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ScienceDirect
American Journal of Otolaryngology–Head and Neck Medicine and Surgery xx (2011) xxx–xxx
American Journal of OTOLARYNGOLOGY
www.elsevier.com/locate/amjoto

Significance of adjunctive mitomycin C in endoscopic dacryocystorhinostomy

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Received 24 August 2010

Abstract

Purpose: The purpose of this study is to observe the effect of intraoperative topical application of mitomycin C (MMC) on the results of endoscopic dacryocystorhinostomy.
Design: This is a prospective, randomized, controlled, single-blind study.
Settings: Hospitalized treatment was done in a tertiary medical college hospital and research center that deals with a predominantly rural population.
Patients: Patients with primary acquired postsaccal obstruction causing chronic dacryocystitis were considered.
Methods: A total of 38 patients were randomized into either a mitomycin group or a control group. Both of these groups were subjected to an identical surgical procedure, except that 0.2 mg/dL of MMC was used in the mitomycin group, whereas normal saline was used in the control group. The follow-up period was at least 6 months. An asymptomatic patient with a visible stoma at nasendoscopy and free flow of saline into the nose with lacrimal syringing after 6 months after surgery was used as criteria for defining a successful result.
Results: The success rate was 82.3% when MMC was used and 85.7% among the controls ($P > .05$). Granulations, adhesions, and obliterative sclerosis occurred in a similar number of patients of both groups. However, granulations and adhesions did not have a bearing on the success rate in either group.
Conclusion: Mitomycin C did not appear to influence the occurrence of granulations, synechiae, or obliterative sclerosis, nor did it alter the success rate significantly.

1. Introduction

Chronic dacryocystitis is a commonly encountered condition and can be treated either by external dacryocystorhinostomy (Ex-DCR) or by endoscopic endonasal dacryocystorhinostomy (En-DCR). Intranasal dacryocystorhinostomy was first described by Caldwell in 1893 [1,2]. Almost a century later, McDonogh and Meiring [3] described the En-DCR. Since then, the advantages of En-DCR over Ex-DCR have been well established. An En-DCR will avoid a facial scar, will not interfere with the lacrimal pump mechanism, preserves the medial canthal ligament, and carries a shorter operating time.

Although En-DCR has several advantages over Ex-DCR, the results are similar [2,4-8], hence, the need for adjuvant measures. Several adjuvant measures have been reported [8-12]. However, these measures are more demanding and have not contributed significantly to the results [9-13].

Recurrence is attributed to obliterative scarring, granulations, and adhesions at the stomal site after En-DCR. Mitomycin C (MMC) is an antibiotic isolated from *Streptomyces caespitosus* by Wakaki et al in 1958 [14]. When applied topically at the operative site, it inhibits

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0196-0709/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.amjoto.2011.01.001

fibroproliferative activity [15,16]. This property of MMC is used by ophthalmologists in pterygium excision and trabeculectomy. In published literature, there are few controlled trials in which MMC has been used as an adjunct to En-DCR [17,18]. Furthermore, the results of these trials do not concur, and the role of MMC remains inconclusive. This study is in the hope that further controlled trials may provide more convincing information on the role of intraoperative topical application of MMC in En-DCR.

2. Patients and methods

This is a randomized, controlled, single-blind study wherein all patients referred by the Department of Ophthalmology with a diagnosis of chronic dacryocystitis due to primary acquired postsaccal obstruction of the lacrimal apparatus were considered. Patients younger than 15 years and those with a history of previous lacrimal sac surgery were excluded.

Institutional consent form was used in which additions were made regarding the inclusion of patients in a study where MMC was used as an adjunct to a standardized surgical procedure. In addition, it was conveyed to the patients that the use of MMC in this procedure was not unprecedented and that the concentration of MMC (0.2 mg/mL) was less than that used in previous studies [18], in which no adverse effects were observed.

