

# Efficacy and Safety of Multiple Needle Revisions and 5-FU Injections in Over 14-month old Dysfunctional Blebs in Thai Patients

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## Abstract

**Objective:** To evaluate efficacy and safety of multiple needle revisions and 5-FU injections in over 14-month old dysfunctional blebs in Thai patients.

**Methods:** Eight eyes of 8 Thai patients who had surgically restored bleb function by using needle revision and 5-FU injection from one ophthalmologist, same technique in over 14-month old dysfunctional blebs in between January 2008 and April 2009 were enrolled, a retrospective study. The dysfunctional bleb was defined if the IOP less than 21 mmHg with anti-glaucoma medication or more than 21 mmHg with or without anti-glaucoma medication. The success of the needling revision was defined as absolute if the intraocular pressure (IOP) was < 21 mmHg without antiglaucoma medications.

Bleb function was evaluated by slit-lamp biomicroscopic examination. Intraocular pressure measurement by applanation tonometry, morpho-

logy and degree of filtering bleb vascularization were evaluated and recorded. Intervention, either or both 5-FU or needling was performed when unsuccessful functioning bleb has been revealed to achieve target IOP less than 21 mmHg without antiglaucoma drugs.

**Results:** Mean of needle revision times and 5-FU injections are 1.25 and 6.25 mg, respectively. There were 100% (8 cases) successes to achieve IOP less than 21 mmHg without anti-glaucoma medication for at least 3 months post-interventional. There was no report of serious complication or infection during and post-intervention.

**Conclusions:** Needle revisions and 5-FU injections in over 14-month old dysfunctional blebs are simple, convenient, safe and effective in Thai patient.

**Key Words:** trabeculectomy, needle revision, 5-FU injection, Dysfunctional bleb

## Introduction

Subconjunctival fibrosis is the most common cause of filtering surgery failure. The increased amount of collagen in the failed bleb suggests that the proliferation of fibroblasts with associated production of collagen and glycosaminoglycans is important in filtering surgery response. Blebs may also be encapsulated, which will cause the increasing of the IOP.

Failed filtering bleb may be restored surgically. In eye that aqueous flow has been limited by subconjunctival fibrosis.

Needle revision has been performed by using a 25- to 30-gauge needle passed underneath the conjunctiva at 5 to 10 mm away from the bleb; in some cases 2% xylocaine with or without adrenaline is injected to balloon up the conjunctiva, and then passed into the bleb to incise the fibrous episcleral tissue. An effective modification is subconjunctival injection of 5 mg of 5-FU (0.5 cc of 10 mg/ml, or 0.1 ml of 50 mg/ml) at the time of the needling.

An effective modification is subconjunctival injection of 5 mg of 5-FU (0.5 cc of 10 mg/ml, or 0.1 cc of 50 mg/ml) at the time of the needling. The pyrimidine analogue 5-FU inhibits fibroblast proliferation and has proven useful in reducing scar formation after filtering surgery. The agent undergoes intracellular conversion to the active deoxynucleotide 5-fluoro-2'-deoxyuridine 5'-monophosphate (FdUMP), which interferes with DNA synthesis through its action on thymidylate synthetase. Higher dosages of 5-FU should be avoided because they can cause corneal endo-

thelial toxicity. Complication can be occurred such as conjunctival wound leak, corneal epithelial defect, and increase late-onset bleb leakage.

There is very little information about performing needle revision in late dysfunctional bleb and no information in Thai patients. In this study we would like to evaluate the efficacy and safety of needle revisions and 5-FU injections in over 14-month old dysfunctional bleb in Thai patients.

## Objective

To evaluate efficacy and safety of needle revisions and 5-FU injections in over 14-month old dysfunctional blebs in Thai patients.

## Method

Descriptive study of 8 consecutive Thai patients who had surgically restored bleb function by using needle revision and 5-FU injection from one ophthalmologist, same technique in over 14-month old dysfunctional blebs in between January 2008 and April 2009 were enrolled. The dysfunctional bleb was defined if the IOP less than 21 mmHg with anti-glaucoma medication or more than 21 mmHg with or without anti-glaucoma medication. The success of the needling revision was defined as absolute if the intraocular pressure (IOP) was < 21 mmHg without antiglaucoma medications at least 3 months post-intervention.

