The treatment of encapsulated trabeculectomy blebs in an out-patient setting using a needling technique and subconjunctival 5-fluorouracil injection

L.E. ALLEN, K. MANUCHEHRI, P.G. CORRIDAN

ARTICLE

Abstract

Purpose **Encapsulation of the trabeculectomy bleb is a common cause of drainage failure in the early post-operative period. The primary management of bleb encapsulation has previously been to restart medical therapy, but recent advances in the technique of needle manipulation and the introduction of adjunctive 5-fluorouracil (5-FU) have increased the popularity of early surgical bleb management. By reporting the results of bleb needling in a series of patients, we aim to illustrate its safety and efficacy.**

Methods **We have reviewed a series of 32 eyes in which needling and 5-FU injection was performed for bleb encapsulation, and analysed the results over a follow-up period of 10.7±2.9 months.**

Results **In 14 (43.7%) cases, primary needling was performed; in the other 18, needling was performed after conservative treatment had proved inadequate. The mean intraocular pressure (IOP) of the group decreased from 29.2±10.5 mmHg prior to needling to 15.9±4.0 mmHg at the most recent attendance (paired *t*-test $p = 1.3 \times 10^{-7}$), with all eyes having a final IOP measurement of 22 mmHg or less. Twenty-three (71.9%) of the cases maintained a target IOP of 18 mmHg or less without additional treatment; 5 (15.6%) were qualified successes with an untreated IOP between 19 and 21 mmHg. The remaining 4 (12.5%) patients, whose IOPs ranged between 20 and 22 mmHg with one hypotensive agent, were considered needling failures. Choroidal detachment complicated the procedure in 2 cases; in each this resolved with conservative management and without long-term visual consequence.**

Conclusion **This technique is recommended as a safe and effective method of treating bleb encapsulation.**

Key words Encapsulated filtering bleb, Needling bleb, 5-Fluorouracil, Trabeculectomy

Encapsulation of the filtering bleb occurs in approximately 13% of eyes following trabeculectomy and is increasing in incidence,[1] partly due to the detrimental effect of topical therapy on conjunctival and episcleral fibroblasts.[2–4] Encapsulation occurs in the early post-operative period, when adhesions form between the episcleral tissues and Tenon's capsule creating a fibrous, vascular cyst that entraps aqueous and creates a localised, dome-shaped bleb. The associated intraocular pressure (IOP) rise peaks in the first 6 weeks post-operatively and may cause additional optic nerve head damage in vulnerable eyes.

Ocular hypotensive agents, steroids and ocular massage are frequently used as the primary therapy for bleb encapsulation, with resort to surgical management should the IOP remain inadequately controlled. Although conservative management may achieve an acceptable reduction in IOP in 70% of cases, 50% of these will require prolonged topical treatment[2,5,6] that may prejudice the results of repeat drainage surgery.[4]

Early needle manipulation of the encapsulated bleb is an alternative approach that is gaining popularity. Primary needling of encapsulated blebs under the operating microscope has been shown to be a safe method of re-establishing function in 69% of cases.[7] Recent advances in the technique and widespread use of 5-fluorouracil (5-FU) have enabled needling to be performed for bleb failure under slit-lamp magnification with success rates between 73% and 91%.[8–12] We report a series of 32 eyes which have been treated with bleb needling and adjuvant 5-FU therapy for bleb encapsulation and analyse our results.

L.E. Allen
K. Manuchehri
P G. Corridan
Wolverhampton and Midland Counties Eye Infirmary
Wolverhampton
WV3 9QR, UK

L.E. Allen ✉
Department of Ophthalmology
Addenbrooke's Hospital
Hills Road
Cambridge CB2 2QQ, UK

Table 1. *Demographics of the study population (number of eyes = 32)*

Demographics	No.	(%)
Race		
Caucasian	26	(81.3)
Asian	4	(12.4)
Afro-Caribbean	2	(6.3)
Sex		
Male	21	(65.6)
Female	11	(34.4)
Glaucoma type		
Open angle	19	(59.4)
Narrow angle	5	(15.6)
Uveitic	3	(9.4)
Aphakic	2	(6.3)
Pseudoexfoliative	1	(3.1)
Normal tension	1	(3.1)
Raised episcleral venous pressure (Low flow carotico-cavernous fistula)	1	(3.1)
Filtering procedures		
First trabeculectomy	26	(81.3)
Repeat trabeculectomy	4	(12.4)
Phacotrabeculectomy and IOL	2	(6.3)
Peroperative application of 5-fluorouracil	21	(65.6)
Lens status at time of needling		
Phakic	24	(75.0)
Pseudophakic	6	(18.8)
Aphakic	2	(6.2)