A total of 38 patients were randomized for either En-DCR with topical application of MMC (mitomycin group) or En-DCR with topical application of normal saline (control group). A combined sample size of 38 patients was arrived at by using the power approach with a power of 90% and an assumed effect size of 35% between the mitomycin and control groups. Random allocation of patients to the mitomycin group or the control group was done by allowing each patient to choose from a bunch of unbiased chits. This was done after counseling and before admission for surgery.

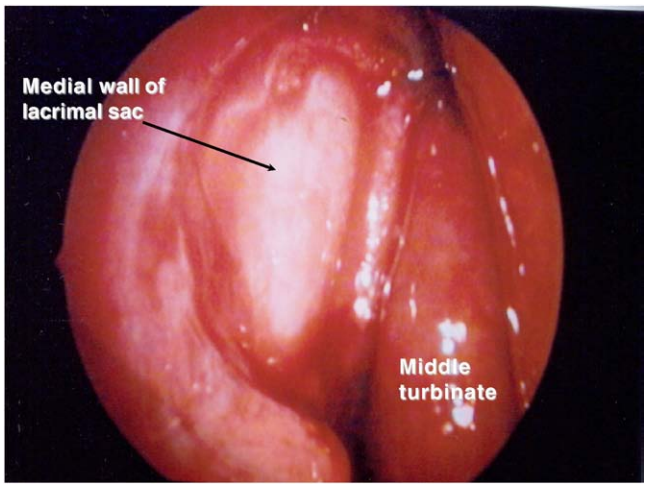

Fig. 1. Extent of exposure of the medial wall of lacrimal sac—from above the level of axilla of MT to the level of insertion of inferior turbinate.

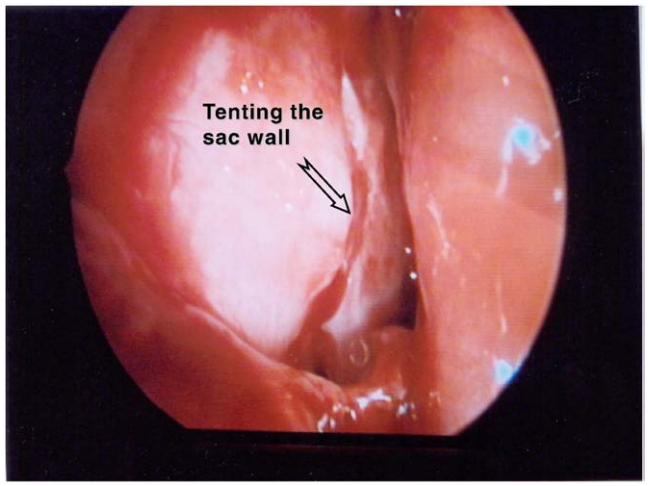

Fig. 2. Tenting of medial wall of lacrimal sac with a Bowman probe prevents injury to lateral sac wall while incising the medial wall.

Mitomycin group consisted of 17 patients, and control group had 21 patients. All of these patients were treated by the Department of Otorhinolaryngology of Sri Devaraj Urs Medical College Hospital between 2003 and 2009.

2.1. Surgical technique

All patients were subjected to a standardized surgical technique. Under sedation and local anesthesia, the middle turbinate (MT) is infractured. The medial surface of the lacrimal fossa was noted just anterosuperior to the axilla of the MT. An oval patch of mucoperiosteum measuring about 2 cm vertically and 1 cm anteroposteriorly surrounding the maxillary line is removed using the otologic drill with a protective sleeve. Bone removal is carried out until the external periosteum of the lacrimal bone and medial wall of lacrimal sac is reached.

Using a Kerrison's punch, the bony window is widened circumferentially until the medial wall of lacrimal sac is exposed for about 8 mm above the axilla of MT to just above the insertion of inferior turbinate (Fig. 1). A Bowman lacrimal probe is passed into the lacrimal sac through the inferior punctum and canaliculus. The limits of the lacrimal sac are probed, and the medial wall of sac is tented medially (Fig. 2). The tented medial wall of sac is removed completely. For patients belonging to the mitomycin group, a cottonoid soaked in 0.2 mg/mL of MMC was placed over the raw edges of stoma for 10 minutes. In the control group, normal saline was used in place of MMC. Selective nasal packing was done, and complete hemostasis was achieved.

