ORIGINAL ARTICLE

Results of Intraoperative Mitomycin C Application in Dacryocystorhinostomy

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Abstract

This study was undertaken to evaluate the long term results of intraoperative mitomycin C application in dacryocystorhinostomy (DCR) surgery compared with results of the conventional procedure. In this prospective randomised controlled study, a total of 44 eyes diagnosed with acquired nasolacrimal duct obstruction were randomly divided into a conventional DCR group and a mitomycin C group in which mitomycin C was used during DCR surgery. The surgical procedures in both groups were exactly the same, except that in the patients in the mitomycin C group, a piece of neurosurgical cottonoid soaked with 0.2 mg/ml mitomycin C was applied to the osteotomy site for 30 minutes. The results of the DCR surgeries were evaluated by objective findings such as irrigation and the height of tear meniscus and subjective symptoms like condition of tearing Among the 22 eyes in the mitomycin C group, 95.45% of patients remained totally symptom free after 9 months of follow up; while in the conventional group, 72.72% of patients were reported to be symptom free and 18% of patients to have an improvement in their symptoms. There was a significant difference between these two groups. As far as objective findings were concerned, there were 21 eyes in the mitomycin C group classified as having normal and one eye with moderate tear meniscus level, compared with 16 eyes and 3 eyes, respectively, in the conventional group. There was also a significant difference between these two groups. The non-patency rate in the mitomycin C group was 4.5% compared with 11.4% in the conventional group. There were no complications such as abnormal nasal bleeding, mucosal necrosis or infection except one patient with delayed wound healing. Thus intraoperative mitomycin C application was effective in increasing the success rate of DCR surgery in standard nasolarcimal duct obstruction and no significant complications resulted from its use.

Key words

DCR, Silicon Insulation, Mitomycin C.

Introduction

Most ophthalmic surgeons accept dacryocystorhinostomy (DCR) as a highly successful procedure in managing epiphora due to nasolacrimal duct obstruction. From previous studies, it appears that the success rate for this procedure is about 90% (1-3). The two most frequent causes of DCR failure are obstruction of the common canaliculus and closure of the osteotomy site (4-6). Thus, if we can inhibit fibrous tissue growth and scarring by applying antiproliferative agents over the anastomosed flaps and osteostomy site, the failure rate may be decreased.

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Mitomycin C, an antiproliferative agent, has been widely used in pterygium excision and trabeculectomy with favourable results (7-8). Our previous study also demonstrated that DCR with intra-operative mitomycin C application can maintain larger osteotomy size than that of the conventional procedure (9). In this paper, we evaluate the long term success rate of DCR surgery with introoperative mitomycin C soaking.

Material and Methods

During 1999-2000, 44 patients with a diagnosis of primary acquired nasolacrimal duct obstruction were randomly assigned into mitomycin C (22) and conventional DCR groups (22). All the procedures were performed by two surgeons. The mean age of the conventional group was 44.9 years and that of the mitomycin C group was 45.4 years. All the patients has been followed up for more than 9 months for the evaluation of objective findings as well as subjective symptoms.

The standard surgical techniques of an external DCR were used in all patients. Local infiltrative anaesthesia, consisting of 2% lognocaine (lidocaine) and 1:100,000 adrenaline (epinephrine) was administered in the region of the medial canthus and lower lid. The nasal mucosa was anaesthetised and vasconstricted with pledgets saturated with a mixture of 5% cocaine and 1:100,000 adrenaline. A skin incision was performed and blunt dissection to the periosteum overlying the anterior lacrimal crest was undertaken. The periosteum was then incised and elevated off the lacrimal sac fossa. The osteotomy was created over the lacrimal fossa with an electric drill. The lacrimal sac was opened in a longitudinal fashion to form anterior and posterior flaps. The nasal mucosa was cut in a similar fashion to the lacrimal sac. Then, the posterior nasal and lacrimal sac flaps were joined with 5-0 Vicryl suture. A silicone tube was used to intubate the lacrimal system and followed by being tied together with a 4-0 silk suture. In the mitomycin C group, once the silicon tube was in place, a piece of neurosurgical cottonoid attached with a long thread, saturated with 0.2 mg/ml mitomycin C was placed over the anastomosed posterior flaps and osteotomy site with the long thread passing out through the nostril, and was then removed transnasally after an application time of 30 minutes. The anterior nasal and lacrimal sac flaps were closed with additional 5-0 Vicryl sutures, as were the periosteum and orbicularis muscle in separate layers. The skin incision was sutured with a running 6-0 nylon suture. The mitomycin C saturated cottonoid was removed transnasally after a 30 minute soak by pulling the long thread out from the nostril. In the conventional group, the same procedures were performed except for the absence of the mitomycin C application. Silicon tubes were removed at 6 months after surgery in all patients.

