

NEEDLE REVISION WITH MITOMYCIN-C IN ENCAPSULATED BLEBS

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Abstract- The most common cause of failure during the first trimester after trabeculectomy is encapsulated bleb and needling bleb revision is a less invasive method in the management of refractory cases. The purpose of this before-after (paired) observation study was to determine the efficacy and safety of mitomycin-C (MMC) augmented bleb revision of failed filtration surgery. A total of 33 patients with failed trabeculectomy because of bleb encapsulation, whose intraocular pressure (IOP) was not reduced under 21 mmHg despite medication and digital massage, underwent needling bleb revision and subconjunctival injection of 0.1 ml MMC (0.4 mg/ml). The mean follow-up time was 9.24 ± 5.27 months (1-20 months). Statistical analysis of the data included the paired two-tailed Student's *t* test for preoperative and postoperative IOP and number of medications. A total of 36 needling procedures were performed on 33 eyes. Patients were between 10-80 years old (mean, 45.67 ± 22.41 years) and mean follow-up was 9.24 ± 5.27 months. IOP decreased from 29.06 ± 5.03 mmHg to 18.21 ± 6.76 mmHg at last follow-up ($P= 0.000$). Antiglaucoma medications decreased from 2.18 ± 0.58 to 1.36 ± 0.29 at last follow-up ($P= 0.000$). Overall, 6 (18.2%) of 33 cases achieved a complete success and 20 (60.6%) of cases achieved a qualified success. The complications of this procedure were subconjunctival hemorrhage (17 cases), hyphema (5 cases) and conjunctival button hole (2 cases). Needling bleb revision with mitomycin-C appears to be an effective and relatively safe way to revive failed filtration surgery.

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INTRODUCTION

The most common cause of failure during the first trimester after trabeculectomy is "bleb encapsulation" which occurs in 10-30% of patients within a few weeks after operation (1-4). Encapsulated bleb (Tenon's cyst) presents as a dome

shaped elevation in the filtration site with stretched conjunctiva over it. Its wall consists of a fibrotic and thickened subconjunctival tissue which is surrounded with a hyperemic ring of conjunctiva (1). This complication usually initiates two weeks postoperatively and establishes in 4-6 weeks (2).

Excision of the thickened Tenon's cyst is rarely effective and accompany with many complications (*e.g.*, choroidal effusion, endophthalmitis, bleb leakage and hypotony) (1). Needling bleb revision (to open Tenon's cyst by a needle) is a less invasive method and it seems logical to try it before excision, but the success of this procedure alone is fair (7.1-50%) (2, 5). The success of the glaucoma surgery

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depends on slowing the healing process by inhibiting the fibroblasts proliferation (6). Combining the needling bleb revision with subconjunctival injection of mitomycin-C (MMC), an anti fibrotic agent, in order to increase the success rate is the object of our study. If so, this procedure (regarding to less invasion and relatively simple technique) can be used as the first choice in encapsulated blebs not responding to medical treatments.

MATERIALS AND METHODS

This before-after (paired) observational study was conducted from 2000 to 2002 at Farabi Eye Hospital. The study was approved by Ethics Committee of Tehran University of Medical Sciences and written informed consent was obtained from all subjects.

There were 90 encapsulated blebs from 317 trabeculectomies and 33 glaucomatous patients with encapsulated bleb after trabeculectomy whose intraocular pressure (IOP) was not reduced under 21 mmHg despite medication and digital massage, were chosen consecutively. All previous filtering surgeries had an initial period of good filtration and all of them had fornix base peritomy.

The needlings were performed in the operating room (because of better management of complications and uncooperative patients) as follows: after prep and drape and under topical anesthesia, first a 27 gauge needle was introduced into subconjunctival space about 6 mm from the bleb and balanced salt solution (BSS) was injected around the bleb. Then the needle was pushed forward to pass through cyst's wall and enter its space. Thereafter with a gentle sweeping motion of the needle tip, the cyst's wall was torn. If the level of resistance was thought to be at the level of the scleral flap, the needle was introduced under the flap to the level of the sclerostomy. After seeing the aqueous flow under conjunctiva, the needle was withdrawn and a cotton applicator was compressed lightly at the entrance site to cease probable leakage. Finally, 0.1 ml MMC (0.04%) was injected subconjunctivally 180 degrees away from the needling site and the eye was patched after instillation of chloramphenicol eye drop.

