COMPARATIVE STUDY OF INTRA OPERATIVE LOCAL APPLICATION OF MITOMYCIN-C IN DACRYOCYSTORHINOSTOMY & ITS EFFECT ON OSTIUM SIZE.

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ABSTRACT: AIMS AND OBJECTIVE : To assess the ostium size after endoscopic endonasal DCR with and without local application of mitomycin-C. **SETTING AND DESIGN:** NKP Salve Institute of Medical Sciences and Research Centre and Lata Mangeshkar Hospital, Nagpur-19. This was a prospective randomized study. **MATERIAL AND METHODS :** 46 patients of epiphora with nasolacrimal duct obstruction, were enrolled in our study. These patients were assigned randomly into 2 groups of 23 patients each. Group A (with Mitomycin-C) group B(without Mitomycin-C) using a random allocation software. Consecutive endoscopic dacryocystorhinostomy was performed with and without local application of mitomycin-C from June 2011 to June 2013. In group A Mitomycin-C was applied with a cotton ball soaked in 0.5 mg/ml concentration to the prepared rhinostomy site. The post operative follow up was done at 1 week, 2 months, 6 months and 1 year to assess lacrimal patency using syringing. The ostium size was assessed at 6 months and 1 year of follow up. **STATISTICAL ANALYSIS :** The result of endoscopic DCR with and without application of Mitomycin-C were then recorded and analysed using paired t-test and Mann Whitney U test. **RESULTS :** The postoperative follow up period was 1 year. The mean area of Ostium at 1 year in group A was 3.8 mm² (SD 1.5) and in group B was 1.3mm² (SD 0.4) which was statistically significant (P value <0.001). The mean decreased in ostium size at the end of 1 year in group A was 3.1 (SD 2.3) and in group B was 1.4 (SD 1.4) which is also statistically significant (p value <0.004) **CONCLUSION :** Intraoperative use of 0.5mg/ml mitomycin-C does not affect the success rates of endonasal endoscopic dacryocystorhinostomy at 1 year follow up. However it was found to maintain a larger ostium at the postoperative observational period.

INTRODUCTION: Evolution of dacryocystorhinostomy which is a surgical therapy for lacrimal obstruction dates back to 1893, where Caldwell described an intranasal DCR performed via trephination of nasolacrimal duct. Although these early approaches were abandoned until the introduction of rigid nasal endoscopes and with improvement in optics and excellent exposure of sac intranasally an endonasal approach was attempted by West in 1910. Ever since this technique has been developed till date, where it stands at par or better in many aspects with the external approach used traditionally by the ophthalmologists¹. Over a past few decades with the advancement in endoscopic equipments, the endoscopic transnasal approach has become popular^{2,3}.

The lacrimal apparatus starts from the lacrimal gland and ends at the nasolacrimal duct. The lacrimal system consists of upper and lower canaliculi, a common canaliculus, lacrimal sac and nasolacrimal duct. In females the nasolacrimal duct is narrow as compared to men and hence more

prone for chronic dacryocystitis. Lacrimal pathway obstruction can be idiopathic or secondary to chronic infections, tumours, trauma or iatrogenic and may occur anywhere along the tract with nasolacrimal duct being the most frequent area to get obstructed. There can be pre-saccal (i.e. canalicular), saccal and post-saccal (nasolacrimal duct) obstruction. Dacryocystorhinostomy is indicated for saccal and post saccal stenosis.

The advantage of an endoscopic approach over external dacryocystorhinostomy is the lack of scar, shorter operating time, done as an outdoor procedure under local anesthesia and less chances of interfering with the physiological lacrimal pump mechanism. There is less bleeding and revision surgery if required is easier. The ability to identify the abnormal intranasal anatomy and to correct it at the same sitting appears to be one of the primary advantages of the procedure³. The main problem of endonasal DCR is regarding long term patency and osteotomy closure by granulation tissue.

Mitomycin- C is derived from streptomyces caespitosus, an alkylating agent with anticancer property. It reduces fibroblast collagen synthesis by inhibiting DNA- dependent RNA synthesis and can suppress cellular proliferation in any period of the cell cycle. The beneficial effect of mitomycin- C as a surgical adjuvant is thought more recently to be related to its potent inhibition of fibroblast proliferation^{4,5} and hence possibly improve the success rates over traditional procedures. Mitomycin – C when used in appropriate doses minimizes postoperative fibrosis, synechiae and granulations thereby maintaining a bigger ostium size in post operative period.

MATERIAL AND METHOD: This study was conducted at NKPSIMS and RC and LMH, Nagpur from June 2011 to June 2013. This was a prospective randomized study which was approved by institutional ethical committee. 46 patients were enrolled in our study, and the inclusion criteria were, primary acquired nasolacrimal duct obstruction in adults above 20 years of age. Patients with failed external DCR, fistula, mucocele or pyocele were also included in our study. These patients were assigned randomly into 2 groups of 23 patients each using random allocation software. Group A patients underwent endoscopic DCR followed by application of Mitomycin- C, Group B patients underwent endoscopic DCR without application of Mitomycin –C. All patients with pre-saccal block, noticeable lid laxity and post traumatic lid and bony deformity were excluded from our study. All patients underwent clinical evaluation both by ophthalmologist and otolaryngologist. Each patient underwent diagnostic nasal endoscopy and syringing to confirm the diagnosis and assess concomitant sinonasal pathology or anatomical changes that could be managed at the same sitting.

