Original Article

Outcomes of Conventional External Dacryocystorhinostomy with and without Mitomycin C: Experience from Eastern Nepal

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Abstract

Introduction: Dacryocystorhinostomy (DCR) is the commonest surgery for nasolacrimal duct obstruction. Inhibition of the scarring process within the anastomosis and rhinostomy site which has been attributed to the failure of this procedure, might improve the success rate of DCR. The objective of this study was to evaluate the outcomes of DCR with Mitomycin-C (MMC) and to compare the results of DCR with and without MMC.

Materials and methods: A hospital based, prospective study was conducted in patients with primary acquired nasolacrimal duct obstruction. Standard conventional DCR was performed upto the level of creation of flaps. Application of MMC 0.2 mg/ml in and around the ostium and underneath the created flaps for two minutes was effected with cotton pledgets. The area was thoroughly washed with normal saline after removal of the pledgets. Rest of the surgery was completed as usual. The patients were followed up on the first postoperative day, one month and three months post surgery.

Results: A total of 60 cases, 30 in each group were allocated. The success rate of DCR with MMC was found to be 96.7% compared to 86.7% (p=0.35) in the DCR group at the end of three months duration.

Conclusions: Intraoperative application of MMC during conventional DCR surgery provides a comparatively higher success rate than DCR without MMC without posing any extra financial burden and adverse drug reaction to the patient.

Key words: Dacryocystorhinostomy, Mitomycin C, Outcomes.

Introduction

Dacryocystorhinostomy (DCR) is among the most commonly performed oculoplastic surgery for the management of epiphora due to nasolacrimal duct obstruction (Tarbet et al, 1995). DCR is a bypass procedure where an anastomosis is created between the lacrimal sac and the nasal mucosa via a bony ostium which is attained by either an external approach or internally by an endoscopic approach. A success rate of approximately 90% is reported in literature (Tarbet et al, 1995; Walland et al,1994). Despite the defined approach of endoscopic DCR, conventional external DCR is still preferred in many parts of the world not only due to cost factor but also to create a large

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bony ostium and a mucosal lined anastomosis (Ali et al, 2012).

There are many factors that has been attributed to the failure of the procedure, but scarring within the anastomosis (Shun-Shin et al, 1997) and soft tissue scarring leading to membranous failure at the rhinostomy site (Yeatts RP et al, 1999), is considered as the most common cause of primary DCR failure. Hence, by inhibiting the process of scarring and fibrous growth over the anastomosed flaps and osteotomy site, the success rate of the conventional DCR surgery could be increased (Yildirim et al, 2007).

Mitomycin C (MMC) is an alkylating chemotherapeutic agent derived from *Streptomyces caespitosus*. It inhibits the DNA dependent RNA synthesis and reduces collagen production by fibroblast (Yildirim et al, 2007). Application of MMC was found effective against excessive scar formation by the prevention of subconjunctival fibrosis (Bergstrom et al, 1991). This use of antifibrotic agents has been accepted in ocular surgeries namely pterygium excision and glaucoma surgery with favourable outcomes (Singh et al, 1988, Megevand et al, 1995).

To the best of our knowledge, there is a lack of similar type of study performed in Nepal to compare the success rate of conventional DCR with and without MMC. We believe that a comparative study will help to establish the role of MMC in enhancing the surgical success rate of conventional DCR. Hence, this study was undertaken to evaluate the role of MMC in maintaining the post-operative patency of anastomosis and ostium and to note down any complications after the use of intraoperative MMC.

Materials and methods

This prospective and interventional study was conducted at Mechi Eye Hospital (MEH), located in eastern Nepal which also serves as a major referral center in this region from July 2017 to December 2017 for a period of six months duration. The cases with presumed primarily acquired naso-lacrimal duct obstruction undergoing DCR surgery were included, whereas pediatric cases, failed DCR, silastic tube intubation and patient unwillingness to participate were excluded.

Approval for the study was taken from the institutional research and ethics committee of MEH. Informed and written consent was obtained from all the participants. The study was conducted in accordance with the tenets of the declaration of Helsinki. Eligible patients were enquired about the presenting complaints, duration of symptoms and the ocular findings recorded. All the patients underwent general physical examination for fitness for surgery and mandatory otorhinolaryngologist consultation. Further necessary blood investigations were performed and normality of the test was assured prior to surgery. The convenience sampling technique was applied, where all the DCR surgeries performed by a single surgeon during the stipulated time of six months were enrolled. The patients were categorized into two groups DCR with MMC and DCR without MMC. The 30 cases who had undergone DCR with MMC were included in one group, and the other 30 cases which had undergone surgery without MMC were included in the conventional DCR group for analyses. The findings of syringing and probing done on an out-patient basis was confirmed on table by the operating surgeon.

