Closed intubation with mitomycin C application for patients older than two years having nasolacrimal duct obstruction

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Purpose The aim was to explore the safety and efficacy of silicon intubation with mitomycin C (MMC) in increasing the success rate of closed intubation in patients older than 2 years.

Patients and methods This prospective study included thirty eyes of 24 consecutive patients with tearing and discharge owing to primary and acquired partial nasolacrimal duct obstruction. Their ages ranged from 2.5 to 40 years, and the male/female ratio was 10/14. Probing of nasolacrimal duct with silicone intubation (SI) (which is soaked in MMC 0.2 mg/ml for 2 min) was done in all cases, but it was abandoned if the resistance or obstruction was too difficult to overcome or if excessive bleeding or a hard blind bony pouch at the end of the nasolacrimal duct was detected. This occurred in five patients (5/35). In these patients, dacryocystorhinostomy was performed, and they were excluded from our study.

Results The procedure was successful in 24 eyes and unsuccessful in six eyes. The success is defined as prevention of recurrence of duct obstruction after removal of silicon tubes 3±1.7 months from intubation. The mean age of the patients with unsuccessful outcomes was 22.4±3.4 years, whereas those with successful outcomes was 8.0±2.8 years, and the difference was statistically significant (P=0.006). Sex (P>0.05) was not statistically different. No serious intraoperative and/or postoperative complications were observed.

Conclusion The results of our prospective study showed that SI with MMC in patients with simple epiphora has a success rate of 80%. This success rate was achieved by other studies using SI alone but in younger age group. In our study, an older patient group was included with almost the same success rate. We can conclude that MMC application during SI does not appear to have additional benefit over SI alone in young children with simple epiphora, as shown in other studies by different authors, whereas the application of MMC during SI would result in better efficacy compared with SI alone in older age patients.

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Introduction

In children, most nasolacrimal duct obstruction (NLDO) cases are congenital. This type of duct obstruction affects approximately 5–8% of normal newborn infants. The most common site of obstruction is Hasner's valve at the distal end of the duct. It is almost equal in both sexes. The spontaneous cure rate is 80–90% within the first year of life, but it decreases as age increases, owing to recurrent dacryocyctitis and fibrosis [1,2].

Probing and syringing is usually a quick, simple procedure. It may be required if medical treatment and massaging the lacrimal sac failed to cure the obstruction and stop tearing and discharge. The success rate of simple probing declines as age increases generally after 24–36 months according to a prospective observational study conducted by Repka *et al*. [3], in which, the success rate was 78%.

Silicone intubation (SI) or duct stent insertion is a procedure in which two ends of one silicon tube are inserted in the lacrimal duct through the upper and lower puncta to meet together down in the nasal cavity. It is used as a primary procedure or following failure of simple probing. The success rate of primary duct stent insertion is estimated to be between 79 and 96% [4].

There is also an other procedure called balloon catheter dilatation, which can be performed as a primary intervention or following failed simple probing by introduction of a LacriCath balloon catheter (Atrion Medical, Birimingham, Alabama) into the duct. The balloon is inflated according to manufacturer's specifications and withdrawn. Its success rate has been estimated between 53 and 95% [5].

Finally, if all the aforementioned measures failed to cure NLDO, dacryocystorhinostomy (DCR) via external or nasal endoscopic approach may be needed to create a new path for tears from lacrimal sac to nasal cavity. After which, a silicon tube is passed through puncta, lacrimal sac, and finally into the upper lateral part of nasal cavity [6].

Some authors added mitomycin C (MMC) with intubation in a trial to decrease fibrosis and increase the success rate. Chen *et al*. [7] were the first authors to use MMC-soaked silicone tubes for intubation. Because MMC has been used in many ocular procedures to reduce scarring and to enhance the success rate, they applied it in lacrimal surgery to study its effect. Liu and Bosley [8] also studied SI of the nasolacrimal duct (NLD) with MMC but did not have beneficial results. In this prospective study, we aimed at evaluating the efficacy of MMC-treated SI technique in patients who may have undergone DCR as an alternative procedure considering protocols of the Liu and Bosley study.

Patients and methods

This study included 30 eyes of 24 consecutive patients, with 10 males and 14 females, of ages from 2.5 to 40 years. All patients had a chief symptom of tearing and discharge owing to primary and acquired partial NLDO and were potential candidates of closed intubation. The study was performed between February 2015 and April 2016. Ethical approval was obtained from the ethical committee of Al Azhar University. Only patients with primary and acquired NLDO, with partial obstruction, negative regurge, and positive Jones fluorescein test, were included in the study (Table 1 and Fig. 1).

