Does Topical Mitomycin-C Improve the Surgical Outcome of Bilateral Congenital Choanal Atresia Repair?


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Abstract:
Bilateral congenital choanal atresia (CCA) in newborns carries significant morbidity and mortality. Many surgical approaches have been described for its correction but none of the approaches have proved superior in preventing postoperative granulation tissue and restenosis. Recently, topical Mitomycin C (MMC) has been used intraoperatively to prevent the formation of granulation tissue and restenosis in choanal atresia repair. We report a series of three consecutive patients who underwent bilateral CCA repair and received topical MMC intraoperatively. We have used topical MMC in CCA repair for the first time in Qatar and report the outcome of these patients. Case 1 was a preterm child (29 gestational weeks) who underwent transnasal repair. Case 2 had CHARGE association and case 3 had no other anomalies, both of whom underwent transpalatal repair. In case 1, we had used topical MMC during revision surgery with improved outcome. In cases 2 and 3, topical MMC was applied during primary repair and in addition both received a second application selectively at the margins of the choanae 6 weeks after stent removal. Case 3 needed further dilatation of the choanae four months after second application of topical MMC. None of our patients developed any local or systemic side effects. To our knowledge, bilateral CCA repair in a 29 weeks gestational age child has not been reported in the literature. Our study suggests that topical MMC may be a useful adjunctive therapy in choanal atresia repair.

Key words: Choanal atresia, surgical management, postoperative complications, mitomycin-C

Introduction:
CCA is the developmental failure of the posterior end of the nasal cavity to communicate with the nasopharynx and was first described by Roderer in 1755 (1,2,3). The incidence of this uncommon condition has been quoted in the literature as 1 in 5000 to 8000 births (2,4,5). It occurs more commonly in females than males (2:1) and unilateral atresia is more common than bilateral atresia (1,2). The standard classification of CCA is bony (90%) or membranous (10%) (1,2,3), though recently this has been subdivided into pure bony, mixed bony-membranous and pure membranous (4,6).

Many theories have been suggested to explain the embryological basis for choanal atresia, but none has been proven. These theories include persistence of the buccopharyngeal membrane; persistence of the nasobuccal membrane of Hochstetter; misdirection of mesodermal flow and formation of mesodermally induced adhesions at the choanae (4,7).

Choanal atresia is associated with many other congenital anomalies in 20% to 50% of the patients and the mnemonic CHARGE association has been used to describe the features. It includes C-Coloboma, H-Heart disease, A-Atresia choanae, R-Retarded growth and development, G-Genital anomalies in males, E-External ear malformation and/or deafness (1,8).

Since newborns are obligate nose breathers, the typical presentation of bilateral CCA is respiratory distress, often present with cyclical apnea and cyanosis. Unilateral choanal atresia may present as chronic unilateral rhinorrhea or respiratory distress, but this is less severe. The gold standard for diagnosis of CCA is axial computer tomographic (CT) scan of the nasal cavity and nasopharynx. It helps to confirm the location, type of atresia and relationship to surrounding structures and assist the operating surgeon to establish a treatment plan. CT scan also helps to exclude other lesions that may produce nasal obstruction at birth such as gliomas, encephaloceles or dermoids (3).

Many surgical procedures have been described in the literature for the correction of CCA, but the most commonly used methods are the transpalatal and transnasal approaches (2,3,6). Rarely, transeptal approach has been used for older patients with unilateral atresia (5). Alternative management includes use of oral airway or McGovern nipple until the child is stable. Long-term endotracheal tube (ET) intubation and tracheotomy are not the ideal choices of treatment because of its inherent complications.
The success of CCA repair depends on various factors and there are no standardized guidelines in the literature to define the success of surgical outcome. Whatever the definition of success, the surgeon is often faced with the problem of restenosis and excessive granulation tissue formation at the site of repair. The rates of restenosis vary from 0% to 85% and until recently no topical medical therapy has been shown to influence the success of surgical repair (6). Recently, MMC has been used intraoperatively during choanal atresia repair to prevent postoperative granulation tissue formation and restenosis (6).

MMC is an antitumor antibiotic isolated from the bacterium streptomyces caespitosis and it selectively inhibits DNA synthesis through MMC induced cross-linking (9). In Ophthalmology, topical MMC has been used routinely during glaucoma filtration surgery to prevent closure of drainage fistula (6,10,11,12). It has also been found useful in reducing the incidence of cicatrix formation in children after laryngotracheal reconstruction (6).

