Surgical Outcome of Repeat External Dacryocystorhinostomy with or Without Mitomycin C for Previously Failed Dacryocystorhinostomy: A Comparative Study of Eastern Nepal

Diwa Hamal[1], Prerna Arjyal[2], Sabin Sahu[3], Rakshya Pant[4], Anjan Bikram Hamal[5], Sanjaya Kumar Singh[6]

[1]Nepal Eye Hospital, [2]Birat Medical Collage, [3]Jyoti Eye Hospital, [4]Biratnagar Eye Hospital, [5]Kist Medical Collage, [6]Siddartha Eye Care

ABSTRACT:

INTRODUCTION: Dacryocystorhinostomy including use of antimetabolites as Mitomycin-C can increase the success rate of surgery for nasolacrimal duct obstruction. Therefore, this study is aimed to compare the surgical outcome of Dacryocystorhinostomy with and without intraoperative use of 0.02% Mitomycin-C in the treatment of failed external Dacryocystorhinostomy surgery.

METHOD: This is a retrospective quasi-experimental study done at Biratnagar Eye hospital from January 2018 to January 2021. We included all 60 failed cases of external Dacryocystorhinostomy previously operated inside the hospital and at other hospitals. The patients underwent External Dacryocystorhinostomy with 0.02 % Mitomycin-C in one group and the External Dacryocystorhinostomy without Mitomycin-C in another group. There were 30 eyes in each group, 60 in total. We used an independent sample t-test, chi-square test and fisher exact test as statistical methods for the data analysis

RESULT: At the end of 12 months 96.7% had success in Dacryocystorhinostomy with the Mitomycin-C group and 93.3% had success in the Dacryocystorhinostomy without Mitomycin-C group. On the other hand, there was 3.3% failure in Dacryocystorhinostomy with Mitomycin-C group and 6.7% failure in Dacryocystorhinostomy without Mitomycin-C group.

CONCLUSION: Although the success rates did not reach statistical significance, slightly higher success has been achieved in patients undergoing Dacryocystorhinostomy with Mitomycin C group. Thus it can be concluded that intraoperative use of Mitomycin-C improves the success rate of revision Dacryocystorhinostomy surgery without any detrimental effects and hence can be considered as a safe and effective modification of conventional Dacryocystorhinostomy.

KEYWORDS: Dacryocystorhinostomy with Mitomycin-C; Mitomycin-C; Revision Dacryocystorhinostomy surgery

INTRODUCTION

External Dacryocystorhinostomy is the gold standard for the management of nasolacrimal duct obstruction. The failure rates of post-Dacryocystorhinostomy (DCR) surgery have been reported to be ranging from 0% to 18%, due to blockage of osteotomy by granulation tissue, scarring, adhesions, and synechiae in the nasal cavity.[1-5] The success rate of repeat DCR surgery has been reported to be 85%.[6]

Correspondence to:
Dr. Diwa Hamal
Consultant orbit plastic and reconstructive surgery
Nepal Eye hospital
diwa222@hotmail.com, +977-9851012243

One of the most frequent causes of DCR failure is obstructive closure of the osteotomy site.[7] After a successful DCR surgery the ostium size can further decrease during the postoperative healing process by scarring.[3] Maintaining the patency of the ostium by using antimetabolites can increase the longevity of the success of DCR. Antimetabolites as mitomycin C (MMC) inhibits circumosteal fibrous tissue growth and scarring. It acts by inhibiting DNA synthesis and interferes with RNA transcription and protein synthesis.[8,9] DCR surgery with MMC prevents the formation of the cicatrix.[10] MMC increases the success rates and reduces the closure rate of the osteotomy after DCR.[11]

To the best of our knowledge, there is a lack of similar studies in Nepal comparing the success rate of DCR with or without MMC in revision DCR cases. Therefore, the objective of this study is to compare the surgical

outcomes of DCR with and without intraoperative use of 0.02% MMC in failed external DCR surgery.