The nasal pack was removed the next day, and patient was discharged from hospital. The patients were reviewed on the seventh postoperative day with nasal endoscopy and removal of crusts and debris. Stomal patency was determined

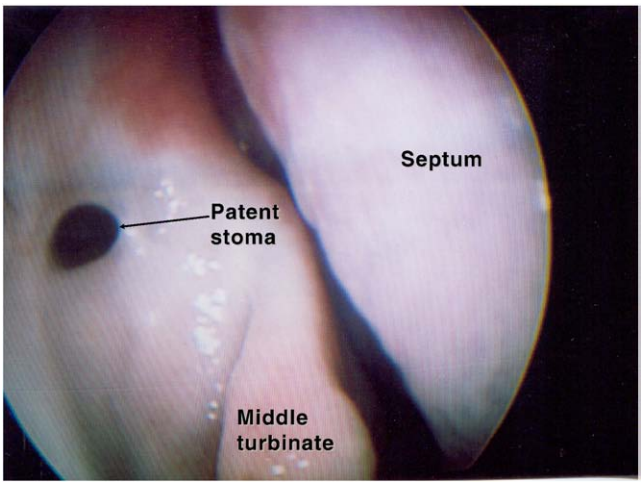

Fig. 3. A patent stoma after completion of the healing process is markedly smaller than that created during surgery.

subjectively by resolution of epiphora and objectively by free flow of saline with lacrimal syringing during nasal endoscopy. Patients were reviewed at monthly intervals for at least 6 months (Fig. 3).

3. Results

A total of 38 patients were part of this study. The youngest was 18 years old, and the oldest was 54 years old. Most patients were between 21 and 30 years old, the average being 33.6 years. Sixteen were men, and 22 were women. The right eye was affected in 28 patients. Most patients belonged to the socioeconomically weaker sections.

A successful outcome of surgery was defined as those patients who were symptom free for more than 6 months and free flow of saline with lacrimal syringing and a visible stoma at nasal endoscopy 6 months after surgery. A

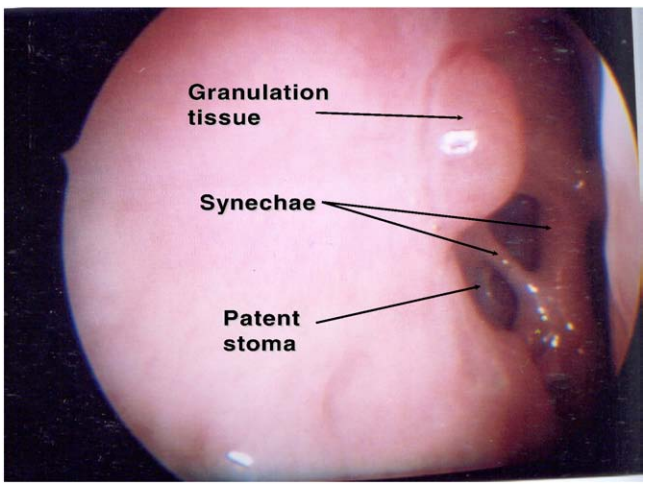

Fig. 4. A patent nasolacrimal stoma even in the presence of granulations and adhesions in a patient where MMC was used as an adjunct.

Table 1
Follow-up nasal endoscopic findings

	Mitomycin group (n = 17)		Control group (n = 21)	
	Successful	Unsuccessful	Successful	Unsuccessful
	13	4	18	3
Granulations	2	1	6	0
Synechiae	1	1	1	1
Obliterative scarring	0	4	0	3

successful outcome in 13 (82.3%) of 17 patients was observed in the mitomycin group and 18 (85.7%) of 21 in the control group.

Among the 13 successful patients of the mitomycin group, granulations were seen in the stomal margins of 2 patients, and synechiae were observed in 5 patients, which did not appear to influence the outcome (Fig. 4). Similarly, among the successful patients in the control group, 6 patients had granulations, and 1 patient had synechiae. All patients with an unsuccessful outcome had obliterative sclerosis (Table 1).