Bleb function was evaluated by slit-lamp biomicroscopic examination. Intraocular pressure measurement by applanation tonometry, morphology and degree of filtering bleb vascularization

were evaluated and recorded. Intervention, either or both 5-FU or needling was performed when unsuccessful functioning bleb has been revealed to achieve target IOP less than 21 mmHg without antiglaucoma drugs.

Needle revision had been performed under slit-lamp. Apply 1–2 drops of 2% xylocaine with adrenaline eyedrop every 5 minutes for 20 minutes and 1–2 drops of 10% phenylephrine pre-interventional to improve subconjunctival vision from conjunctival injection and decrease vascular injury during the procedure. The needling technique has been performed under slit-lamp by using a 27-gauge needle passed beneath the 5–7 mm away from conjunctival bleb and passed into the bleb to incise the fibrotic episcleral tissue. The accomplishment of needle revision would be accomplished by observing the balloon-up sign from the aqueous outflow at the incision site. No subconjunctival xylocaine injection in the study.

Subconjunctival injection of 5 mg of 5-FU has been injected at the 10 mm posterior to the bleb. The injection sites would be observed for bleeding until controlled, if occurred and 10 ml of sterile normal saline were soaked to wash out the retained 5-FU from conjunctival area followed by one drop of tobramycin eyedrop. Multiple procedures will be performed if only there were evidences of unsuccessful functioning bleb at the time of follow up.

Age, sex, date of surgery, preinterventional intraocular pressure, preinterventional medication, type and time of intervention, IOP and antiglaucoma medication prescribed at the last follow-up have been recorded.

## Results

Eight patients enrolled in the study. Women and men were equal (50%), and the mean age was 71.71 years (range 67 to 87 years). Mean dysfunctional blebs' age was 57.1 months (range 14.8 to 158.4 months). Mean pre-operative IOP were 29.5 mmHg (range 18 to 45 mmHg). There were 7 from 8 cases (87.5%) that had been taking more than 3 anti-glaucoma medications pre-operatively.

Needle -revision times and 5-FU injections are mostly only one intervention. Mean of needle -revision times and 5-FU injections are 1.25 times (range 1 to 2 times) and 6.25 mg (range 5 to 10 mg), respectively. There were 100% (8 cases) successes to achieve IOP less than 21 mmHg without anti-glaucoma medication for at least 3 months post-interventional. Mean post-operative follow-up period and post-operative IOP were 22.3 months (range 7.5 to 44 months) and 15.13 mmHg (range 11 to 18 mmHg), respectively. There were reported of superficial keratitis, burning sensation and filamentous keratitis after the procedure and all cases completely recovered after using Vislube® every 1–2 hours for 2–3 days. There was no report of serious complication or infection during and post-intervention. [Table 1]

**Table 1**

Case no.	Diagnosis	Dysfunctional bleb age (months)	intervention		Post-intervention complication	Post-operative follow-up period (months)
			Needle Revision (times)	5-FU Injection (mg)		
1	POAG	14.8	1	5		8
2	2 <sup>nd</sup> glaucoma	36.5	1	5		44
3	PACG	48.7	1	5		32
4	2 <sup>nd</sup> glaucoma	65.7	2	10	Burning sensation with superficial punctate keratitis	7.5
5	POAG	158.4	1	5		44
6	PACG	70.7	2	10		7.5
7	POAG	36.5	1	5	Filamentous keratitis	17.7
8	POAG	25.4	1	5	Superficial keratitis	17.7

**Discussions**

The conventional bleb revision or revised old dysfunctional trabeculectomy has usually been performed in the operating room and requires subconjunctival fibrotic tissue removal by incising the conjunctival tissue above the scleral flap to regenerate the aqueous outflow. Report of complications such as hypotony, choroidal detachment, endophthalmitis or bleb leak are not uncommon. The needle revision also tries to achieve the same goal by using the needle rather than wide opening the conjunctival tissue which may offer less serious complication. Needle revision and anti-fibrotic agent has been accepted worldwide in maintaining bleb function post-operatively. However, there are not many evidences about late dysfunctional bleb.

In the study, multiple needle revisions and 5-FU injections were performed in over 6-month dysfunctional blebs with the same technique from

one surgeon. The procedures were done within 5–10 minutes under slit-lamp at the out-patient department. There are no reports of serious complication from needle revision or 5-FU injection. One patient reported discomfort eye with filamentous keratitis after the procedure and recover without sequelae after couple days of vigorous preservative free tear. According to variety of surgical techniques such as needling techniques, sites and doses of 5-FU injection or surgical personal skill might have some effects to the success of this procedure. The accomplishment of procedure in this study is the balloon-up sign of aqueous at the incision site, which prove the certain re-functional bleb.