The standard techniques of an external DCR surgery (Ali et al, 2012) were performed in all patients. The surgical procedures were similar in both groups except for the application of intraoperative MMC. In the DCR-MMC group, after creation of the standard 'U' shaped nasal mucosal flap and lacrimal sac flap, a small ball of cotton pledget soaked in 0.2 mg/ml MMC was applied in and around the ostium and underneath the created flap for two minutes. After application, the pledget was

removed and the area irrigated thoroughly with approximately 20 ml of normal saline, and rest of the surgical steps were carried out in the normal fashion. The nasal pack was removed and a freshly prepared nasal pack soaked in 1:100000 adrenaline, two percent xylocaine and oxymetazoline was repacked subsequently. Postoperatively oral antibiotics and topical steroid antibiotic combination drops were prescribed for seven days. Nasal decongestant drop was advised in the operated side of nostril for two weeks. Topical steroid-antibiotic drops were prescribed for a duration of one month in a tapering fashion. The patients were followed up on the first postoperative day and at the end of the first and third month postoperative period.

All the procedures were performed by a single surgeon (S.Khadka). The results of surgery were evaluated by interrogating the absence or improvement of symptoms as a subjective parameter and confirming the patency of irrigation as an objective parameter. The surgical procedure was considered as successful if the patients had no symptoms or improvement in tearing and patent lacrimal drainage system confirmed by irrigation at the end of three months post-operative period. Whereas redundancy of symptoms, persistent epiphora and non-patent irrigation was considered as surgical failure. The complications by the use of MMC whenever encountered at the end of the three month period were also documented.

The collected data was analyzed in a statistical package for the social sciences software (SPSS v20, IBM, Armonk, NY, USA). Continuous variables were reported as mean ± SD. Independent sample t test was used to compare means between the groups, Mann–Whitney U test for continuous variables and Fisher's exact test was applied to detect differences in categorical variables. P value <0.05 was considered statistically significant.

Results

Sixty patients were enrolled in this study and allocated in two groups namely DCR with MMC group and conventional DCR, each group comprising 30 cases respectively.

The number of female patients were comparatively more than males in both groups. The mean ± standard deviation (SD) age of the DCR MMC group was 38.9 ± 9.2 (25-59) years and that of the conventional DCR group was 36.6 ± 10.7 (20-60) years. However, there was no significant difference in gender (p=0.36) and age (p=0.77) between the two groups. The patients presented with the duration of symptoms ranging from four months to 12 years with the median duration of 12 (3 – 132) months in DCR MMC group and 24 (6 – 144) months in DCR group. The median duration of symptoms was significantly higher for conventional DCR group compared to the other (24 months vs. 12 months, p=0.03). Table 1 represents the patient characteristics.

The mean ± SD duration of surgery in the DCR MMC group was 34.5 ± 5.5 minutes, whereas, the surgical time was 32.5 ± 5 minutes in the DCR group. No statistically significant difference was found in surgical duration in between the groups (Table 2). The intra operative bleeding from the mucosal anastomotic site was the commonest complication encountered in 1/30 (3.33%) cases in DCR MMC group and in 3/30 (10%) cases in DCR group.

The post-operative events from the first postoperative day, end of one month and at the end of three months period are depicted in table 3.

Twenty eight eyes of 30 cases (93.4%) were symptom free in the DCR MMC group following the surgery and 1/30 (3.3%) case reported improvement in symptom after one month follow-up. Only one eye (3.3%) in the DCR MMC group had excess watering at the end of final follow-up visit. Similarly,

in the DCR group 22/30 (73.4%) cases were symptom free, 4/30 (13.3%) cases improved and the remaining 4/30 (13.3%) had persistent complaints of tearing. Comparing the status of tearing in both groups, it was found that the subjective complaints of tearing condition improved in the MMC group compared to conventional DCR group but it was not statistically significant (p=0.13). The patency rate which corresponds to the surgical success rate was higher (96.7%) in the DCR MMC group compared to (86.7%) in the DCR group. However, on comparison of the patency by irrigation following surgery, the patency rates did not differ significantly between two groups (p=0.35) (Table 4).

During the follow up visits, no complications such as delayed wound healing, abnormal nasal bleeding, mucosal necrosis, infection or atrophic rhinitis were encountered in any of the patients. No nasal or gastrointestinal irritation had been observed during or after the intra-operative MMC application. Repeat DCR was considered in case of surgical failure after one month from the duration of persistent symptoms despite conservative management.