Patients with symptoms secondary to identifiable or treatable causes such as dry eyes, lid abnormalities (trichiasis, distichiasis, entropion, ectropion, and lid laxity), glaucoma, refractive error, tumor of the eyelid, and secondary causes of NLDO such as fractures of the facial bones, nose structural abnormalities, severe atrophic rhinitis, tumors of the lacrimal system, canalicular and common canalicular obstruction, and previously failed DCR were excluded.

Informed consent was obtained from all patients. Preoperative workup included obtaining patient medical and ocular history, testing the visual acuity, and thorough slit-lamp examination of the conjunctiva and cornea to rule out possible ocular surface disorders.

Table 1 Descriptive data of the study group

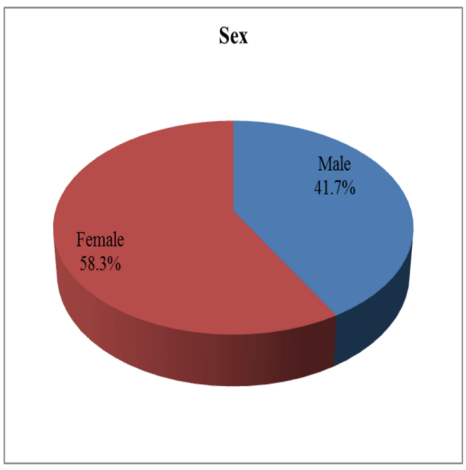
	Total (*N*=24)
Age (years)	2.5–40 (21.7±2.5)
Sex	
Male	10 (41.7)
Female	14 (58.3)
Mean follow-up period	6–9 (6.8±2.4)
Silicone tube removal time	3–4 (3.2±1.1)

The eyelids were examined for proper closure and possible laxity or misdirected lashes. Whenever needed, Schirmer I and II tests, tear break-up time, Jones test I, or a dye disappearance test, and fluorescein staining were performed. Regurge test was also performed, and patients with positive regurge were excluded. Irrigation with saline solution revealed the nature and location of the obstruction.

The procedure was performed under general anesthesia in all patients. A blunt-tipped probe was used for dilating and probing of both upper and lower puncta. A Crawford SI set (27 G; BD Visitec, California, USA) which is soaked in MMC 0.2 mg/ml for 2 min was used in all patients. If resistance was felt, its location was recorded. Probing of NLD with SI was abandoned if the resistance or obstruction was too difficult to overcome or if there was excessive bleeding or a hard blind bony pouch at the end of the nasal lacrimal duct; this occured in five patients (5/35). In these patients, DCR was performed, and these patients were excluded from our study. After overcoming the obstruction, the Crawford silicone was slightly withdrawn and then the nasal cavity was suctioned. Care of the soaked silicon tube with MMC was taken so that there was no spill over the cornea, and constant corneal irrigation with saline solution was done during this period. Copious irrigation with gentle suctioning followed, and SI proceeded in the usual manner.

After surgery, a small amount of tetracycline ointment was instilled on the operated eye. A few hours after surgery, patients received betamethasone eye drops 6 h, and chloramphenicol eye drops 4 h, which were tapered off after 1 week. Patients also received oral cephalexin for 1 week. Follow-up visits were scheduled at 1 week, 1, 3, and 6 months postoperatively.

Figure 1



Pie chart of sex distribution of the study group.

During each visit, the same relevant lacrimal function tests were repeated and failures were recorded. In documented failed cases, DCR was offered if the patient's symptoms could not be managed with nonsurgical managements. The silicone was left in place for 3 months. Any complication during this time was recorded and managed appropriately.

After completion of the study, all records were reviewed and analyzed. Statistical evaluations included means analysis with the one-way analysis of variance test with the Student-Newman–Keuls test. Success rates were analyzed by two-tailed χ^2-test. *P* value less than 0.05 was regarded as significant.

Results

The mean age was 21.7±2.5 years (range: 2.5–40 years). Of the 24 patients, 10 were male and 14 were female. All patients had symptoms of chronic NLDO within the several months before surgery with repeated medical treatment trials. A bicanalicular MMC-soaked silicone tube (0.2 mg/ml for 2 min) was successfully placed in 30/35 patients. Inferior turbinate infracture was required in two (6%) cases. The operation was classified as successful by absence of epiphora or discharge, patent NLD in irrigation test, and the patient being symptom free up to 3 months after removal of the silicone tube (Table 1).