METHOD

This is a retrospective quasi-experimental study done at Biratnagar Eye Hospital (BEH). The hospital is a high-volume surgical center located in Eastern Nepal, the Terai plain near to Nepal India border. Over 1000 DCR surgeries are performed every year. The chart review of operated cases by two surgeons from January 2018 to January 2019 was done that followed up to 2021 January. The cases had followed up after 3 months, 6 months, 12 months, and then after every 6 months.

Sample size- 60 cases in total.

The sample size was calculated using the formula

$n = Z2 \times p \times q / e2$

$= Z2 \times p \times (1-p) / e2$

$= (1.96)\ 2 \times 15 \times (1-15) / (4)\ 2$

$= 3.8416 \times 15 \times 14/16$

$= 50.421$

$= 51.$

Where,

n = required sample size

Z = 1.96 at 95% Confidence Interval (CI)

p = prevalence of 15% failure after repeated DCR in reference population6

(The success rate of repeat DCR surgery has been reported to be 85%.6)

e = margin of error, 4% in this study.

Sampling Method: Consecutive sampling

Participants

After adding 10% (5.1) of the missing data the sample size was (56.1) that is 57, however we took 60 as sample size as total number of failed DCR presented and operated by repeat DCR from January 2018 to January 2019 was 60 in number.

Inclusion criteria- All the previously operated cases of nasolacrimal duct obstruction (NLDO) operated by external DCR technique inside the hospital or from other hospitals that presented with watering and those were diagnosed as a case of failed DCR surgery at BEH by lacrimal irrigation were included in this study. The patients that were included in the study underwent External DCR with MMC in one group and the other group underwent only External DCR surgery without MMC. The case selection for either group was not planned, but due to the unavailability of MMC during the course of surgery.

Exclusion criteria- those patients who did not have a minimum follow-up of 6 months post-surgery were excluded. Patients with any systemic illnesses contraindicating for DCR surgery and pediatric patients age below 18 were also excluded from the study.

Surgical Procedure

All the surgical steps of External DCR surgery were performed under local anesthesia with 2% Lignocaine with adrenaline 1:2,00,000. The subcutaneous injection was administered in parallel and anterior to the anterior lacrimal crest, posterior to the anterior lacrimal crest in the lacrimal sac fossa, and superior and posterior to the medial canthal tendon. Injection of the last area blocked the ethmoid nerve and the infratrochlear nerve. Lacrimal irrigation was done with betadine 1% and normal saline solution on the operation table to confirm the site of obstruction and to clear out the nasolacrimal sac. Anesthesia and hemostasis of the nasal mucosa were accomplished with the nasal pack with ribbon gauze soaked in Lignocaine jelly 2% and adrenaline 1:1000, 2ml and placed at the anterior limit of the middle turbinate, the intranasal site of the ostium just before surgery.

The skin incision was made over the site of the previous scar to avoid creating multiple scars. Orbicularis fibers were separated by blunt dissection till the anterior lacrimal crest was exposed. The periosteum was then incised and a subperiosteal plane was created. We tried to preserve the nasal mucosal tissues as far as possible. A bowman's lacrimal probe was placed into the lacrimal sac to help demonstrate the site of the previous fistula and osteotomy. If scar tissue was seen to be covering the osteotomy, it was excised gradually. If the osteotomy was small in size or not in the proper position, the opening was enlarged using a Kerrison rongeur. The opening of the common canaliculus was clearly seen and any bone or soft tissue in its vicinity was removed.

Bleeding was controlled with epinephrine-soaked cotton and cautery. Cautery use was avoided as far as possible to minimize complications like scarring in the ostium or delayed wound healing.

Once the ostium was cleared and enlarged to adequate size, MMC 0.02% soaked cotton ball was applied to the ostium for 3 minutes.

