

Original Research Article

Efficacy of mitomycin c in endoscopic dacryocystorhinostomy

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ABSTRACT

Background: Endoscopic dacryocystorhinostomy is a procedure done to drain the lacrimal sac due to post saccular lacrimal obstruction. The most common cause of failure of dacryocystorhinostomy is blockage of ostium created in lacrimal sac. Various methods are employed to prevent the blockage such as stenting, mitomycin C and steroidal nasal sprays. In this study we evaluated the efficacy of mitomycin C in reducing the stomal closure following dacryocystorhinostomy.

Methods: Fifty patients who were diagnosed with chronic dacryocystitis due to nasolacrimal duct obstruction were chosen for the study. They were randomly divided in to two groups. In group I 25 patients under went endoscopic dacryocystorhinostomy with intraoperative mitomycin C application and in group II 25 patients underwent endoscopic dacryocystorhinostomy without application of mitomycin C. Patients were followed up at the end of one week, three weeks, three months and six months. Surgical success was evaluated objectively at the end of six months.

Results: The success rate of endoscopic dacryocystorhinostomy with use of mitomycin c was 86% in group where mitomycin c was used and 62% in group where mitomycin c was not used.

Conclusions: Mitomycin C is a safe drug which can keep the stoma created patent and reduces the chance of recurrence following endoscopic dacryocystorhinostomy.

Keywords: Chronic dacryocystitis, Nasolacrimal duct obstruction, Dacryocystorhinostomy, Endoscopic endonasal dacryocystorhinostomy, Mitomycin C

INTRODUCTION

Dacryocystitis is an infection of lacrimal sac. Dacryocystitis is a commonly encountered condition wherein blockage of the lacrimal apparatus leads to stagnation of secretions from the lacrimal gland which in turn leads to acute and subsequently chronic dacryocystitis. The condition is characterised by epiphora, pain, chemosis, edema of lower eyelids.

Nasolacrimal duct obstruction is a common cause for epiphora. The advent of dacryocystorhinostomy provided a revolution in the management of epiphora secondary to nasolacrimal duct obstruction. It can be performed through an external or endonasal approach.

Endoscopic endonasal dacryocystorhinostomy has been accepted as a highly successful procedure, because of less surgical trauma, less interference with lacrimal pump function, shorter postoperative and hospitalization time, low postoperative discomfort, and greater cosmetic acceptance.

In a recent systematic review of outcomes after dacryocystorhinostomy in adults, the success rate of endoscopic dacryocystorhinostomy was found to range from 82 to 95%.¹⁻⁴ Though endoscopic dacryocystorhinostomy is a widely accepted surgical procedure, like all surgeries it has a percentage of failure which at times become a point of contention in the evaluation of success rate.

During dacryocystorhinostomy the main emphasis is focused towards opening the wall of lacrimal sac as the nasolacrimal duct is blocked. At times inspite of the level of surgical expertise the opening made in the wall of lacrimal sac closes spontaneously leading to recurrence of symptoms. Closure of osteotomy site may be due to granulations, fibrosis, scarring, synechiae. Fibrous tissue and granulation formation are associated with surgical failure because they diminish ostium size and lead to nonpatency.

To circumvent this; various retarding agents were experimented with to keep the stoma patent, and mitomycin C is one such agent which has been used with fair amount of success. Application of mitomycin C is a modality adopted to prevent closure of lacrimal sac after endoscopic dacryocystorhinostomy. Mitomycin C is derived from *Streptomyces caespitosus*. It is an alkylating, antimetabolic and anti-neoplastic agent. It inhibits the synthesis of DNA, inhibits the cellular RNA, inhibits fibroblast proliferation, inhibits the synthesis of collagen by fibroblasts and also inhibits the protein synthesis.

Intraoperative mitomycin C application was a safe adjuvant that could reduce the closure rate of the stoma created in the lacrimal sac after endoscopic dacryocystorhinostomy. Due to the potential for adverse effects mitomycin C is typically administered for brief durations (2-10 minutes) at doses of 0.2 to 0.4 mg/mL. It has been found that 0.2 mg/mL of mitomycin C administered to an ostium for 30 minutes might be favorable to increase success rates with no significant increase in adverse effects.

