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Original Research Article

A Comparative Assessment of Topical Mitomycin-C Versus Nasolacrimal Stent in Endoscopic Dacryocystorhinostomy for Chronic Dacryocystitis

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Abstract

Aim: A comparative study in the use of topical mitomycin-C versus nasolacrimal stent in endoscopic dacryocystorhinostomy for chronic dacryocystitis.

Methods: This prospective study conducted in the Department of ENT, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India. 40 consecutive patients were enrolled and randomly divided into two groups. Patient undergoing EnDCR with mitomycin-C as adjuvant were assigned as Group A and those undergoing NLD stenting were assigned as Group B.

Results: Total 40 patients were finally enrolled in the study. There were 62.5% females (n=25) and 37.5% male (n=15) in the study. 75% patients presented with symptoms of chronic dacryocystitis while 25% patients presented with simple epiphora. Sac syringing was done in all the patients which showed NLDO. DCG was done in 25 patients who showed lacrimal sac and blockage in NLD. It was performed in patients with inconsistent findings on sac syringing. It was not performed in balance 15 patients where sac syringing was confirmatory. Among the study subjects, age wise distribution revealed that chronic dacryocystitis was most prevalent in 5th and 6th decade of life, with mean age of 54.54 and standard deviation of 11.5. Out of 40 patients enrolled, only 3 patients (7.5%) patient reported within 06 months of onset of symptoms, balance 37 (92.5%) patients reported after 06 months of onset of symptoms. 20 patients had DNS, however, only in 7 patients it was severe enough to limit access to the sac per se during surgery. These patients underwent access endoscopic septoplasty. 20 patients underwent EnDCR with mitomycin-c application while rest 20 underwent EnDCR with stenting. At 06 months follow up 95% patients of group A (n=19) had a patent sac while in group B 85% (n=17) had a patent sac. Patients in grade 0 and 1 of Munk et al were considered as successful patients. 90% patients in Group A (n=18) and 80% (n=16) patients in Group B had subjective benefit.

Conclusion: EnDCR, beyond doubt is now the preferred and established modality of treatment for patients suffering from chronic dacryocystitis**.**

Keywords: dacryocystitis, mitomycin-C, DNS

Introduction

Dacryocystitis is the infection of lacrimal sac most often as a result of obstruction of nasolacrimal duct[1]. This disease may be acute or chronic. Watering from the eye is the presenting complaint of chronic dacryocystitis[2] A swelling at the inner canthus, that is usually painless, is often the presenting sign in chronic dacryocystitis[3]. Sometimes swelling may not be obvious but pressure over the lacrimal sac can result in regurgitation of mucopurulent discharge through the canaliculi[1].

For the management of epiphora, as a result of nasolacrimal duct obstruction, external dacryocysto- rhinostomy (DCR) is the most popular procedure[3,4]. In this procedure, a surgical anastomosis is done between the lacrimal sac to the nasal mucosa of middle meatus by creating an opening in the intervening bone[5]. Fibrous tissue growth in the flap anastomosis, obstruction at common canalicular end and closure of osteotomy site[6] constitute the most common causes of failure of external DCR. Success rate can be increased if growth of fibrous tissues is prevented. This goal can be achieved by applying anti-fibrotic agents like mitomycin-C[7]. Mitomycin-C is an alkylating antibiotic, derived from Streptomyces caespitosus. It inhibits DNA-dependent RNA synthesis[8] and prevents collagen synthesis. Mitomycin-C use during external DCR surgery is safe and effective and it results in good outcome of DCR surgery[9,10]. Races with higher level of melanin in body tissues are more prone to develop tissue fibrosis during wound healing[11]. This prospective study has been conducted to compare the efficiency of intraoperative use of mitomycin-C vis a vis use of silicone stenting in enhancing the success rate of EnDCR and to find out if any modification can be done to provide suitable cure to this benign troublesome condition. EnDCR is now a well-established procedure to relieve NLDO, becoming ENT surgeons' domain.