4. Discussion

Endoscopic dacryocystorhinostomy has several advantages over Ex-DCR, such as avoidance of a facial scar, noninterference with the lacrimal pump mechanism, preservation of medial canthal ligament, simultaneous correction of the intranasal causes contributing to the nasolacrimal duct obstruction, and shorter operating time. However, the results of En-DCR and Ex-DCR are similar, averaging around 85% [2,4-8].

Several adjuvant methods and techniques are in use to improve the results of En-DCR, such as creation of mucosal flaps [12], use of special-powered instruments [12], lacrimal stenting [9,10], and laser-assisted dacryocystorhinostomy [11]. These adjuvants to En-DCR have not contributed significantly to the results [9-13]. Failures and/or recurrence after En-DCR are attributed to obliterative sclerosis, granulations, and synechiae at stomal site.

MMC is an alkylating agent with properties to inhibit fibroblastic proliferation and scar formation when applied topically. In a study by Ugurbas et al [15], the histologic changes in nasal mucosa after topical application of MMC were evaluated under light and electron microscopes. They concluded that MMC can enhance the success rate of surgery by causing a decrease in density and cellularity of nasal mucosa. Hu et al [16] observed the effects of MMC on cultured human nasal mucosa fibroblasts. They opined that short exposure times to MMC have a variable cytotoxic effect and inhibit proliferation of fibroblasts. They found that MMC can also induce apoptosis when exposed for 5 minutes and concluded that MMC has a complex effect in dacryocystorhinostomy.

In our literature search published over the last 20 years, we found few controlled studies where MMC was used, and their conclusions differed. In a small series of 14 patients (15 eyes), intraoperative topical application of MMC with stenting in Ex-DCR was found to be 100% successful, whereas the controls showed a success rate of 87.5% (failed in 1 patient). In addition, the average size of the ostium after the sixth postoperative month was double the size of those in the control group. Septo-osteotomy adhesions were found only in the control group [17]. Zilelioglu et al [18] found that the results of En-DCR were similar with or without intraoperative topical application of MMC. Of 40 patients, 22 were treated with topical adjuvant MMC in a concentration of 0.5 mg/mL applied to the stomal site for 2.5 minutes. Their mean follow-up period was 18.2 months. Success rate in the group that received MMC was 77.3%, and in control group, it was 77.8%. However, Camara et al [19] suggest significant advantages of using MMC. They had a larger series of 171 patients of which 123 received adjuvant topical MMC intraoperatively in laser-assisted En-DCR. These patients were observed for an average period of 51 months. The success rate was 99.2% when MMC was used and 89.6% when MMC was not used.

After surgery, there is a natural tendency for the stoma to contract during the healing process. Hence, the follow-up period must be adequate to accommodate completion of this healing process. An analysis by Boush et al [11] showed that most surgical failures occurred within the first 4 months after surgery. Similar findings were reported by Kong et al [13] who observed that the average onset of stomal closure after primary operation was 12.7 weeks. Woog et al [20] reported that the average onset of failure was 7.5 weeks postoperatively. Therefore, a minimum follow-up period of 6 months was observed in our study; the mean follow-up period was 2 years. All our failed En-DCRs occurred within 3 months of surgery.

In our study, a success rate of 82.3% was observed when MMC was used. When MMC was replaced by normal saline, the success rate did not vary significantly—85.7% (Student t test, $P > .05$). In addition, the occurrence of granulations, synechiae, and/or obliterative scarring did not vary significantly with the use of MMC. Presence of granulations or adhesions did not seem to influence the success rate either. We, therefore, did not find a distinct advantage of adjuvant MMC in En-DCR. However, the histologic evidence of the beneficial effects of MMC is compelling enough to suggest further studies. A controlled study with a large sample is suggested in which various concentrations of MMC are used and applied topically for different durations. This may provide more conclusive information.

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