Patients and methods

Patient selection

We have reviewed the notes of the 29 patients (32 eyes) who underwent needling and adjunctive 5-FU therapy by one of the authors (P.G.C. or L.E.A.) for bleb encapsulation in the year interval May 1995 to May 1996. The average age of the patients was 63.9±10.8 years (range 38–85 years); further demographic information is summarised in Table 1.

Twenty-one (65.6%) of the patients studied had characteristics associated with an intermediate or high risk of bleb failure[13] (Table 2) and had been treated with an intraoperative sponge application of 5-FU. All eyes had an initial period of good IOP control after drainage surgery, the mean interval between this surgery and bleb encapsulation being 9.7 ± 26.9 weeks (range 2–156 weeks). Four patients developed encapsulation more than 8 weeks after trabeculectomy; in each case an intraocular procedure had been performed in the intervening period (3 eyes underwent cataract extraction, 1 a vitrectomy). The mean interval between the last intraocular procedure and encapsulation in all 32 eyes was 3.3 ± 1.2 weeks (range 2–8 weeks).

Table 2. *High-risk characteristics for bleb failure (total number of eyes = 32)*

Characteristic	No.	(%)
Repeat filtering surgery	4	(12.4)
Uveitic glaucoma	3	(9.4)
Aphakia	2	(6.3)
Afro-Caribbean race	2	(6.3)
Use of adrenergic agents	2	(6.3)
Cataract extraction (involving conjunctiva)	2	(6.3)
Age < 40 years	1	(3.1)
Multiple risk factors	5	(15.5)
Total	21	(65.6)

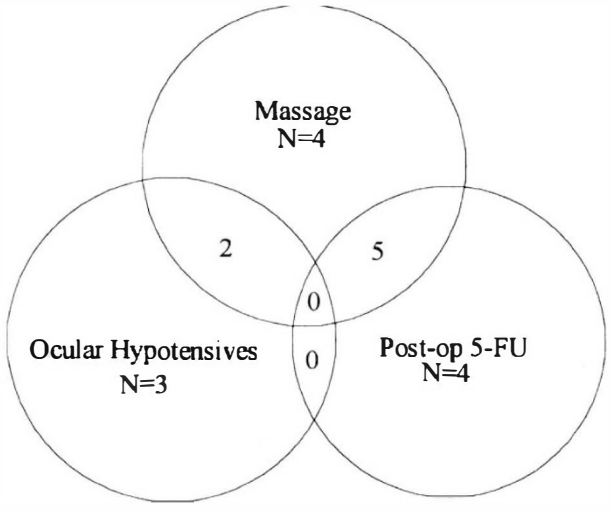

Fig. 1. *Conservative management given prior to needling (number of eyes = 18).*

Encapsulation of the bleb was diagnosed on the basis of the appearance of the bleb (a domed, localised bleb with absent conjunctival microcystic changes) and the presence of a patent sclerostomy on gonioscopic examination. Where these features were accompanied by an IOP that was considered higher than acceptable for the degree of optic disc cupping and visual field loss, bleb needling was performed. In this group, all patients had an IOP of 18 mmHg or more (mean 29.2 ± 10.5 mmHg, range 18–60 mmHg) prior to needling.

Needling was performed as a primary procedure in 14 eyes (43.7%); in the other 18 (56.3%) needling was performed 1.1 ± 1.3 weeks (range 1–4 weeks) after conservative therapy had been initiated and subsequently proved inadequate for IOP control (Fig. 1).

