneal epithelial defects or hypema were noted in all cases.

## Discussion

Encapsulated bleb formation is a fairly uncommon complication following filtering surgery. Since it was first reported in detail by Van buskirk in 1982, the incidence ranged from 2.4% to 29%<sup>1,5,6</sup>. Several risk factors have been associated with the development of bleb encapsulation, including male gender, preoperative argon laser trabeculoplasty (ALT), previous topical use of  $\beta$ -blockers and sympathomimetics, previous conjunctival surgery, prior Tenon's cyst in the other eye, and surgical glove power<sup>1,2,5,7-9</sup>.

Encapsulated blebs may lead to an IOP elevation to compromise vision in the early postoperative stage, but controversy exists about the extent of the IOP rise necessary to make the diagnosis. In our series, the diagnosis of encapsulation was mainly based upon bleb appearance with no regard to IOP level. It typically occurs between the second and eighth weeks following operation, and the median time to diagnosis in our study was  $23.85 \pm 10.66$  days.

Its management consists of medical therapy, digital massage maneuvers, and surgical interventions, mainly needling and bleb revision. Though conservative therapy has been reported to be sufficient in most cases, the complete success rate of conservative management alone was not totally acceptable. It was reported that 46% ~74% cases required prolonged topical antiglaucoma medication<sup>1-3</sup>.

Needling revision of the encapsulated bleb with subconjunctival injection of 5-FU has been confirmed to be effective in many cases. Hodge et al<sup>10</sup> observed that 15 (88.2%) of 17 eyes with encapsulated blebs ultimately had good IOP control after bleb needling, and among which 7 (41.2%) eyes required additional topical hypotensive agents. Allen et al<sup>11</sup> reported the result of encapsulation needling revision of 32 eyes observed for 4 to 18 months.

**Table 1** Demographics of the Study Population (number of eyes=27)

Demographics	No.	(%)
Sex		
Male	14	66.0
Female	11	34.0
Diagnosis		
Acute angle closure glaucoma	6	22.2
Chronic angle closure glaucoma	4	14.8
Open angle glaucoma	14	51.9
Uveitic glaucoma	2	7.41
Combined mechanism	1	3.7
Filtering procedures		
First trabeculectomy	26	96.3
Trabeculectomy after NPT*	1	3.7
Peroperative application of MMC	15	55.6
0.25 mg/ml	11	40.7
0.28 mg/ml	3	11.1
0.33 mg/ml	1	3.7
Lens status		
Phakic	26	96.3
Pseudophakic	1	3.7

\* NPT=nonpenetrating trabeculectomy

Twenty-one (65.6%) eyes required two or more needling procedures. Overall 23 (71.9%) achieved a completely successful result. However, as an antifibrotic agent, 5-FU is toxic to both corneal and conjunctival epithelial cells and the use of 5-FU may cause corneal epithelial defects, bleb leaks. If it gains access to the anterior chamber via the bleb, serious intraocular complications may happen.

IFN  $\alpha$ -2b is a cytokine that has been shown to have antifibrotic effects both in vitro and in vivo without corneal complications<sup>4</sup>. It could inhibit proliferation of human Tenon's capsule fibroblasts as well as collagen and glycosaminoglycan production in vitro studies. Gillies MC et al<sup>12</sup> performed a phase II trial of IFN  $\alpha$ -2b after trabeculectomy. In their study, patients were divided randomly into three groups and received three subconjunctival injections of IFN  $\alpha$ -2b or 5-FU or both agents per week for 3~4 weeks postoperatively. It was reported that subconjunctival injection of IFN  $\alpha$ -2b was well tolerated and no significant difference existed between IFN  $\alpha$ -2b and 5-FU with respect to efficacy. But up till now studies on managing encapsulated blebs with subconjunctival injection of IFN  $\alpha$ -2b have not ever been reported.

In our retrospective study, we collected 25 cases (27 eyes) who received bleb needling with subconjunctival injection of IFN  $\alpha$ -2b after they developed bleb encapsulation. It demonstrated that needling with IFN  $\alpha$ -2b treatment was effective in controlling IOP. Over a follow-up period of 12 months, 25 (92.6%) eyes had reasonable IOP control, among which 15 (55.56%) eyes achieved a complete success result and 10 (37.04%) were qualified success. Strict comparison of treatment efficacy between 5-FU and IFN  $\alpha$ -2b in different studies is difficult because of minor variations in definition of encapsulated bleb, different demographic natures and preoperative managements. However, this study does indicate that needling with IFN  $\alpha$ -2b is an effective method in treating encapsulated blebs.

IFN  $\alpha$ -2b injection was more simple and convenient than 5-FU injection because needling and 5-FU injection should be separated and the injection spot should be far away from the filtering area. If 5-FU gains access to the anterior chamber, it may cause serious intraocular complications. The most commonly complications in previous needling studies included wound leaks at the piercing site, corneal epithelial toxicity, hypotony with or without choroidal detachment and small hyphemas. In our group, only minor complications such as self-limited piercing site leaking and hypotony were detected and resolved within 3 days. No corneal epithelial defects or consistent bleb leakage or other reported complications happened.

A retrospective design and lack of control group made it impossible to compare needling with IFN  $\alpha$ -2b with conservative medication therapy or needling with 5-FU. It also prevented analysis of risk factors contributing to development of encapsulation. A randomized, controlled, prospective study in the next step would be helpful to answer these issues. The results from our retrospective study show that needling with IFN  $\alpha$ -2b can successfully control IOP after bleb encapsulation and it appears to be a safe and effective method in treating encapsulated blebs.

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