A bicanalicular silicone intubation tube was then introduced in the ostium from the upper and lower canaliculi and its free ends were tied in the nasal cavity. Anterior flaps of the remaining nasal mucosa and lacrimal sac were then sutured to each other. In

cases where intact nasal mucosa was not seen, the periosteum from the anterior lacrimal crest was used to create a flap with the sac mucosa. The cutaneous incision was then closed in layers.

The patients were given cap ampicillin 250 mg + cloxacillin 250 mg one cap four times daily per orally for 1 week, tab analgesic one tab per oral 3 times a day for 3 days, and then as needed, tab Serratiopeptidase 10 mg 3 times a day for 1 week, eye drop ciprofloxacin 0.3% with dexamethasone 0.1% 4 times a day for 2 weeks, ointment ciprofloxacin over the skin wound twice daily for 4 weeks, oxymetazoline nasal drop 2 drops 3 times a day for 2 weeks. The suture was removed after 1 week. After 2 weeks, the antibiotic steroid drop was stopped and only antibiotic drop Ciprofloxacin 0.3% 4 times a day was used for the next 1 month. The silicone tube was removed after 3 months. The causes of failure were diagnosed during the revision surgery and categorized as inadequate osteotomy, inappropriate ostium location, inadequate sac marsupialization, cicatricial closure of osteotomy, and ostium granuloma.

Inadequate osteotomy was defined as when the removed bone did not completely expose the lacrimal sac including its fundus. Inappropriate ostium location was defined as small osteotomy, inferiorly, anteriorly, or posteriorly related to the internal common opening. Inadequate sac marsupialization was defined as failure to achieve full-thickness sac wall cut along its entire length and failure to reflect the lacrimal sac flaps noted intraoperatively. The duration of complaints after primary surgery was recorded in months.

Variables: We compared the two groups in terms of demography (age, gender, nationality). We identified the causes of failure of previously done DCR surgeries. Duration of surgery, surgical success, failure, and endoscopic finding of the failure of repeat surgery (cicatricial ostium closures, organizing granulomas, bone neogenesis) were recorded. The duration of surgery was categorized as <30, 30-60, and 60-90 in minutes. We recorded the complications related to surgery, tube, MMC as bleeding, laceration of punctum, and difficulty in making bony windows in both the groups. In addition, we recorded the complications as epistaxis, nasal synechiae, granulation tissue formation, and obstruction at the rhinostomy site.

We determined the success rate subjectively by Munk's subjective scoring system for watering and objectively by lacrimal irrigation that was done in each follow-up visit at the third month, the sixth month, twelve months, and then every 6 months.

Munk's score of epiphora was graded into five grades. Grade zero was determined when there was no epiphora. Grade one was determined by occasional epiphora requiring dabbing less than twice a day. Grade two was determined by epiphora requiring dabbing two to four times per day. Grade three was determined by epiphora requiring dabbing 5–10 times per day. Grade four was determined by epiphora requiring dabbing more than 10 times per day. Grade five was determined by constant tearing.

Good outcome was considered in cases where the fistulous opening was freely patent and patients had subjective epiphora of Munk's score 0 to 1. The fair outcome was labeled when a passage was patent on syringing but with some resistance to flow and the patient has Munk's score of 2 to 3. Poor outcome was when the passage was not patent on syringing and the patient's epiphora scored 4 to 5.

Surgical success was defined as when a fistulous opening was freely patented and patients had subjective epiphora of Munk's score 0 to 1.

Surgical failure was defined as non-patency of ostium on lacrimal irrigation and subjective epiphora of Munk's score is above 4.

Data collection: We collected the data retrospectively from the patient's chart, where the data entry was done during each patient's visit.

Statistical Analysis:

The collected data were recorded in Microsoft Excel 2013 and imported to R version 4.0.3 (2020-10-10), available from the comprehensive R Archive Network (http://cran.r-project.org/) for statistical analysis. The categorical variables were presented with frequency and percentages. In addition, parametric numerical variables were presented with mean and standard deviation, whereas the non-parametric numerical variables were presented with median and interquartile range. The statistical methods used for data analysis were independent sample t-test, chi-square test, and fisher-exact test.

