

# Effect of Mitomycin C In Reducing External Dacryocystorhinostomy Failure

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## ABSTRACT

**Objective** To find out effectiveness of mitomycin C soaked gauze during external dacryocystorhinostomy surgery in reducing the failure rate of the procedure.

**Study design** Quasi experimental Study.

**Place & Duration of study** Khalid Eye Clinic Karachi, from November 2018 to January 2020.

**Methodology** Patients were evaluated with regurgitation test for site and severity of obstruction. Lacrimal sac syringing was performed for documenting patency of lacrimal system. Bowman's probe was used where distal obstruction was suspected. External dacryocystorhinostomy surgery was performed with intra operative use of MMC 0.02% soaked gauze piece passed through the anastomosed dacryocystorhinostomy flaps and the osteotomy site for 2 minutes. Silicone tube was passed through the ostium into the nasal cavity and skin was sutured. Silicon tube was removed six months after the surgery. Patients were followed up to nine months.

**Results** Fifty patients of both genders were recruited. Age of the study subjects was from 20 year to 40 year with the mean age of  $31.3 \pm 5.3$  year. Forty-seven (94%) patients had a patent postoperative nasolacrimal system which was proven by nasolacrimal syringing test. Three (6%) patients complained of watering and discharge and required revision surgeries.

**Conclusions** Use of mitomycin C during external dacryocystorhinostomy surgery reduced the postoperative surgical failure.

**Key words** Mitomycin C, External dacryocystorhinostomy, Dacryocystitis.

## INTRODUCTION:

Dacryocystitis is an acute or chronic infective disease of the lacrimal sac due to obstruction of the nasolacrimal duct. Acute stage is usually treated conservatively whereas chronic dacryocystitis is painless and may present as a bulge adjacent to the inner canthus due to a mucocele and reflux of mucopurulent discharge on regurgitation test (pressure on the lacrimal sac).<sup>1</sup>

The surgical procedure dacryocystorhinostomy (DCR)

is performed for the removal of retained mucus within the lacrimal sac with subsequent drainage of the tears to eliminate watering of the eyes (epiphora). DCR comprises of the surgical exclusion of the bone next to the nasolacrimal sac followed by amalgamation of the lateral nasal mucosa with the lacrimal sac, thereby evading the obstruction of the nasolacrimal duct and letting the direct drainage of tears from the lacrimal canaliculi into the nasal cavity having decreased resistance.<sup>2</sup> Dacryocystorhinostomy with a success rate of about 90% has proven itself to be a successful surgical procedure in managing epiphora caused by nasolacrimal duct obstruction (NLDO) resulting in reduced tear outflow.<sup>1-3</sup>

Nasolacrimal duct obstruction may be congenital or acquired and can occur anywhere from the lacrimal puncta to the nasolacrimal duct owing to number of reasons which makes a thorough detailed history imperative, such as enquiring about the symptoms,

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functional status, associated co-morbidities, medications used and other risk factors, in making the diagnosis of obstruction of the nasolacrimal duct, as the cause of tearing, in contrast with reflex tearing due to other reasons.<sup>4</sup>

Despite having a good surgical success rate, significant failure rate still exists in external DCR, mainly due to obstructive postoperative adhesions, common canaliculi obstruction and obstruction via granulation tissue formation at the osteotomy site.<sup>5,6</sup> Intra operative adjuncts that prevent the expansion of fibrous tissue along with reduction of scarring above the anastomosed flaps and osteotomy site should enhance the accomplishment rate.<sup>7</sup>

Mitomycin-C has been used for the prevention of excessive scarring at the ostium site following DCR.<sup>8</sup> The mode of action involves inhibiting DNA synthesis, and subsequently of cellular RNA and protein, leading to decrease in by fibroblasts.<sup>9-11</sup> This study was conducted to find out the role of MMC 0.02% soaked gauze placed through the anastomosed dacryocystorhinostomy flaps and the osteotomy region to evaluate external DCR failure rate.

#### **METHODOLOGY:**

This interventional study was carried out at Khalid Eye Clinic Karachi, from November 2018 to January 2020. Patients between ages of 20 year to 40 year, of both genders with obstruction of the nasolacrimal duct, were recruited. Approval of study was obtained from the ethical review committee of the hospital. Permission was obtained from all the patients and the aim and objective of the surgical procedure was conveyed to them. Patients with the history of previous DCR, canalicular block, presence of deviated nasal septum on same side, chronic rhinosinusitis and nasal tumors were excluded.

The initial evaluation for the site and severity of obstruction was done by observing the regurgitation test. Thereafter, lacrimal sac syringing with saline was performed. Fluid reflux from the opposing puncta meant distal obstruction of the nasolacrimal duct whereas reflux of fluid from the ipsilateral puncta meant obstruction proximally. Absence of reflux with free passage of the fluid through the nose showed patency of the lacrimal system with no requirement for surgical intervention. Bowman's probe was used for probing where there was suspicion of distal obstruction.

