The Role of Mitomycin C in Endoscopic Dacryocystorhinostomy Mitomycin C in Endoscopic Dacryocystorhinostomy

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Objectives: The objective of this work is to compare the result of using topical Mitomycin C in endoscopic dacryocystorhinostomy associated with probing and bicanalicular silicon stenting in primary cases of epiphora due to post-saccal obstruction.

Background: Epiphora is a very troublesome symptom that may annoy the young as well as the old in both sexes. The goal of endoscopic DCR is to re-establish tear flow from the lacrimal sac into the nasal cavity through endonasal Approach.

Patients and Methods: Forty patients complained of epiphora were included in this study in the period from February 2015 to march 2017 . All were primary cases and all of them were chronic dacryocystitis (post-saccal obstruction). Assessment of epiphora was done both subjectively and objectively both preoperatively and postoperatively utilizing both Jones 1 and Jones 11 tests. All cases were followed up for at least one year and in some cases up to two years.

Results: We find that the total success rate is (87.5%), with (90%) in group (A) and (85%) in group (B) with insignificant use of topical Mitomycin C in endoscopic endonasal DCR in cases of post-saccal obstruction.

Conclusion: Endoscopic endonasal dacryocystorhinostomy with probing and bicanalicular silicon stent intubation is an effective treatment modality in the management of epiphora due to post-saccal obstruction, but using topical Mitomycin C has no benefit in such cases.

Keywords: lacrimal pathway, lacrimal system, lacrimal pathway obstruction, Endonasal endoscopic dacryocystorhinostomy, mitomycin.

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Introduction

Epiphora or abnormal tearing is a medical problem causing discomfort to the patient. It occurs as a result of blockage in the lacrimal drainage system which impairs normal tear channelling into the nose. As a result of lacrimal stagnation, infection may also occur. The Dacryocystorhinostomy operation, which involves fistulization of the lacrimal sac into the nasal cavity, may alleviate the symptoms.It was first described via an external approach by Toti in 1904. [1]

The first intranasal DCR was described by Caldwell in 1893. [2] McDonogh and Meiring [3] described the endoscopic transnasal DCR. Since this description a number of modifications had been developed with good instrumentation and also using different kinds of lasers such Holmium: Yag, argon, carbon dioxide and also KTP laser. [4]

The endoscopic approach has several advantages;it provides a better ethetic result with no external scar. It avoids injury of medial canthus.It preserves the pumping mechanism of orbicularis oculi muscle. [5]

The two most common causes of failure in DCR surgery are closure of the surgically created osteotomy with soft tissue obstruction at the common canaliculus. Many surgeon elect to insert bicanalicular silicone stents at the time of surgery. [6] While others prefer not to use them because of concerns related to silicone tubing induced granulomatous inflammation, which may compromise long term ostium patency. [7] The success rates without using the stents reaching up to 100%. [8]

Analyses of Boush et al series showed that majority of the surgical failures occurred withen 4 months after endoscopic surgery. Zilelioglu et al preferred to leave the siliastic tubes for 4-6months after endoscopic surgery. The stent interval proposed by different authors range from 4weeks to 24weeks. [9] The longer duration of tube retention is associated with higher chances of infection. The reported success rates with intubation range from 70 to 100%. Antiproliferative agent applied at the osteotomy site may reduce the fibrosis and hence the failure rate. Mitomycin C (MMC) and 5-fluorouracil have been equally successful in this regard. [10]

Dolmetsch [11] reported a success rate of 95% with adjunctive use of MMC (0.5mg/ml for 10minutes) in a follow up of 18.2 months in a non laser endoscopic endonasal DCR.

She also reported that intubation more than 3months was associated with higher rates of obstruction.

In this prospective randomized study,we have two groups, group (A) in which we use topical Mitomycin C and group (B) done without Mitomycin C.

