

# **EFFECT OF USE OF MITOMYCIN C ON THE OUTCOME OF CHOANAL ATRESIA REPAIR,**

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**Key words;** choanal atresia, mitomycin C, nasal obstruction.

## **Abstract**

### **Introduction**

Congenital choanal atresia (CA) is an uncommon anomaly which is reported in 1 in 5000 to 8000 births.<sup>1,2</sup> It was first described by Roederer in 1755.<sup>3,4</sup>

This anomaly is more commonly encountered in female with an estimated female to male ratio ranging between 1.6:1 and 2:1.<sup>1,2,4</sup>

Isolated CA may be seen more frequently, however association with other congenital anomalies can be seen in 20% to 50% of cases.<sup>1,2</sup> Finding of CA should prompt search for other congenital anomalies such as CHARGE association (ocular colobomas, heart defects, choanal atresia, retarded growth and central nervous system issues, genitourinary hypoplasia, and ear anomalies).<sup>2</sup>

Unilateral CA is reported to be twice as common as bilateral CA.<sup>1</sup>

Bilateral CA is commonly discovered immediately after birth with obvious upper airway obstruction, necessitating emergency management with either oropharyngeal airway, McGovern nipple, or intubation, until surgical repair of CA is performed.<sup>1</sup> Unilateral CA, on the other hand, usually presents with less acute features, such as unilateral nasal obstruction and discharge, which commonly manifests latter in life.

Opening of the posterior choana is the procedure to establish normal nasal breathing in case of CA . Many approaches have been used including the transpalatal, transnasal, transantral and trans-septal route.<sup>5</sup> However repair of CA by endoscopic technique has become very popular in recent years. This can safely correct the difficult anatomical areas that have caused high failure rates in the past, ie, the lateral bony narrowing and the posterior septum.<sup>4</sup>

Outcome of endoscopic repair, however, is variable based on different studies.<sup>6,7,8,9,10,11,12</sup> Search for tools to improve outcome is very extensive.<sup>13</sup>

Topical mitomycin C (MMC) was introduced previously in an attempt to improve outcome and to maintain patent posterior choana. However, most of the studies in the literature using topical MMC are applying this drug to cases undergoing revision surgeries and cases with use of nasal stent. Therefore, it becomes difficult to evaluate the effectiveness of MMC in the presence of these confounding factors.

The present study was undertaken to evaluate the effect of the application of MMC without the use of nasal stent during endoscopic repair of CA in cases with no previous history of choanal surgery.

## Patients and methods

Thirty-seven consecutive children with the diagnosis of congenital choanal atresia were managed at King Abdulaziz University Hospital between January 1999 and October 2005.

We excluded from this study; cases with history of prior attempt to open or dilate the posterior choana (5 children), children who were operated and endonasal stent was used(6 children), not operated upon because of medical reasons (2 children), and operated with Nd:YAG laser (one child).

Twenty-three children fulfilled our selection criteria; none of them had prior surgical intervention, all underwent endoscopic repair of CA, and none of them had nasal stent post operatively.

The cases were distributed randomly in an alternating way into one of two groups.

The first group of children had an intraoperative application of topical MMC (0.4 mg / mL) to the dilated area by cotton

pledget for 4 minutes. Followed by irrigation with 15cc of saline to the site of application. This group included 13 children.

In the second group, no MMC was used. This group included 10 children. Unfortunately 3 cases were lost to follow up in this group.

Endoscopic repair of CA was performed utilizing 0° telescope (2.7 or 4 mm) connected to a camera and a monitor.

Opening of the soft tissue and dilatation was performed utilizing microdebrider. Microdebrider drill or skeeter drill were used to dilate the bony atresia laterally and to resect the posterior margin of the septum along with backbiting forceps.

All of our cases received saline nasal wash for one month after surgical intervention.

Criteria for successful outcome included all of the following; size of the posterior choana of at least 4mm in diameter by fiberoptic examination, absence of symptoms of nasal obstruction or discharge, and lack of the need for further intervention or dilatation.

Follow up of our patients ranged between 9 months and 6 years with a mean follow up period of about 32 months.

Fisher's Exact test was used to compare categorical variables. A p-value of less than 0.05 indicated statistical significance  
OBJECTIVE; To investigate the effectiveness of topical mitomycin C (MMC) on outcome of endoscopic repair of choanal atresia (CA) in cases that had never had this operation and when nasal stent was not used.

METHOD; Endoscopic repair of choanal atresia was performed in 20 children at King Abdulaziz University Hospital between January 1999 and October 2005. Intra-operative application of topical MMC (0.4mg/mL for 4 minutes) was done in 13 children, and 7 children did not receive MMC. Follow up period ranged between 9 months and 6 years.

The association between two categorical variables was investigated using Fisher's Exact test.

RESULTS: Sixty-nine percent of the cases who received MMC had a successful outcome compared to 57% of non-MMC cases,

but the difference was not statistically significant ( $P= 0.230$ ). In unilateral CA 70% of those who received MMC had a successful outcome compared to 60% of those who did not, again the difference was not statistically significant ( $P= 0.566$ ). Successful outcome was considered when the posterior choana was patent during the successive follow up, without the need for revision surgeries.

## Results

A total of 20 children were included our study. Their age ranged between 11 days and 17 years, with a mean of 7.9 years.

Eight of our patients were boys and 12 were girls. Five cases had bilateral CA, and 15 cases had unilateral CA. All of our cases had mixed bony and membranous atresia, except one who had bony atresia only.

Nine cases (69%) of the MMC group had successful outcome compared to 4 cases (57%) of the children in non-MMC group. however, this difference was not statistically significant ( $P= 0.230$ ).

