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# Efficacy of probing adjunctive with low-dose mitomycin-C irrigation for the treatment of epiphora in adults with nasolacrimal duct stenosis

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**Abstract:**

**PURPOSE:** The purpose of the study was to investigate the efficacy of adjunctive low-dose mitomycin-C (MMC) during successful lacrimal duct probing in adults with nasolacrimal ducts (NLDs) stenosis.

**MATERIALS AND METHODS:** This is a prospective case–control study on patients with NLD stenosis who were randomized into two groups. All patients underwent probing without or with an application of MMC. Former group received 0.2 mg/ml MMC irrigation for 5 min. The main outcome measures were objective evaluation of patency with irrigation, as well as patients' subjective assessment of improvement.

**RESULTS:** There were 73 eyes in 58 consecutive patients; patient mean age ranged from 19 to 78 years (mean 44 years). Female included larger group of patients (63%) and mean duration of the symptoms was 26.1 months (range, 2–120 months). After mean follow-up of 11 months (range, 9–14 months), 23 (60%) of the 38 eyes in the MMC groups and 8 (22%) of the 35 eyes in control group had complete response and remained symptom free. This difference was statistically significant ($P$ = 0.005). According to the patient's satisfaction, epiphora was partially improved in 6 (17%) eyes of control group and 4 (10%) eyes in MMC group. Application of MMC has a better outcome in patients with severe stenosis ($P$ = 0.007); patients who had symptoms more than 12 months ($P$ = 0.02) and patients with constant epiphora were compared with intermittent symptoms ($P$ = 0.001). No complications were detected during patients follow-up.

**CONCLUSION:** This study suggests acceptable long-term results for probing adjunctive with MMC irrigation for adults with NLD stenosis that can be recommended as a simple and effective procedure for these patients.

**Keywords:**

Adults, epiphora, mitomycin-C, nasolacrimal duct stenosis, probing

## Introduction

Epiphora is a common disorder in ophthalmology practice and it could be a serious problem that can interfere with daily activities. Dacryocystorhinostomy (DCR) is the gold standard treatment for nasolacrimal duct obstruction (NLDO) with more than 90% success rate,[1,2] but it is an invasive procedure that has considerable risks and expenses.[2,3] Recently, there has been a trend toward the application of the less invasive procedures for treating NLDO problems, especially for patients who have not complete NLDO.[1,4]

Probing is a minimally invasive, cost-effective, easily performed procedure that can be done by topical anesthesia in the outpatient setting. There are many studies in favor of its effectiveness in congenital

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NLDO in children, but its effectiveness in treating adults with NLDO lacks support of enough evidence.[1,4]

Mitomycin-C (MMC) is an antibiotic antineoplastic agent. It has been used intraoperatively and postoperatively for the prevention of recurrent pterygium, re-stenosis of fistula in glaucoma filtration surgery, and for the treatment of conjunctival and corneal epithelial dysplasia and some neoplasia.[5-8] The beneficial effects of adjunctive MMC for DCR surgery success rate improvement have been studied.[9,10] Furthermore, a few studies demonstrated a combined effect of probing and MMC in adult NLDO.[11-13] However, to the author's best knowledge, MMC has not been applied in conjunction with probing for treating patients with nasolacrimal duct (NLD) stenosis.

The aim of this prospective comparative study was to evaluate the safety and efficacy of the adjunctive use of MMC irrigation after probing for treating adults with NLD stenosis.

## Materials and Methods

This is a prospective comparative interventional case–control study conducted in Farabi Eye Hospital, Tehran University of Medical Sciences, which enrolled adult patients complaining of epiphora due to primary NLD stenosis. The study protocol was based on the tenets of the Declaration of Helsinki and was approved by the Institutional review board of Tehran University of Medical Sciences (IR.PR.REC.1390.08). Informed consent was obtained from all patients after detailed information about the procedure had been provided. On the first visit, demographic and other information including duration of symptoms and frequency of symptoms were collected.

Patients with a history of facial trauma, obvious facial bone deformity, orbital or periorbital neoplasm (nose, sinus, and lacrimal system), nasal surgery, sinusitis, and chronic allergic rhinitis; patients with secondary epiphora (reflex hyper secretion) due to any causes of ocular surface irritation such as corneal erosion, conjunctivitis, trichiasis, and dry eye,; and patients with eyelid or punctal malposition, punctal atresia, or obstruction due to scar or conjunctivochalasia were excluded from the study.