To evaluate the long terms results of both groups, we documented the subjective symptoms and classified them as symptom free (no tearing), improvement and no improvement in tearing by asking patients about the tearing conditions during 3 months follow up after operation. In addition, two objective findings such as the height of tear meniscus and patency of irrigation were documented at the same time. We measured the height of tear meniscus mixed with a fixed amount of fluorescein stain (5µl flourescein by using micropipette) under cobalt blue light at slit lamp for each patient, and graded it as high tear meniscus (0.2 mm), moderate meniscus (0.1mm << 0.2 mm), and normal tear meniscus (≤ 0.1mm). All the examinations were done by the same physician with double blind control. If non-patency was noted, transasal endoscopy was used to verify the area of obstruction.

Results

There were 44 DCR surgeries in this study; 22 eyes were in the mitomycin C group and the remaining 22

eyes were in the conventional group. There was no significant difference in age between the two groups ($p>0.1$). All patients except one in the mitomycin group remained symptom free (21 eyes) after 9 months follow up. The satisfaction rate in the mitomycin C group was 95.45% (21/22) while in the conventional group there were 3 eyes with excessive tearing after DCR surgery. 16 eyes (72.72%) remained symptom free (no tearing) and 4 eyes improved. There was a significant difference between the two groups ($p<0.05$).

As far as the objective finding were concerned, there were two eye samples in the mitomycin C group classified as having a high tear meniscus. One eye sample was classified as having moderate and 19 eye samples as having normal tear meniscus levels. In the conventional group, 3 eye samples were classified as having a higher tear meniscus, 3 eye samples as a moderate tear meniscus and 16 eye samples as a normal tear meniscus. The objective findings of tear meniscus height showed a significant difference between the two groups ($p<0.05$).

In the mitomycin C group, all eyes except one showed patency of the lacrimal drainage system; while in the conventional group six eyes revealed non patency of the drainage system. Transnasal endoscopic findings in these seven eyes (one in the mitomycin group and six in the conventional group) showed either total septo-osteotomy adhesion or complete obstruction of the osteotomy area, revealing that fibrous tissue growth, scarring or granulation tissue formation had been noted at the osteotomy area. The patency rate of the lacrimal drainage system in the mitomycin C group was 95.45% and that in the conventional group was 72.72%.During the follow up period, no complications such as abnormal nasal bleeding, mucosal necrosis or infection were noted in any of the patients. One patient showed delayed wound healing. Wound disruption was noted during skin suture removal about 7 days after surgery; it might have been the result of accidental contact of mitomycin C soaked sponge on the skin wound and could have been prevented be carefully managing the sponge. Fortunately, the wound healed within 2-3 weeks after DCR surgery leaving a barely visible scar with a successful result.

Discussion

Dacryocystorhinostomy has been accepted as a highly successful procedure in dealing with epiphora from nasalacrimal duct obstruction. A review of the literature reveals an average failure rate of 9.4% (1-3). Failure is generally defined as having symptoms of excessive tearing with the inability to irrigate. McPherson and Egelston noted that three out of seven patients in their study who underwent a second operation were found to have dense scar tissue present at the osteotomy site (10). Pico started that in every instance, the cause of failure was found at the secondary surgery to be an obstruction of the new drainage channel by an occluding membrane, which on histologic examination was shown to be composed of organised granulation tissue (11). Allen and Berlin reported 20 failed DCRs with the postoperative obstruction distal to common canaliculus. In their study, there were 13 cases with cicatricial closure of the rhinostomy with granulation tissue and three cases with cicatricial closure of the rhinostomy with granulation tissue and three cases with scarring of the osteotomy to the turbinate or septum (4). Mc Lachlan *et. al.* on the other hand, proposed the higher incidence of common canalicular obstructions as a cause of DCR failure (6). Linber *et. al.* showed that an appropriately large osteotomy made during surgery can narrow down to a final size of approximately 2 mm due to tissue growth and scarring (12). Thus, if we can reduce fibrous proliferation at the osteotomy site and at the anastomosed flaps, the success rate of DCRs may become much higher.

