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TOPICAL MITOMYCIN IN PREVENTION OF RESTENOSIS IN CONGENITAL CHOANAL ATRESIA REPAIR.

ENT

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ABSTRACT

Objective : congenital choanal atresia (CCA) is a rare disease. Prevention of restenosis has been the main concern of choanoplasty. Granulation tissue start forming after removal of stent post operatively in case of choanal atresia.[3] Mitomycin is generally used in cancer chemotherapy and it was established to interfere with the growth and spread of cancer cells in the body.[4] Mitomycin is clarified as antitumor drug and activated in vivo to a bifunctional and trifunctional agent which finally bind to DNA which leads to cross linking and inhibit of DNA synthesis and function.[5] Mitomycin is cell cycle phase non specific drug.[6] In this study I try to established a relation between topical use of mitomycin during surgical repair of choanal atresia and its outcome as compare to control group in which no topical mitomycin is used during surgical intervention as well as try to established statical significance if any between two treatment group. Current literature has very few research publications on choral atresia and use of mitomycin and this research will submit a strong background in the medical literature.

Methods : This is a retrospective cohort study carried out in government medical college Kota after proper ethical clearance from medical college ethical committee and with patient consent. Previous cohort is examined and two groups of patients are formed with topical mitomycin exposure and without exposure respectively. 6 patients with use of topical mitomycin is taken into study and 8 patients without topical mitomycin during surgery are taken respectively. Restenosis is measured by the use of dilatation required post operatively.

Number of dilatation required post operatively in follow up period and final outcome after removal of stent 6-8 weeks later are considered and studied. Analysis is done using excel software.

Results : two groups are formed with mitomycin exposure and non exposure during surgery and after proper analysis it is observed that with mitomycin exposure M ± SEM = 0.67 ± 0.304 (M=mean , SEM = standard error of mean) and without topical mitomycin exposure M ± SEM = 3.871 ± 1.369.

Unpaired student t test is applied using excel software and alpha comes out to be 0.2 (degree of freedom = 12) thus null hypothesis is rejected since p <<<0.2 (p = 0.01). Results are statically significant and shows that after using topical mitomycin frequency of restenosis is reduced by 81.26% with relative risk of the study being 5.336.

Conclusion: Restenosis significantly reduced in the patients where topical mitomycin is applied during endoscopic choanal atresia repair and need of dilatation post operatively is less as compare to those where topical mitomycin are not used as a adjuvant treatment during repair surgery.

KEYWORDS

Topical mitomycin, restenosis, congenital choanal atresia

INTRODUCTION:

congenital choanal atresia (CCA) is a rare cause of paediatric airway complete or partial obstruction with an estimated incidence of around 1:5000 — 1:8000 birth.[1] Choanal atresia results from a failure of embryonic nasobuccal membrane of Hochstetter to rupture that usually occurs during 5th or 6th weeks of intrauterine life. Nasal cavity is narrowed by a bony obstruction of the choanae by the pterygoid plate laterally and a thickened vomer medially; most cases also have a mucosal membrane component to the obstruction.[2] majority of patients (70) have a mixed bony membranous atresia and approximately two third have a unilateral malformation.[7] as many as 50% of all the patients may have other associated congenital abnormality such as CHARGE syndrome or CROUZON'S syndrome.[8] and this number may be as high as 75% in case of congenital bilateral atresia.[9]

Patients with unilateral disease may be diagnosed at birth by a snorting cry and inability to pass a suction catheter, though presentation is often delayed with complaints of nasal obstruction, unilateral rhinorrhea, delayed speech, and mouth breathing. Bilateral atresia results in respiratory distress in the neonate and patients characteristically present with cyclic cyanotic spells that improve with crying. Bilateral atresia necessitates immediate intervention, unless the airway is improved with an oral airway. Delayed repair is occasionally sought to allow for facial and nasal growth.

Almost all cases are now repaired via an endoscopic approach with the aid of powered instruments. Unfortunately, post-operative stenosis is not uncommon secondary to scar and/or granulation tissue formation. In such cases, dilation of the stenosis with rigid dilators or even balloons may be performed. Occasionally, revision surgery may even be required in cases of severe stenosis or if the vomer is exceptionally thick. Adjunct therapies and techniques have been employed to avoid such problems. Stenting of the choanae has long been employed to avoid restenosis[10]

MATERIAL AND METHODS:

Retrospective cohort study is being carried out in a tertiary medical college and hospital in government medical college Kota after proper ethical committee clearance and patient consent. Cohort of 14 patients are being analysed and are categorised into two groups. 6 patients are categorised in exposed group in which adjuvant topical mitomycin is given during endoscopic choanal atresia repair and 8 patients are categorised in another group of non exposed in which no topical mitomycin is used during endoscopic choanal atresia repair. Age, sex, type of choanal atresia, duration of stunting done post operatively and need of dilatation required post operatively is noted for each patient and tables are formed. Statical analysis is done using excel and SPSS software. Need of dilation surgery post removal of stent 6-8 week post endoscopic choanal atresia repair is taken into consideration and this determine the main variable in study. We try to remove the confounding factor my matching the age. Random cohorts are being selected to remove any bias. No patient bias is present in this study as it is a retrospective cohort.