Material and Methods:

This prospective study conducted in the, Department of ENT, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India. 40 consecutive patients were enrolled and randomly divided into two groups. Patient undergoing EnDCR with mitomycin-C as adjuvant were assigned as Group A and those undergoing NLD stenting were assigned as Group B.

Patients who satisfy following criteria were included-

(a) adult patients suffering from acquired NLDO with history of epiphora and discharge; (b) confirmed patient suffering from NLDO in which other causes of epiphora were excluded; (c) no h/o undergoing any type of surgery for epiphora previously.

Exclusion criteria were- (a) patients suffering from other causes of epiphora like lid malposition, entropion, ectropion, punctual abnormalities, and blepharitis; (b) patients having acute dacryocystitis; (c) tumors of lacrimal sac; (d) prior failed DCR; (e) previous history of eye trauma; (f) anatomic mal-position of lacrimal duct or bony canal.

Out of 40 patients, 15 patients were male and 25 patients were female in age group ranging from 30 to 65 yrs. Out of these, 40 patients were referred from Ophthalmology department who were incidentally found to be suffering from dacryocystitis prior to cataract surgery.

Surgical technique:

The standard surgical technique of endoscopic DCR was adopted. Nasal decongestion with infiltration of local anesthesia 2% and 1:100000 adrenaline and soaked neuropatties was done in lateral nasal wall just superior and anterior to the attachment of middle turbinate. A 4 mm O^0 or 30^0 nasal endoscope with single chip CCD camera and xenon light source was used. Using number 15 blade mucosal incision were made. The first horizontal incision made 8 to 10mm above axilla of the middle turbinate starting about 3mm posterior to axilla and brought about 10mm anterior to axilla onto the frontal process of maxilla. The incision turned vertically to about 2/3rd of the vertical height of middle turbinate stopping just above the insertion of inferior turbinate into the lateral nasal wall. The incision is than continued horizontally and posteriorly till the insertion of uncinate process. The mucosal flap was raised posteriorly and elevated backwards off the maxillary bone up to uncinate process. In the middle meatus the lacrimal bone is exposed, a round knife is used to elevate the lacrimal bone off the thin posterior inferior region of the sac. A forward biting Hajek Koeffler punch is used to remove thick bone of frontal process of maxilla. This bone lies over the antero-inferior aspect of the lacrimal sac. Bone removal is continued till the bone becomes too thick for the punch to engage. A 2.5 mm diameter burr was also used in a few patients to remove the thick bone overlying the upper half of the sac. Entire sac was exposed and identified as a bluish white translucent structure which moved with pressure over the lacrimal fossa and to a lesser extent with movement of eyeball. Punctum dilator was used to dilate the lower punctum and a Bowman's lacrimal probe was inserted through the inferior canaliculus into the lacrimal sac. The sac wall was indented against it. This also helped in sac identification, once the sac was identified and confirmed, it was incised with a number 12 blade or a sickle and the presence of mucopurulent material within sac and escaping into the nasal cavity was confirmatory of chronic dacryocystitis. The probe was seen coming through the common canaliculus. A large flap was made and rotated onto the frontal process of the maxilla. The original mucosal flap that was raised was trimmed and adjusted in size to cover the denuded bone surrounding the opened sac. The lacrimal sac flaps are incised, everted and adjusted to accurately oppose the nasal mucosa.

Patients assigned in Group A- underwent mitomycin-C application over the sac area with the help of the gel foam in a concentration of 0.2 mg/ml for 3 min. It was followed with saline irrigation to wash out excess mitomycin-C. Eyes were also given saline wash to prevent any complication due to exposure to mitomycin-C. A total of 23 patients of group A and 03 patients of group B underwent mitomycin-C due to failed nasolacrimal intubation. Patients in Group B underwent bicanalicular siliastic stenting. Stent was passed through upper and lower lacrimal punctum into the sac. The parts of the stent within the eye were kept a little loose so to prevent damage to lacrimal puncta and the medial caruncle (preventing cheese wiring). The stents were secured in place with a silastic tube over the stent used as spacer and slid up into the lacrimal sac and about 6-7 knots below it. The stent was kept for minimum of 03 months duration. This procedure was employed in 20 patients out of 23 patients assigned to undergo nasolacrimal intubation. In 03 patients the metallic probe of the nasolacrimal stunt could not be negotiated through the common canaliculi. These 03 patients underwent mitomycin-C application.