Informed consent was obtained before surgery from all the patients. Patients were operated under local anaesthesia with sedation by one surgeon. After appropriate premedication, nasal packing was done with 4% xylocaine with adrenaline for local decongestion of nasal mucosa. Local infiltration with xylocaine 2% with 1:2,00,000 adrenaline was given over lateral nasal wall anterior, above and below the anterior attachment of middle turbinate. Both 0° and 30° rigid nasal endoscopes were used during surgeries which were connected to high resolution video system. After incision of the mucosa, anterior and inferior to the attachment of middle turbinate over the lateral nasal wall, mucoperiosteal flap was raised using Freer's elevator and removed using Blackesley forceps. Frontal process was removed using Kerrison's punch and sometimes micromotor drill was used in difficult cases.

The lacrimal sac was identified and incised vertically using a sickle knife. Ball probe was used to break adhesions between medial and lateral wall. The medial wall of the sac was removed with the help of thrucut forceps. Syringing was done using normal saline to confirm the patency. In group A patients a cotton ball soaked in 0.5 mg/ml solution of Mitomycin-C was applied to the rhinotomy site for 5 min. After removal of cotton ball the area was irrigated thoroughly with saline solution. A change in the colour of nasal mucosa from red to white gray was visible immediately after application. Patients were followed up for a period of 1 year postoperatively.

Lacrimal sac irrigation was performed by surgeon to assess lacrimal patency at 1 week, 2 months , 6 months and 1 year (Fig 1). Diagnostic nasal endoscopy was performed to measure the rhiniostoma size using a curved tipped suction canula at 6 months and 1 year followup. The results of endoscopic DCR with and without mitomycin-c were then recorded and analysed using paired t-test and Mann Whitney U test.

RESULTS: There were 46 patients recruited into the study. There were 29 females and 17 males with a male to female ratio of 1:1.7. The mean age was 39.84 yr. The majority of the patients were from poor socioeconomic background. In our study 22 patients had right eye affection and 18 patients had left eye affection while 4 cases had bilateral disease. The commonest presenting symptom was tearing from the eye which was seen in all the patients of both groups. Other symptoms noted were purulent discharge in 32% patients of group A and 26% of group B, mucocele in 4.34% patient of group A and 4.34 % of group B. The duration of symptoms varied for 3 months to 18 months with majority of patients in both groups presenting within 10 months of onset of symptoms. On syringing the nasolacrimal duct was found to be blocked in all 46 patients. The middle turbinate head was resected where it was found enlarged. The middle turbinate head resection was done in five patients in group A and 4 patients in group B. Intra operatively septal correction was done in 4 patients of group A and 6 patients of group B. No complications, such as delayed wound healing, abnormal nasal bleeding, necrosis or infection were noted in any patient in both the groups.

After 1 year of follow-up, 22 patients of group A were having complete relief of symptoms of epiphora while, 21 patients of group B had complete relief. 1 patient of group A and 2 patients of group B had no relief. Result of syringing was assessed periodically and at 1 year of follow-up. 22 patients of group A and 20 patients of group B had patent lacrimal passage on syringing. 1 patient in group A and 3 patients in group B had regurgitation on syringing because of partial or complete obstruction in the lacrimal passage. Ostium size was assessed endoscopically at 6 months and 1 year of follow-up. The mean area of the ostium at 6 month in group A was 7 mm² (SD 2.2) and at 1 year was 3.8 mm² (SD 1.5) which is statistically significant (P value < 0.001). The mean area of ostium in group B was 2.7 mm² (SD 1.17) and at 1 year it was 1.3 mm (SD 0.4) which was also statistically significant (P value < 0.001). The mean decrease in size of ostium at 1 year in group A was 3.1mm (SD 2.3) and in group B was 1.4 mm (SD 1.4). On applying Mann Whitney U test, it was found to be statistically significant (p value < 0.004).

Ostium size mm ² (SD)	Time of assessment of ostium size		P value
	6 months	1 year	
Group A (n=23)	7 (2.2)	3.8(1.5)	<0.001
Group B (n=23)	2.7 (1.17)	1.3(0.4)	<0.001

Table – 1: The ostium size at 6 months & 1 year of follow up.

S.D. standard deviation

Group	Mean (SD)	P value
Group A	3.1 (2.3)	} 0.004
Group B	1.4 (1.4)	

Table – 2: The mean decrease in ostium size at the end of 1 year.

DISCUSSION: Endoscopic DCR is widely accepted technique for correction of nasolacrimal duct obstruction. The decrease in the size of the healed intranasal ostium after surgery is the result of a normal wound healing response. Mitomycin-C has been used to modulate fibrosis after glaucoma and pterygium surgeries. Several studies have recently investigated adjunctive Mitomycin-C for dacryocystorhinostomy to augment success rate.