Ethical clearance:

The study was done after the ethical clearance from the institutional review board of Biratnagar Eye Hospital. The IRC Approval No is BEH- IRC-22/A.

RESULT

A total of 60 failed DCR cases, 30 in each group, were included in the study. Out of the total 60 cases, 35 failed DCR cases were from BEH and 25 failed DCR cases were referred from other hospitals. The prevalence of the failed cases during the study period (Confidence Interval = x to y).

Where the confidence Interval (C.I.) = $p \pm Z \times \sqrt{p\,q/n}$

CI (x) = $15 + 1.96 \times \sqrt{15 \times 14/60} = 16.77$.

CI (y) = $15 - 1.96 \times \sqrt{15 \times 14/60} = -13.23$.

CI (x to y) = 16.77 to -13.23.

The demographic characteristics of the patients included in this study are presented in (Table 1).

Table 1. The demographic characteristics of the patient included in this study				
Characteristics	DCR with MMC n (%)	DCR without MMC n (%)	Overall	P-value
Age (in years)				
Mean (SD)	41.4 (15.4)	44.5 (12.9)	42.9(14.2)	0.4915
Range [Min, Max]	19.0, 74.0	19.0, 67.0	19.0, 74.0	
Gender				
Female	22 (48.9%)	23 (51.1%)	45(75%)	1
Male	8 (53.3%)	7 (46.7%)	15(25.0%)	
Nationality				
Bangladesh	4 (66.7%)	2 (33.3%)	6(10.0%)	0.0103
India	16 (38.1.7%)	26 (61.9%)	42(70.0%)	
Nepal	10 (83.3%)	2 (16.7%)	12(20.0%)	

The age of the patients ranged from 19 to 74 years, with the mean age of 41.4 (SD=15.4) in DCR with MMC group and 44.5 (SD=12.9) in DCR without MMC group. Three fourth (75.0%) of the patients included in this study were female. There were 41 right eyes and 19 left eyes included in this study.

The reasons for failed DCR surgery were included in the study (Table 2).

Table 2. The reasons for failed DCR surgery included in this study.				
Reasons for failed DCR included in the study	DCR without MMC n (%)	DCR with MMC n (%)	Total	P-value
Inadequate osteotomy	8 (26.7)	8 (26.7)	16 (26.7)	0.9923
Inadequate sac marsupialization	9 (30.0)	10 (33.3)	19 (31.7)	
Cicatricial closure of osteotomy	12 (40.0)	11 (36.7)	23 (38.3)	
Canalicular obstruction	1 (3.3)	1 (3.3)	2 (3.3)	

The majority of patients had cicatricial closure of the osteotomy (38.3%) followed by inadequate sac marsupialization (31.7%), inadequate osteotomy (26.7%), and canalicular obstruction (3.3%). There were no intraoperative complications. Postoperative complications included 3 failed cases, 1 eye each with canalicular cheese wiring, hemorrhage needing nasal packing, and lacrimal sac abscess. Surgical time taken ranged from 25 min to 60 min in DCR with MMC group and 20 min to 55 min in DCR without MMC group.

At 6 months, 1 eye in each group showed poor Munk's score. One eye in DCR without the MMC group showed Fair Munk's score. At the end of 12 months, 29 eyes showed subjective success in DCR with the MMC group and 28 eyes in DCR without the MMC group. The subjective improvement in epiphora after DCR with and without MMC in previously failed DCR cases is shown on (Table 3).

Subjective improvement of epiphora by munk's score at last visit		
Munk's score	DCR without MMC n (%)	DCR with MMC n (%)
Good (0-1)	28 (93.3)	29 (96.7)
Fair (2-3)	1 (3.3)	0 (0)
Poor (4-5)	1 (3.3)	1 (3.3)

Table 3. The subjective improvement in epiphora after DCR with and without MMC in previously failed DCR cases.