Technique of bleb needling

Informed consent was obtained from all patients prior to needling. After instillation of topical anaesthetic, the patient was seated at the slit-lamp and directed to look down while an assistant retracted the upper lid. With the superior conjunctiva adequately exposed and taking care not to desterilise the needle on the lid margins or lashes, a 30 gauge needle attached to an insulin syringe was

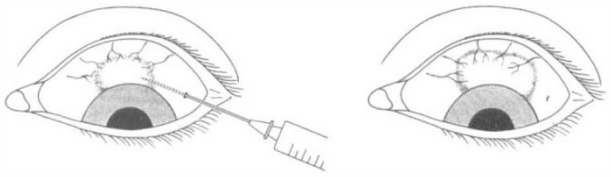

Fig. 2. *Method of bleb needling: Advance the 30 gauge needle in the subconjunctival space towards the lateral bleb wall. Repeatedly puncture the cyst and gently sweep the needle tip up and down until bleb inflation is seen.*

used to enter the subconjunctival space approximately 10 mm temporal to the cyst. The needle was advanced in the subconjunctival space and the needle point was used to perforate the wall of the cyst several times – as the needle pierced the cyst wall it was eased from side to side, thus enlarging the perforations until a rush of subconjunctival aqueous and bleb inflation was seen (Fig. 2). Great care was taken not to button-hole the conjunctiva overlying the drainage site. Following slow withdrawal of the needle, the conjunctival entry point was examined for the presence of an aqueous leak using the Seidel test. If Seidel-positive, the puncture point was tamponaded for several minutes with a sterile cotton bud. Using a strict isolation technique and care to avoid accidental spillage, 5 mg (0.2 ml of 25 mg/ml solution) of 5-FU was then drawn into a second insulin syringe. The needle point was directed into the subconjunctival space 2–3 mm superior to the upper limit of the bleb and the 5-FU injected to form a subconjunctival fluid bubble. A single dose of antibiotic ointment (chloramphenicol) was applied following the procedure. Any ocular hypotensive agents that had been used prior to needling were discontinued, topical steroid (dexamethasone 2-hourly) was prescribed and patients whose IOP remained above 15 mmHg after the procedure were advised to perform digital ocular massage three times daily.

All patients were reviewed 1 week after bleb needling and regularly thereafter. At each review, the characteristics of the bleb, presence of wound leak, anterior chamber depth and presence of choroidal detachment were noted. Repeat needle revision was performed, using the same technique as detailed above, if the IOP exceeded the target of 18 mmHg and there were signs of recurrent encapsulation (scarred, flattened blebs were not reneedled).

A number of studies have suggested criteria for judging the success of needling. Mardelli *et al.*[14] have proposed the most stringent criteria in their study of needling with adjunctive mitomycin C: the procedure was considered a success if the long-term IOP was 18 mmHg or less without the use of ocular hypotensive medication, a qualified success if 18 mmHg or less with medication, and a failure if more than 18 mmHg with medication or if further conventional surgery was required. Since it was not our policy routinely to restart glaucoma therapy if the IOP was between 19 and 21 mmHg, we have modified the definition of qualified success in this study to include those patients whose untreated IOP was in this range.

Statistical analysis of the data included the use of the paired, two-tailed Student's *t*-test for pre-operative and post-operative data, an unpaired, two-tailed *t*-test for comparing primary and secondary needling results and χ^2 tests to study the relationship between needling success and patient characteristics.

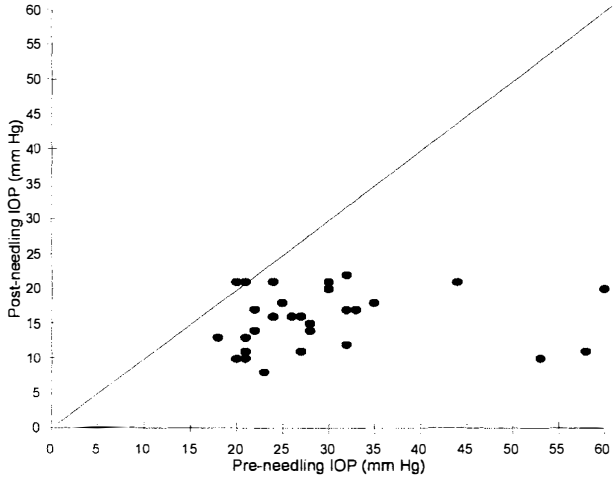

Fig. 3. *Comparison between pre-needling and post-needling IOP.*

Results

Number of needling procedures

In total, 64 needling procedures (mean 2 ± 0.9 revisions per eye, range 1–4) were performed on 32 eyes. The mean length of follow-up was 10.7 ± 2.9 months (range 4–18 months) after the last needle revision. Eleven (34.4%) eyes required one needling procedure, 12 (37.5%) required two procedures (mean interval between first and second needling: 2.1 ± 1.6 weeks), 7 (21.8%) required three procedures (interval between second and third needling: 2 ± 1.2 weeks), and 2 (6.3%) eyes required four procedures (interval between third and fourth needling: 3 weeks).

