

Comparison of recurrent rate in Nasolacrimal duct obstruction, with and Without Mitomycin C associated with probing

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Abstract: Nasolacrimal duct obstruction is the most common cause of tearing in children. Patients with Lacrimal duct obstruction have various symptoms such as tearing, infection, acute or chronic lacrimal sac, conjunctivitis, red eye or eczematous skin reactions to their lower eyelids. This study Compared recurrent rate of Nasolacrimal duct obstruction, with and without Mitomycin C associated with probing, a double blind randomized clinical trial. This study is a double blind randomized clinical trial. 150 patients diagnosed with cramps tearing the tear duct, patients allocated randomly to experimental and control groups. 3 patients from control group and 2 patients from trial group were drop from to follow up. 91 eyes from 72 patients in control group and 98 eyes from 73 patients from trial group were diagnosed with cramps tearing the tear duct. All patients, received general anesthesia, then Patients in control group treated with probing and patients in trial group treated by probing associated with 2 cc solution of Mitomycin 10 mg per cent Mitomycin C injected into the nasolacrimal duct after probing. Each patient followed for one month after treatment at intervals of ten days and one month. After 1 month follow up in 89 from 91 eyes (97/1%) in trial group and 88 from 98 eyes (89.79%) in control group, nasolacrimal duct was symptomatically satisfied and no complication was observed. This study showed that probing and irrigation with Mitomycin c was a method with significantly better success rate and could be an appropriate additive option for treated congenital nasolacrimal duct obstruction.

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1. Introduction

Tearing is one of common complaints of ophthalmology patients that can be very annoying for patient. Other than those factors that may increase secretion of tears, congenital nasolacrimal duct obstruction is the main cause of tearing in children. Congenital nasolacrimal duct obstruction commonly is the result of nasolacrimal duct distal end non-canalized and obstruction is rare in nasolacrimal duct. Patients with nasolacrimal duct obstruction refer to a doctor with multiple symptoms such as tearing, lacrimal sac acute or chronic infection, conjunctivitis, eye redness or skin reaction eczema of lower eyelids. Tearing occurs in nearly 20 percent of infants, and in more than 90 percent of cases, spontaneous recovery occurs during first 12 months. The incidence of congenital nasolacrimal duct obstruction is 4-7 percent. Treatment of congenital nasolacrimal duct obstruction is hydrostatic pressure on lacrimal sac and using topical antibiotics in early months. In case that obstruction was not healed with supportive treatments, catheterization is a standard method to treat and remove obstruction, and its success rate is high. Mitomycin C application has been started in ophthalmology since about 1993 and it applies in

different eye diseases as an adjunct therapy. Mitomycin C is a drug that prevents fibroblasts division and in human and animal studies, it cause to control proliferation of under conjunctiva fibroblasts. Therefore, so far in trabeculectomy operation, preventing recurrence of carcinoma of cornea, reducing recurrence of pterygium, DCR operation (Dacryocystorhinostomy), reducing posterior capsule opacity and vernal conjunctivitis treatment which is resistant against treatment have been used. In study of Kumar, 27 patients have been divided into two groups of subject and control, that mitomycin C (0.4 mg/ml) was used in 15 patients during catheterization and recovery rate of disease symptoms was reported 80% (12 eyes) after one year follow-up in this group and in it was reported 8.3% (1 eye) in control group. No side effects have been observed in using mitomycin.

Tsai study was conducted with the purpose of determination of effective rate and safety of using mitomycin C (0.2 mg/ml) during catheterization on adult patients with nasolacrimal duct obstruction; from 36 under study eyes, 32 eyes (89%) had open nasolacrimal duct and 4 eyes infected recurrent obstruction. This study showed that the use of

mitomycin C has good results in catheterization of nasolacrimal duct in long term. In study of Dolmetsch on children of 16 years or less, 94.4% success was shown in nasolacrimal duct obstruction treatment and safe use of mitomycin C. In a study of Shenasi and colleagues on 80 adult patients with nasolacrimal duct obstruction, a comparison was conducted between the use of mitomycin C during catheterization and using DCR method without use of mitomycin C on recovery rate of nasolacrimal duct obstruction symptoms, and in this study in two weeks follow-up after operation, 95.5% of catheterization group, and 97.5% of subjects of DCR group had recovery symptoms and in six months follow-up, 77.5% subjects of catheterization group and 92.5% subjects of DCR group had recovery symptoms. This research showed that the use of mitomycin during catheterization is beneficial for treatment of nasolacrimal duct obstruction, although its efficacy is reduced over time.