Complete preoperative ophthalmology workup including slit-lamp examination for rule out of ocular surface disorder and eyelid evaluation for laxity, ectropion, or entropion was performed.

Definite NLD stenosis diagnosis was based on lacrimal drainage system irrigation which is confirmed with dacryoscintigraphy. A symptomatic patient was called stenotic when after forced irrigation, fluid passed to the nasal cavity with or without reflux from Puncta, and in diagnostic probing, a hard touch was felt. With lacrimal drainage system scintigraphy, the diagnosis of NLD stenosis was confirmed when there was a significant delay in dye passage. Patients with soft contact felt during diagnostic probing and upper drainage system (canalicular) obstruction were excluded. The important point was to distinguish between NLD stenosis of complete NLD obstruction (NLDO). When a hard touch was felt during diagnostic probing but, with forced irrigation, no fluid passage to the nasal cavity was detected, the patient suggesting as complete NLDO. Of course, after doing a lacrimal drainage system scintigraphy, no dye passage should have been seen even in the delayed phases.

Based on the irrigation, the severity of stenosis was classified into three grades:

- Grade1: Fluid passes to the nasal cavity with a gentle push without reflux from the puncti
- Grade 2: Most of the fluid passes to the nasal cavity with a small portion reflux from the puncti
- Grade 3: Most of the fluid reflux from puncti and a small portion pass to the nasal cavity.

Patients were divided into two groups (Groups A and B) according to block randomization. Group A patients underwent simple lacrimal duct probing. The procedure was performed with a gauge 00 Bowman's probe. After dilating one of the upper or lower puncta, the probe was passed through the canaliculus to reach the hard stop and then was rotated in the direction of NLD and advanced to enter the nasal cavity. Feeling the metal-to-metal touch of the probe to another instrument which was entered to the nasal cavity through nostrils was the final reassurance of the procedure being successfully done. In Group B, after performing probing procedure as we mentioned before, 0.5 cc of MMC 0.2 mg/ml was injected to the lacrimal drainage system and care was taken to avoid direct corneal contact with the medication. The ocular surface was also irrigated with normal saline. During MMC injection, to minimize systemic absorption of drug, a cotton-tipped applicator was placed into the nasal cavity and patients were instructed not to swallow the solution. After MMC irrigation, water for gargling was used to help clear any residual MMC. The medication was left in the lacrimal system for a total of 5 min, and then, copious irrigation with gentle suctioning was followed.

Patients were visited the day after procedure for any possible complication and they were prescribed 0.5% chloramphenicol and 0.1% betamethasone eye drops, 4 times per day, for 1 week. Follow-up examination was conducted 1 week and then 1, 3, and 9 months after procedure. During each visit, we documented subjective

**Table 1: Demographic data and clinical characteristics of sub-groups**

| Parameters | Probing (Group A) *n*=35 | Probing + MMC* (Group B) *n*=38 | *P* |
|---|---|---|---|
| Age (mean±SD, year) | 45.94±15.88 | 42.18±12.27 | 0.223 |
| Sex | | | |
| Male | 14/35 (40.0%) | 13/38 (34.2%) | 0.60 |
| Female | 21/35 (60.0%) | 25/38 (65.8%) | |
| Duration of symptoms | | | |
| ≤1 year | 15/35 (42.9%) | 18/38 (47.4%) | 0.699 |
| >1 year | 20/35 (57.1%) | 20/38 (52.6%) | |
| Frequency of symptoms | | | |
| Intermittent | 20/35 (57.1%) | 14/38 (36.8%) | 0.06 |
| Constant | 15/35 (42.9%) | 24/38 (63.2%) | |
| Severity of NLD stenosis | | | |
| Mild | 0/35 (0.0%) | 0/38 (0.0%) | 0.63 |
| Moderate | 8/35 (22.9%) | 7/38 (18.4%) | |
| Severe | 27/35 (77.1%) | 31/38 (81.6%) | |

*MMC=Mitomycin C; NLD=Nasolacrimal Duct

evaluation of epiphora improvement by asking about tearing condition. Furthermore, NLD patency was confirmed by irrigation and slit-lamp examination of puncta, conjunctiva, and cornea was performed.

According to patients complain from epiphora, there were three groups: (1) completely resolved (complete improvement), (2) partially improved (more than 50% improvement in subjective symptoms), or (3) not improved at all (unsatisfied patient). The patients who were unsatisfied with the result and their symptoms persisted were proposed for DCR surgery.