The aim is to identify the role of Mitomycin C in endoscopic endonasal DCR to correlate the efficasy of endoscopic DCR with and without MMC.MMC has been used in different concentrations and time by various authors such as 0.5 mg/ml for 2.5, 5 and 10 minutes.Also 0.4mg/ml has been used for 3 and 5 minutes. [12]

Patients and Methods

This prospective case control study started in February 2015 to march 2017 was conducted on forty cases, all of them were selected from Ophthalmology and ORL Departments of Menoufia University hospital after approval of ethical committee of the hospital. A written consent was taken from all patients and they were informed with the results of the study. All of them were primary cases suffering from epiphora due to nasolacrimal duct obstruction (post-saccal), but revision cases and those with proximal obstruction, severe maxillo-facial trauma, suspicious malignancy were excluded from this study.All patients underwent endonasal endoscopic dacryocystorhinostomy with application of silicon tubes.

Patients were forty in number divided randomly into two groups, group (A) and group (B), twenty patients for each group. Group (A) patients were subjected to topical Mitomycin C after surgery while group (B) not. Fifteen females (37.5%) and twenty five males (62.5%) with a mean age (35.6 plus or minus 22.67) . All cases were diagnosed as chronic dacryocystitis (post-saccal obstruction).

Methods:

Preoperative preparation:

Preoperatively, all patients were subjected to detailed history taking and general examination. Local examination was done by Ophthalmologist including inspection (to exclude lid patholoy), palpation of the lacrimal sac (in case of dacryocystitis), nasal endoscopy (to examine the nasal cavity). Jones 1 test (in which we put lacal anaesthetic eye drops in the eye followed by putting fluorescein patches in both conjunctival fornices and putting a piece of cottonoid in each nostril in the inferior meatus it is considered negative if the cottonoid does not take the stain of fluorescein dye after 5 minutes) and Jones 11 test (in which a size 0 or 00 Bowman lacrimal probe is then put through the inferior or superior canaliculus to palpate the common internal punctum and also irrigation using 25 gouge blunt lacrimal canula in the inferior punctum to test patency).

CT- scan axial and coronal cuts without contrast were done to assess the nearby structures and also laboratory investigations were done.

Operative procedure:

- All the operations were done under general anaethesia with hypotesive technique in Ophthalmology operative theatre.
- Haemostasis done by lacal application of 2% xylocain with 1:10.000 adrenaline solution in acotton wads then infiltration with the same solution with concentration of 1;100000.
- Head of the patients were raised 30 degrees upwards and turned to the right of the patient towards the surgeon. A 4 mm, 0 or 30 degrees rigid endoscope was introduced in to the nasal cavity and the whole nasal cavity was visualized.
- The 1.5×2 cm piece of mucosa anterior to the anterior attachment of middle turbinate removed off but posteriorly based and corresponding lacrimal bone and frontal process of maxilla were removed.
- Probing (using bowman lacrimal probe) and dilatation (using netel dilator) of the inferior and superior puncti and canaliculi to the common canaliculus and then toward the medial wall of the sac and tenting it.
- The lacrimal sac then opened vertically using sickle knife (as an open book),
- Patency checked by saline irrigation ,then application of 0.5 Mitomycin C for 5 minutes in the osteotomy site in half of patients group(A) then all patients were stented and packed.

Postoperative follow up for 12 months:

- The nasal pack was removed after 24 hours and stents after 3 months.
- Regular endoscopic assessment of the operation regarding ostium size, presence or absence of granulation tissue, adhesions or synechia with immediate management of such cases.
- All patients were assessed postoperatively subjectively and objectively (flourescein test and irrigation test) in Ophthalmology department as regard resolution of epiphora after one month, after six months and at the end of the first year.
- The operation considered succeeded if the patient is symptome free after twelve months of the operation.

Statistical analysis:

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis.

According to the type of data qualitative represent as number and percentage , quantitative continues group represent by mean ± SD , the following tests were used to test differences for significance;. Differences between frequencies (qualitative variables) and percentages in groups were compared by Chi-square test.