Exclusion criteria :

1. Age below 1 year
2. Patients with any other co-morbidities.
3. Patients where endoscopic repair is not possible otherwise.
4. Loss of follow up.

Inclusion criteria :

1. Age above 1 year
2. Patients with unilateral or bilateral choanal atresia proven otherwise.
3. Patients where follow up cohort is available.

Study design:

Hospital based Retrospective cohort study.

Study tools :

Endoscopic surgery setup, topical mitomycin, excel software, computer, paper, pen.

Study technique :
Cohort and data are taken from tertiary medical college and hospital of all those patients who underwent endoscopic choanal atresia repair with or without topical mitomycin used as an adjuvant therapy during surgery and taking into consideration of all exclusion and inclusion criteria two groups are formed among them.

One with use of adjuvant mitomycin during endoscopic choanal atresia repair and one without use of any topical mitomycin during endoscopic choanal atresia repair.

Since it is a retrospective cohort design thus two groups are divide into exposed and non exposed group and proper statical analysis is carried out between the two groups.

Follow up is seen after removal of stent 6-8 weeks later which is placed during endoscopic choanal atresia repair. Need of dilation or repeated surgery is taken into consideration on long follow up of 1 year and number of dilatation attempt or any surgery post repair if done is noted.

Number of dilatation attempt post repair is taken into consideration as a measure of restenosis and data is analysed.

Ethics : ethical clearance is taken from the medical college ethical committee
Patient consent : work is channelise through and after proper patient consent.
Statical analysis : This is a retrospective cohort study and statical analysis is done using excel and SPSS software. Following analysis used in study
Results - M ± SEM in case of adjuvant topical mitomycin used = 0.67 ± 0.304 (SD = 0.746) M ± SEM in case of no adjuvant mitomycin used = 3.871 ± 1.369 (SD = 3.871) SD - standard deviation Unpaired t test is applied as a statical significance test which comes out to be 1.32075. Alpha comes out to be 0.2 with degree of freedom as 12. Since p value p<<<0.2 (p = 0.01) test results can be considered as significant rejecting null hypothesis.

Relative risk is calculated which comes out to be 5,336 along with attributable risk which is calculated as 81.26%.

Coefficient of variation (COV) when adjuvant mitomycin is used is 113.03% while COV when adjuvant mitomycin is not used is 83.69%.

Maximum choanal atresia are mixed with both bony and membranous component with approx 78.5%. Remaining are either bony or membranous while bony are greater in frequency than pure membranous.

No statical significance found among incidence related to sex. Maximum choanal atresia are congenital but age of presentation vary significantly because greater number of choanal atresia are unilateral thus produced no severe respiratory distress. Mean age of presentation comes out to be 10 years approximately.

Discussion :
Success in endoscopic choanal atresia repair depends on various factors like age of patient, type of choanal atresia (bony, membranous, unilateral, bilateral), presence or absence or other congenital anomaly , etc. Many research have been done in this regard but very few mentioned that whether or not patient require post operative dilatation or not and whether restenosis is here post operative or not. In this study we have mentioned through cohort the exact number of patients require post operative dilatation procedure and in what numbers.

Mitomycin is a antitumor alkylating agent and have a anti-inflammatory action as well.[4][5] although mitomycin is most commonly used as an intravenous agent but topically it is used to prevent stenosis and improved outcome in many surgeries. Findings from cultured fibroblasts have shown that exposure to 0.4 mg/mL of mitomycin for 1 minute and 5 minutes caused a 77% and 90% reduction in 3H- thymidine uptake, respectively.23 At this concentration, the drug is not cytocidal to fibroblasts, but concentrations of 1 mg/mL (1%) and higher are cytocidal. Mitomycin has recently been investigated in rabbit models in which it was used topically after maxillary antrotomy; it reduced the rate of restenosis of the antrotomies, and the surrounding nasal ciliary epithelium regained its normal microscopic morphologic characteristics and physiologic mucociliary clearance within 2 weeks of application. Thus, it seems that mitomycin should be ideal in reducing fibroblast proliferation and restenosis without causing any long-term Harm to the surrounding mucosa.Adjuvant mitomycin therapy during choanal atresia repair comes out to be a promising method in prevention of restenosis and this study provide a valid data and proof about the same. Intranasal steroids have been used by some authors, although no information was given about the concentration or frequency of use, and few comments were made about their efficacy other than that they may reduce stenosis and granulation tissue formation.

Acc to Bradford W. Holland, MD; William F. McGuirt, Jr, MD study is done to check the restenosis after choanal atresia. They found in their study that mitomycin is effective in preventing the restenosis after endoscopic choanal atresia repair.

