Needling: A Potential option for Trabeculectomy Bleb Failure

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ABSTRACT

Trabeculectomy still remains the standard procedure of choice for a patient with uncontrolled glaucoma on maximum tolerated medical therapy and/or after laser. Although it has a high success rate of its own, a small number of patients continue to have a failing or a failed bleb despite a good bleb management. Needling had been a well-known modality of bleb management described in literature which has refined itself through years. However, in most of the situations, this modality of treatment is least considered. In this review, we will go through the evolution of needling procedure and various related options, their success rates, complications and emerging trends.

Keywords: Trabeculectomy, Bleb needling, Bleb failure.

INTRODUCTION

What is needling: Needling is a type of revision procedure with needle incisions, for a failing or a failed bleb after an excessive healing response leading to fibrosis following trabeculectomy.

Normal wound healing in trabeculectomies: A normal wound healing occurs in four overlapping phases.1
1. Phases of inflammation or clotting
2. Phase of fibroblastic proliferation
3. Phase of collagen synthesis
4. Phase of remodeling.

Immediately following trabeculectomy, the bleb is usually relatively vascular but should have a definite characteristic with a well-formed AC and an IOP in lower teens. The phase of inflammation consists of recruitment of inflammatory mediators, kinins, complements, and cytokines, which starts immediately after operation and reaches its peak at around 3 to 5 days. This phase is accompanied by clot formation to immediately but temporarily seal the wound. Topical steroids given immediately after operation helps to combat excessive inflammation. This phase is then overlapped by phase of fibroblastic proliferation, which occurs through recruitment of fibroblasts in the wound. As they proliferate, they tend to form collagen, along with new vessels which will again form bed for more fibroblast synthesis. The VEGF, b-FGF, TGF-β and other interleukins help in continuation of this cycle.2 This process ultimately leads to formation of an acute scar, which approximately takes around 2 weeks. Intraoperative use of bevacizumab (avastin) during trabeculectomy helps to combat excessive vascularization of bleb. Intraoperative and postoperative MMC 3 and 5-FU 4 are some of the well-known antimitotic agents that help to downregulate fibroblastic proliferation and subsequent collagen synthesis. The phase of collagen synthesis occurs at around 2 to 4 weeks in which they orient themselves in variable ways.

There are studies that have shown that amniotic membrane grafting might be a good option with7 or without MMC during trabeculectomy to reduce failure rates. However, in normal situations the sclerostomies never get fully healed due to the antifibrotic property of aqueous humor. The last phase of remodeling takes around 3 to 6 months and at times continues for years. There is reorientation of the collagen fibres that gives rise to secondary changes in bleb characteristics. A new product named oloGen6 has a porous collagenous structure that help to modify the phase of remodeling, but the relevant studies have not shown a significant success rate.

NEEDLING—IN WHICH CASES?

Despite all available options, some of the blebs are notorious to fail either early or late and may require further treatment. Thus indication for needling consist of (1) early failing bleb, (2) encapsulated bleb and (3) late failed bleb, all of which are due to excessive fibrosis.

Bleb Characteristics

Ideal bleb (Fig. 1): An ideal bleb should be a low lying diffuse bleb of mild vascularity, having relatively thick wall but translucent enough to be able to see the superficial scleral flap, has cystic changes in the wall with IOP in lower teens , a well-formed AC, tightly closed conjunctival wound and patent sclerostomy.

Failing bleb (Fig. 2): It is caused by excessive fibroblastic proliferation within 2 weeks leading to scarring at the conjunctival and episcleral interface. It is characterized by a high IOP, deep AC, flat bleb with high vascularity with a patent sclerostomy and not responding to digital massage.
Encapsulated or encysted bleb (Fig. 3): It is caused by excessive collagen synthesis within 2 to 4 weeks and is characterized by a high IOP, deep AC, a tense, elevated, thick-walled bleb with large vessels present over the bleb but with intervening avascular areas and there are very few or no microcysts in the wall.

Late failing/Failed bleb: It is caused by secondary changes in bleb characteristics due to remodelling that occurs 3 to 6 months after surgery. Scarring occurs at conjunctival and episcleral interface. The condition is associated with a high IOP, deep AC, an elevated fibrosed bleb with thick wall and having reduced vascularity.

**WHEN TO DO?**

**Systematic approach to a failing bleb:** When we find a flat bleb with a high IOP and a deep AC, we must perform a gonioscopy to rule out any blockage at the sclerostomy site for which the treatment would be entirely different. If in doubt we can go for an anterior segment OCT or an UBM if available although in most cases, it is not required. When the sclerostomy is found patent, the first step is to perform a digital massage so that the aqueous flows through the sclerostomy and the bleb is formed. If repeated massages are not successful, we should move to release a suture, if a releasable suture has been applied, or we can go for an argon laser suturolysis. Also, associated inflammation is to be addressed with increasing the dose of topical steroid which should be early within first 3 to 5 days. If the bleb continues to be nonresponsive, then a diagnosis of a failing bleb is made and needling may then be considered.