Betamethasone and chloramphenicol eye drops were administered to all patients for one week and

antiglaucoma medications were regulated according to the measured IOPs in follow-up visits. For the purpose of this study, the procedure was considered a complete success if IOP was less than or equal to 21 mmHg without the use of antiglaucoma medications as measured at latest visit. A qualified success was defined as IOP less than or equal to 21 mmHg with the aid of antiglaucoma medications. A failure was defined as IOP more than 21 mmHg despite medication or if further conventional surgery to lower IOP was required.

This procedure was performed on all patients by a certain individual and was repeated in failed cases within one month, if possible. The routine program of follow-up was 1 day, 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months, 12 months, and 24 months after procedure, but additional visits were performed if needed in complicated cases. The minimum follow-up time was considered one month because failure most commonly occurs within this period.

Statistical analysis of the data included the paired two tailed Student's *t* test for preoperative and postoperative IOP and number of medications.

RESULTS

A total of 36 needling procedures (mean, 1.09 ± 0.21 revisions per eye; range, 1-2) were performed on 33 eyes of 33 patients. Patients were between 10-80 years old (mean, 45.67 ± 22.41); 14 patients (42.4%) were female and 19 patients (57.6%) were male.

The most common type of glaucoma was primary open angle glaucoma (Table 1). The mean duration between trabeculectomy and needling was 9.54 ± 3.58 weeks (range, 6-24) and the mean follow-up from the last needling procedure was 9.24 ± 5.27 months (range, 1-20). The mean number of antiglaucoma medications decreased from 2.18 ± 0.58 at baseline to 1.36 ± 0.29 at last follow-up (two tailed Student's *t* test; $P=0.000$). The mean IOP decreased from 29.06 ± 5.03 mmHg at baseline to 18.21 ± 6.76 mmHg at last follow-up (two-tailed Student's *t* test; $P=0.000$) (Fig. 1). Overall, 6 (18.2%) of 33 patients achieved a complete success, 20 patients (60.60%) achieved a qualified success and others were classified as failure. Complications are listed in Table 2.

Table 1. Types of glaucoma

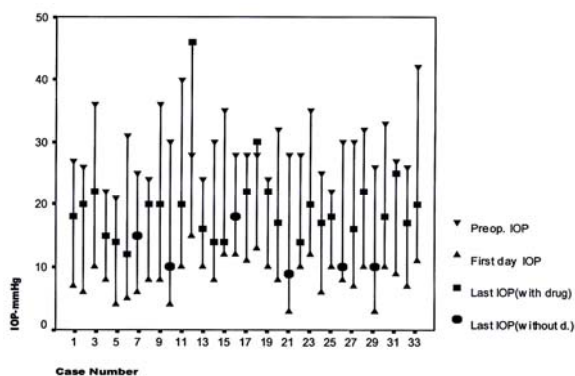
	Number	Percent
Axenfeld-Reiger syndrome	1	3.0
Acute angle closure glaucoma	1	3.0
Angle recession chronic angle	1	3.0
Closure glaucoma	3	9.1
Congenital glaucoma	6	18.2
Juvenile glaucoma	4	12.1
Pseudoexfoliation glaucoma	7	21.2
Primary open angle glaucoma	9	27.3
Postoperative glaucoma	1	3.0
Total	33	100.0

Hyphema and subconjunctival hemorrhage resorbed within two weeks without any sequelae. Two eyes required suturing (with Nylon 10/0) because of button hole formation. The sample of the failure group was too small to draw a conclusion on the predictors of failure.