Mitomycin C, an anticancer agent isolated from Streptamyces caespitosus, has the ability to significantly suppress fibrosis and vascular ingrowth after exposure to the filtration site of the trabeculectomy for glaucoma (13,14). The effect of mitomycin C in glaucoma filtering surgery has been widely discussed and proved to be effective in reducing intraocular pressure (8,15). In DCR surgery, we tried to use mitomycin C soaking over the osteotomy site and the anastomosed flaps to suppress fibrous proliferation and scar formation. In our previous study, the mean actual osteotomy size in mitomycin C group shrank from 66.28 mm^2 (100%) initially to 27.10 mm^2 (40.89%) 6 months after DCR surgery. On the other hand, the mean actual osteotomy size in control group shrank from 65.44 mm^2 (100%) initially to 10.83 mm^2 (16.52%) 6 months after DCR surgery (9). It is concluded that application of the mitomycin C over the osteotomy site is effective in maintaining a larger osteotomy site. Ugurbas *et. al.* studied the histopathological effects of mitomycin C on transnasal DCR by using 0.5 mg/ml mitomycin C and soaking for 2½ minutes over the osteotomy site. The light and electron microscopy showed attenuated epithelium as well as looser and hypocellular subepithelial connective tissue on mitomycin C soaking specimens. They concluded that mitomycin C soaking can result in a decrease in density and cellularity of mucosa, and hence, enhance the success of DCR surgery (16). Yeatts and Neves reported eight cases of repeat DCR using mitomycin C soaking with successful results (17). They recommended that the adjunctive use of mitomycin C may increase the success rate of repeat DCR.

In the present study, regarding patency of the lacrimal drainage system and transnasal endoscopic findings, we found that one eye in the mitomycin C group showed non-patency of the lacrimal drainage system when irrigated and an obstruction over the osteotomy area. In the conventional group, 6 eyes were reported to be non-patent with obstruction over the osteotomy site diagnosed by irrigation as well as transnasal endoscopy. The patency rate of the lacrimal drainage system after DCR surgery was 95.5% in the mitomycin C group compared with 72.72% in the conventional group.

Many complications due to mitomycin C application have been reported in both pterygium and glaucoma filtration operations. Severe secondary glaucoma, corneal perforation, corectopia, secondary cataract and scleral calcification are documented as complications in using topical mitomycin C as medical adjunct to pterygiem surgery (18). Hypotony related maculopathy, infection and endophthalmitis have been found in patients undergoing glaucoma filtration surgery after exposure to mitomycin C (10-19). Fortunately, in our study, there were no complications such as abnormal nasal bleeding, mucosal necrosis, or infection noted with mitomycin C soaking. Only one case initially presented with delayed would healing which may have been due to accidental contact of mitomycin C soaked sponge on the skin wound. The wound healed within 2-3 weeks after DCR surgery leaving a barely visible-scar and with a successful result.

In summary, although a high success rate of external DCR surgery has been reported, 10% of cases still fail. In our experience, DCR with intraoperative mitomycin C soaking over the osteotomy and anastomosed flaps can minimize the adhesions around the septoostotomy area as well as the opening of the common canaliculus. In this way, mitomycin C soaking during DCR surgery is a useful modified procedure to improve the success rate of external DCR. Recently, new reports have shown that endonasal laser assisted DCR can be an alternative to conventional external DCR (20- 22). May be it will be helpful

to apply mitomycin C over a laser created osteotomy site to increase the success rate of laser assisted DCR and revised DCR surgery.

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