The diagnosis of an encapsulated bleb is rather easy due to its typical characteristics and also to diagnose a late failed bleb is also easy because of its duration and association of a deep AC and a high IOP.

**Principle of needling:** To perforate a fibrosed bleb (Fig. 4) through conjunctiva with a needle and thus re-establish aqueous flow.
flow to form a normal bleb with subsequent normal IOP. Various agents can be injected sub- or transconjunctivally to increase success rate.

Results of Needling

History

In 1941, Ferrer described a procedure called conjunctival dialysis which was described for incising scar tissue and separating conjunctiva from sclera with a spatula (Am J Oph, 1941). In 1985, Pederson and Smith reported first the term needling of blebs with a success rate of 69% in their study, however many of them required medical therapy post needling. (Ophthalmol, 1985). In 1990, Ewing and Stamper were the first to describe 5-FU in postoperative period of needling. They had a success rate of 91.6%, where 63.6% required post needling medication (Am J Oph 1990). In 1993, Shin et al first administered 5-FU during needling. 80% was the success rate where only 21% did not require medications postoperatively. The success rate was higher in cases with late failed bleb (Oph Surg, 1993).

Recent Studies on Needling with Various Adjunctive Agents

Subconjunctival 5-FU as antifibrotic agent in needling: Alan P Rotchford and Anthony J King (2008) had a detailed study of subconjunctival 5-FU along with needling. Both early and late failing blebs (up to 6 months) were included in the study. The cases were followed up up to an average of 2 years. Performed under slit lamp, it was done with 28 G needle from temporal side along a long tract to avoid later conjunctival wound leak. Multiple punctures and/or sweeping movements were done to release all fibrotic tissues. 5-FU (5 mg in 0.2 ml) was injected through a separate site 10 mm superior to limbus away from the bleb. Both the sites of entry were left unsutured. Success after 2 years was 59% with single needling and 29.7% with multiple. Absolute success was 35.8% at 2 years and it was better with needling within 3 months, better with elevated blebs if they were also vascular/had microcysts. Risk factors for poor outcome were young age, lack of MMC during primary surgery, prior exposure to sympathomimetics, pseudophakia/aphakia and high preneedling IOP. Good prognostic factor was immediate reduction of IOP post needling. They concluded that needling with 5-fluorouracil (5-FU) is an effective intervention in the short to medium term, but long-term results show that additional intervention is necessary in the majority of cases. Also, bleb morphology can be used to predict success in recent, highly vascularized, or microcystic trabeculectomy blebs.

Transconjunctival MMC in bleb needling: Andrew G Iwach, Maria F et al (2003) used a 25 G needle to puncture the episcleral scar tissue in failing blebs, the entry site was sutured with 8-0 vicryl. A cut piece of sponge soaked in MMC 0.5 mg/ml kept in contact with conjunctival for 6 minutes and then irrigated thoroughly with saline. Some subjects received postoperative subconjunctival 5-FU. Qualified success was IOP reduced to at least 30% and no further surgery, complete success was no hypotensive medication used postoperative the follow-up period was 2 to 48 months. Analysis showed probability of continued success at 12 months of 76.1%, at 24 months 71.6%, at 36 months of 40.0%. Failure rate was slightly higher in only MMC group as compared to MMC + 5-FU (44% and 23%) group. They concluded that transconjunctival MMC may enhance success of the needling procedure in failing filtering blebs.

Subconjunctival MMC in needling: Mardelli et al had earlier (1996) used a combination of MMC 0.01ml (0.4 mg/ml) and bupivacaine (0.02 ml) subconjunctivally as an adjunct to needling. Average follow-up was up to 9.9 ± 3.7 months. Total success was 75.8%, qualified success 16.1%, failure 8.1%. Around 41.9% underwent multiple needling.

Comparing subconjunctival 5-FU with subconjunctival MMC: C Kranemann, IK Ahmed and AS Crandall (2004) performed slit-lamp bleb needling for failing filters in 86 patients. Adjunctive 5-FU (10 mg) was injected in 36 patients and adjunctive MMC (20 ug) in 50 patients at least 20 minutes prior to the needling procedure. When required, multiple needlings/antimetabolite injections were given. Pre- and post-needling intraocular pressure (IOP) and medications, success rate (IOP less than 18 mm Hg without medications and greater than 30% IOP reduction) and complications were compared. Mean pre- and post-needling IOP was similar between those patients 5-FU (24.1 to 15.7 mm Hg) or MMC (24.5 to 14.2 mm Hg). Patients needled with 5-FU required an average of 2.8 needlings versus those with MMC (average 1.1) p = 0.001. After a mean follow-up of 12.6 months, complete success was 48.7% in the 5-FU group versus 70.0% in the MMC group. Major complications included three patients with persistent hypotony requiring intervention and one patient developed a postneedling suprachoroidal hemorrhage. They concluded MMC appears to provide improved efficacy when compared versus 5-FU as an adjunct to needling of failing blebs after trabeculectomy, requiring fewer repeat needlings and a superior success rate.

