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Comparison of the Success Rate of External Dacryocystorhinostomy with Intramucosal Injection and Sponge Application of Mitomycin C to Circumosteal Mucosa

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ABSTRACT

Objective: To compare the success rate of external dacryocystorhinostomy with intramucosal injection and sponge application of Mitomycin C to circumosteal mucosa.

Study Design: Quasi-experimental study

Place and Duration of Study: Eye Department, Combined Military Hospital, Jhelum Cantt Pakistan, from Feb 2019 to Dec 2021.

Methodology: One hundred ten patients were selected and randomly allocated into two equal Groups labelled Group-A and Group-B. Group-A patients received 0.1ml of intramucosal injection of 0.02% Mitomycin C, and Group-B patients had 0.02% Mitomycin C applied with a sponge to the circumboreal mucosa. The result of DCR was evaluated at six months and declared successful if the patients were asymptomatic of epiphora and a patent lacrimal passage was found on probing and irrigation. Failure was defined as symptomatic epiphora along with regurgitation on probing and syringing. In failed cases, nasal endoscopy was performed along with probing.

Results: Success rates of external dacryocystorhinostomy in the Intramucosal Injection Group was 96%, and in the Sponge Application Group, it was 92%. A comparison of both techniques depicted a statistically insignificant difference in success rate (p=0.60).

Conclusion: Mitomycin C use as an adjunctive agent during external dacryocystorhinostomy is a safe and effective technique in achieving a high rate of success, and the route of application, whether applied topically or injected intramucosal does not significantly affect the outcome of this procedure.

Keywords: Dacryocystorhinostomy, Injection, Mitomycin C, Mucosa.

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INTRODUCTION

Mitomycin C (MMC) is an antibiotic with anti-tumour properties as it can inhibit collagen synthesis by fibroblast cells and suppress vascular proliferation by cytotoxic activity on microvascular endothelial cells.[1] There is a vast array of MMC applications in ophthalmology which includes ocular surface tumours, allergic conjunctivitis and many ocular surgeries such as pterygium, glaucoma, refractive, squint and dacryocystorhinostomy(DCR) employ MMC as an adjunctive agent.[2,3]

In DCR, MMC is postulated to suppress scarring and the development of granulation tissue around the osteotomy site and the common canaliculus, as these two are the most common causes of failure of DCR surgery.[4] In primary external DCR, a meta-analysis reported that MMC is a safe agent for reducing the osteotomy's closure rate.[5]

Intraoperatively, MMC can be applied in a variety of ways. Some surgeons use cotton tips or soaking, also pro-mote antibiotic stewardship, preventing inju-while others irrigate MMC. Similarly, the area of application is either on the nasal mucosa, osteotomy site or under the lacrimal flaps.[6,7] Intramucosal injection of MMC to the osteotomy mucosa with a needle is a different method of drug delivery that a few surgeons have employed to enhance the outcome of DCR.[8]

Previously published studies have shown that the failure rate of DCR with MMC use has consistently been above that when the procedure was performed without MMC.[9] On the other hand data regarding the comparison of one application technique with another method of drug delivery is lacking;[10] therefore, the objective of our study was to compare the technique of intramucosal injection of MMC with sponge application technique on the success rate of external DCR to refine the methodology of MMC application further and avoid MMC related complications.

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METHODOLOGY

The quasi-experimental study was conducted at the Eye Department of Combined Military Hospital, Jhelum, from February 2019 to December 2021 after approval by the Ethical Review Committee (Certificate No. 1121/02/Estb/2019). A sample size was calculated taking a success rate of 96.4% and 73.8% from formerly published data,[11] utilizing similar surgical methods with the help of WHO calculator.

Inclusion Criteria: Patients aged 15 years and above who presented in the Outpatient Department with epiphora and chronic dacryocystitis and demonstrated nasolacrimal duct obstruction on syringing were included in the study.

Exclusion Criteria: Patients who required repeat DCR surgery or had canalicular obstruction, involutional ectropion and traumatic nasolacrimal duct obstruction were excluded from the study.

Based on a computer-generated random numbers table, one hundred ten patients were selected and randomly allocated into two equal Groups labelled Group-A and Group-B. Group-A patients received intramucosal injections of MMC, and Group-B patients had MMC applied with a sponge to the circumboreal mucosa.