In a study done by Apuhan et al on effect of mitomycin-C in endoscopic dacryocystorhinostomy, on 43 patients found that mitomycin C used in 0.5 mg/ml for 2.5 minutes intraoperatively had a success rate of 91% compared to external dacryocystorhinostomy, which had 71.5% success rate.⁵

Another study done by Selig et al found that, mitomycin-C in concentrations of 0.2 mg per ml is applied topically to the dacryocystorhinostomy ostium site decreases scarring and adhesions. Hence stomal patency is maintained, decreasing the failure rate of endoscopic dacryocystorhinostomy.⁶

Mitomycin C when used in appropriate doses minimizes postoperative fibrosis, synechiae and granulations thereby maintaining a bigger ostium size in the postoperative period. The aim of this study is to endoscopically assess the ostium size and patency after endonasal dacryocystorhinostomy with and without mitomycin C application in cases of chronic dacryocystitis secondary to primary post saccal stenosis.

METHODS

This is a randomized clinical trial. Study was conducted at Dr. D.Y. Patil medical college, Pune. The time period of study was from May 2015- May 2018. Data for study was collected from the patients undergoing endoscopic dacryocystorhinostomy surgery. Institute Ethics Committee clearance was obtained before starting the study

A predesigned proforma was used to record relevant information including Patient's data, clinical findings, investigation reports, from patients selected considering inclusion and exclusion criteria.

The study was carried out in 50 patients, 25 patients in study group (Group I) underwent endoscopic dacryocystorhinostomy with mitomycin-C and 25 patients in control group (Group II) underwent endoscopic dacryocystorhinostomy without mitomycin-C. Out of these 4 patients in study group had bilateral dacryocystitis and had undergone bilateral dacryocystorhinostomy and one patient in control group had bilateral dacryocystitis and had undergone bilateral dacryocystorhinostomy. Therefore number of surgeries in study group is 29 and number of surgeries in control group is 26.

Inclusion criteria

Inclusion criteria were patients with nasolacrimal duct blockage willing to undergo endoscopic dacryocystorhinostomy; patients above twelve years of age.

Exclusion criteria

Exclusion criteria were patients less than twelve years of age; patients with presaccal obstruction; malignant conditions; secondary dacryocystitis; medical contraindications to undergo surgery; pregnant and lactating female patients; revision endoscopic dacryocystorhinostomy.

Methodology

Patients were selected according to systematic random allocation method considering inclusion and exclusion criteria.

Patients were evaluated as follows:

A detailed history was taken. All patients underwent a complete ophthalmic examination before the surgical procedure. Syringing of the lacrimal drainage system was done to look for patency. A dacryocystogram was done in all patients to confirm the diagnosis of Nasolacrimal duct obstruction and the absence of canalicular block. Nasal endoscopy was performed as a routine pre-operative assessment and to rule out any other intranasal pathology.

Acute dacryocystitis patients were treated on medical line of management and then subjected to surgery.

All routine blood investigations were done. All patients received a course of antibiotics starting one day prior to surgery and continued for five days.

These patients were subjected to endoscopic endonasal dacryocystorhinostomy. In half number of patients Mitomycin C was applied postoperatively to ostium made in lacrimal sac. The other half was served as control.

Surgical procedure

All procedures were done under local or general anaesthesia. Topical nasal decongestion with 4% xylocaine with adrenaline was done 10 min prior to procedure.

Nasal endoscopy was performed with a 0 degree endoscope.

Middle turbinate was identified and its anterior arch was traced laterally as the maxillary line.

The area in front of maxillary line is the lacrimal sac area. The sac is covered by the lacrimal bone which is removed to access lacrimal sac.

Infiltration was done with 2% xylocaine with adrenaline at root of middle turbinate and on lateral wall of nose and around upper attachment of inferior turbinate.



Figure 1: Key landmark.

Key land mark is ridge formed by frontal process of maxilla and the root of middle turbinate on lateral nasal wall (Figure 1).

A vertical incision is given 0.5 to 1 cm anterior to the base of middle turbinate vertically down till the upper attachment of inferior turbinate.