In another study - The Endoscopic Repair of Choanal Atresia by James A. Stankiewicz, MD, endoscopic repair is done in 4 patients and 3 out 4 need revision surgery due to restenosis. No significant study about adjuvant medical therapy is done in this study.

In my study it was found that the need of revision surgery or dilatation is reduced when mitomycin is used as a n adjuvant therapy during endoscopic choanal atresia repair. In 2 patients out of 6 underwent endoscopic choanal atresia repair along with adjuvant mitomycin therapy 2 need revision surgery or dilation but the number of times revision surgery required after removal of stent (6-8 weeks later) is less as compare to those groups where no mitomycin or adjuvant medical therapy is used during endoscopic choanal atresia repair. Thus the significance of this study lies in the number of times dilatation or revision surgery done in exposed and non exposed group and a valid conclusion is driven.

Conclusion : After proper statical analysis it is found in my study that restenosis is significant reduced when adjuvant mitomycin is applied during endoscopic choanal atresia repair and thus need of further dilatation surgery also reduced significantly on long follow up.

Table 1 : Table Showing Endoscopic Choanal Atresia Repair Using Mitomycin As An Adjuvant Therapy During Surgery.

S.NO	TYPE	REPAIR	AGE	DURATION OF STENT IN WEEKS	NO. OF POST OPERATIVE DILATATION
1	Mixed	Endoscopic	10y2m	7w4d	2
2	Mixed	Endoscopic	9y1m	6w4d	0
3	Bony	Endoscopic	8y6m	7w4d	0
4	Mixed	Endoscopic	12y9m	8w2d	2
5	Mixed	Endoscopic	14y2m	8w4d	0
6	Mixed	Endoscopic	8y5m	8w4d	0

In the above table Mean (M) = 0.67, Standard deviation (SD) = 0.746, Variance (V) = 0.5558, Coefficient of variation (COV) = 113.03%, Standard error of mean (SEM) = 0.304, M ± SEM = 0.67 ± 0.304.

Table 2 : table showing endoscopic choanal atresia repair without mitomycin as an adjuvant therapy during surgery.

S. NO	TYPE	REPAIR	AGE	DURATION OF STENT IN WEEKS	NO. OF POST OPERATIVE DILATATION
1	Mixed	Endoscopic	10y4m	9w4d	4
2	Mixed	Endoscopic	9y2m	7w4d	8
3	Membranous	Endoscopic	8y7m	6w4d	2
4	Bony	Endoscopic	12y1m	8w2d	2
5	Mixed	Endoscopic	14y3m	8w4d	10
6	Mixed	Endoscopic	8y7m	8w4d	1
7	Mixed	Endoscopic	9y1m	7w2d	0
8	Mixed	Endoscopic	12y1m	7w2d	10

In above table Mean (M) = 4.625, Standard deviation (SD) = 3.871, Variance (V) = 14.985, Coefficient of variation (COV) = 83.69%, Standard error of mean (SEM) = 1.369, M ± SEM = 3.871 ± 1.369.

Table 3: table showing relative risk among exposed and non exposed.

	Exposed to mitomycin	Non exposed to mitomycin
Restenosis absent	4	1
Restenosis present	2	7

In above table relative risk (RR) = 0.667/0.125 = 5.336, attributable risk (AR) = 81.26%. This shows that restenosis is absent in 5.336 times among those who are exposed with mitomycin during surgery as compared to those who are not exposed to mitomycin. This also shows that restenosis is absent in 81..26% of patients attributable to mitomycin exposure.

Image 1 : image showing CT scan of patient having choanal atresia.

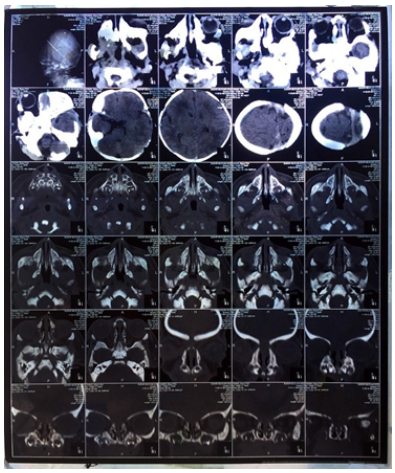
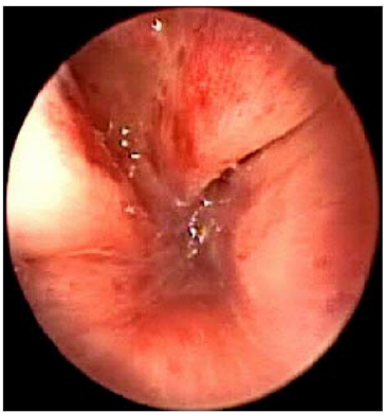


Image 2 : image showing endoscopic picture of right choanal atresia .



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