DISCUSSION

Many authors believe in conservative management (topical steroid, antiglaucoma medications and digital massage) as the first step in encapsulated blebs and mention the success rate of this strategy to be more than 90% (1-4). Surgery will be required when cyst wall remains thick and without any evidence of micro cystic changes for 4-12 weeks and IOP is not controlled despite of relevant measures (2).

Shingleton *et al.* mentioned a 50% success rate of needling (without antifibrotic agents) although many of their cases required antiglaucoma medications after this procedure (7).

**Fig. 1.** Pre and postoperative intraocular pressures.**Table 2.** Complications

	Number	Percent
Button hole	2	6.1
Extensive subconjunctival hemorrhage	2	6.1
Hyphema	5	15.2
Without complication	9	27.3
Subconjunctival hemorrhage	15	45.5
Total	33	100.0

In the Pederson and Smith study, the success rate was 69% but firstly, the sample size was too small (13 cases) and secondly, the target IOP was considered equal to or less than 22 mmHg. The only power point of this study was its relatively long follow-up period of 20 months (8). Costa *et al.* studied 14 cases and after 10 months from needling (without antifibrotic agents) only one patient had IOP less than 20 mmHg without antiglaucoma medications (5).

Ewing and Stamper were pioneers in combining the needling procedure with the application of 5-FU (an antifibrotic agent), but their study didn't indicate any significant difference between this new method and needling alone (9). Shin and colleagues studied needling with subconjunctival injection of 5-FU in 30 patients. The success rate of this study was 80%, but most of cases were dependent to antiglaucoma medications at last visit (10).

MMC, an antitumor antibiotic isolated from *Streptomyces caespitosus*, inhibits the proliferation of fibroblasts and alters conjunctival vascular endothelium. It is 100 times more potent than 5-FU. These effects have been shown to have a prolonged nature (11). Although the success rates of filtration surgery have been reported as being equal when 5FU or MMC are used, the latter achieves lower IOP and longer duration of success. The MMC also offers the advantage of single application during the filtration surgery as opposed to the repeated and painful subconjunctival injections of 5-FU (9, 12, 13). Mardelli *et al.* examined the needling with subconjunctival injection of MMC on 62 eyes during a retrospective study and stated a complete success rate (without antiglaucoma medications) of more than 75% (6).

As mentioned in the results, the main success in our study was qualified and most of the patients

were under antiglaucoma medications at last visit. The probable causes of this problem are as follows: 1) the mean number of needling procedures in our study was significantly less than Mardelli's (1.09 in comparison with 1.90 revisions per eye), 2) in our study MMC was injected 180 degrees away from the bleb and after needling procedure but Mardelli injected the MMC at the needling site and 30 minutes before the procedure, 3) these two studies were performed on two different races and therefore the healing process may be different between them, too, and 4) other probable causes are difference in age, glaucoma type and complications between these studies.

One of the most feared complications of subconjunctival injection of MMC is endothelial toxicity. The amount of MMC used in our study was insufficient to cause endothelial toxicity, even if the entire amount inadvertently was washed into the anterior chamber. If this unlikely event were to occur, the anterior chamber concentration of 16 ug/ml (based on an anterior chamber volume of 0.25 ml) would be well below the level known to cause corneal endothelial toxicity (approximately 200 ug/ml) (14) and in our study none of the patients presented significant corneal edema. Scleral melting is another major complication of MMC, especially in pterygium surgery. However, regarding its minimal applied dose, none of the patients in our and previously mentioned studies presented this complication. Although choroidal hemorrhage and effusion were reported in previous articles, none of our cases presented these complications. It may be due to relatively small number of cases in our study. Other minor complications such as subconjunctival hemorrhage and microhyphema were similar to previous studies.

In conclusion, considering relatively simple technique and transient complications, this method is recommended as the first choice in patients with encapsulated blebs that don't respond to conservative management. Also, a large study with a control group is recommended in which the procedure is performed at the slit lamp; thus, needling can be repeated inexpensively, if needed.

Conflict of interests

We have no competing interests.

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