In a study by Angela And colleagues that was done to determine prognosis and safety of using mitomycin C during DCR operation on adult patients with nasolacrimal duct obstruction (congenital, acquired, traumatized), it was shown in eighteen-months follow-up that using mitomycin C (0.5 mg/ml) during DCR operation had 95% success in eliminating secretion and epinephrine immediately.

Study of Tabatabai and colleagues was done on adults with nasolacrimal duct obstruction, it aimed to evaluate the effect of catheterization on nasolacrimal duct in association with mitomycin C 0.2 mg/ml, 58 eyes of 56 patients were studied, after catheterization, nasolacrimal duct was washed with 1 cc mitomycin solution with a concentration of 0.2 mg/ml. After eight months follow-up, 30 eyes (51.7%) had an open nasolacrimal duct, 23 eyes (39.7%) had partial obstruction and 5 eyes (8.9%) had complete obstruction. From Clinical symptoms point of view, it was reported that 35 patients (60.3%) had complete loss of epiphora, 17 patients (29.3%) had reduction of epiphora and 6 patients (10.3%) had no recovery. No complications were reported in the use of mitomycin C. In a study by Razaghie and colleagues on 17 eyes with nasolacrimal duct obstruction that was done to evaluate the effect of using mitomycin C during catheterization on adults; in last patients visit, 4 eyes (23.6%) had no tearing, 2 eyes (11.7%) had little tearing, 3 eyes had moderate tearing and 8 eyes (47%) had severe tearing. In this study it was shown that catheterization with mitomycin C injection can be considered as an alternative for reducing the severity of tearing in patients who are not suitable candidates for surgery, or those who don't tend to perform DCR operation.

In Bazazie and colleagues study whose aim was to evaluate the effect and complications of mitomycin C during catheterization, 40 patients were studied that 6 patients had bilateral nasolacrimal duct obstruction and 34 patients had unilateral obstruction, after six months follow-up, nasolacrimal duct was wide open in 20 eyes (43.6%), and symptoms recovery were satisfied in 21 eyes (52.5%). In six-month follow-up of patients, no complications were reported in the use of mitomycin. The result of this study showed that this treatment could be a suitable method of partial nasolacrimal duct obstruction on adults. Some advantages of this method are simplicity, no need for general anesthesia, additional and expensive equipment and its low rate of morbidity.

In a study of Michanicie and colleagues that was done to compare the therapeutic effect of catheterization with and without use of mitomycin C in treatment of nasolacrimal duct obstruction, 120 eyes of 106 adults with nasolacrimal duct obstruction were studied. Patients were randomly divided in two groups of 60 eyes. First group was under catheterization operation and in second group in addition to above operation, their nasolacrimal ducts were washed with 1 cc of mitomycin C solution whose concentration was 0.2 mg/ml. One month after operation, treatment success was 55% in catheterization group and 96.6% in catheterization with mitomycin group and after one year follow-up, treatment success was reported 40% in catheterization group and 95% in catheterization with mitomycin C group. The result of this study showed that using mitomycin C during catheterization is an effective method for opening nasolacrimal duct obstruction. Despite the fact that several studies were done about effectiveness of using Mitomycin during catheterization on adults with acquired nasolacrimal duct obstruction and they had acceptable results, but no study has been done on children with congenital nasolacrimal duct obstruction treatment by catheterization in association with mitomycin C injection. This study aims to determine the effect of 0.1 mg/ml dose of mitomycin C injection with nasolacrimal duct catheterization to prevent nasolacrimal duct recurrent in children under eighteen months.