The patient follow-up ranged from 6 months to 30 months. The mean follow-up was 16.2 months in the DCR without the MMC group and 18.1 months in DCR with the MMC group. At the end of 12 months, 29 eyes (96.66%) were patent in lacrimal syringing in DCR with MMC group and 28 eyes (93.33%) were patent in DCR without MMC group. The patency of the lacrimal apparatus on lacrimal irrigation after DCR with or without MMC is mentioned in (Table 4).

Patency on lacrimal irrigation on last visit		
	DCR with MMC n (%)	DCR without MMC n (%)
Complete block	1(3.3)	1 (3.3)
Partial block	1 (3.3)	0 (0)
Patent	28 (93.3)	29(96.7)

Table 4. The patency on syringing of lacrimal apparatus after DCR with and without MMC in previously failed DCR cases.

Twenty- nine (96.66%) patients showed anatomical success in the DCR with the MMC group, and 28 (93.33%) showed anatomical success in DCR without the MMC group. There was 1 case (3.33%) of failure in DCR with the MMC group and 2 cases (6.66%) of failure in DCR without the MMC group. The reasons for failure identified by endoscopic examination of the surgical site were cicatricial closure of osteotomy in one eye and ostium granuloma in one eye in the DCR group and cicatricial closure of osteotomy in DCR with the MMC group. The failure of the cases was noted 5, 16, and 28 months post repeat surgery.

DISCUSSION

Chronic dacryocystitis is more common in adults over middle life from the fifth to seventh decade.[12,13] In our study, the age range of patients was 19-74 years, with the mean age of 44.5 years and more common in the 30th to 60th decade of life. In this study, the age range in the conventional DCR group was 19-74 years (average 41.36 years) and the age range in the MMC group was 19–67 years (average 44.47 years). Thus this is comparable with previous studies with no significant difference in age between the two groups.[12]

In this study, 45 (75%) patients were female and 15 (25%) were male, thus showing female preponderance. This is in agreement with previous studies that demonstrate female predilection of dacryocystitis with a male: female ratio 1:3.[14]

This is assumed to be due to the presence of a narrower lumen of a bony lacrimal canal and lower nasolacrimal fossa in females. Contrary to previous studies, the majority of the study cases (68.3%) had dacryocystitis on the right side. A study by Qadir M, et al. also showed results similar to our study, with more patients presenting in RE.[15]

Various authors have described different concentrations and techniques of instilling intraoperative MMC. Gonzalvo et al. studied the effects of intraoperative MMC on the clinical evolution and osteotomy size following an external DCR with helical computed tomography. They concluded that intraoperative MMC may increase the success rates over the traditional DCR procedure and is effective in reducing the closure rate of the osteotomy after DCR16 (Gonzalvo Ibáñez FJ et al, 2000). There have been further variations in the duration of application and concentration. Deka et al. used 3 groups: Control group 1, operated without MMC; experimental group 2, with MMC at a concentration of 0.05 mg/ml for 2 min; and experimental group 3, with MMC applied at a concentration of 0.4 mg/ml for 2 min. Furthermore, half of the cases in each group underwent single‐flap DCR, and half underwent double‐flap DCR surgery. They concluded that the ostium size in group 3 was found to be significantly bigger in comparison with group 1 and with group 2 .[3]

The minimum effective concentration appeared to be 0.2 mg/ml for 3 min as it prevents the proliferation of the fibroblasts by inducing cell cycle arrest, without causing extensive apoptosis.[17] We have used 0.2% of MMC instilled in cotton and applied it at the bony ostium for 3 minutes. We did not see any complications associated with MMC. Ali et al. studied the effect of varying concentrations of MMC and treatment durations on cellular proliferation and viability of the fibroblasts. Nasal mucosa harvested from patients undergoing a DCR was used to establish primary cultures by explant culture method. The cells were then treated with different concentrations of MMC (0.1–0.5 mg/ml) for different time periods (3, 5, and 10 min). Cell viability, cellular proliferation, and the actin cytoskeletons of fibroblasts were studied. The significant findings of this study were that the doubling time of cultured nasal mucosal fibroblasts was found to be approximately 24 h. MMC at 0.4 mg/ml beyond 5 min and 0.5 mg/ml concentration at all time points were lethal and caused extensive cell death when compared with controls.[17]