We report a series of three consecutive patients who had bilateral CCA repair and received topical MMC intraoperatively and discuss the outcome of the surgery.

Case Report:

Case 1:

A preterm (29 gestational weeks) female child had respiratory distress after a normal delivery and a diagnosis of bilateral CCA was made when a catheter could not be passed down through the nasal cavities. Figure 1 shows the preoperative axial CT scan findings. The child did not require intubation and was managed with an oral airway until surgery. At 5 days of age and weight of 1300 grams, the child underwent transnasal repair. Because of the low birth weight, prematurity and narrowness of the nasal cavities, we performed a two-staged procedure. The aim was to establish a nasal airway without significant morbidity or mortality. Transnasal puncture was done with a 2.7mm 0° Storz- Hopkins telescope to visualize the atretic plate and the plate was perforated carefully at the inferomedial aspect using a mastoid curette. Clutton urethral sounds were used to dilate the opening. 2.5mm inner diameter (ID) ET tube nasal stents were left in place for six weeks and on removal, we improved the size of the choanae by removing the bony components of the atretic plate. Conventional endoscopic biting instruments were used during this procedure. Nasal cavities were restented with 3.5mm (ID) ET tubes for further four weeks. The child developed difficulty in breathing due to granulation tissue and restenosis of choanae within 6 weeks of stent removal and underwent dilatation of choanae with removal of granulation tissue and fibrous tissue contracture. MMC soaked neurosurgical patties were placed on the mucosa of the choanae for 3 minutes on each side as described in the literature (6).

Postoperatively, saline nasal drops and regular suctioning were used to maintain the patency of nasal stents. Figure 2a and 2b show postoperative endoscopic views of newly created choanal openings after topical MMC application. One year follow up showed adequate nasal airway.

Figure 1: Preoperative computerized tomography scan (axial view) of nasal cavities of case 1 showing bilateral choanal atresia.

Figure 2a: Postoperative endoscopic view of right nasal cavity of case 1 showing newly formed choanal opening after topical MMC application.

Figure 2b: Postoperative endoscopic close up view of choana as in figure 2a.
Case 2:
A near term (37 gestational weeks) female child was delivered by lower segment caesarean section due to pregnancy induced hypertension and fetal distress. The child was intubated after delivery due to multiple congenital anomalies (CHARGE association) and respiratory distress secondary to bilateral CCA. Axial CT scan showed bilateral mixed bony-membranous choanal atresia.

The child underwent transpalatal repair of choanal atresia after 10 days of delivery. The transpalatal repair was performed as described by Owens in the literature(13). Careful attention was given to avoid excessive mucosal injury. After the removal of the atretic plate, MMC at a concentration of 0.4 mg/ml was applied to the mucosa of the choanae for 3 minutes on each side. 3.5mm (ID) ET tube stents were positioned for six weeks. Postoperatively, saline nasal drops and regular suctioning were used to prevent crusting and blockage of the nasal stents.

Six weeks after removal of the stents, the child presented with signs of nasal blockage without desaturation. Examination of the nose under general anaesthesia revealed granulation tissue at the craniomedical borders of choanae without significant fibrous tissue contracture. Topical MMC (0.4 mg/ml) was reapplied to the base of granulation tissue after its removal. Six months follow up showed adequate nasal airway.

Case 3:
A full term female child was intubated immediately after delivery due to respiratory distress. Clinical examination and subsequent axial CT scan of the nasal cavities confirmed the diagnosis of bilateral CCA (mixed bony-membranous type). The child had no other systemic anomalies. The child underwent transpalatal repair of choanal atresia at 7 days old. After removal of the atretic plates, mitomycin (0.4 mg/ml) was applied to the mucosa of the choanae for 3 minutes. 4mm (ID) ET tubes were used as the nasal stents for six weeks. Regular suctioning and saline drops were used to maintain the patency of the nasal stents. Examination of the child at 6 weeks after removal of stents revealed nasal blockage without desaturation. The child underwent elective examination of the nasal cavities under general anaesthesia and it showed granulation tissue at the medial border of the choanae on both sides. Mitomycin was reapplied to the base of granulation tissue after its removal. Examination of the child at four months after second application of topical MMC showed minimal narrowing of choanal opening and the child had dilatation of the choanae with urethral dilators. Six months follow up showed adequate nasal airway.