All patients were followed up to 06 months postoperatively. Sac syringing was done at regular intervals, starting from second post op day in patients who were not stented, then weekly for one month followed by syringing at 03 months and 06 months after surgery. It was performed in every visit to verify the patency of ostium along with nasal endoscopy to remove crusts and debris from ostium gently.

In patients undergoing stenting, sac syringing was done at 03 months, after removal of nasolacrimal stent, to confirm the patency of neo ostium. The surgical outcome was evaluated both subjectively and objectively. In subjective assessment, patients were asked to grade the degree of epiphora relief on a scale described by Munk et al.[12]. In objective assessment, sac syringing was performed with simultaneous nasal endoscopy and saline dropping into nasal cavity was observed. Tear meniscus level was measured using slit lamp. The results were documented and studied.

Results:

Total 40 patients were finally enrolled in the study. There were 62.5% females (n=25) and 37.5% male (n=15) in the study (Table 1).

Table 1: Gender distribution of case

Gender	No of cases (%)
Male	15 (37.5)
Female	25 (62.5)
n=40	

75% patients presented with symptoms of chronic dacryocystitis while 25% patients presented with simple epiphora (Table 2).

Table 2: Clinical presentation

No of cases (%) (n=40)	
Chronic dacryocystitis	30 (75)
Simple epiphora	10 (25)

Sac syringing was done in all the patients which showed NLDO. DCG was done in 25 patients who showed lacrimal sac and blockage in NLD. It was performed in patients with inconsistent findings on sac syringing. It was not performed in balance 15 patients where sac syringing was confirmatory.

Among the study subjects, age wise distribution revealed that chronic dacryocystitis was most prevalent in 5th and 6th decade of life, with mean age of 54.54 and standard deviation of 11.5 (Table 3).

Table 3: Age-wise distribution of study subjects

Age groups (yrs)	No of patients (%) (n=40)
31-40	04 (10)
41-50	6(15)
51-60	18 45)
61-70	12 (30)

Age: mean-54.44, S.D.-11.5.

Out of 40 patients enrolled, only 3 patients (7.5%) patient reported within 06 months of onset of symptoms, balance 37 (92.5%) patients reported after 06 months of onset of symptoms.

20 patients had DNS, however, only in 7 patients it was severe enough to limit access to the sac per se during surgery. These patients underwent access endoscopic septoplasty. 20 patients underwent EnDCR with mitomycin-c application while rest 20 underwent EnDCR with stenting.

At 06 months follow up 95% patients of group A (n=19) had a patent sac while in group B 85% (n=17) had a patent sac (Table 4, 5). Improvement in epiphora was evaluated subjectively as per criteria given by Munk et al and objectively by measuring height of tear meniscus by slit lamp examination at the end of 6 months of follow up.

Table 4: Patency of Sac at 6 months

Group	Type of Surgery	No of cases (n=40)	Number of successful cases (n=36)	Number of failure cases (n=4)	Success percentage (%)	Failure percentage (%)
Group A	DCR with MMC	20	19	1	95	5
Group B	DCR with stent	20	17	3	85	15

Table 5: Patency of Sac on follow up (group A v/s group B)

Post op follow up	Group A (n=20) Patients (%) with patent sac	Group B (n=20) Patients (%) with patent sac
01day post op	20 (100)	-
01 month post op	20 (100)	-
03 months post op	19 (95)	18 (90)
06 months post op	18 (90)	16 (80)

Table 6: Subjective benefit based on grading by Munk et al.