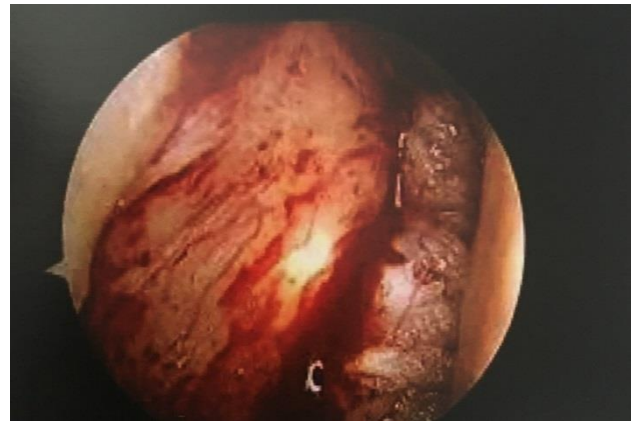


Figure 2: Elevated mucoperiosteal flap.

Mucoperiosteal flap was elevated (Figure 2). Lacrimal bone is identified and punched out with Kerrison's punch forceps. Lacrimal sac is identified. The movement of medial wall of sac in endoscopic view will confirm the lacrimal sac. Lacrimal sac is incised and a wide stoma is made.

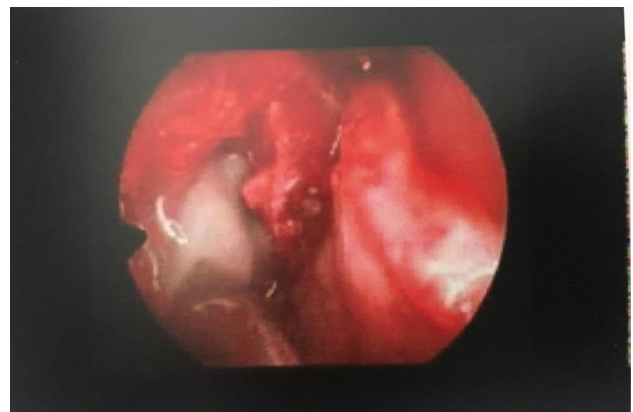


Figure 3: Free flow on sac syringing.

Sac syringing is done to look for free flow of saline or mucopus (Figure 3).

Intraoperative mitomycin C was applied via neurosurgical cotton patties; each measuring 1 cm in length, which are soaked in Mitomycin C at a concentration of 0.2 mg/ml.

These patties were placed directly over lacrimal sac ostium for 3 min. After removal of patties, the operative site was rinsed with normal saline

Anterior nasal packing was given which was removed after 48 hours.

Postoperative care

Patient was started on broad spectrum antibiotics, analgesics, nasal decongestants, antibiotic and steroid eye drops which was given for five days. Nasal endoscopy

was done after pack removal to remove crusts and clots a traumatically.

The results of the dacryocystorhinostomy were assessed using objective findings like

- Nasal endoscopy and visualization of wide stoma
- Nasolacrimal duct irrigation and assessing patency at the end of 1 week, 3 weeks, 3 months and 6 months

Statistical methodology

The data collected was analysed using Friedman test (Chi-square test) and Proportion tests to calculate the Z value and P value.

RESULTS

In group I where mitomycin C was used postoperative complications were seen like three patients had synechia, 2 cases had fibrosis around ostium and one patient had infection which was treated with antibiotics. None of the patients had developed granulations around ostium.

In group II where mitomycin C was not used; 6 cases had developed granulations around ostium thereby blocking the ostium. Three cases had fibrosis and narrowing of ostium. The occurrence of granulations was higher in control group where mitomycin C was not used whereas in study group where mitomycin C was used there was no occurrence of granulations. This result is statistically significant with $p < 0.01$. Thus proving that Mitomycin C has an inhibitory effect on granulation tissue formation

Rest of the complications in both groups were not statistically significant with $p > 0.05$

In group I and group II; in the first week the ostia were patent in all cases (100%)

In group I where mitomycin C was used at the end of 3 weeks 27 cases had patent ostia; and at the end of 3 months and 6 months 25 cases had patent ostia.

In group II where mitomycin C was not used at the end of 3 weeks only 19 cases had patent ostium and by the end of 3 months and 6 months only 16 cases had patent ostium on sac syringing. This result is statistically significant with $p < 0.05$. The inference is that use of mitomycin C as an adjuvant in endoscopic DCR has a major role in maintaining the patency of ostium and gives good long term results.