2. Material and Methods

In this study which was done during 2010-2011, children less than eighteen months who refer to Department of Ophthalmology in Yasuj city and had a complaint of tearing were entered into the plan with their parents' informed written consent. Entry requirements: complaint of tearing, less than 18 months old, and no secondary symptoms include: eye

dryness, entropion, ectropion, glaucoma, eyelids tumors and lacrimal system and no history of nasolacrimal duct surgery. Those patients, who did not regularly refer for follow ups, were excluded from plan. Sampling procedure: Available sample was based on target, and given the limitations and type of study and according to similar studies; sample size was considered 80 people for each group that finally 70 children from experimental group and 75 children from control group were participated in the plan until the end.

Treatment method: All patients were examined by a doctor and after general anesthesia they underwent catheterization operation with similar method. In children from experimental group, after catheterization, 2cc mitomycin solution of 0.1 mg per cent was injected into nasolacrimal duct and only catheterization was done in control group. Each patient had follow-up for two months after treatment and they were visited at intervals of ten days, one month and two months after catheterization, and the results were recorded.

Catheterization procedure: At first, patients were anesthetized generally by anesthesiologist in operating room. After washing around eyes with Betadine and preparation, because upper punctum is dilated under general anesthesia, using zero probe bowman, it was vertically inserted into upper punctum then probe is rotating in horizontal direction parallel to upper canaliculus, at the same time upper eyelid was pulled out to ensure that canaliculus is unruffled, simultaneously probe is driven inside too slowly until it is stopped and then it slowly pulled out and then it is vertically rotated until slip on inside nasolacrimal duct. Because obstructions often occur in lower level of nasolacrimal duct, probe needs to have a bend so that it could go directly into lower and back of duct, when it arrives to lacrimal sac.

After probing lacrimal duct and assurance of duct openness, using a 2 cc syringe with dull tip that has been passed from punctum and canaliculus, 2 cc mitomycin 0.1% which had already been prepared was injected into duct of patient slowly and over several seconds. During injection, the patient's nose and pharynx were suctioned to prevent leakage of mitomycin into throat. After one minute of injection time, nasolacrimal duct was washed with normal saline and finally the eye was dried and two drops of gentamicin were dripped into each eye. Patients were evaluated at intervals of ten days, one month and two months after catheterization and in each follow-up; child tearing and any eye secretion were asked from parents and eye was examined for cornea and conjunctiva complications. Data collection tool was a questionnaire in which a check list was recorded by therapist physician for situation and symptoms

including: age, sex, symptoms, involvement of left or right eyes or both of them, age at diagnosis time, catheterization history, drug history, age at the time of catheterization, date of catheterization, interval follow-up of ten days, one month and two months after catheterization. Collected data was analyzed by SPSS-17 software and Fisher's exact test. Central and dispersion indices and frequency distribution tables were used to report data.

3. Results

The average age of diagnosis of nasolacrimal ducts obstruction was 6.5 ± 2.1 , average age at surgery, with a minimum 9 and maximum 18 months was equal to 12 ± 1.5 months and the interval between diagnosis and surgery was equal to 5.6 ± 1.2 months. Patients were under examination and evaluation for 10 days, one month and two months after catheterization. Profile Details of patients are presented in Table 1. In first follow-up of experimental group, 89 eyes of 91 eyes with 97.1% success and in control group, 88 eyes of 98 eyes with 89.79% success, had no re-obstruction of nasolacrimal duct and this situation did not change until the end of study. Using mitomycin C significantly prevented nasolacrimal duct re-obstruction in patients. Success rate in one month follow-up after operation of 97.1% with 95% confidence was 95.35-98.96. Also no special effect was observed for mitomycin C injection in experimental patients group. Details of patients' treatment are presented in Table 2.

4. Discussions

Nasolacrimal duct catheterization has been accepted as a standard method with high achievement in children with congenital nasolacrimal duct obstruction. The success rate of catheterization is 85-95% in children less than one year, and its prognosis is reduced with increasing patient's age and increasing number of catheterization. In Honavar and colleagues study on 2 years children and older, catheterization success rate was reported 80% and it is significantly different with results in children under one year. Factors that had caused failure: older than 36 months, failure of supportive therapy, and failure in early catheterization, dilated lacrimal sac, and bilateral obstruction. This study was done on children under eighteen months with nasolacrimal duct obstruction in order to have no effect of age for success rate. In Sturrock and colleagues study that was conducted to examine long-term results of catheterization operation in children with nasolacrimal duct obstruction, after 4-13 years follow-up, 30% of patients still had symptoms of obstruction. Mitomycin C is an antibiotic with anti-