Grade	Group A (DCR with MMC) n=26 (%)	Group B (DCR with stent) n=20 (%)
0	18 (90)	16 (80)
1	1 (5)	1 (5)
2	1 (5)	1 (5)
3	0	1 (5)
4	0	1 (5)
5	0	0

Patients in grade 0 and 1 of Munk et al were considered as successful patients. 90% patients in Group A (n=18) and 80% (n=16) patients in Group B had subjective benefit (Table 6).

Objective evaluation of epiphora was done by measuring tear meniscus level at 6 months. Patients with tear meniscus levels of less than 0.1mm were considered as successful surgical outcome.

A few post-operative complications were noticed, however none of them was major complication. In Group A, 10% patient and in group B, 25% patient had post- operative complications.

Chi-square test with Yate's correction was employed to give a value of 0.1 with confidence interval of 3.14–0.07. P value of greater than 0.05 (p=0.56) was obtained, therefore the difference in results obtained by two techniques were insignificant. Similarly chi square test was employed to assess the difference in tear levels obtained after employing two techniques, p value obtained were 0.675, which means there is no significant difference in tear levels obtained post-surgery. As far as complications between the two groups are concerned the difference was statistically insignificant (p=0.24).

Discussion:

Chronic dacrocystitis is due to an obstruction for drainage in the lacrimal system, mainly at the level of nasolacrimal duct, with subsequent infection of the lacrimal sac[13]. Tearing and intermittent swelling of the medial canthus are the most frequent symptoms of the impaired drainage of the lacrimal system. The obstruction occurs primarily at 2 levels- (i) proximal - where the common canaliculus enters the lacrimal sac, (ii) distal- where the narolacrimal duct (NLD) enters the inferior meatus (dacryocystor- hinostenosis). The goal of the surgery is to re-establish intranasal drainage of the lacrimal sac, which can be achieved by a number of surgical methods.

Endoscopic dacryocystorhinostomy was initially described by Caldwell in 1893; however fell into disrepute due to limitation of technology at that time[14]. In Toti described the external procedure and later modified in 1921 by Dutemps et al.[15,16]

The endoscopic endonasal approach as performed today was pioneered by West (1910) who substituted a window resection over the lacrimal sac for wide resection[17]. This approach did not gain much popularity at that time because of poor visualization of intra nasal anatomy. The endonasal technique remained at best a neglected operation. With the introduction of endoscopes of different degrees of angulations, led to renewed interest in late 1980's and early 1990's by McDonogh, Merring and Massaro. The procedure is a valid alternative approach for NLDO and remained largely unchanged since then[18,19]. The success rate has been reported as approx 85% to 95% by both endonasal and external approach[20-22]. The endonasal approach has the added advantage of avoiding an external scar, maintaining the integrity of the pump mechanism and tackling any associated nasal pathology in the same sitting.

Causes of failure of EnDCR are mainly due to granulation tissue around the neo-ostium due to scarring or fibrosis at mucosal/submucousal level. In order to enhance the success rate of dacryocystorhinostomy, intraoperative adjuncts were employed. These are (a) Intraoperative topical application of mitomycin-C, an antimetabolite that affectively reduces fibroblastic capillary proliferations at osteotomy site (commonly used by ophthalmologists) in external DCR procedure and also used in EnDCR by otolaryngologists[23,24] (b) Intraoperative use of nasolacrimal silicone stent to maintain the patency of canaliculi and neo-ostium by preventing post-operative synechiae[25]. (c) Wide exposure of lacrimal sac with marsupialization of lacrimal sac with the nasal

mucosa, thereby minimizing the formation of granulation tissue and synechiae.

In our study all patients underwent marsupialization of widely exposed sac into nasal cavity with either intra-op mitomycin-C application or silicone stent to enhance the post-operative success rate. The surgical techniques employed in this study has been extensively described by Wormald.

In endonasal lacrimal surgery, osteotomy closure by granulation tissue, fibrosis and cicatrisation has been reported as most important reasons for failure[19]. Thus if an adjunct like applying mitomycin-c over osteotomy site, or using silastic stent can decrease the failure rate[26-28].