The complication from 5-FU injection mostly from corneal toxicity which should be prevented by using conjunctival NSS irrigation. In this study, there are some lag times between the

procedure and irrigation period because of the technician's availability. Normal saline irrigation right after the procedure is recommended in all 5-FU injected cases. There were no infection or hypotony reported in this study. There were only 8 cases enrolled in this study, which may not represent the whole picture. The study of more enrolled group and longer follow up time may provide us more information.

## Conclusions

Needle revisions and 5-FU injections in over 14-month old dysfunctional blebs are simple, safe and effective in Thai patient. The single intervention could satisfactorily restore bleb function, multiple interventions might be as well necessary.

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## References

1. Kapasi MS, Birt CM. The efficacy of 5-fluorouracil bleb needling performed 1 year or more posttrabeculectomy: a retrospective study. *J Glaucoma*. 2009 Feb; 18(2):144-8.
2. Feldman RM, Tabet RR. Needle revision of filtering blebs. *J Glaucoma*. 2008 Oct-Nov; 17(7):594-600. Review.
3. Mardelli PG. Slitlamp needle revision of capsular block syndrome. *J Cataract Refract Surg*. 2008 Jul; 34(7):1065-9.
4. Li G, Kasner O. Review of consecutive phacotrabeculectomies supplemented with early needle revision and antimetabolites. *Can J Ophthalmol*. 2006 Aug; 41(4):457-63.
5. Shetty RK, Wartluft L, Moster MR. Slit-lamp needle revision of failed filtering blebs using high-dose mitomycin C. *J Glaucoma*. 2005 Feb; 14(1):52-6.
6. Broadway DC, Bloom PA, Bunce C, Thiagarajan M, Khaw PT. Needle revision of failing and failed trabeculectomy blebs with adjunctive 5-fluorouracil: survival analysis. *Ophthalmology*. 2004 Apr; 111(4):665-73. Erratum in: *Ophthalmology*. 2005 Jan; 112(1):66.
7. Fagerli M, Løfors KT, Elsås T. Needling revision of failed filtering blebs after trabeculectomy: a retrospective study. *Acta Ophthalmol Scand*. 2003 Dec; 81(6):577-82.
8. Iwach AG, Delgado MF, Novack GD, Nguyen N, Wong PC. Transconjunctival mitomycin-C in needle revisions of failing filtering blebs. *Ophthalmology*. 2003 Apr; 110(4):734-42.
9. Durak I, Ozbek Z, Yaman A, Soylev M, Cingil G. The role of needle revision and 5-fluorouracil application over the filtration site in the management of bleb failure after trabeculectomy: a prospective study. *Doc Ophthalmol*. 2003 Mar; 106(2):189-93.
10. Ben-Simon GJ, Glovinsky Y. Needle revision of failed filtering blebs augmented with subconjunctival injection of mitomycin C. *Ophthalmic Surg Lasers Imaging*. 2003 Mar-Apr; 34(2):94-9.

11. Chang SH, Hou CH. Needling revision with subconjunctival 5-fluorouracil in failing filtering blebs. *Chang Gung Med J*. 2002 Feb; 25(2): 97-103.
12. Ophir A, Wasserman D. 5-Fluorouracil-needling and paracentesis through the failing filtering bleb. *Ophthalmic Surg Lasers*. 2002 Mar-Apr; 33(2):109-16.
13. Costa VP, Correa MM, Kara-Jose N. Needling versus medical treatment in encapsulated blebs. A randomized, prospective study. *Ophthalmology*. 1997 Aug; 104(8):1215-20.
14. Chen PP, Palmberg PF. Needling revision of glaucoma drainage device filtering blebs. *Ophthalmology*. 1997 Jun; 104(6):1004-10. Erratum in: *Ophthalmology* 1997 Oct; 104(10):1532.
15. Greenfield DS, Miller MP, Suner IJ, Palmberg PF. Needle elevation of the scleral flap for failing filtration blebs after trabeculectomy with mitomycin C. *Am J Ophthalmol*. 1996 Aug; 122(2):195-204.
16. Apostolov VI, Siarov NP. Subconjunctival injection of low-dose Mitomycin-C for treatment of failing human trabeculectomies. *Int Ophthalmol*. 1996-1997; 20(1-3):101-5.
17. Chalfin S, Memmen JE. Corneal endothelial toxic effect secondary to fluorouracil needle bleb revision. *Arch Ophthalmol*. 1995 Sep; 113(9):1093-4.
18. Mazey BJ, Siegel MJ, Siegel LI, Dunn SP. Corneal endothelial toxic effect secondary to fluorouracil needle bleb revision. *Arch Ophthalmol*. 1994 Nov; 112(11):1411.
19. Ewing RH, Stamper RL. Needle revision with and without 5-fluorouracil for the treatment of failed filtering blebs. *Am J Ophthalmol*. 1990 Sep 15; 110(3):254-9.
20. Heuer DK, Parrish RK 2<sup>nd</sup>, Gressel MG, Hodapp E, Palmberg PF, Anderson DR. 5-fluorouracil and glaucoma filtering surgery. II. A pilot study. *Ophthalmology*. 1984 Apr; 91(4):384-94.