The mean follow-up period was 6.8±2.4 months (range: 6–9 months). The mean silicone tube removal time was 3.2±1.1 months (range: 3–4 months). Although the silicone tubing was well-tolerated in most of the cases, three (10%) patients experienced epiphora and minimal mucopurulent secretion with the tubes in place which resolved after the removal of the tubes. The complete resolution of signs and symptoms with dye disappearance test grade 0–1 was observed in 24 of 30 eyes (80%) during the last 3 months of follow-up period after removal of the silicone tube. In six (20%) cases, improvement of the signs and symptoms could not be achieved after the procedure. One (3.3%) case developed lacrimal fistula at site of medial canthus 3 weeks after surgery, which was treated conservatively, and then shifted to DCR. However, in the other five cases, signs and symptoms of epiphora and discharge remained after removal of the tube.

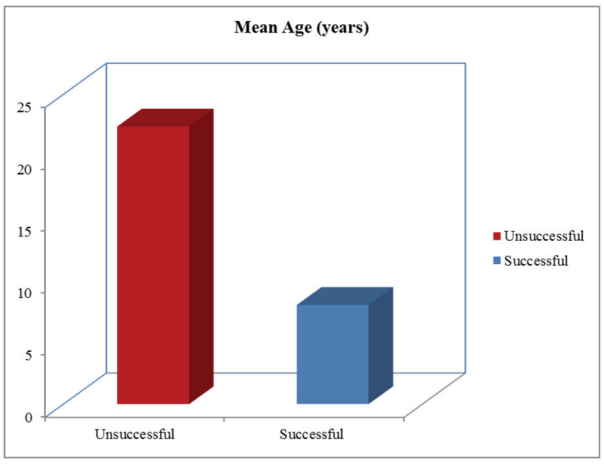
So the procedure was successful in 24 eyes and unsuccessful in six eyes. The mean age of the patients with unsuccessful outcomes was 22.4±3.4 years, whereas that of the patients with successful outcomes was 8.0±2.8 years, and the difference was statistically significant (*P*=0.006). Sex and time at mean silicone tube removal (both *P*>0.05) were not statistically different. No serious intraoperative and/or postoperative complications, including excessive bleeding, punctal damage, 'cheese wiring', dacryocystitis, or pyogenic granuloma formation, were observed (Fig. 2, Table 2).

Discussion

The present study showed that SI of nasolacrimal duct with MMC had favorable results as a primary treatment of persistent NLDO in older children as well as adult patients with acquired NLDO. This could be stated because the mean age of unsuccessful cases was 22.4±3.4 years despite having ages up to 40 years. Ages before and beyond this mean age showed success, so failure could be owing to other factors than age.

Congenital NLDO is a common lacrimal system disorder in children. Conservative therapy has been found to be sufficient in most cases during the first 12 months, and probing has been proposed as the most effective procedure in cases aged between 12 and 18 months [9]. Although SI is generally used after failure of conservative therapy and probing, it has been suggested as the primary procedure in children older than 1.5–2 years, owing to the decreasing success of probing with age. Silicone tubing avoids annular obstruction and contraction inside the nasolacrimal canal during wound healing, by acting as a

Figure 2



Bar chart with success and failure outcomes according to mean age (years).

Table 2 Comparison between mean age (years) with successful and unsuccessful outcomes

Outcomes	Mean age (years)	*t*-test	*P* value
Unsuccessful	22.4±3.4	7.244	0.006
Successful	8.0±2.8		

temporary stent. Previous studies have shown high success rates of SI in the treatment of CNLDO in children aged up to 7 years, and others showed higher failure rate beyond this age [10,11]. Orhan and Onerci (12) used SI with the help of nasal endoscopic viewing in children with an age range of 18–48 months in the treatment of CNLDO. They found a 100% success rate for a follow-up period ranging from 4 to 24 months [12]. Repka *et al*. (3) reported a 90% success rate in children aged 6 to 45 months with no prior nasolacrimal surgical procedure. Andalib *et al*. [13] achieved an 86.2% success rate for monocanalicular and an 89% success rate for bicanalicular SI in children younger than 7 years. Okumuş *et al*. [14] showed a success rate of 73.3%, which was slightly lower than in the previous studies, probably owing to the fact that success of nasolacrimal duct intubation reduces with increasing age. In addition, in accordance with previous study [14], we showed that the mean age of the patients with unsuccessful results was significantly higher than that of the patients with successful results. This may be caused by increased fibrosis at the site of obstruction in older patients.