In group I endoscopic dacryocystorhinostomy was carried out with adjuvant use of mitomycin C. 25 (86%) cases had a successful outcome with a patent nasolacrimal drainage system and complete resolution of epiphora. Where as in group II endoscopic dacryocystorhinostomy was carried out without using mitomycin C and was

successful only in 16 (62%) cases. The success rate was more in group I than group II where intraoperative mitomycin C was used. The outcome is also statistically significant with $p < 0.01$. Thus the adjuvant use of mitomycin C in endoscopic dacryocystorhinostomy has a significant role in increasing the success rate of the surgery.

Table 1: Postoperative complications wise distribution of cases in group I and group II.

Post op complication	Group I (N=29)	Group II (N=26)	P value
Fibrosis	2	3	0.659
Granulations	0	6	0.008
Infection	1	0	1.00
Synechia	3	0	0.238

Table 2: Patency of ostium wise distribution of cases in Group I and Group II.

Patent at	Group I (N=29)	Group II (N=26)	P value
1 st week	29	26	NA
3 rd weeks	27	19	>0.05
3 rd months	25	16	<0.05
6 th months	25	16	<0.05

Table 3: Outcome of surgery.

Outcome	Group I (N=29)	Group II (N=26)	P Value
Success	25	16	<0.01

DISCUSSION

In our study postoperatively in group I three patients had synechia, two cases had fibrosis around ostium and one patient had infection which was treated with antibiotics. None of the patients had developed granulations around ostium.

In group II 6 cases had developed granulations around ostium thereby blocking the ostium. Three cases had fibrosis and narrowing of ostium. The occurrence of granulations were higher in control group where mitomycin C was not used whereas in study group where mitomycin C was used there were no occurrence granulations. This result is statistically significant with $p < 0.01$. Thus proving that mitomycin C has an inhibitory effect on granulation tissue formation

Ressionitis et al found that obstruction of neo-ostium by granulation tissue or fibrosis is the most common cause of failure. Adhesion may also form between the flaps of nasal mucosa, flaps of lacrimal sac and sometimes between the nasal mucosa at the margins of ostium and nasal septum if there is damage to the nasal mucosa covering the nasal septum.⁷

In our study in group I where mitomycin C was used at the end of 3 weeks 27 cases (93%) had patent ostia; and at the end of 3 months and 6 months 25 cases (86%) had patent ostia. Patients had successful outcome with a patent nasolacrimal drainage system and complete resolution of epiphora.

In group II where mitomycin C was not used at the end of 3 weeks only 19 (73%) cases had patent ostium and by the end of 3 months and 6 months only 16 (62%) cases had patent ostium on sac syringing. This result is statistically significant with $p < 0.01$. The inference is that use of mitomycin C as an adjuvant in endoscopic dacryocystorhinostomy has a major role in maintaining the patency of ostium and gives good long term results.

The success rate was more in group I than group II where intraoperative mitomycin C was used. The Outcome is also statistically significant with $p < 0.01$. Thus the adjuvant use of mitomycin C in endoscopic dacryocystorhinostomy has a significant role in increasing the success rate of the surgery.

In studies on intraoperative mitomycin C with dacryocystorhinostomy, Kao et al, You and Fang, Shimming Cheng et al, Gonzalvo et al, Rathore et al, Deka et al, found that the osteotomy site was significantly larger in the mitomycin C group than the control group. Our study had results comparable to these studies. Hence it was found that intraoperative use of mitomycin C was a safe adjuvant that can maintain the patency of neo ostium and significantly increase the success rate in endoscopic dacryocystorhinostomy.⁸⁻¹³

CONCLUSION

The conclusions that can be drawn from the study are endoscopic endonasal dacryocystorhinostomy is the surgery of choice for primary acquired nasolacrimal duct obstruction. It is a simple, safe, cosmetically acceptable, minimally invasive procedure with less interference of lacrimal pump function. Intraoperative mitomycin C prevents narrowing of ostium. Topical mitomycin C is safer with no local adverse effects. Use of adjuvant mitomycin C enhances the success rate of surgery with less chances of recurrence.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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