Slit lamp examination of the lids, conjunctiva, cornea and particularly puncta were performed for malposition and stenosis. A regurgitation test was performed under the slit lamp biomicroscope, and probing and sac syringing were done in the operation theatre under topical anaesthesia in all the patients. Schirmer`s test, Jones dye test or Dacryocystography was not carried out in any patient. All patients underwent nasal examination and completed the general physical examination. History of diabetes mellitus, hypertension, ischaemic heart disease, bleeding disorder, aspirin use and antiplatelet therapy was elicited. For patients taking aspirin, it was discontinued two weeks before surgery. Surgery was performed under general anaesthesia after obtaining the fitness to undergo general anaesthesia. An external DCR procedure with silicone intubation was executed in every patient. Written informed consent was taken from all those patients who were declared fit to undergo general anaesthesia Patients with acute on chronic dacryocystitis were treated with systemic Ciprofloxacin 500mg twice a day for one week before surgery. The same surgeon performed external DCR in every patient.

Anesthetist was advised to give hypotensive anaesthesia in selected cases to minimize bleeding. Nasal packing was done. The skin incision was made 8-10mm from the medial canthus, starting just superior to the medial canthal tendon and carrying inferiorly for 15-20mm along the nose. Splitting of the orbicularis oculi was done. During this procedure, care was taken not to injure the angular vein. An incision was made on the medial canthal tendon to reveal the lacrimal sac. Periosteum was incised anterior to the anterior lacrimal crest and reflected posteriorly, thereby displaying lacrimal fossa.

Using a periosteal elevator, osteotomy was commenced at the thin bone at the intersection of the lacrimal bone and maxillary bone and broadened anteriorly up to 5mm anterior to anterior lacrimal crest, backwards up to the posterior lacrimal crest, upward to the insertion of medial canthal tendon and downwards to the inferior orbital margin. The lower punctum was dilated, and a probe was directed into the lacrimal sac. The lacrimal sac was incised with the crescent knife at the site where the probe was tenting the medial wall of the sac down to the nasolacrimal duct. Flaps of the lacrimal sac and nasal mucosa were created. Both posterior lacrimal and nasal flaps were excised.

In the intramucosal injection Group, 0.1ml of 0.02% MMC was injected employing an Insulin syringe at a total of 04 equally spaced points with two points in the edge of the anterior nasal mucosal flap and two points in the posterior cut edge of the nasal mucosal flap. In the sponge application, Group 0.02% MMC was applied all around to the edges of the anterior and posterior nasal sac mucosa for five minutes with a cellulose sponge. Then Silicone intubation was done in all the procedures. All patients' anterior flaps were sutured with 6/0 vicryl on a half-circle needle with 04 stitches. The orbicularis muscle was closed. 7/0 vicryl mattress sutures were utilized to appose the skin edges. A nasal pack was inserted.

Postoperatively steroid plus antibiotic combination eye drops, thrice daily and ointment at bedtime were prescribed for one month. Tablet Ciprofloxacin 500mg twice a day was prescribed for one week only. Patients were examined in the evening, and the nasal pack was removed. They were discharged after 24 hrs. Follow-up was at one week and then at monthly intervals for 06 months. In all the patients, the silicone tube was removed at three months. At six months, the result of DCR was evaluated and declared successful if. The patients had symptomatic relief of epiphora, and a patent lacrimal passage was found on probing and irrigation.

In contrast, failure was defined as symptomatic epiphora and regurgitation from the opposite punctum. In failed cases, nasal endoscopy and probing were performed to determine the cause of the blockage. Revision surgery or intranasal procedure was then performed later in recurrent cases.

SPSS ver 24 was used for the data analysis. Kolmogorov–Smirnov test and the Shapiro–Wilk test were applied to check the normality of the data. Data were found to be not normally distributed. Therefore, median and interquartile ranges were reported for quantitative variables and qualitative variables were expressed as frequency and percentages. Mann Witney U test and chi square test were applied for inferential statistics at *p*-value value lower than or up to 0.05 considered statistically significant.

RESULT

One hundred four procedures were performed, with 52 cases receiving the intramucosal injection and 52 receiving sponge application of MMC in each Group. Of these 104 procedures, two patients from each Group did not report for follow-up after the first visit and were excluded from the study cohort. The final study cohort, therefore, comprised 100 patients.