In a comparative study, the most common causes of DCR failure were inadequate osteotomy (69.8% in the external group and 85.1% in the endoscopic group, P = 0.19) followed by inadequate or inappropriate sac marsupialization (60.2% in the external group and 77.7% in the endoscopic group, P = 0.16) and cicatricle closure of the ostium (50.6% in the external group and 55.5% in the endoscopic group, P = 0.83).[18] The majority of failed DCR cases included in this study had cicatricle closure of the osteotomy 12 (40%) in DCR without MMC group and 11(36.7%) in DCR with MMC group, followed by inadequate sac marsupialization,

inadequate osteotomy, and canalicular obstruction.

In our study, postoperative complications included three failed cases, one (1.66%) eye each with canalicular cheese wiring, hemorrhage needing nasal packing, and lacrimal sac abscess, all in DCR with MMC group. Tarbet and Custer have reported postoperative epistaxis in 3.9% of cases of external dacryocystorhinostomy.[19] In one study by Qadir M et al., epistaxis was seen postoperatively in five (10%) cases, three in the Mitomycin C group and two in the conventional DCR group. In that study surgical time taken ranged from 25 min to 60 min in DCR with the MMC group and 20 min to 55 min in the conventional DCR group.[15] In this study, one eye in each group showed a poor Munk's score at six months of follow up. One eye in DCR without the MMC group showed Fair Munk's score. At the end of 12 months, 29 eyes showed subjective success in DCR with the MMC group and 28 eyes in DCR without the MMC group.

In this study, at the end of 12 months; 29 eyes (96.7%) were patent in lacrimal syringing in DCR with the MMC group and 28 eyes (93.3%) were patent in DCR without the MMC group. Twenty- nine (96.7%) patients showed anatomical success in the DCR with the MMC group and 28 (93.3%) showed anatomical success in the conventional DCR group. There was 1 case (3.3%) of failure in DCR with the MMC group and 2 cases (6.7%) of failure in the conventional DCR group.

Endoscopic evaluation of failed cases may show many possible causes of tear drainage failure and include cicatricle ostium closures, scarred common canaliculus, obstructed distal canaliculi, organizing granulomas, and bone neogenesis. The intraoperative surgical complication that may lead to or contribute to subsequent failures includes the inability to correctly localize the sac, inappropriate osteotomy, inadequate sac opening, significant septal deviations, and concha bullosa.[20-27] In this study, the reasons for failure identified by endoscopic examination of the surgical site were cicatricle closure of osteotomy in one eye and ostium granuloma in one eye in DCR without MMC group, and cicatricle closure of osteotomy in DCR with MMC group. In a study by Qadir M et, at the end of 6 months, 20 (80%) cases in the DCR without MMC group and 24 (96%) cases in DCR with MMC group had patent passage on lacrimal syringing.[15] Failed cases showed either clear fluid regurgitation or mucopurulent regurgitation on lacrimal sac syringing. In the study of Ari S et al. on lacrimal sac syringing, 96% had patent passage in the MMC group and 84% in the conventional DCR group had patent passage at the end of 1 year.20 Our results are also comparable to the study conducted by Liao S et al, where 88.4% of cases in the conventional group and 95.5% of cases in the MMC group had patent passage on lacrimal sac syringing.[28] This indicates the effectiveness of MMC in increasing the patency rate of the lacrimal drainage system, although the statistical difference is not significant. All 6 failed cases in both groups showed narrow ostium and soft tissue scar and membrane across the ostium on anterior rhinoscopy.[15] Various studies reported that there are no complications due to MMC.[9, 28, 29] In this study, we did not see any complications associated with the use of MMC. The application of MMC in revision DCR appears to be safe, but a larger sample size must be assessed before a definite conclusion can be made. The strength of this study is that this is the first study from Nepal and has a good follow-up. The small sample size is the limitation of this study. Since the patients visiting our hospital were from Eastern Nepal as well as neighboring countries such as India and Bangladesh, it was difficult to maintain regular follow-up. Therefore, we had only 60 cases included in the study group who fulfilled the inclusion criteria. The potential biases in this study can be due to the surgery being done by two surgeons and the two groups were not identified before surgery. Those patients who were in the DCR without MMC group were due to the unavailability of MMC at that time.