Few studies have investigated the results of nasolacrimal duct SI in children with wider age ranges [15]. Agarwal *et al*. [16] achieved complete resolution of symptoms in 80% of patients, in a population including children with ages varied from 11 months to 9 years. They stated that this approach might avoid a DCR in more than 80% of children with epiphora [16]. Kraft *et al*. [17] analyzed the outcomes of SI s in children aged 6 months to 16 years and found an overall success rate of 80.3%. However, in the aforementioned studies, no specific analysis for the patients older than 7 years was undertaken. To the best of our knowledge, we are the first in the literature to report the results of SI in children older than 16 years and adults whose ages were up to 40 years.

The reported success rates in different studies are based on individuals with different ranges of ages up to 16 years, but all of them were done without the addition of MMC. We reported 80% success rate, which issimilar to Kraft *et al*. [17] and Agarwal *et al*. [16] However, in the study by Krat *et al*. [17], the range of ages was between 6 months and 16 years, in the study by Agrawal *et al*. [16], the range of ages was between 11 months and 9 years, whereas in our study, the range of ages was between 2.5 and 40 years, with the same success rate. The difference between our study and their studies is the use of MMC, which may be considered in increasing the success rate with increasing age of patients.

Syed-Ziaeddin *et al*. [18] had carried out a randomized, prospective study using MMC during SI at concentrations of 0.2 mg/ml to evaluate its effect. The success rate was 75.9%. They also found that the duration of symptoms before surgery affected the success rate even with MMC. Duration of symptoms before procedure in patients who had only epiphora without discharge well correlated with the success rate, so that in the control group, patients with less than 6 months of duration of symptoms had significantly better results (83.3%) than patients with more than 6 months of symptoms (29.4%) [18]. Addition of MMC to SI in patients with simple epiphora and less than 6 months of symptoms did not have additional effect on the efficacy of treatment. However, in patients with simple epiphora and more than 6 months of symptoms, success rate in placebo group and SI+MMC group was 29.4 and 71.4%, respectively.Ugurbas and de Souza [19] used 0.5 mg/ml MMC for 2.5 min with good histopathologic effects. Yazici *et al*. [20] reported application of 0.2 mg/ml MMC and 0.5 mg/ml MMC for the same time of application (5 min), which yielded success rates of 100% and 94%, respectively, without any complication. Liu and Bosley used 0.2 mg/ml MMC without any complication. Randomized studies involving variable dosing schemes and long-term follow-up visits would help to elucidate the optimum drug regimen. SI of the NLD in adults has a success rate ranging from 22 to 83%, they performed SI with MMC for complete NLDO in adults and found a 53% success rate with a mean follow-up of 18 months. Liu and Bosely [21] found a 22.2% success rate for complete NLDO and 77.8% for incomplete NLDO following SI with MMC.

The range of ages in the study by Syed-Ziaeddin and colleagues was up to 30 years, and success rate in MMC group was 75.9%, so, the present study showed higher success rate of 80% with higher age of up to 40 years.

Limitations of the present study were the relatively small sample size and short follow-up period. Studies with larger sample sizes, longer follow-up periods, and in addition, a similar study with monocanalicular intubation (as this would avoid the use of general anesthesia) would make useful contributions to the literature in the treatment of older children with persistent CNLDO.

Conclusion

In summary, the results of this prospective study showed that SI with MMC in patients with simple epiphora has a success rate of 80%. This success rate was achieved by other studies using SI alone, but in

younger age group. In this study, older patient group was included with almost the same success rate.

So, it can be concluded that MMC application during SI does not appear to have additional benefit over SI alone in young children with simple epiphora. However, the application of MMC during SI would result in better efficacy compared with SI alone in older ages. In longer duration of symptoms of epiphora, application of MMC would increase success rate significantly, as compared with the other authors.

We recommend SI in patients with NLDO and simple epiphora with no discharge when the eventual cosmetic outcome is important for them, SI alone is sufficient when the duration of symptoms is less than 6 months, and SI with application of MMC is a better choice in patients with more than 6 months of duration of symptoms. We do not recommend these procedures in patients with chronic dacryocystitis and positive regurge. We also propose that a larger prospective study be conducted to more definitely evaluate the long-term outcome.

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Conflicts of interest
There are no conflicts of interest.

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