Statistical analysis was performed using SPSS Statistics software, version 22 (IBM, Armonk, NY) and Chi-square/Fisher exact test was used for the analysis. $P < 0.05$ was regarded as statistically significant.

## Results

Of the 73 patients enrolled in this study, 46 patients (63%) were female and 27 (37%) were male with a mean age of 44 years (ranged from 19 to 78 years) and the mean duration of the symptoms was 26.1 months (range: from 2 to 120 months). Thirty-four (46.6%) patients had intermittent symptoms and for other 39 (53.4%) patients, symptoms were constant and present most of the time. According to the grading system described before, the severity of NLD stenosis was assessed as severe in 58 (79.5%) eyes, moderate in 15 (20.5%) eyes, and mild in non. In 33 eyes (45%), the duration of symptom was ≤12 months.

Probing was performed alone in 35 (47.9%) eyes (Group A) and in combination with MMC irrigation in 38 (52.1%) eyes (Group B). There was no statistically significant difference of age, sex, duration of symptoms, frequency of symptoms, and severity of NLD stenosis between patients and control group [Table 1]. Successful outcome

**Table 2: Comparison of success rates between the subgroups**

| Parameters | Probing (Group A, *n*=35), *n* (%) | Probing + MMC (Group B, *n*=38), *n* (%) | *P* |
|---|---|---|---|
| Complete response | 8/35 (22) | 23/38 (60) | 0.005 |
| Partial response | 6/35 (17) | 4/38 (10) | 0.2 |
| Duration of symptoms (years) | | | |
| ≤1 | 15/35 (42.9) | 18/38 (47.4) | 0.02 |
| >1 | 20/35 (57.1) | 20/38 (52.6) | 0.05 |
| Frequency of symptoms | | | |
| Intermittent | 20/35 (57.1) | 14/38 (36.8) | 0.30 |
| Constant | 15/35 (42.9) | 24/38 (63.2) | 0.001 |
| Severity of NLD stenosis | | | |
| Moderate | 8/35 (22.9) | 7/38 (18.4) | 0.26 |
| Severe | 27/35 (77.1) | 31/38 (81.6) | 0.07 |

MMC=Mitomycin C, NLD=Nasolacrimal duct

in patients, who were treated with MMC, does not appear to have a significant relationship with age, gender, or laterality ($P > 0.05$). There were not any remarkable intraoperative and postoperative complications.

For both the groups, the mean follow-up interval was 11 months (range, 9–14 months) in which subjective improvement was happened completely in 22% (8/35) of the patients in Group A and 60% (23/38) of the patients in Group B. This difference was remarkable ($P = 0.005$). Furthermore, 17% of the patients in Group A and 10% of the patients in Group B had partial improvement [Table 2].

The impacts of variables such as frequency of symptoms, duration of symptoms, and severity of stenosis on the outcome of the treatment were also evaluated. Therefore, the patients were separated into two groups: who had complaints of intermittent epiphora (34 eyes) and patients with permanent symptoms (38 eyes). There was no statistically significant difference between subjective

symptoms relief if MMC was applied or not in patients with intermittent symptoms, but it was significant in patients with permanent symptoms ($P = 0.3$ vs. $P = 0.001$).

Subjective symptom relief in patients who had severe stenosis (58/73 patients) in preinterventional evaluation compared to cases with moderate NLD stenosis (15/73) had statistically significant difference ($P = 0.007$ vs. $P = 0.26$).

According to the duration of symptoms, we had two subgroups: 33 eyes had ≤12 months, and in 40 eyes, patients had more than 12 months duration of symptoms. If MMC was applied, subjective symptom relief in patients who had ≤12 months duration of symptoms was less than patients who had symptoms for more than12 months ($P = 0.05$ vs. $P = 0.02$) [Table 2].

## Discussion

DCR is indicating for patients with complete obstruction of NLD and also in patients with intractable NLD stenosis that epiphora interfere with daily activity.[1-3] It is logical, cost-effective, and beneficial for patients to have a noninvasive and simpler procedure performed whenever possible.