Differences between parametric quantitative independent groups by t test in non parametric by Man Whitney,. P value was set at <0.05 for significant results &<0.001 for high significant result.

Data were collected and submitted to statistical analysis. The following statistical tests and parameters were used.

Results

Side distribution in group (A) were 12 right side and 8 left side, in group (B) there were 9 right side and 11 left side ,all cases were diagnonsed as chronic dacryocystitis **(Table 1)**.

Additional surgeries were more or less similar in both groups (no significant difference **(Table 2)**.

Complication distribution in both groups nearly there is no significant difference except granulation tissue formation at ostium site which is more in group (B) than in group (A) which gives slight benefit to the use of topical mitomycin C **(Table 3).**

The succeeded cases were 19 in group (A) and 19 in group (B) with success rate after one month was 95% in both groups **(Table 4).**

After one year of follow up the Succeeded cases were 18 in group (A) with success rate of (90%) and 17 cases in group (B) with success rate (85%) so it is nearly the same success rate in both groups with insignificant effect of Mitomycin C **(Table 5)**.

Table 1 Characters among both groups

			Mitomycin		Total	X^2	P
			Group (A)	Group (B)			
Side	Right	Count	12	9	21	0.902	0.34
		%	60.0%	45.0%	52.5%		
	Left	Count	8	11	19		
		%	40.0%	55.0%	47.5%		
Diagn-osis	Chronic dacryocystitis	Count	20	20	39	1.02	0.31
		%	100.0%	100%	100%		
	Trauma	Count	0	0			
		%	0.0%	0.0%	0.0%		
	Total	Count	20	20	40		
		%	100.0%	100.0%	100.0%		

P value as regarding side on which we operate is 0.34.
p value as regarding diagnosis of cases 0.31

Table 2 Additional surgeries done in both groups

			Mitomycin		Total	X^2	P
			Group (A)	Group (B)			
Additional	No	Count	10	9	19	0.14	0.98
		%	50.0%	45.0%	47.5%		
	Septoplasty	Count	2	2	4		
		%	10.0%	10.0%	10.0%		
	Turbinoplasty	Count	5	6	11		
		%	25.0%	30.0%	27.5%		
	Septoplasty + turbino-plasty +Fess	Count	3	3	6		
		%	15.0%	15.0%	15.0%		
	Total	Count	20	20	40		
		%	100.0%	100.0%	100.0%		

P value as regarding additional surgeries done with the main surgery is 0.98.

Table 3 Complication among groups

			Mitomycin		Total	X^2	P
			Group (A)	Group (B)			
Complication	No	Count	13	12	25	3.72	P1 0.81
		%	65.0%	60.0%	62.5%		
	Synaechia	Count	1	1	2		
		%	5.0%	5.0%	5.0%		
	Granulation	Count	1	2	3		
		%	5.0%	10.0%	7.5%		
	Skin abrasion	Count	2	2	4		
		%	10.0%	10.0%	10.0%		
	Stent loss	Count	2	1	3		
		%	10.0%	5.0%	7.5%		
	Orbital complication	Count	1	0	1		
		%	5.0%	0.0%	2.5%		
	Cheek swelling	Count	0	1	1		
		%	0.0%	5.0%	2.5%		
	Bleeding	Count	0	1	1		
		%	0.0%	5.0%	2.5%		
Complication	Not	Count	13	12	25	0.107	P2 0.74
		%	65.0%	60.0%	62.5%		
	Complicated	Count	7	8	15		
		%	35.0%	40.0%	37.5%		
Total		Count	20	20	40		
		%	100.0%	100.0%	100.0%		

P1 value as regarding complications among cases is 0.81.
P2 value as regarding complicated and non complicated cases is 0.74.