Mitomycin-C, an alkaline agent is isolated from fermentation filtrate of '*Streptomyces caespitosus'*. After intracellular enzyme reduction of the quinine and loss of methoxy, mitomycin-C becomes bifunctional or trifunctional alkylating agent. It covalently binds with and alkylates DNA and inhibits its synthesis. It also inhibits DNA dependent RNA synthesis thereby inhibiting protein synthesis. It inhibits cell mitosis in all phases of cell cycle, most predominantly during late G1 and early S phase of cell cycle. It affects both replicating and non-replicating cells and thus no cell can proliferate after exposure to MMC. MMC decreases proliferation of fibroblasts as well as growing capillary endothelium of conjunctival vasculature and may alter ciliary epithelium as well. MMC has been shown to induce apoptosis in human tenon capsule fibroblasts and bovine trabecular meshwork cells[29]. Application of mitomycin-C in dosages of 0.2 mg/ml to 0.5 mg/ml was effective in sub conjunctival fibroblasts for 1 to 3 min[30,31]. Liao et al used 0.2 mg/ml of MMC externally on the posterior flap and on the osteotomy site and removed after 30 min[21]. They reported 95.5% success rate.

Silicone intubation is a commonly suggested procedure in external DCR, especially in previous acute dacryocystitis, a small lacrimal sac, canalicular disease, or poor mucosal flap formation. Silicone tubing has been proposed to maintain the patency of the fistula by impeding fibrous closure during post-operative healing period.[32] It is also recommended for EnDCR procedures, because the surgical ostium created during surgery heals with granulation, and silicone stent has shown to maintain the patency of neo-ostium. Silicone stent should be placed both from superior and inferior canaliculi into lacrimal sac[33].

In this comparative study there were 40 patients who underwent EnDCR. We had made an attempt to find out whether intra operative mitomycin-C application increases the postoperative success rate by preventing scarring during the healing stage as compared to DCR with stenting.

In our study, the age of patients in our study ranged from 30 years to 65 years, mean being 54.44 yrs. Thus there being a predilection to elderly age group, this corresponds to studies conducted by Bartley[34]. Various studies have indicated that females suffer more from this condition than compared to males[20]. Total 40 patients were finally enrolled in the study. There were 62.5% females (n=25) and 37.5% male (n=15) in the study. Females are more prone to lacrimal obstruction due to narrower lumen of bony canal. Menstrual and hormonal fluctuations have been stated as factors to explain the prevalence in the middle aged and elderly.

Epiphora was the dominant symptom and was present in all 40 patients, being the commonest symptom of uncomplicated chronic dacryocystitis[22,35]. 20 patients had DNS, however, only in 7 patients it was severe enough to limit access to the sac per se during surgery. These patients underwent access endoscopic septoplasty. 20 patients underwent EnDCR with mitomycin-c application while rest 20 underwent EnDCR with stenting.

Subjective improvement in symptoms was assessed by a questionnaire presented to all the patients to evaluate the improvement in epiphora based on grading system described by Munk et al. Patients in grade 0 and 1 after 6 months were considered as successful operations.

Grade 0– no epiphora; Grade 1– occasional epiphora requiring drying or dabbing less than twice a day; Grade 2– epiphora requiring drying 2-4 times/day; Grade 3– epiphora requiring drying 5-10 times/day; Grade 4– epiphora requiring drying >10 times/day; Grade 5– constant tear flow. Patients in grade 0 and 1 of Munk et al were considered as successful patients. 90% patients in Group A (n=18) and 80% (n=16) patients in Group B had subjective benefit Objectively the improvement was assessed by measuring height of tear meniscus level by slit lamp examination at ophthalmology dept. 88.46% patients in group A and 85% patients in Group B had significantly better tear levels.

Conclusion:

EnDCR, beyond doubt is now the preferred and established modality of treatment for patients suffering from chronic dacryocystitis. Several studies have been conducted to compare the results in use of mitomycin-C versus no mitomycin-C, Nasolacrimal stent versus no stent, but as far as review of literature is concerned, we were unable to find any study which directly compared the results of mitomycin-C versus nasolacrimal duct stent, and hence this study was undertaken.

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