proliferation cell property that it has been used in various reports. There has been a significant difference ($P=0.0014$) between success rate 97.1% that was obtained in this study and Sturrock and colleagues study' success rate 86% that was obtained by catheterization without using mitomycin C. In michanic and colleagues study on adult patients with nasolacrimal duct obstruction, after catheterization, duct was washed with 0.2 mg/ml dose of mitomycin and after a month, the success rate in catheterization with mitomycin group was reported 96.6% in comparison with no mitomycin group that its success rate was 55%, and in one-year follow-up, success rate was reported 95% in mitomycin group while this rate was 40% in without mitomycin group. This study showed that the use of mitomycin, during catheterization, increase considerably success rate in long-term, results of our study on one-month follow-up of patients (97.1%) is near to results of this study in one-month follow-up of their patients. Tabatabai and colleagues studied adult patients with nasolacrimal duct obstruction, after catheterization, they washed nasolacrimal duct with 1 cc mitomycin solution with a concentration of 2 mg/ml. After eight months follow-up, 51.7% of subjects had an open nasolacrimal duct, 39.7% of subjects had partial obstruction and 8.9% of subjects had complete obstruction. No complications were reported in the use of mitomycin C in study. Its success rate is less than present study. Dolmetsch and colleagues in a study conducted on children aged 16 years and under, showed success rate of 94.4% in nasolacrimal duct obstruction treatment with the use of mitomycin C, therefore they indicate mitomycin as an effective drug for increased likelihood of successfulness of operation. Our study success rate has been more than this study. In a study by Bazzazi and colleagues that was conducted on patients with nasolacrimal duct obstruction, after catheterization, nasolacrimal duct

was washed with mitomycin C that after a six-month follow-up nasolacrimal duct was completely open in 20 eyes (43.6%) and 21 patients (52.5%) were satisfied with improvement in symptoms. In six-month follow-up of patients, no complications were reported in using mitomycin. Result of this study showed that this treatment could be an appropriate method for treatment of nasolacrimal duct obstruction in adults. Some advantages of this method are simplicity, no need for general anesthesia, additional and expensive equipment and its low rate of morbidity. Its result is lower than the results of present study. Kumar and colleagues in a study on patients with nasolacrimal duct obstruction, after catheterization, washed duct with dose of 0.4 mg/ml, and they obtained 80% for rate of improvement in symptoms after one year follow-up (compared to 8.3% in control group). In this study, no side effects caused by mitomycin were observed.

In a study by Tsai and colleagues that was conducted with the purpose of determination of effective rate and safety of using mitomycin C (0.2 mg/ml) during catheterization on adult patients with nasolacrimal duct obstruction; after 9 months follow-up, 89% of subjects had widely open nasolacrimal duct. It was concluded in this study that the use of mitomycin C has good results in long term in nasolacrimal duct catheterization and it is suggested as a simple, effective and yet least invasive technique. Final result is that the use of mitomycin C during nasolacrimal duct catheterization leads to increase the success rate of catheterization and prevention of duct re-obstruction in children with congenital nasolacrimal duct obstruction.

Limitations of study: it was better to follow study in 3,4,5,6 months and it was not possible due to dispersion of patients and specific problems of province.

Table 1: General conditions of children under 18 months participants in the project.

Discussion	Sex			Eye			History	
	Female	Male	Total	Right	Left	Both eyes	Drug use History	Family History
Control	41(55)	34 (45)	75(100)	28(37)	24(32)	23(32)	70(93)	2(3)
Cases	40(57)	30(43)	70(100)	25(36)	24(32)	21(30)	68(97)	1(1)
Total	81(56)	64(44)	145(100)	53(65)	48(59)	44(54)	138(95)	3(1)

Table 2: Distributions of Eye surgery in terms of re-occlusion or obstruction of lacrimal canal in two groups

Discussion	Without Recurrent	With Recurrent	Eyes	Successful Rate (%)
Controls	88	10	98	89.79(87.86, 92.24)
Cases	89	2	91	97.80(94.86, 99.64)
Total	180	9	189	----

$$\chi^2 = 5.09 \quad df=1 \quad P < 0.05$$

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