For patients with incomplete NLDO, a variety of noninvasive treatment modalities have been proposed, including probing, silicone intubation, and balloon dacryocystoplasty using an antegrade or retrograde technique.[14-16] Some studies have investigated the efficacy of silicone intubation in the management of (partial) lacrimal duct obstruction in adults. Success rate was noted in 22%–62%.[14,15] Recently, another noninvasive treatment method, balloon dacryocystoplasty, has gained popularity, especially for the treatment of congenital NLDO. The success rate of balloon dacryocystoplasty in adults with partial NLDO has been reported from 25% to 90%.[16]

NLD probing is a minimally invasive and easily performed procedure that could be available by topical anesthesia in the clinic. There are many studies in favor of its effectiveness in congenital NLDO in children with unresponsive to trial conservative treatment with massage and/or topical antibiotics.[17] Although probing for congenital NLDO is an effective treatment, but effectiveness of nasolacrimal probing in treating adults with NLDO lacks support of enough evidence.[1,4] Bell's study[4] demonstrated 52% improvement of epiphora in adults with NLDO after doing simple probing. Guinot-Saera and Koay study showed that 35% of their adult NLDO patients were completely and 17% were partially symptom free after performing probing.[1] Although these two study have suggested relatively good efficacy, the efficacy of probing for adult cases remains controversial due to the risk of inducing trauma and significant recurrence rate.[1,4]

Since 1983, MMC has been used in many ocular procedures to enhance success rate with reduce scaring.[5-9] MMC is an antineoplastic antibiotic which is isolated from *Streptomyces caespitosus* and acts as a potent fibroblastic inhibitor and significantly inhibits the synthesis of DNA, cellular RNA, and proteins. Topical usage of MMC in conjunction with ophthalmology surgery has increased considerably because it modulates the wound-healing process.[5-7] It has been used intraoperatively and postoperatively for the prevention of recurrent pterygium, re-stenosis of fistula in glaucoma filtration surgery, and for the treatment of conjunctival and corneal epithelial dysplasia and neoplasia and ocular cicatricial pemphigoid.[5-9] Kao *et al*. applied MMC intraoperatively in external DCR (EXT-DCR). In comparison to regular EXT-DCR, the success rate in the MMC group was 100% versus 87.5% in the control group.[9] They did not report any significant complications. Histopathology examination after MMC usage for endoscopic transnasal DCR showed loose and hypocellular subepithelial connective tissue with significant reducing scar formation.[10,18]

The optimal dosage and exposure time of MMC are still controversial. Liao *et al*.[19] applied 0.2 mg/mL of it for 30 min and some authors have been used in 0.3 mg/mL dosage for 3 min with favorable results.[10] MMC potentially has toxic effects including superficial punctate keratitis, iritis, glaucoma, cataract, and late-onset corneal and scleral necrosis and rarely cornea melting.[20] In this study, after successful probing, we applied 0.5 cc of MMC 0.2 mg/ml slow irrigation during 5 min. No acute or chronic complications were observed.

Although the efficacy of adjunctive low-dose MMC irrigation during lacrimal duct probing for adults with NLDO has been evaluated,[11,13] in authors' best knowledge, MMC has not been applied in conjunction with probing for patients with NLD stenosis. At the end of this prospective study, we found that the application of MMC during simple probing caused acceptable results up to 60% of the NLD stenosis patients. There was a statistically significant difference in subjective improvement of symptoms, in contrast to patients who underwent probing alone (20%) ($P = 0.005$). Furthermore, low-dose MMC irrigation had more significant effect in relieving symptoms of patients who had subjectively complaint of constant epiphora ($P = 0.001$), patients with severe NLD stenosis ($P = 0.007$), and in eyes who had >12 months duration of symptoms ($P = 0.02$).

Apparently, our reported success rate for complete subjective satisfaction is lower than DCR (85%–90% vs. 69%), but it holds several advantages including the procedure is a nonincisional method and the normal anatomy of NLD pathway is preserved otherwise; there is a possibility of repeat procedure. Compared to other noninvasive surgical methods, silicone intubation (22%–62%),[14,15] and balloon dacryocystoplasty in adults (25%–90%),[16] the success achieved is remarkable for our new version of NLD stenosis treatment. On the other hand, silicone tubing may cause complications in itself,[15] and balloon dacryocystoplasty occasionally may prove impossible because of the difficulty in introducing the catheter in the narrowed NLD.[16]

## Conclusion

Our findings suggest that simple probing adjunctive with MMC irrigation has acceptable results in adult patients with NLD stenosis and it would add neither significant extra time nor cost to probing procedure. In addition, we did not find any noticeable complications in our cases. However, this study was a preliminary study, and a larger sample size with longer follow-up is planned to determine the definite effect of MMC in adjunctive with probing for the treatment of adult NLD stenosis.


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### Conflicts of interest
The authors declare that there are no conflicts of interests of this paper.

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