

Results of the application of intraoperative mitomycin C in dacryocystorhinostomy

M.H. ROOZITALAB, M. AMIRAHMADI, M.R. NAMAZI

Department of Ophthalmology, Shiraz University of Medical Sciences, Shiraz - Iran

PURPOSE. *Dacryocystorhinostomy (DCR) is widely accepted as the procedure of choice for surgical correction of lacrimal drainage system obstruction distal to common canaliculus in adulthood. The success rate of DCR has been reported to be from 63% to 99%. DCR failure has been attributed to membranous occlusion of the rhinostomy site caused by soft tissue scarring. More recently, use of mitomycin C (MMC) has been described in lacrimal drainage surgery. The beneficial effect of MMC as a surgical adjunct is thought to be related to its potent inhibition of fibroblast proliferation.*

METHODS. *To improve the success rate of DCR, the authors used MMC as an adjunct to surgery in 130 patients with nasolacrimal duct obstruction undergoing lacrimal surgery. They were assigned randomly into a MMC DCR group and a regular DCR group (control group).*

RESULTS. *The mean age of the MMC group was 40 ± 15 years and that of the control group was 42 ± 16 years. The standard surgical techniques of an external DCR were used in all patients of both groups. Patients were followed for 6 months. The authors evaluated the patients with subjective symptoms (improvement in tearing) and objective findings such as the height of tear meniscus, fluorescein dye test, and patency at the time of irrigation. There was no significant difference in the age between the two groups ($p=1.00$). Six patients in the mitomycin group were symptomatic after 6 months' follow-up; probe and irrigation showed non-patency of lacrimal system. The success rate in the MMC group was therefore 90.5% (59/65), and in the conventional group it was 92.4% (60/65). No significant difference between the two groups was present ($p=0.75$).*

CONCLUSIONS. *The authors conclude that the use of intraoperative MMC in DCR surgery does not change the success rate of this procedure. (Eur J Ophthalmol 2004; 14: 461-3)*

KEY WORDS. *Dacryocystorhinostomy, Mitomycin C, Lacrimal drainage obstruction, Treatment*

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INTRODUCTION

Dacryocystorhinostomy (DCR) is widely accepted as the procedure of choice for surgical correction of lacrimal drainage system obstruction distal to common canaliculus in adults. The success rate of DCR has been reported to be from 63% to 99%. Factors influencing the outcome of lacrimal drainage system surgery include the surgical approach (i.e., intranasal DCR, vs external DCR), the

presence of preoperative acute dacryocystitis or postoperative soft tissue infection, a history of trauma to the lacrimal drainage apparatus, and the use of silicon tubes. DCR failure has been attributed to membranous occlusion of the rhinostomy site, common canalicular obstruction, and an inappropriate size or location of bony ostium. Membranous failure, caused by soft tissue scarring at the rhinostomy site, is considered by many authors as the most common cause of primary DCR failure (1). More

recently, use of mitomycin C (MMC) has been described in lacrimal drainage surgery. The beneficial effect of MMC as a surgical adjunct is thought to be related to its potent inhibition of fibroblast proliferation (1). To evaluate the effectiveness of MMC in improving the success rate of DCR, we used this agent as an adjunct to surgery in patients undergoing lacrimal surgery, comparing the long-term success rate of conventional DCR surgery with that of DCR surgery with intra-operative MMC soaking.

SUBJECTS AND METHODS

From November 2001 to August 2003, 130 patients diagnosed with nasolacrimal duct obstruction (congenital and acquired) were assigned randomly into a MMC DCR group (MMC group) and regular DCR group (control group). A total of 130 DCRs were performed by one surgeon (MHR). The mean age of the MMC group was 40 ± 15 years and that of the control group was 42 ± 16 years. In the MMC group, 75% were female and 25% were male. In the control group 62% were female and 38% were male.

The standard surgical techniques of an external DCR were used in all patients of both groups. All of patients were operated under general anesthesia. A mesh soaked in epinephrine was inserted in the nose. A skin incision was performed 10-12 mm medial to medial canthus, 2-3 mm above medial canthus, and 10 mm below medial canthus), and blunt dissection to the periosteum overlying the anterior lacrimal crest was undertaken. The periosteum then was incised and elevated off the lacrimal sac fossa. A nasal osteotomy of 15-18 mm was created over the lacrimal fossa with Kearson bone punch. The lacrimal sac was opened in a longitudinal fashion to form anteroposterior flaps. The nasal mucosa was cut in a similar fashion to the lacrimal sac. Then, the mesh in the nose was removed. In the MMC group, a piece of cotton saturated with 0.2 mg/ml MMC attached with a long thread was placed over the posterior flaps and osteotomy site with the long thread passing out through the nostril. The mesh was then removed in the recovery room transnasally after an application time of 30 minutes. Once the MMC-saturated cottonoid was in place, anterior nasal and lacrimal sac flaps were closed with 6-0 Vicryl sutures, as were the periosteum and orbicularis muscle in separate layers. The skin incision was sutured with 6-0 nylon suture. The MMC saturated cottonoid was removed transnasally after a 30-minute soak by pulling the long thread out from the nos-

tril. In the control group, the same procedures were performed except for the absence of the MMC application.