CONCLUSIONS

Although the success rates did not reach statistical significance, slightly higher success has been achieved in patients undergoing DCR with MMC group compared to patients undergoing DCR without MMC. Intraoperative use of MMC improves the success rate of revision DCR without any detrimental effects and hence can be considered as a safe and effective modification of conventional DCR.

ACKNOWLEDGMENTS

I would like to acknowledge Dr. Nisha Shrestha and Dr. Archana Shrestha for continuous support in the construction and revision of this manuscript.

Conflict of Interest: None.

REFERENCES

1. Allen K, Berlin AJ. Dacryocystorhinostomy failure: association with nasolacrimal silicone intubation. Ophthalmic Surg. 1989 Jul; 20 (7): 486–9.
2. Nemet AY, Wilcsek G, Francis IC. Endoscopic dacryocystorhinostomy with adjunctive mitomycin C for canalicular obstruction. Orbit. 2007 Jun;26(2):97-100.
3. Deka A, Bhattacharjee K, Bhuyan SK, Barua CK, Bhattacharjee H, Khaund G. Effect of mitomycin C on ostium in dacryocystorhinostomy. Clin Exp Ophthalmol. 2006 Aug; 34(6): 557-61.
4. HALLUM AV. The Dupuy-Dutemps dacryocystorhinostomy. Am J Ophthalmol. 1949 Sep; 32(9): 1197-1206.
5. Samuel D. McPherson, DuBose Egleston. Dacryocystorhinostomy: A Review of 106 Operations, American Journal of Ophthalmology.1959 March; 47(3): 328-31.
6. Welham RA, Wulc AE. Management of unsuccessful lacrimal surgery. Br J Ophthalmol. 1987 Feb;71(2):152-7.
7. Korkut AY, Teker AM, Ozsutcu M, Askiner O,

Gedikli O. A comparison of endonasal with external dacryocystorhinostomy in revision cases. Eur Arch Otorhinolaryngol. 2011 Mar; 268(3): 377-81.