Table 4 Follow up after one month among both groups

			Mitomycin		Total	X^2	P
			Group (A)	Group (B)			
Subjectively	Nosymptomes	Count	19	19	38	-------	-------
		%	95.0%	95.0%	95.0%		
	Symptoms (epiphora)	Count	1	1	2		
		%	5.0%	5.0%	5.0%		
Flourecein test (objective test)	+VE	Count	19	19	38	-------	-------
		%	95.0%	95.0%	95.0%		
	-VE	Count	1	1	2		
		%	5.0%	5.0%	5.0%		
Regurge test (objective test)	+VE	Count	1	1	2	-------	-------
		%	5.0%	5.0%	5.0%		
	-VE	Count	19	19	38		
		%	95.0%	95.0%	95.0%		
Total		Count	20	20	40		
		%	100.0%	100.0%	100.0%		

Table 5 Follow up after one year among both groups

			Mitomycin		Total	X^2	P
			Group (A)	Group (B)			
Subjectively	No symptomes	Count	18	17	35	0.22	0.63
		%	90.0%	85.0%	87.5%		
	Symptoms (epiphora)	Count	2	3	5		
		%	10.0%	15.0%	12.5%		
Flourecein test (objective test)	+VE	Count	18	17	35	0.22	0.63
		%	90.0%	85.0%	87.5%		
	-VE	Count	2	3	5		
		%	10.0%	15.0%	12.5%		
Regurge test (objective test)	+VE	Count	2	3	5	0.22	0.63
		%	10.0%	15.0%	12.5%		
	-VE	Count	18	17	35		
		%	90.0%	85.0%	87.5%		
Total		Count	20	20	40		
		%	100.0%	100.0%	100.0%		

P value as regarding post-operative follow up after one year is 0.63.

Fig 1 Skin abrasion, one of complication during drilling of left lacrimal bone in a 2 years old male

Fig 2 Flourescein patches (Jones 1 test) in a 8 years old male (primary case)

Fig 3 Jones 11(irrigation) test using blunt lacrimal cannula in the right eye of the previous patient

Fig 4 56 years old female patient one of primary cases with EX-DCR on the left eye and EN-DCR on the right eye (noting silicone tubes and minimal skin abrasion at the vestibule)

Discussion

Dacryocystorhinostomy which had been performed in the past hundred years is a surgical procedure by which lacrimal flow is diverted into the nasal cavity through an artificial opening made at the level of the lacrimal sac. The operation can be carried out using either an external or endoscopic endonasal approach. [12]

Tsirbas et al. [12] stated that the endoscopic approach has several advantages over the external approach:

- It is less traumatic and there is no facial scar and no dammage to angular vein or medial canthal tendon or orbicularis oculi muscle and thus preserving lacrimal pump function and avoiding double site dissection of the lacrimal sac.
- Additional surgeries can be done during the procedure as septoplasty and FESS.
- Relative disadvantages are:
- Deep learning curve and massive surgical equibments needed.
- Relatively narrow field with relative risk of injury to nearby structures like the eye.

In the present study we evaluate the topical effect of antimetabolite agent namely Mitomycin C (MMC) as an adjuvant therapy in cases of endoscopic endonasal DCR. Complete relief from epiphora twelve months after surgery as well as nasolacrimal patency confirmed by lacrimal irrigation were the index for a satisfactory procedure. We use the relief of symptoms as the measurement for success of surgery. This meet the guidelines of the Royal college of Ophthalmologists published in 1999. All of the patients had preoperative diagnosis of the level of obstruction which was done by the Ophthalmologist.

In our study, we operate on forty cases suffering from epiphora they were divided randomely into two groups, group (A) and group (B) , twenty patients for each group . In both groups we did endoscopic endonasal DCR with topical use of Mitomycin C in group (A) and without Mitomycin C in group (B). Patients of two groups have insignificant age difference with a mean age (35.6 year plus or minus 22.67). The mean operative time in group (B) is about 42 minutes , and increased 5 minutes in group (A) and this matches with (Hehar et al., 1997) who stated that excellent haemostasis and easy access to the rhinostomy site were the main causes for this short operative time.

Male patients are more than female patients (62.5% for males and 37.5% for females). Right sided nasolacrimal blockage occurs in 52.5% of patients while left sided occurs in 47.5% of the patients. All patients were diagnosed as chronic dacryocystitis in 40 cases (100%).