To evaluate the long term long-term results of both groups, we documented the subjective symptoms and classified them as symptom free (no tearing) and no improvement in tearing by asking patients about the tearing condition at 6 months follow-up after operation. In addition, two objective findings such as the height of tear meniscus, fluorescein dye tests, and patency of irrigation were documented. We measured the height of tear meniscus and fluorescein dye tests with fluorescein paper applied in unanesthetized lower fornix under cobalt blue light at slit lamp for each patient, and graded it as high tear meniscus (≥ 0.1 mm) and or normal tear meniscus (≤ 0.1 mm), and then measured residual color after 5 minutes and graded intensity of residual dye (grade 0-4; 0 = no dye, 4 = all the dye). All the examinations were done by the second author, who was blinded to the procedures. All of patients with high tear meniscus and subjective finding (tearing) underwent probe and irrigation at 6-month follow-up after operation.

Chi-square test was used to compare the success rate between the two groups.

RESULTS

A total of 130 DCR surgeries were conducted in this study: 65 eyes were in the MMC group and the remaining 65 eyes were in the conventional group. There was no significant difference in age between the two groups ($p=1.00$). Six patients in the mitomycin group were symptomatic after 6 months follow-up. The success rate in the MMC group was 90.5% (59/65). In the control group there were five eyes with excessive tearing after DCR surgery and the remaining were symptom free, with success rate of 92.4% (60/65). There was no significant difference between the two groups ($p=0.75$).

One week after operation, height of tear meniscus was measured; six eyes in the MMC group were classified as having a high tear meniscus and grade 4 fluorescein dye test. In the control group, five patients had high tear meniscus and grade 4 dye fluorescein test. Therefore, estimation of tear meniscus height showed no significant difference between the two groups ($p=0.75$).

In the MMC group, all eyes except six showed patency of the lacrimal drainage system, with patency rate of 90.5%, while in the conventional group, five eyes revealed

non-patency of the drainage system, with patency rate of 92.4%, which was not significant ($p=0.75$). No complications such as abnormal nasal bleeding, mucosal necrosis, or infection were noted in any patients.

DISCUSSION

DCR is a widely accepted technique for correction of nasolacrimal obstruction. (2). The decrease in the size of the healed intranasal ostium after surgery is the result of a normal wound healing response. Antimetabolites which can inhibit DNA or RNA replication, cell division, protein synthesis, and fibroblast proliferation have been used as adjunctive therapy to prevent excessive scar formation in DCR surgery, glaucoma surgery, and pterygium removal. MMC is the most popular antifibrotic agent used intraoperatively. It is highly toxic when used systemically in anti-tumor therapy. Intraoperative application of MMC in lacrimal surgery is a new indication. When used as a 0.5 mg/ml concentration for 2.5 minutes, intraoperative application of MMC favorably affected the wound healing process. (3).

Fibroblasts have other actions besides proliferation during wound healing, including migration collagen production, and contraction. MMC causes cell death by toxicity and induced apoptosis and also may influence these steps when it is used in DCR. The interaction of epithelial and vascular endothelial cells with fibroblasts also may influence the scar formation (3).

In this study the effect of intraoperative MMC application in DCR was evaluated. In the MMC group 75% were female and 25% were male. In the control group 62% were female and 38% were male. In this study female/male ratio was approximately 3/1, illustrating that females are more susceptible to nasolacrimal duct obstruction. Patients were followed for 6 months and evaluated by subjective symptoms and objective findings. The success rates in the MMC and control groups were 90.5% and 92.4%, respectively, which shows no statistical difference ($p = 0.75$).

Shu et al (4), Shine et al (5), Patrick and Robert (1), and Camara et al (6) found MMC to be effective in increasing the success rate of DCR, whereas Zilelioglu et al (3), reported that MMC could not increase the success rate of DCR. The current study, which unlike previous studies was performed on a large number of cases, negates the effectiveness of MMC in increasing the success rate of DCR.

Proposed reasons for this ineffectiveness are as follows.

DCR wounds typically are bloodier than trabeculectomies when compared with the conjunctiva, Tenon's capsule, and sclera, because of increased vascularity of the nasal mucosa, lacrimal sac, and nasolacrimal duct mucosa, and bone. Increased vascularity of the DCR surgical field may dilute the effects of MMC. This variation was thought to decrease the possible penetration of drug beyond surgical borders (7).

Also, MMC at concentrations of 0.1 to 0.4 mg/ml sometimes has no effect on trabeculectomy results, therefore concentrations greater than 0.5 mg/ml may be required to have a clinical effect on the inhibition of wound healing in DCR. Therefore, the MMC concentration used for trabeculectomies may not be as beneficial as that for lacrimal drainage surgery.

We conclude that intraoperative application of 0.2 mg/ml MMC in DCR surgery does not change the success rate of this procedure.

Reprint requests to:
M.R. Namazi, MD
P.O. Box 71955-687
Shiraz, Iran
Namazi_mr@yahoo.com

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