IOP control

The mean IOP of the group decreased from 29.2 ± 10.5 mmHg (range 18–60 mmHg) prior to the first needling to 15.9 ± 4.0 mmHg (range 8–22 mmHg) at last follow-up (two-tailed paired Student's *t*-test $p = 1.3 \times 10^{-7}$). The scatterplot in Fig. 3 illustrates the relationship between pre-needling and follow-up IOP measurements. Overall, the mean drop in IOP associated with needling was 15.9 ± 8.3 mmHg (range 2–40 mmHg): the IOP reduction in eyes needled as a primary procedure was 16.4 ± 2.9 mmHg compared with 15.4 ± 4.7 mmHg in those needled after initiation of glaucoma medication (two-tailed unpaired *t*-test $p = 0.5$).

Of the 32 eyes, 23 (71.9%) achieved a successful result, 5 (15.6%) were qualified successes (all had IOPs of less than 22 mmHg without treatment) and the remaining 4 (12.5%) were considered failures, with IOPs between 20 and 22 mmHg with one topical medication (beta-blockers in two cases, dorzolamide and latanoprost in one case each). The relationship between number of needling revisions and outcome is illustrated in Table 3. The long-term success rate after one needling revision was 25%; after two needlings the cumulative success rate was 56.3%. Fifteen (65.2%) of the eyes that maintained successful IOP control required more than one needling procedure.

Table 3. *Number of needling procedures with 5-FU and outcome (number of eyes = 32)*

No. of needlings	Success		Qualified success		Failures	
	No.	(%)	No.	(%)	No.	(%)
1	8	(25.0)	3	(9.4)	0	
2	10	(31.3)	1	(3.1)	1	(3.1)
3	4	(12.5)	1	(3.1)	2	(6.3)
4	1	(3.1)	0		1	(3.1)
Total	23	(71.9)	5	(15.6)	4	(12.5)

The success rate for phakic eyes was 70.8% and that for pseudophakic and aphakic eyes 75% (χ^2 test $p>0.5$). The success rate for primarily needled eyes was 78.6% and that for eyes needled after initiation of medication 66.7% (χ^2 test $p>0.5$).

In the group with a successful result the IOP decreased from a mean of 28.0 ± 9.6 mmHg prior to needling to 13.9 ± 2.9 mmHg (two-tailed paired Student's *t*-test $p = 2.0 \times 10^{-7}$); the mean IOP decreased from 27.8 ± 8.8 mmHg to 20.8±0.4 mmHg ($p = 0.19$) in the qualified success group. In the failure group the IOP decreased from 38 ± 12.7 mmHg to 21 ± 0.7 mmHg ($p = 0.11$), but all patients in this group had a long-term decrease in IOP of at least 30% of their initial measurement.

Bleb appearance

The long-term appearance of the needled blebs was unusual, most of the blebs being shaped like an inverted L with extension towards the side where the needling had been performed. At the last review none of the blebs was thin-walled or Seidel-positive.

Complications

The procedure was generally well tolerated, only one patient refusing a second needling procedure (he maintained an IOP of 21 mmHg without treatment and was a qualified success). Over the follow-up period none of the 32 patients lost more than one line of Snellen visual acuity. Twenty-two (68.8%) patients maintained the same visual acuity as that recorded prior to trabeculectomy and in 4 (12.5%) cases the Snellen visual acuity improved by two lines or more (these patients had undergone phacotrabeculectomy or secondary cataract extraction). Two (6.3%) eyes developed choroidal detachments that occurred within 3 days of needling; the IOP drop with needling prior to choroidal effusion was 15 mmHg and 25 mmHg respectively. The detachments resolved within 1 month after conservative treatment with mydriatics and topical steroids and did not result in long-term reduction in visual acuity. No persistent bleb leaks or corneal epithelial defects were noted at the clinic visits after the needling procedures.