No additional procedure was needed in 19 cases (47.5%) , 9 cases in group (A) and 10 cases in group (B). In 21 cases (52.5%) we did additional procedure. Septoplasty were done in 4 cases (10%), 2 in group (A) and 2 in group (B) , bilateral inferior turbinoplasty were done in 11 cases (27.5%), 5 in group (A) and 6 in group (B).

Combination of septoplasty, inferior turbinoplasty ,and functional endoscopic sinus surgery were done in 6 cases (15%), 3 in group (A) and 3 in group (B).

Wormald [13] in forty seven endoscopic DCR procedures, using powered instrumentation, had performed septoplasty in 29% of patients.

Complications were absent in twenty five cases (62.5%) and

present in fifteen cases (37.5%). Minimal skin abrasion of the upper lip from bur occur in four cases (10%) two of them in group (A) and two in group (B). Stent loss occurs in three cases (7.5%) two of them in group (A) and one in group (B) , in late cases we added a silk ligature over the sillicon stent to prevent stent loss.Granulation tissue at the ostium site occures in three cases (7.5%) one in group (A) and two in group (B). Synaechia occurs in two cases ,one in each group. Orbital complication (orbital fat exposure) occurs in one case of group (A).Cheek swelling occurs in one case of group (B).

Bleeding (epistaxis) occur in one case of group (B). Skin abrasion significantly happened in primary cases as there is excessive use of electric bur to create a wide bony ostium at the level of the lacrimal sac, during bony work trauma can be happened from the shaft of the bur so care should be taken during the use of electric bur in order to protect the upper lip or the entrance of the vestibule specialy the collumella and the most anteroinferior part of the nasal septum.

Wormald [13] reported exposure of orbital fat in one patient. By analysis of the results of this study as regarding the success rate we find the following:

- Total success rate in both groups is (87.5%) as all cases were diagnosed as chronic dacryocystitis (post-saccal obstruction) and they were all primay cases, the reported success rate of EN-DCR using silicon tubes vary from (82%-95%) according to Weidenbecher et al., (1994) Sprekelson and unlu (1996) Eloy et al., (1995) unlu et al.,(2000) and thus similar to our study.

- The effect of Mitomycin C on primary cases it seems it has no effect , as the success rate in group (A) is (90%) and (85%) in group (B), with only one case difference in both groups and these results matching with Zilelioglu et al.(9) who found that the success rate of endoscopic DCR with intraoperative use of topical Mitomycin C is (77.3%) where as without the use of Mitomycin C was 77.8%. Hence there was no difference between two groups regarding ostium size or success rate. Farahani and Ramezani [14] conducted prospected double blind randomized clinical trial and showed that patient with nasolacrimal duct obstruction who underwent endoscopic DCR did not benefit adjunctive topical application of Mitomycin C. Although, clinically there were lesser complications as regarding granulation tissue formation with Mitomycin C group as compared to control group but statistically they were not significant as they were two cases in group (B) and only one case in group (A).Our study not Matching with the result of Apuhan et al. [15] and Selig et al., [16] both found favourable effect of topical use Mitomycin C in primary cases.As Mitomycin C has no role in primary cases of endoscopic DCR and also is relatively expensive and should be used within 2 weeks after preparation due to its instability after this period,so its use in EN-DCR not advised.

We can say that factors that determine or by another word factors that enhance the success rate of EN-DCR should include all of the following:
Wide bony ostium, complete marsipulization of the medial wall of the lacrimal sac leaving the fundus and intensive post-operative care.

Conclusion

Endoscopic endonasal dacryocystorhinostomy with probing and bicanalicular silicon stent intubation is an effective treatment modality in the management of epiphora due to post-saccal obstruction, but using topical Mitomycin C has no benefit in such cases. Future studies are needed to clarify the role of EN-DCR in certain cases of pre-saccal obstruction and the role of topical MMC in revision cases.

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