The usual external dacryocystorhinostomy surgery was performed on all the patients with intra operative use of MMC 0.02% soaked gauze piece passed through the anastomosed dacryocystorhinostomy

flaps and the osteotomy site for 2 minutes. Thorough irrigation of the region with the oral packing in place was then done. Silicone tube was passed through the ostium into the nasal cavity and skin was sutured. Nasal packing was done for 24 hours postoperatively. Silicon tube was removed six months after the surgery.

After the procedure patients were evaluated for improvement or relapse for a period of nine months. Patients were assessed for severity of, absence/presence of purulent discharge, positive/negative dye disappearance test in the nasal cavity, passage of fluid freely during washing or obstruction, pressurized thin jet of fluid using a plunger causing movement of the fluid into the nasal cavity, the existence of a fashioned ostium or cicatricial deformation of the formed ostium. Statistical package for social science (SPSS) version 21 was used for data analysis. Student t test was used to assess the significance of the procedure in terms of patency of nasolacrimal duct. A  $p < 0.05$  was taken as statistically significant.

#### **RESULTS:**

Fifty patients were recruited in this study with 23 (46%) females and 27(54%) males. The mean age of the patients was  $31.3 \pm 4.3$  year. By the conclusion of the nine months follow up period, forty seven (94%) patients had a patent postoperative nasolacrimal system documented with nasolacrimal syringing test. This was statistically significant ( $p < 0.004$ ). Three (6%) patients complained of watering and discharge. They were managed conservatively and required revision surgeries.

#### **DISCUSSION:**

The failure rate of dacryocystorhinostomy procedure is reported as high as 18%, due to blockage of ostium site owing to granulation tissue, scarring and formation of adhesions in the nasal cavity.<sup>6,12</sup> Unusual watering of the eyes after the surgical procedure along with failure to irrigate the lacrimal system is generally regarded as an unsuccessful surgical attempt. A study was done among patients requiring a repeat surgical procedure and noted the presence of a thick scar tissue at the osteotomy site.<sup>13</sup> Similarly another study done on patients requiring a second surgical procedure found the occurrence of an occluding membrane composed of organized granulation tissue resulting in failure of the primary surgery.<sup>14</sup> These observations lead to the belief that limiting the proliferation of fibrous tissue at the osteotomy site and the anastomosed flaps would result in enhancement of the surgical outcome after DCR.

MMC, chemotherapeutic agent, is a derivative of *Streptomyces caespitosus*, which blocks the production of DNA, cellular RNA and protein by stopping collagen production through fibroblasts.<sup>15</sup> Kao et al compared and documented the surgical outcome of external DCR with intraoperative MMC use versus DCR without MMC application.<sup>16</sup> They observed that MMC favorably affects the ostium and enhances the success rate of the surgery. It was also found that there were no adhesions in the MMC group. This was in accordance with our study. MMC treated nasal mucosa shows significant changes in the epithelial, glandular, vascular, and fibrocollagenous tissues compared to the normal untreated tissue and these changes were restricted to treated areas only. This suggested that MMC may have a role in preventing the formation of subsequent cicatrix.<sup>17</sup>

A meta analysis done on the concurrent use of mitomycin C for primary and repeated, external and endonasal dacryocystorhinostomy showed that the use of MMC at the osteotomy region is a secure and successful mean of escalating surgical achievement rate in primary external DCR.<sup>18</sup> A study done by You and Fang evaluated the effectiveness of dissimilar dosages (0.2 mg/ml MMC for 5 min in one group and 0.5 mg/ml MMC for 5 min in the other group) in external DCR and established no considerable disparity among the two MMC groups.<sup>19</sup> Whereas in another study MMC at 0.4 mg/ml past 5 min and 0.5 mg/ml dosage application were found to be fatal resulting in widespread cell death when compared with controls. The minimum effective dosage was found to be 0.2 mg/ml for 3 min as it prohibited cell propagation of the fibroblasts by seizing the cell cycle with no widespread apoptosis.<sup>20</sup> In our study we used 0.2mg/ml of MMC for 2 minutes to maximally inhibit fibrosis. Another study observed the durable results of intra-operative mitomycin C usage in external DCR surgery as compared to the traditional DCR procedure and demonstrated that 95.5% of patients were entirely symptom-free by the end of the ten months follow up period. The traditional DCR group showed 70.5% of patients as free from preoperative symptoms.<sup>21</sup> Our study showed a similar result with 94% of our patients having a patent postoperative nasolacrimal system with no symptoms at the conclusion of the follow up period.

Nasolacrimal duct obstruction after primary DCR is mainly due to decrease in the size of the healed intranasal ostium site with granulation tissue as a result of a normal wound healing response.<sup>22</sup> To prevent closure of the stoma, local application of

antimetabolites such as MMC is used for the reticence of the wound remedial course and the prevention of scar development in the ostium site. With newer techniques constantly evolving, the core surgical principle of DCR remains constant, making it a less invasive, safe procedure with long lasting success. In the wake of recent studies, the role that MMC has proven to improve the successful accomplishment rate of DCR.<sup>23</sup>

#### CONCLUSIONS:

Intra operative use of MMC in external DCR for primary nasolacrimal duct obstruction is safe, with no local adverse effects and enhances the success rate of surgery with lesser chances of recurrence.

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Khalid Mahmood: Data collection, final review.

Conflict of Interest:

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