Discussion:
Bilateral CCA is an uncommon life threatening condition in the newborn. Since its first description by Roederer in 1755, many articles have been published in the literature on various surgical approaches to repair the CCA and their advantages and disadvantages. The commonly used methods are the transpalatal and transnasal endoscopic approaches(2,3,6,7). Other methods have been described, which includes a transseptal repair(5,7) and transantral approach that is no longer used. None of the approaches have proved superior to one another in preventing postoperative stenosis and granulation tissue formation(8). The preference and success of a particular approach depends on various factors that include the age of the patient, type of atresia (bony, mixed or membranous), unilateral or bilateral, surgeon’s experience and other associated congenital anomalies.

Surgeons who perform surgical repair of CCA require easy access and good visualization of operative field with minimal blood loss. The approach selected should give long-term success with minimal postoperative morbidity and fewer revision procedures.

Whatever the method of approach selected, failure due to restenosis and granulation tissue formation are the two main obstacles to a successful surgical outcome(6). Many articles report the use of stenting for a variable period to improve the outcome of choanal atresia repair. But, restenosis and granulation tissue can develop in spite of postoperative stenting(2,4,5,6). Topical nasal steroids have been suggested to reduce the formation of granulation tissue, but evidence is lacking. Topical saline nasal drops have been used universally with frequent suctioning to prevent crusting and blockage of nasal stents in the postoperative period.

MMC is an antineoplastic antibiotic used mainly as an intravenous agent in transitional cell carcinoma of bladder and in combination with other agents in advanced squamous cell carcinoma of uterine cervix and in metastatic breast cancer. It has been used topically at a concentration of 0.4 mg/ml for 5 minutes during glaucoma filtration surgery to prevent restenosis of the drainage fistula(10).

In an in vitro experiment, human Tenon’s capsule fibroblasts were exposed to MMC at a concentration of 0.4 mg/ml for duration of 1 and 5 minutes. There was no cytotoxic effect noted at this concentration. The study concluded that MMC has an antiproliferative effect on fibroblasts and may have effects on other components of wound healing such as cell migration, extracellular matrix production and on the vasculature(11).

Although topical MMC has been widely used in glaucoma filtration surgery for many years, its introduction to the clinical use in the field of otolaryngology, head and neck surgery is recent. In one small clinical study, topical MMC was used in the treatment of tracheal cicatrix after tracheal reconstruction, with favorable outcome(10).

A recently published article evaluated the use of topical MMC on 8 patients during choanal atresia repair (2 bilateral & 6 unilateral) and compared the results with their own historical
controls. The historical control included 15 patients (9 bilateral and 6 unilateral) who had CCA repair without the use of topical MMC. It concluded that topical MMC is an effective agent to prevent restenosis and granulation tissue formation compared to the historical controls.

Recently, in our unit we have used topical MMC on 3 consecutive patients who had bilateral CCA repair. In Case 1, we did not use topical MMC at the time of initial repair because of low birth weight and prematurity. We do not have data to support the use of topical MMC in similar cases and review of literature did not show any such described cases presenting with bilateral CCA. Many articles mentioned age of the patient is a key to a successful outcome, but none have quoted any age limit for surgical intervention.

In our case, the child was initially managed with an oral airway and orogastric feeding. Because of intermittent desaturation and difficulties in maintaining the airway, we decided to establish a definitive nasal airway by means of transnasal procedures. The child developed partial restenosis and granulation tissue formation 6 weeks after removal of stents. Topical MMC was applied to the mucosa of the choanae after the revision surgery. Postoperative follow up after MMC therapy shows patent choanae and the patient did not require further dilatations or revision surgery.

The critical period to develop restenosis and granulation tissue formation is within 4 to 8 weeks of stent removal. In our series, Cases 2 and 3 were presented with nasal blockage without desaturation at 6 weeks follow up and had examination of nasal cavities under general anaesthesia. The children did not develop any systemic side effects (myelo suppression, renal toxicity and pulmonary fibrosis) after second application of MMC.

We followed the principle used in glaucoma filtration surgery where second application of MMC is sometimes necessary to reestablish a drainage fistula. We believe that repeat use of topical MMC is safer and may have a role in revision cases, but need a larger series. We suggest a randomized control study to compare CCA repair with and without MMC therapy.

References: