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Efficacy of Mitomycin C in Dacryocystorhinostomy Operation: A Clinical Study - A Research Article

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Abstract: ***Aim: To study the effect of Mitomycin C(MMC) in Dacryocystorhinostomy (DCR) surgery. Materials and methods: The study included 101 cases of chronic dacryocystitis with or without complications over a period of one year which were divided into 2 groups; the control group with 51 cases where standard External Dacryocystorhinostomy (EXT-DCR) was performed and MMC group with 50 cases where 0.2 mg/ml MMC was used intra-operatively. A detailed history was taken and proper ocular examination was done. Blood investigations were done wherever indicated. A Rhinological examination by E.N.T specialist was done in all the cases in the Out Patient Department of E.N.T. The operative techniques used were: Type I (Single Flap DCR), Type II (Double Flap DCR), and Type III (Periosteal anastomosis). Results: The success rate in Control group was 86.27% and in MMC group was 96%. The difference was statistically significant (p value <0.05). Conclusion: Thus, intra-operative MMC is a safe and useful adjunct that helps to achieve long term success rate in EXT-DCR.***

Keywords: Dacryocystorhinostomy, Mitomycin-C, Dacryocystitis

1. Introduction

'Epiphora' is a Greek word meaning 'sudden outburst'. It is defined as an abnormal outflow of tears due to defect in the lacrimal passage pathway. Dacryocystorhinostomy is the surgical procedure by which tears are diverted from the lacrimal sac into the middle meatus of nose by forming an anastomosis between the sac and the nasal cavity by using their mucosa and thus, re-establishing the tear drainage through this alternate route. Thus, epiphora and other complications can be managed.

In 1904, it was Toti[1], an Italian Rhinologist who introduced external dacryocystorhinostomy to relieve nasolacrimal duct obstruction. By 1951, external DCR became the treatment of choice for nasolacrimal duct obstruction by the ophthalmologists.[2] The success rate for this procedure is about 90% as per the previous studies.[3,4,5]

Failed DCR may result due to obstruction of the common canaliculus or closure of the osteotomy site by granulation tissue or scarring. Therefore, the use of anti-proliferative agents over the anastomosed flaps and osteotomy site to prevent fibrous tissue growth and scarring, the failure rate may be decreased. Mitomycin C(MMC), a chemotherapeutic agent is an anti-proliferative agent obtained from the broth of *Streptomyces caespitosus*. Cross linkage of the DNA base pairs, adenine and guanine inhibits DNA synthesis in all phases of life cycle. MMC also cause breakage of single stranded DNA.

We included 101 cases, 51 cases in the control group and 50 cases in the MMC group who were followed up for a period of one year. It was a control study using MMC in external DCR to soak the area of anastomosed flaps and osteotomy site to evaluate the long term effect on osteotomy size and thus the success rate following External DCR surgery.

2. Materials and Methods

This study included 101 cases of chronic dacryocystitis who presented in the Out Patient Department of a tertiary care hospital which was carried out for a period of one year and were prepared for dacryocystorhinostomy operation. They were divided into two groups:

Control Group: 51 cases where External DCR were performed.

MMC Group: 50 cases; 0.2 mg/ml MMC was applied intra-operatively for one minute and washed off thoroughly with sterile normal saline solution.

Selection criteria

Inclusion criteria- cases with fibrosed or small shrunken sac, recurrent acute on chronic dacryocystitis, failed DCR cases, chronic dacryocystitis with external lacrimal fistula and cases of chronic dacryocystitis with or without mucocele.

Exclusion criteria- cases with Grossly deviated nasal septum, septal spur, hypertrophied middle turbinate, polyps, allergic and atrophic rhinitis. Intra-operative and post-operative findings were recorded.

A detailed history was taken and proper ocular examination was done. Blood investigations including R/E blood, RBS, Bleeding and Clotting time etc were done. A rhinological examination by E.N.T specialist was done in all the cases in the Out Patient Department of E.N.T. and cases with gross nasal pathology were excluded from the study. Pre-operatively , each patient was started on oral systemic antibiotics, nasal decongestant drops three times daily, antihistaminic at bedtime and antibiotic eye-drops six times daily 1 day prior to the scheduled operation. Informed and written consent were obtained from each of the patient. Most of the operations were performed under local anaesthesia

except in children where general anaesthesia were used. Local anaesthesia consists of (i) local infiltration with 2% lignocaine HCl with or without adrenaline solution (1:200000) and (ii) endonasal anaesthesia with ribbon gauze soaked with 4% xylocaine and nasal decongestant drops (xylometazoline).

The operative techniques used were: Type I (Single Flap DCR), Type II (Double Flap DCR),and Type III (Periosteal anastomosis).

Stages of operation: Basic surgical steps were same for all the above techniques except in the preparation and the anastomosis of the flaps. Blood Pressure, pulse and respiratory rate were recorded prior to the surgery. After skin incision, exposure of the lacrimal sac and creation of the bony osteum, sac and nasal mucosal flaps were prepared

Application of Mitomycin C: In MMC group, a piece of cotton soaked with 0.2mg/ml MMC (2mg MMC diluted with 10 ml of distilled water and mixed thoroughly) was applied intra-operatively to both the surfaces and edges of the nasal mucosal flaps, the mucosal flaps of the lacrimal sac and edges of the bony osteum. Then it was washed thoroughly with a sterile normal saline after a contact time of one minute.

Suturing of the flaps: Haemostasis was achieved and any debris were removed.
Type I: The large anterior flaps of the sac and nasal mucosa was sutured with 6-0 Vicryl by 2-3 interrupted sutures.
Type II: The posterior flaps of the sac and the nasal mucosa was sutured first with 2 interrupted knots followed by the suturing of anterior flaps of the sac and the nasal mucosa.
Type III: The anterior flap of the sac was sutured to the periosteum and the adjacent tissues just anterior to the bony margin with 3 interrupted knots.

Wound closure: The medial palpebral ligament was sutured with a single 6-0 absorbable suture and the orbicularis muscle by 3-4 interrupted knots. After cleaning the wound and surrounding area, the skin is sutured by continuous or interrupted 6-0 vicryl.

Bandages: The wound was then cleaned with betadine and normal saline, antibiotic ointment was applied over the wound and the conjunctival sac. The eye was gently closed and pressure bandage applied.

Postoperative managements:
The patient's head was kept in a slightly elevated position to prevent oozing. Pulse, BP recorded and monitored for any bleeding. Those done under general anaesthesia was kept empty stomach for another 6 hours.

The same systemic antibiotic was continued for another 6 days.

Nasal decongestant drops three times daily for 10 days; local antibiotic eye drops 6 times daily in the conjunctival sac for 4 weeks and antibiotic ointment over the wound thrice daily to be applied from the first post-operative day after antiseptic dressing for 3 weeks; antihistaminic tablet at bedtime for 7 days to be continued.
On second post-operative day, syringing was done with normal sterile saline. Most of them were discharged on the second postoperative day and stitches removed after 7-10 days.

At the time of discharge, patients were advised to avoid contact with water on the operated side for 2 weeks, to avoid rubbing of the eye and wound site, to avoid sneezing, to contact immediately if any nasal congestion or bleeding occurs and to visit on 7-10th postoperative day for stitch removal.

Postoperative evaluation was done using-

a) Munk's score(Score 0 – IV)
   0-No epiphora; 1- occasional epiphora requiring dabbing with handkerchief less than twice daily; 2- epiphora requiring dabbing 2-4 times daily; 3- epiphora requiring dabbing 5-10 times daily; 4- epiphora requiring dabbing >10 times daily.
b) Syringing done on 2nd postoperative day, 2 weeks, 1 month, 2 months, 3 months and 6 months from the day of operation.
c) Endoscopic evaluation of the bony osteum was done by E.N.T specialist on 2nd day, 14th day, 1 month, 3 months and 6 months from the day of operation.

3. Results and Observations

Age and sex distribution*:* The lowest age at which DCR was done was 4 ½ years old, and the maximum age was 73 years. Females were found affected more than males in both the groups. Out of 101 cases, 78.22% was female and 21.78% was male.

Table 1: Showing age and sex distribution of the cases in Control Group:

Age in years	Male	Female	Total
0-10	1	--	1
11-20	2	2	4
21-30	2	14	16
31-40	3	15	18
41-50	2	5	7
51-60	1	4	5
61-70	--	--	--
71-80	--	--	--
Total	11	40	51

Table 2: Showing age and sex distribution of the cases in MMC Group:

Age in years	Male	Female	Total
0-10	--	1	1
11-20	--	3	3
21-30	3	11	14
31-40	2	14	16
41-50	3	9	12
51-60	1	1	2
61-70	1	--	1
71-80	1	--	1
Total	11	39	50

***Occupation*:** The highest number of DCR operation was done among housewives with 70.59% in control group and 66% in MMC Group.

Table 3: Showing occupation of patients in whom DCR operation was done

Occupation	*Number of cases*
Housewife	69
Student	12
Teacher	4
Service	8
Business	3
Rickshawpuller	1
Unemployed	1
Shopkeeper	1
Farmer	1
Nurse	1
Total	101

Indication for DCR surgery: In the present study, maximum patients with simple chronic dacryocystitis(65) were operated, chronic dacryocystitis with mucocele(20), encysted mucocele(1),6 patients with external lacrimal fistula(5 discharging; 1 healed), acute on chronic dacryocystitis(3), recurrent acute dacryocystitis(3), post DCT dacryocystitis(1) and 2 cases of failed DCR.

Table 4: Showing various indications of DCR operation and other associated conditions along with post-operative success rate.

Indications	No. of cases	Associated conditions			No. and percentage of success
		DNS	Hypertrophied inferior turbinate	Hypertrophied middle turbinate	
Simple chronic dacryocystitis	65	11	15	1	60(92.31%)
Chronic dacryocystitis with mucocele	20	1	2	--	19(95%)
Encysted mucocele	1	--	--	--	1(100%)
Fistula	6	--	--	--	6(100%)
1. Discharging.	5	--	--	--	--
2. Healed.	1	--	--	--	--
Acute on chronic dacryocystitis	3	--	2	--	1(33.33%)
Recurrent acute dacryocystitis	3	--	--	--	3(100%)
Post-DCT dacryocystitis	1	--	--	--	1(100%)
Failed DCR	2	--	--	--	2(100%)
Total	101	12	19	1	93(92.07%)

Indication for MMC: Intra-operative MMC was used mostly in cases of chronic dacryocystitis with mucocele(18) and encysted mucocele(1), 6 patients with external lacrimal fistula, 1 case of recurrent acute on chronic dacryocystitis, 3 cases with recurrent acute dacryocystitis, 2 cases of failed DCR and 1 case of post DCT dacryocystitis. Intra-operative decision were also taken in certain cases.

Table 5: Showing various indications for use of intra-operative MMC

Indications.	No. of cases	No. of successful cases.
Simple chronic dacryocystitis with fibrosed and shrunken sac.	9	9
Chronic dacryocystitis with extensive pericystic fibrosis.	2	2
Cases with intra-operative flap laceration.	2	2
Recurrent acute on chronic dacryocystitis.	1	1
Failed DCR surgery.	2	2
Post-DCT dacryocystitis using pseudosacs.	1	1
Chronic dacryocystitis with external lacrimal fistula.		
1. Discharging.	5	5
2. Healed.	1	1
Chronic dacryocystitis with-		
1. Mucocele.	18	17
2. Encysted mucocele.	1	1
Chronic dacryocystitis with normal sac condition.	5	4
Recurrent acute dacryocystitis.	3	3
Total.	50	48

***Types of operative technique**:* Type I was carried out in 37 patients of control group and 32 patients of MMC group. In the rest four techniques, there were equal number of cases in both the groups with 8 operations for Type II, 8 in Type III.

***Success rate**:* Complete success was seen in 47 cases in control group and 48 cases in MMC group at 2 weeks; 42 cases in control group and 48 cases in MMC group at 6th month. Partial success was seen in 4 cases in control group and 2 cases in MMC group at 2 weeks, and 2 cases in control group at 6 months with no case of partial success in MMC group. Therefore, success rate in control group was 86.27% and 96% in MMC group at 6th month that is found to be statistically significant ($p<0.05$). The success rate was 100% in both the groups at 2 weeks.

Out of 51 cases, 7 were unsuccessful in control group and 2 out of 50 cases in MMC group.

Causes of failure: Closure of the bony osteum due to fibrosis(3 in control group and 1 in MMC group), synechia between middle turbinate and lateral nasal wall in 2 patients of control group, epithelial membrane covering the osteum seen in 1 patient of MMC group and 2 cases with unknown cause in control group.

Table 6: Showing success rate in different age group at 6 months in Control (CON) Group and MMC Group

Age	No. of cases.		No. of success.						No. of failure.		Success rate.	
	CON	MMC	Complete success		Partial success		Total success		CON	MMC	CON	MMC
			CON	MMC	CON	MMC	CON	MMC				
0-10	1	1	1	1	--	NIL	44	48	--	--	86.27%	96%
11-20	4	3	3	3	--				1	--		
21-30	16	14	12	13	1				3	1		
31-40	18	16	16	16	--				2	--		
41-50	7	12	6	11	--				1	1		
51-60	5	2	4	2	1				--	--		
61-70	--	1	--	1	--				--	--		
71-80	--	1	--	1	--				--	--		
Total.	51	50	42	48	2				7	2		

Osteum sizes: It was measured in 11 cases in control group and in 11 cases in MMC group in successful DCR. The average osteum size at 2 weeks in control group was 10.81mm^2 and in MMC group was 11.27 mm^2. Whereas average osteum size at 6 months in control group and in MMC group were respectively 2.81mm^2 and 6.36mm^2.

Table 7: Showing average osteum sizes at 2 weeks and at 6 months in Control group and in MMC group in successful DCR

Average osteum size at 2 weeks (mm^2)		Average osteum size at 6 months (mm^2)	
CON	MMC	CON	MMC
10.81	11.27	2.81	6.36

4. Discussion

1) Age and sex incidence

The maximum number of cases were found in the 4th decade (18 cases in the control group and 16 cases in MMC group). The number of female was more than male (40 in control group and 39 in MMC group). The incidence of female and male are 78.22% and 21.78% respectively. Age variations reported was between 3 and 90 years. Dacryocystitis was mostly seen in the 3rd to 5th decade with female preponderance in the previous studies. However, according to Pico [6] (1971), before 20 years of age, males predominate but after menopausal years, the cases were more in females. Duke-Elder[7] (1974) observed the highest incidence of chronic dacryocystitis was seen in the 5th decade, with 75-80% female cases that is similar to our findings.

2) Occupation

The occupation most commonly involved with dacryocystitis in our study were housewives with lower incidence in the higher social classes. Wolf[8], (1946) reported that chronic dacryocystitis were more in poorer social classes and in the housewives and that probably the lack of personal hygiene being responsible for higher frequency in them (Duke-Elder[7]).

3) Effect of MMC

In our study, 48 patients in MMC group were free from epiphora with 2 cases that failed to respond to surgery. Whereas in control group, 42 patients were totally free from epiphora and 2 cases relieved from symptom (MUNK Score 1 in both), but failure seen in 7 out of 51 patients. The success rate in control group was 86.27% and in MMC group was 96% at 6th month.

The osteum size in the control group (2.81mm^2) and MMC group(6.36 mm^2) at 6 months was found statistically significant in our study. Shine et al[9] (1996), found the osteum size in MMC soaked eye was three times more than that without MMC at 6 months follow up thus indicating improvement in the success rate of DCR. Shu L. Liao et al[10] (2000) reported the patency rate of the lacrimal drainage system after DCR surgery was 95.5% in MMC Group compared to 88.6% in the conventional group that is similar to our study. Camara, Jorge G. Et al[11] (2000), reported significant difference between the success rate of MMC group and control group that correlates with our study.

4) Causes of failure

In our study, it was observed that incidence of fibrosis and synechia formation as the cause of failure is less in MMC group. Shine C.S. Kao et al[9] (1996) found septo-osteotomy adhesion in 2 patients in the control group but not such adhesion was seen in MMC group thus indicating that MMC can minimize this adhesion formation. Huang HS[12] (1998) also found the long term surgical failure was due to fibrous tissue growth, scarring and granulation tissue formation at the osteotomy site.

In our study, post-operative follow-up was done by syringing on 2nd day, 2nd week, 1st month, 2nd month, 3rd month and 6th month with sterile normal saline. In partially patent cases on 2nd day in both the groups, syringing were done using dexamethasone solution resulting in complete patency in the following visits. This is similar to that reported by Sarda et al[13] (1961) in his study. The cortisone solution used for syringing was helpful in preventing closure of the anastomosis by granulation tissue and fibrosis.

5. Conclusion

From our study, it has been observed that the intra-operative application of MMC is a safe and useful adjunct that helps to achieve long term success rate in DCR surgery. The osteum size in control group and MMC group at 6 months were 2.81mm^2 and 6.36mm^2 respectively which is statistically significant. The success rate in control group was 86.27% and in MMC group was 96% at 6th month of follow-up, the difference being statistically significant ($p<0.05$).

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