In this study 15 of the cases had unilateral CA; 10 of them received MMC and 5 did not receive it. Seventy percent of those who received MMC had successful outcome compared to 60% of those who did not. Statistically there was no significant difference between the two results ( $P= 0.566$ ).

A total of 5 cases had bilateral CA; Three of them received MMC. Sixty-seven percent of those who received MMC had successful outcome compared to 50% of those who did not. This difference was not statistically significant ( $P= 0.700$ ).

Seventy percent of the unilateral CA who received MMC had successful outcome compared to 67% of the bilateral cases. Statistically there was no significant difference between the two results ( $P=0.706$ ).

Isolated CA was seen in 13 cases. On the other hand, seven of the cases were associated with other congenital anomalies including; CHARGE, Treacher Collins syndrome, Down syndrome, Apert syndrome, isolated cardiac, renal and ear anomalies.

Forty percent of the cases with associated other anomalies had successful outcome compared to 50% of the cases without

associated anomalies. This difference was not statistically significant (P = 0.58).

## Discussion

Mitomycin C is an aminoglycoside antibiotic made by the fungus *Streptomyces caespitosus*.<sup>6</sup> It acts by inhibiting DNA synthesis and breaking DNA strands. It is a drug which is long been used as an antineoplastic agent.<sup>14</sup>

Because of the inhibitory effect of this drug on fibroblast proliferation and migration, it is successfully used to maintain trabecular patency in glaucoma surgeries<sup>15</sup>, preventing scarring and maintain patency in laryngeal surgeries.<sup>12</sup>

The use of MMC as an adjunct to surgical repair of CA was introduced before, with studies indicating favorable outcome.<sup>6,7,16</sup>

Prasad et al<sup>6</sup>, in their review of 20 children who underwent endoscopic repair of CA and application of MMC (0.5mg/mL) for 3 minutes, reported a success rate of 85%. However, in 40% of their patients surgical intervention and use of MMC had to be repeated twice and 60% of their patients were revision cases.

Bradford et al<sup>16</sup>, compared cases who had MMC (0.4mg/mL) for 3 minutes at the time of surgical repair of CA to historical controls for which MMC was not used. They reported a success rate of about 60% in the MMC group compared to 7% in the control group.

Use of MMC in airway surgeries may precipitate early obstruction because of delayed wound healing with formation of sloughs, debris, or cartilage collapse of unhealed cartilage.<sup>17</sup>

Kubba et al<sup>18</sup>, didn't notice any significant difference in outcome of repair of choanal atresia for those who received MMC and those who did not. However, they used a smaller dose of topical MMC and shorter application time (0.2mg/mL for 2 minutes). Also there was variability in the time of use of MMC in the post-operative period, and their data was limited by random use of steroids and KTP laser for some of the patients.

In our study decision was made at the beginning to use topical MMC in a higher concentration (0.4 mg/mL) and longer

application time of 4 minutes compared to concentration and duration used in Kubba's study.

Our results , however, did not show a major difference in outcome between those who received MMC (success rate 69%) and those who did not receive it (success rate 57%). This difference in result was not statistically significant (P= 0.230).

When comparing the outcome of unilateral to bilateral cases who received MMC, we found that the success rate in unilateral cases was 70% and in bilateral cases was 67% , which was not a statistically significant difference (P= 0.706). The number of bilateral cases , however, was small in our study, which may have affected this result.

An attempt also was made in this study to assess the effect of use of MMC among the unilateral cases. Seventy percent of the unilateral cases who received MMC had a successful outcome, and 60% of the unilateral cases who did not receive MMC had a successful outcome. Statistically the difference in results was not significant (P=0.566). This indicated that there was no major benefit in the use of MMC in unilateral cases.

This is not in agreement with the results of Rombaux et al.<sup>10</sup> They indicated patent posterior choana with the use of MMC in unilateral CA in 85% of cases compared to 47% of cases without use of MMC.

The use of MMC, however, lacks standardization, with no agreement on dose, period of application or frequency of application .<sup>6,7,16,18</sup>

Animal research suggests a higher dosage MMC may have more beneficial effect<sup>19</sup>, which was also used in human studies.<sup>20</sup> This may represent the way to improve outcome of surgical intervention in case of CA. However, we still need further studies in this area.

Presence of other anomalies did not seem to have major effect on the outcome of intervention in our cases. This is in keeping with results from other studies.<sup>2</sup>

There is no statistically detected difference between children with CHARGE association and other patients in the number of procedures needed for the cure or in the need for follow-up surgery.<sup>2</sup>

In order to get a pure effect of mitomycin in our study, we avoided the use of endonasal stent. Use of stent may be associated with poor outcome due to local irritation, ulceration and infection.<sup>21</sup> Recommendation of other studies is ranging between, no use of nasal stents<sup>8,11</sup>, to a variable period of stenting.<sup>9,22</sup>

Van Den et al<sup>9</sup>, reported a success rate of endoscopic repair of CA in 80% of cases with a brief stenting for 2 days.

The present study suffers from the drawback of being based on a small sample size of just twenty children. This shortcoming may be responsible for the failure to detect a difference between the success rates for the two groups of children that were investigated. The study may be said to have had low statistical power, and this was inevitable due to the rarity of CA cases, and the only inclusion of cases with no prior surgical repair.

Further research need to be conducted using larger series of cases in order to arrive at reliable conclusions about the efficacy of MMC as an adjunctive to endoscopic repair of CA. But for uncommon anomaly like CA, such large scale series may take too long to accomplish.

In conclusion, the results from our study did not demonstrate statistically significant difference between the percentages of children treated with MMC versus no-MMC who remained patent after surgery.

## CONCLUSION;

The results from our study did not demonstrate statistically significant difference between the percentages of children treated with MMC versus no-MMC who remained patent after surgery.

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