Late bleb needling: CT Ung, H Von Lany and KG Claridge (2003) reported results of five cases of late bleb needling with 5FU where trabeculectomy was performed between 8 and 30 years earlier. No case had antimiotics been used at the original surgery. Conjunctiva was entered several mm from the flap site with a 27 gauge needle. In one case aqueous flow established after perforating scar tissue around an encysted bleb, whereas in others it was necessary to dissect beneath the scleral flap and enter the AC. After creating a bleb and confirming a reduction in IOP, 5 mg 5-FU (25 mg/ml) injected into the subconjunctival space around the bleb. Repeat injections of 5-FU with or without needling were given, according to the IOP and appearance of the bleb. After 12 months follow-up, average IOP reduced from 29.4 mm Hg (range 19-58) to 14 mm Hg (range 9-17). There was no change in the patients’ visual acuity. Two
cases developed a mild corneal epitheliopathy that healed within 8 weeks. There were no other complications. They concluded that bleb needling may be successful in achieving a long-lasting IOP reduction even several years after the original surgery.


Intrableb triamcinolone acetonide after needling: Tham et al (2006) in a pilot study of 11 patients, undergoing trabeculectomy, phacotrabeculectomy, and needling revision during the study period of 3 months, injected 0.03 ml of TA (40 mg/ml) using a bent 27 G needle into the filtration bleb at the conclusion of surgery. Entry site was at least 1 cm from the scleral flap, and covered by the upper eyelid. The needle was passed between conjunctiva and sclera towards the scleral flap. Three eyes underwent phacotrabeculectomy (with MMC 0.4 mg/ml applied to sclera for 3 min), three eyes trabeculectomy (with MMC), and five eyes underwent needling revision (with single intraoperative subconjunctival 5-FU 5 mg). Mean IOP reduced from 23.77.1 mmHg preoperative to 12.25.7 mm Hg at 1 month and 11.95.1 mmHg at 3 months after surgery. The mean number of topical glaucoma drugs reduced from 3.41.0 (range, 2-5) preoperatively to 0 in all eyes at both 1 month and 3 months. There was minimal postoperative anterior segment inflammation in all cases. Microcystic and spongy blebs were achieved in all cases. All corneas were clear before surgery, and at 1 and 3 months after the procedure. The only complication was persistent subconjunctival TA deposit in one case of needling up to 3 months after surgery with no other consequences. The authors concluded that intrableb TA injection in bleb-forming filtration surgery is compatible with a desirable clinical outcome, and appears to be safe up to 3 months after surgery.


Bevacizumab (avastin) in needling: The utility of needle bleb revision with bevacizumab in a patient with a failing bleb following trabeculectomy was explored by Kahook et al (2006). In a case report, a patient had previously failed needle bleb revision with mitomycin C. After needling and injection of 1 mg of bevacizumab, the bleb noted to be more diffuse with a decrease in surface neovascularization. The authors mentioned a possibility of bevacizumab to be an effective medication for rescuing failing filtering blebs that exhibit neovascularization.


Complications of Needling

Minor
i. Subconjunctival hemorrhage
ii. Needling site leak with or without hypotony
iii. Overdraining bleb
iv. Hyphema
v. Corneal epithelial defect (5-FU)
vi. Intrableb deposit (TA).

Major
i. Persistent large choroidal effusion
ii. Large leak causing iridocorneal touch/corneal decompensation
iii. CME
iv. Choroidal hemorrhage.


Prediction of Risk Factors of Failure of Needling

Dong H Shin, Yong Y Kim et al (2001) investigated the risk factors for failure of 5-FU needling revision, a useful procedure for restoring a failed filtration bleb. It was an interventional case series and retrospectively conducted study of 64 eyes of 64 patients who underwent trabeculectomy/phacotrabeculectomy with or without MMC and failed subsequently. Successful outcome of initial 5-FU needling revision was defined as target IOP control with not more than two topical glaucoma medications and no additional 5-FU needling or other surgical procedures. Risk factors for failure of initial 5-FU needling revision analyzed by Cox proportional hazards regression analysis. success rate of the initial 5-FU needling was 45% at 1 year, 33% at 2 years, and 28% at 4 years. Failure of the initial 5-FU revision correlated significantly with preneedling IOP > $30\,mm\,Hg$ (p = 0.0003), lack of MMC use during the previous filtration surgery (p = 0.013), and IOP > $10\,mm\,Hg$ immediately following needling revision (p = 0.0012). They concluded that Pre-needling IOP > $30\,mm\,Hg$, lack of MMC use during the previous filtration surgery, and IOP > $10\,mm\,Hg$ immediately after needling were found to be significant risk factors for failure of the initial 5-FU needling procedure. They are more likely to require additional therapeutic interventions, including repeat needling revisions.


CONCLUSION

Needling is still a good option for failing/failed bleb with/without adjunctive agents to avoid resurgery. The adjunctive agents will depend upon timing, characteristic of bleb, risk factors in the patient and choice of the surgeon. Long-term success rate is unknown and complications are not uncommon. Further studies in future may provide us with a better success rate with other adjunctive agents, combination of agents or a modification of technique.


REFERENCES