Table 1: Patient Characteristics

Variables	DCR with MMC group (n=30)	DCR group (n=30)	p-value
Age (years)	38.9 ± 9.2	36.6 ± 10.7	0.36#
Gender Male (%) Female (%)	 9 (30%) 21 (70%)	 8 (26.7%) 22 (73.3%)	0.77#
Duration of symptoms (months)	12 (3 – 132)	24 (6 – 144)	0.03**

Independent sample t test, ** Mann–Whitney U test

Table 2: Duration of surgery in between the groups

Surgery	Duration in range (minutes)	Mean duration (minutes)	p-value
DCR with MMC	25 - 45	34.5 ± 5.5	0.14#
DCR	25 - 40	32.5 ± 5.0	

Independent sample t test

Table 3: Post-operative events

1st Post-operative day			
Surgery	Subjective Symptom	Improvement	Syringing
DCR with MMC	None (28), Headache(2)	30	Patent
DCR	None	30	Patent
One month follow up			
Surgery	Subjective Symptom	Improvement	Syringing
DCR with MMC	None	30	Patent
DCR	None	30	Patent
3rd month follow up			
Surgery	Subjective Symptom	Syringing	
DCR with MMC	Watering (1), None (29)	Patent (29), Not patent(1)	
DCR	Watering (4)	Patent(26) Not Patent (4)	

Table 4: Comparison of tearing condition and patency following surgery at the end of three months period

Tearing Condition	DCR with MMC group (n=30 cases)	DCR group (n=30 cases)	p-value
Symptom free	28 (93.4 %)	22 (73.4 %)	0.13*
Improved	1 (3.3%)	4 (13.3%)	
No Improvement	1 (3.3%)	4 (13.3%)	
Syringing	DCR with MMC group (n=30 cases)	DCR group (n=30 cases)	p value
Patent	29 (96.7%)	26 (86.7%)	0.35*
Not-patent	1 (3.3%)	4 (13.3%)	

**Fisher's exact test*

Discussion

DCR has been accepted as a highly successful surgical procedure for treatment of epiphora from nasolacrimal duct obstruction (Kao et al, 1997). The documented success rate of DCR surgery is around 90% and is also validated by various literatures (Tarbet et al, 1995; Ali et al, 2012). Failure of the surgery is defined as the persistent symptoms of excessive tearing with the inability to irrigate during syringing (Kao et al, 1997). The cause of failed DCR determined during revision surgery revealed an obstruction of the lacrimal drainage channel by an occluding membrane. The histopathological examination of the membrane was composed of organized granulation tissue (Picó et al, 1971). Thus, the use of adjunctive MMC is advocated to reduce fibrous proliferation in or around the osteotomy site and at the anastomosed flaps to increase the success rate (Kao et al, 1997).

Acquired nasolacrimal duct obstruction commonly affects people during fifth to seventh decades of life and is three times more likely to affect females than males (Shigeta et al, 2007). Similarly, the female preponderance was present in this study. Nonetheless, the two groups did not differ by age and gender. The surgical duration was not significant between the groups, thus use of MMC did not escalate the operating time.

All the patients remained symptom free at the end of the first month, and four patients in the conventional DCR group and only one patient in the MMC group were declared as surgical failure at the end of three months. This accounted to the surgical success rate of 96.7% in the MMC group compared to 86.7% in the conventional DCR group. This encouraging result was supported by various other studies with similar type of success pattern (Yildirim et al, 2007 and Kao et al, 1997). The duration and concentration for the use of MMC in DCR has an incongruous distribution (Feng et al, 2012). To date, the appropriate dose of MMC in DCR surgery has not been standardized (Deka et al, 2006). The present study recommends a concentration of 0.2 mg/ml of MMC for the duration of two minutes to be applied in and around the ostium and underneath the created anastomotic flap. The rationale is to prevent fibroblastic cell proliferation by induction of arrest in cell cycle but without causing significant apoptosis (Ali et al,2013).

The improvement in subjective parameters with reduction in tearing condition as experienced by the subjects was better in the MMC group, however, the objective parameters of patency rates were not significantly different between the two groups. This accounts to the improvement of only the satisfaction rate

following intraoperative MMC application. Nonetheless, the lack of correlation of failure with regard to different surgical techniques in most of the studies including ours is desired. Moreover, for the successful outcome of DCR surgery following determinants play a pivotal role; atraumatic handling of soft tissue, uniform as well as adequately fashioned rhinostomy with smooth edges, careful exposure of the true lumen of lacrimal sac followed by careful mucosal flaps suturing and nonetheless, individual response to the process of tissue healing (Ali et al,2013).

Small sample size, single center study, surgeries not compared with other surgeons and short follow up time were the limitations of this study.

In conclusion, the present study advocates for the use of intra-operative MMC being effective in increasing the surgical success rate of DCR. MMC application in conventional DCR could be a safe adjuvant that might prevent the closure rate of the osteotomy site. The surgical success rates were also found to be higher compared to conventional DCR. No deleterious effect of MMC was noted with its use at the end of the three months period. Application of an anti-fibrotic agent may be considered as an effective modification of conventional DCR surgery without posing a huge financial problem and detrimental effect on the subjects rather than a new treatment modality in conventional DCR. A myriad of studies consisting of larger sample size and a longer follow up period is recommended before affirming a definitive statement.

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