8. Cheng SM, Feng YF, Xu L, Li Y, Huang JH. Efficacy of mitomycin C in endoscopic dacryocystorhinostomy: a systematic review and meta-analysis. PLoS One. 2013 May 13;8(5): e62737.
9. You YA, Fang CT. Intraoperative mitomycin C in dacryocystorhinostomy. Ophthalmic Plast Reconstr Surg. 2001 Mar; 17(2): 115-9.
10. Ali MJ, Baig F, Lakshman M, Naik MN. Electron microscopic features of nasal mucosa treated with topical and circumostial injection of mitomycin C: implications in dacryocystorhinostomy. Ophthalmic Plast Reconstr Surg. 2015 Mar-Apr; 31(2): 103-7.
11. Shams PN, Chen PG, Wormald PJ, Sloan B, Wilcsek G, McNab A, et al. Management of functional epiphora in patients with an anatomically patent dacryocystorhinostomy. JAMA Ophthalmol. 2014 Sep; 132(9): 1127-32.
12. Iliff CE. A simplified dacryocystorhinostomy. 1954-1970. Arch Ophthalmol. 1971 May; 85(5): 586-91.
13. Picó G. A modified technique of external dacryocystorhinostomy. Am J Ophthalmol. 1971 Oct; 72(4) :679-90.
14. Akcay E, Yuksel N, Ozen U. Revision External Dacryocystorhinostomy Results After a Failed Dacryocystorhinostomy Surgery. Ophthalmol Ther. 2016 Jun; 5(1): 75-80.
15. Qadir M, Ahangar A, Dar MA, Hamid S, Keng MQ. Comparative study of dacryocystorhinostomy with and without intraoperative application of Mitomycin C. Saudi J Ophthalmol. 2014 Jan; 28(1): 44-8.
16. Gonzalvo Ibáñez FJ, Fuertes Fernández I, Fernández Tirado FJ, Hernández Delgado G, Rabinal Arbués F, Honrubia López FM (2000). External dacryocystorhinostomy with mitomycin C. Clinical and anatomical evaluation with helical computed tomography. Arch Soc Esp Ofthalmol; 75: 611□7.
17. Ali MJ, Mariappan I, Maddileti S, Ali MH, Naik MN. Mitomycin C in dacryocystorhinostomy: the search for the right concentration and duration--a fundamental study on human nasal mucosa fibroblasts. Ophthalmic Plast Reconstr Surg. 2013 Nov-Dec; 29(6): 469-74.
18. Dave TV, Mohammed FA, Ali MJ, Naik MN. Etiologic analysis of 100 anatomically failed dacryocystorhinostomies. Clin Ophthalmol. 2016 Jul 28; 10:1 419-22.
19. Tarbet KJ, Custer PL. External dacryocystorhinostomy. Surgical success, patient satisfaction, and economic cost. Ophthalmology. 1995 Jul; 102(7): 1065-70.
20. Ari S, Gun R, Surmeli S, Atay AE, Caca I. Use of adjunctive mitomycin C in external dacryocystorhinostomy surgery compared with surgery alone in patients with nasolacrimal duct obstruction: A prospective, double-masked, randomized, controlled trial. Curr Ther Res Clin Exp. 2009 Aug;70(4):267-73.
21. Choussy O, Retout A, Marie JP, Cozlean A, Dehesdin D. Endoscopic revision of external dacryocystorhinostomy failure. Rhinology. 2010 Mar;48(1):104-7.
22. Elmorsy SM, Fayk HM. Nasal endoscopic assessment of failure after external dacryocystorhinostomy. Orbit. 2010 Aug;29(4):197-201.
23. El-Guindy A, Dorgham A, Ghoraba M. Endoscopic revision surgery for recurrent epiphora occurring after external dacryocystorhinostomy. Ann Otol Rhinol Laryngol. 2000 Apr;109(4):425-30.
24. Hull S, Lalchan SA, Olver JM. Success rates in powered endonasal revision surgery for failed dacryocystorhinostomy in a tertiary referral center. Ophthalmic Plast Reconstr Surg. 2013 Jul-Aug; 29(4):267-71.
25. McMurray CJ, McNab AA, Selva D. Late failure of dacryocystorhinostomy. Ophthalmic Plast Reconstr Surg. 2011 Mar-Apr;27(2):99-101.
26. Liang J, Hur K, Merbs SL, Lane AP. Surgical and anatomic considerations in endoscopic revision of failed external dacryocystorhinostomy. Otolaryngol Head Neck Surg. 2014 May;150(5):901-5.
27. Welham RA, Wulc AE. Management of unsuccessful lacrimal surgery. Br J Ophthalmol. 1987 Feb;71(2):152-7.
28. Liao SL, Kao SC, Tseng JH, Chen MS, Hou PK. Results of intraoperative mitomycin C application in dacryocystorhinostomy. Br J Ophthalmol. 2000 Aug;84(8):903-6.
29. Liu D, Bosley TM. Silicone nasolacrimal intubation with mitomycin-C: a prospective, randomized, double-masked study. Ophthalmology. 2003 Feb;110(2):306-10.