The age ranged from 31-70 years. Both Groups were found to be age-matched, as there was no statistical difference in the median(IQR) ages of the two Groups (Table-I). Out of 100 patients, 64% were female and 36% were male. All 100 patients comp-leted their 6-month follow-up. A surgical procedure in 94% out of 100 cases went routinely.

Table-I: Comparison of age between Intramucosal Injection Group and Sponge Application Group (n=100)

Group	Age(Years)	*p*-value
Median(IQR)		
Intramucosal Injection (n=50	61(14)	0.887
Sponge application (n=50)	61(15)	

After six months, 48(96%) patients out of 50 from Group-A were free from the symptom of epiphora, and 46(92%) patients out of 50 were alleviated of epiphora in Group-B. Syringing and probing of the canaliculi validated patency of osteotomy passage in both Groups. Comparison of the success rates of DCR in both Groups was statistically insignificant (Table-II).

Table–II: Comparison of the Success Rate of External Dacryocystorhinostomy between Intramucosal Injection Group and Sponge Application Group of MMC (n=100)

Groups	Successful DCR	Failed	*p*-value
Intramucosal Injection (n=50)	48(96%)	2(4%)	0.887
Sponge Application (n=50)	46(92%)	4(8%)	

DISCUSSION

We recorded similar success rates in both Groups, with statistically insignificant differences in whether MMC is applied topically or delivered via injection. To conclude, using Mitomycin C during external dacryocystorhinostomy is a safe and effective procedure in achieving a high rate of success, and the route of application, whether applied topically or injected intramucosal, does not significantly affect the outcome of this procedure.

Our dose selection of MMC was 0.2mg/ml. This was selected based on previous data. Ali *et al*. found out in their study that the minimum effective concentration of MMC that would inhibit fibroblast proliferation and, at the same time, prevent cell cycle arrest and apoptosis is 0.2mg/ml. 10 They also concluded that concentrations at and above 0.4mg/ml would cause cell death on a massive scale. 10 The outcome measures of DCR surgery are comparable to whether a concentration of 0.2mg/ml or 0.5mg/ml is employed.[11,12] Therefore, we choose to work with 0.02% concentration to achieve uniformity in methodology with previous analysis and compare results.

We applied MMC for five minutes on the evidence that duration beyond five minutes causes extensive cell necrosis.[13] Previous authors' intraoperative duration of MMC application in DCR varies considerably from 2 minutes to 30 minutes.[14] and no definite conclusion can be drawn on the optimum concentration. However, the minimum effective and safe duration is three minutes.[15] For the duration, we compared five minutes application with intramucosal injection in which the role of duration is irrelevant; however, we achieved similar results in both cases; therefore, it can be concluded that duration did not play a significant role in our study.

The modality of delivering MMC via intramucosal injection was first performed by Kamal *et al*.[8] Another study also performed the same technique.[16] Both studies used 0.02% concentration of MMC and injected 0.1ml of MMC at each point. To date, our study is the third to employ the intramucosal injection technique. None of our failed cases showed any MMC-related complications on endoscopy with a concentration of 0.02% and 0.1 ml at each injection point.

The success rate of external DCR is higher in younger patients than in older patients. This is caused by the higher incidence of eyelid laxity, dry eye with reflex lacrimation and conjunctivochalasis in the older age groups.[17] Age is a significant factor in causing

functional failure of DCR in the elderly despite anatomical success.[18]

Reported adverse effects of adjunctive use of MMC in DCR surgery include wound gape, infection, lacrimal sac fistula, mucosal necrosis and nasal or gastrointestinal irritation.[18,19] Howevera metanalysis study depicted that MMC does not increase the incidence of abnormal nasal bleeding, mucosal necrosis or infection. Majority of studies have not reported even a single MMC-specific complication.[3,4,19] Similarly, complications related to MMC were not recorded in our study.

The results of our study are limited to cases where primary external DCR was performed since we did not include repeat or failed DCR cases and we did not perform Endoscopic DCR; therefore, our results do not mention the efficacy of MMC in endoscopic DCR.

CONCLUSION

Mitomycin C use as an adjunctive agent during external dacryocystorhinostomy is a safe and effective technique in achieving a high rate of success, and the route of application, whether applied topically or injected intramucosal does not significantly affect the outcome of this procedure.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

FAK: Data acquisition, data analysis, drafting the manuscript, approval of the final version to be published.

SPN: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

MFH: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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