R. Mudhol et al⁶ reported the surface area of the osteotomy site at the end of 6 month and 1 year in mitomycin-C group was 31.6mm² and 30.9 mm² respectively while in control group it was 25.7 mm² and 25 mm² respectively. Suppamong Tirakunerichcha et al⁷ reported the surface area of the osteotomy site at the end of 6 month and 1 year in Mitomycin – C group as 10.8 mm (3.17) and 3 mm (1.78) respectively while in control group it was 7.1mm (2.62) and 1.6 mm (1.18). Kao et al⁸ Liao et al⁹ Roozitalb et al⁴ and You and Fang¹⁰ evaluated the role of intraoperative mitomycin-C in external DCR. Liao et al¹⁰ and You and Fang¹⁰ concluded that intraoperative Mitomycin-C application was effective in increasing the success rate of external DCR surgery, whereas Roozitalb et al⁴ concluded that mitomycin-C does not change the success rate of this procedure. Ugurbas et al¹¹ performed endoscopic intranasal DCR and sent the tissue around the ostium for histopathological examination which revealed attenuated epithelium with intracytoplasmic vacuoles formation in specimens of mitomycin-C while there was normal epithelium with no vacuoles in the specimens of control group. They suggested that by causing decrease in density and cellularity of mucosa, topical use of mitomycin may enhance the success rate of surgery. Camara et al¹² conducted a study to evaluate the role of intra operative Mitomycin-C in endonasal endoscopic laser assisted DCR. The success rate of the Mitomycin-C group was 99.2% compared with 89.6% in the control group which is comparable to our study. Zilelioglu et al⁵ did not find any change in the success rate after using intra operative mitomycin-C in endoscopic DCR, which is not in accordance with our study.

The success rate depends upon the size of rhinostome. A large rhinostoma was created by removing the frontal process of maxilla and lacrimal bone approximately 1x1cm dimensions were made in all patients. All the patients had been followed up for 1 year. The average onset of ostium closure with granulation tissue formation after endoscopic endonasal DCR is reported to be 7.5 to 12.7 weeks by Ugurbas et al¹¹. According to Boush et al majority of surgical failures occur within four months postoperative

CONCLUSION: Mitomycin –C in appropriate dose minimizes postoperative fibrosis and granulations thereby maintaining a bigger post operative ostium throughout the post operative observation period.

REFERENCES:

1. Jarbet KJ, Custer PL. External dacryocystorhinostomy. Surgical success, patient satisfaction and economic cost. *Ophthalmology*. 1995;102:1065-1070.
2. Vigit O, Samancioglu M, Taskin U, et al. External and endoscopic dacryocystorhinostomy in chronic dacryocystitis comparison of results. *Eur Arch Otorhinolaryngol*. 2007; 264:879-885.
3. Feretis M, Neuton JR, Ram B, et al. Comparison of external and endonasal dacryocystorhinostomy *J Laryngol Otol*. 2009; 123:315-319.
4. Roozitalab MH, Amerahmadi M, Namazi MR. Results of the application of intraoperative Mitomycin-C in dacryocystorhinostomy *Eur Ophthalmology* 2004; 14(6): 461-3.
5. Zilelioglu G, Ugurbas SH, Anadolu Y, Akiner M, Akturk T, Adjunctive use of mitomycin-C on endoscopic lacrimal surgery. *Br J Ophthalmol*. 1998; 82:63-66.
6. Rekha R. Mudhol, N.D. Zingade, RS Mudhol and Amal Das Endoscopic Ostium Assessment following Endonasal Dacryocystorhinostomy with Mitomycin-C. *Application At Ameen J. Med. Sci.* 2012; 593):320-324.
7. Tirakunerichcha et al. Efficacy of Mitomycin-C in Endonasal Endoscopic Dacryocystorhinostomy. *Laryngoscope* 2011; 121: 433-436.
8. Kao SC, Liao CL, Tseng JH, et al. Dacryocystorhinostomy with intraoperative mitomycin-c *Ophthalmology* 1997; 104:86-91.
9. Liao-SL, Kao SCS, Tseng, Chen MS, Hou PK. Results of intraoperative mitomycin-c application in dacryocystorhinostomy *Br Ophthalmol*. 2000; 84(8):903-06.
10. You YA, Fang CT. Intraoperative Mitomycin C in dacryocystorhinostomy with intraoperative mitomycin-C. *Ophthalmology* 1997; 104:86-91.
11. Ugurbas SH, Zilelioglu G, Sargon MF, Anadob Y, Akiner M, Akturk T, Histopathologic effects of mitomycin-c on endoscopic transanal dacryocystorhinostomy. *Ophthalmic surgery and laser* 1977;28(4):300-04.
12. Camara JG, Bengzon AU, Henson RD. The safety and efficacy of Mitomycin C in endonasal endoscopic laser- assisted dacryocystorhinostomy. *Ophthal Plast Reconstr Surg*. 2000; 16:114-118.

Fig_1__Showing_ostium_at_1_year_of_follow-up.

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