## การศึกษาความปลอดภัยและประสิทธิภาพของการเปิดทาง ระบายน้ำโดยใช้เข็มและฉีด 5-FU ในผู้ป่วยที่ล้มเหลว จากการผ่าตัดต่อหิหนานกว่า 14 เดือน

ผู้ช่วยศาสตราจารย์ แพทย์หญิงมัญชิมา มะกรวัฒน์  
ภาควิชาจักษุวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์

### บทคัดย่อ

**วัตถุประสงค์:** เพื่อประเมินความปลอดภัยและประสิทธิภาพของการเปิดทางระบายน้ำโดยใช้เข็มและฉีด 5-FU ในผู้ป่วยที่เคยได้รับการผ่าตัดและล้มเหลวจากการผ่าตัดต่อหิหนานกว่า 14 เดือน

**วิธีการศึกษา:** การศึกษาย้อนหลัง ผู้ป่วยคนไทย 8 ราย จำนวน 8 ตาที่ได้รับการเปิดทางระบายน้ำโดยใช้เข็มและฉีด 5-FU จากจักษุแพทย์ท่านเดียว วิธีการเดียวกัน ในกลุ่มผู้ป่วยต่อหิหนานที่ได้รับการผ่าตัดและไม่สามารถควบคุมความดันตาได้โดยไม่ต้องใช้ยาลดความดันตาเป็นเวลานานกว่า 14 เดือนในช่วงเวลาระหว่างมกราคม 2551 ถึงเมษายน 2552 ความสำเร็จของการแก้ไขพิจารณาจากความดันตาหลังการเปิดทางระบายน้ำโดยใช้เข็มและฉีด 5-FU ต้องน้อยกว่า 21 มิลลิเมตรปรอทโดยไม่ต้องใช้ยาต่อหิหนาน จักษุแพทย์ประเมินการทำงานของทางระบายน้ำโดยใช้กล้องขยาย ทำการวัดความดันตาโดยเครื่องมือแอปเพลนเช้น ประเมินลักษณะรูปร่าง เส้นเลือด และพังพืดของทางระบายน้ำ หากมีความดันตามากกว่า 21 มิลลิเมตรปรอทหรือน้อยกว่า 21 มิลลิเมตรปรอทโดยต้องใช้ยาต่อหิหนานร่วมด้วย จะพิจารณาเปิดทางระบายน้ำโดยใช้เข็มและฉีด 5-FU

**ผลการศึกษา:** ความสำเร็จในการเปิดทางระบายน้ำโดยใช้เข็มและฉีด 5-FU คิดเป็นร้อยละหนึ่งร้อย คือสามารถลดความดันตาในผู้ป่วยทุกรายได้น้อยกว่า 21 มิลลิเมตรปรอท โดยไม่ต้องใช้ยาต่อหิหนานอย่างน้อย 3 เดือนหลังการเปิดทางระบายน้ำ จำนวนครั้งในการเปิดทางระบายน้ำโดยใช้เข็มและปริมาณยาฉีด 5-FU เป็น 1.25 และ 6.25 มิลลิกรัม ตามลำดับ ไม่มีรายงานผลข้างเคียงที่รุนแรงในผู้ป่วยทุกราย

**สรุป:** การเปิดทางระบายน้ำโดยใช้เข็มและฉีด 5-FU ในผู้ป่วยไทยที่ล้มเหลวจากการผ่าตัดต่อหิหนานกว่า 14 เดือน เป็นวิธีการที่ง่าย สะดวก มีความปลอดภัยและประสิทธิภาพสูง