Discussion

The safe and efficient treatment of bleb encapsulation is becoming an increasingly important skill in glaucoma management. Whilst aggressive medical therapy may lower the IOP in 70% of cases, the level of control may not be sufficient to prevent further glaucomatous damage and it may become a prolonged requirement.[1,2,5,6] Several reports have indicated that prophylactic, post-operative 5-FU therapy inhibits bleb scarring (leading to a flattened bleb) but does not influence bleb encapsulation.[3,15,16] In our study, 65.6% of the eyes with encapsulated blebs had received prophylactic, per-operative 5-FU. Furthermore, 28.1% of these needled blebs had initially been treated with subconjunctival 5-FU injection (5 mg in 0.2 ml), without response, suggesting that 5-FU therapy alone does not alter the natural history of bleb encapsulation. Four (12.5%) of the eyes in this study developed bleb encapsulation only after a second intraocular procedure. Aggressive post-operative steroid therapy may be required to reduce the incidence of subsequent bleb encapsulation in these eyes.

Surgical bleb revision has been performed under the operating microscope with a similar success rate to medical therapy.[7] More recently, the less invasive technique using a 30 gauge needle under slit-lamp magnification has become popular.[8–12,14] This technique is particularly suitable for encapsulated blebs, where the resistance to aqueous drainage is a localised, raised, fibrous barrier in the subconjunctival layer that is amenable to perforation. Theoretically, the use of adjuvant anti-metabolites such as 5-FU and mitomycin C (MMC) after needling may inhibit subsequent bleb scarring, if not re-encapsulation, but no prospective, controlled studies have been performed to confirm this.

In our retrospective study, 28 of 32 eyes (87.5%) with encapsulated blebs treated with needling and 5-FU injection had reasonable IOP control without hypotensive therapy over a mean follow-up period of 10.7 months (71.9% were successes with an untreated IOP of 18 mmHg or less; 15.6% were qualified successes with an untreated IOP less than 22 mmHg). This is the largest report of needling results in eyes with bleb encapsulation. Pederson and Smith[7] reported the results of one needling procedure without adjunctive anti-metabolites in 13 eyes with encapsulated blebs. Over the 20 month follow-up period, 23% maintained an IOP of 22 mmHg or less without treatment, although the success rate doubled after further surgical revision. Hodge *et al.*[8] have reviewed their results of needling with 5-FU in 17 eyes with encapsulated blebs. Forty-seven per cent of eyes were successfully needled and an additional 41.2% classified as qualified successes. Gillies and Brooks[9] performed needling with 5-FU on 8 eyes with bleb encapsulation with a 75% success rate. Several other needling studies have reported success rates of 73–91% in the treatment of other types of bleb failure.[10–12,14]

The most commonly encountered complications in previous studies of needling with 5-FU have been corneal epithelial defects, hyphaema and bleb leaks,[8-11] but 5-FU may cause additional serious intraocular complications if it gains access to the anterior chamber via the bleb.[18,21] We advise performing the needling and 5-FU injection separately; injecting the 5-FU 3–4 mm superior to the upper limit of the bleb, which maximises its concentration around the bleb but prevents its direct entry into anterior chamber. Choroidal effusions have been associated with the IOP drop following needling with 5-FU and MMC.[14,19] Two of 32 (6.3%) eyes developed choroidal effusions in our study that resolved with conservative therapy and without visual sequelae. It would seem wise to treat those cases where the IOP is over 30 mmHg with ocular hypotensive therapy prior to needling, in order to reduce the risk of choroidal effusion and detachment. To our knowledge there has been only one case of endophthalmitis following needling,[12] but, since needling is an intraocular procedure, all possible precautions should be taken to prevent its occurrence. Although povidone-iodine 5% was not used to clean the lids and ocular surfaces prior to needling in this retrospective study, its efficacy in decreasing the conjunctival bacterial count has been demonstrated.[17,20] We now advise the use of povidone-iodine prior to needling and a prophylactic course of topical antibiotics after the procedure.

This retrospective study reviewed the results of bleb needling and 5-FU in a small and disparate group of glaucoma patients and its design limits the conclusions that can be drawn from the data. It does illustrate, however, that needling is effective in immediately lowering the IOP and providing continued control over a 10 month period in patients with bleb encapsulation, that many patients will require two or more needlings to successfully maintain IOP control and that the complication rate is low. A long-term, prospective, case-controlled study is required to confirm its advantages over conservative therapy for bleb encapsulation.

Bleb encapsulation is becoming an increasingly common challenge for the ophthalmologist. Although medical therapy may be successful in many cases, early bleb manipulation appears to offer a convenient, safe and efficacious method of gaining immediate IOP control and reducing the requirement for long-term glaucoma therapy.

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