# Mitomycin-C as a Preventive Measure of Adhesion after Functional Endoscopic Sinus Surgery (FESS)

# Original Article

Fatma Mohamed Elhussieny<sup>1</sup>, Doaa Abd Elhalim Saif Eldin<sup>1</sup>, Yasmin Ahmed Elsharawy<sup>2</sup>

<sup>1</sup> Department of ENT, Faculty of Medicine for Girls, Al-Azhar University, Cairo, Egypt, <sup>2</sup>Drug and Poison Information Center, Pharmacy Department, King Saud University Medical City, Riyadh, Saudi Arabia

#### **ABSTRACT**

**Background:** Synechia formation in a postoperative nasal cavity is a major factor for suboptimal clinical outcome in functional endoscopic sinus surgery (FESS). Nasal packs medicated with topical agents like mitomycin C have been shown to reduce the formation of synechiae in postoperative patients.

**Aim:** To assess the role of mitomycin-c (MMC) in preventing synechia formation and ostial stenosis following endoscopic nasal surgery.

**Patients and Methods:** This is a prospective comparative study performed at the department of Otorhinolaryngology, El-Zhraa University hospital from January 2018 to December 2019 to evaluate the effect of MMC in prevention of nasal adhesions after endoscopic nasal surgery. A total of fifty (50) patients of different age groups and both sexes were involved in the study and divided into two groups, each group include 25 patients, group A with applying MMC and group B without applying MMC.

**Results:** In the MMC group, there was a reduction of synechia and crustration formation in group A that use MMC than group B without using MMC but with no significance.

Conclusion: Mitomycin C (MMC) is safe and beneficial in decreasing adhesion formation after endoscopic nasal surgery.

Key Words: Endoscopic nasal surgery, FESS, mitomycin-C.

Received: 16 July 2020, Accepted: 30 July 2020

Corresponding Author: Fatma Mohamed Elhussieny, MD, ENT Department, Al-Azhar University, Faculty of Medicine for

Girls, Tel.: 00201003483916, E-mail: fatmaelhussieny@yahoo.com

ISSN: 2090-0740, November 2020 Vol.21, No.3

# INTRODUCTION

Endoscopic sinus surgery (ESS) has been accepted as the choice treatment modality of chronic sinus disease. This is mainly because this approach maintains the sinus mucosa, establishes the sinus ventilation and sinus drainage pathway from the natural openings and eliminates the pathology effectively<sup>[1]</sup>.

Efficacy of ESS is clearly described within the past two decades, however, narrowing and adhesion formation after ESS is a potential cause of surgical failure<sup>[2]</sup>.

Plain packing and packing with medication have shown reduction in the formation of synechiaepostoperatively. Nasal packs medicated with topical agents like mitomycin C have been shown to reduce the formation of synechiae in a postoperative patient<sup>[3]</sup>.

Mitomycin-c (MMC) has been used successfully in other fields to decrease post-operative scar formation due to its ability to suppress fibrosis and vascularity in both vivo and vitro<sup>[4]</sup>.

# **AIM OF THESTUDY:**

To assess the role of mitomycin-c (MMC) in preventing synechia formation and ostial stenosis following endoscopic nasal surgery.

#### **PATIENTS AND METHODS:**

The current study is a prospective comparative study performed at the department of Otorhinolaryngology, El-Zhraa University hospital from January 2018 to December 2019 to evaluate the effect of MMC in prevention of nasal adhesions after endoscopic nasal surgery.

A total of fifty (50) patients of different age groups and both sexes were involved in the study. We excluded from the study any patients with traumatic nasal deformity, cystic fibrosis, abnormalities of cilia transport as kartegners syndrome.

The participants were divided into two groups: Group A that included 25 patients with applying MitoMycin C and Group B that included 25 patients without using MitoMycin C.

Personal non-commercial use only EJENTAS copyright © 2020. All rights reserved

DOI: 10.21608/ejentas.2020.26708.1189

#### Ethical considerations:

This study was discussed with the participants. A written informed consent was taken after an explanation of the study to them and before the initiation of the research study. The patients and the control groups had the right to withdraw from the study at any time without giving any reasons.

All patients were subjected to detailed history taking, complete ENT examination including diagnostic nasal endoscopy, CT of nose and paranasal sinus coronal and axial viewand routine preoperative investigations.





Fig. 1: intraoperative maxillary sinus ostium (RT and LT).

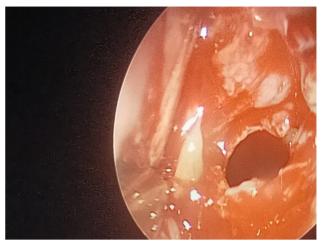


Fig. 2: Immediate post operative maxillary sinus ostium.

Follow up was done after two weeks, three months and after 6 months to assess the effect of MMC after the functional endoscopic sinus surgery.



**Fig. 3:** postoperative patent maxillary sinus ostium (after 2 weeks).

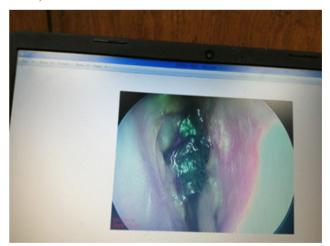


Fig. 4:  $2^{nd}$  week follow up crustation of nasal crustation



Fig. 5: postoperative synechia at 3<sup>rd</sup> month.

To obtain a concentration of 0.5 mg/ml of MMC, the content of the 5 mg vial is dissolved, on the same day, into 10 ml of saline; this solution has a characteristic light violet colour and is effective for 2 weeks if kept in the refrigerator. If it is kept at room temperature (15° - 30°) it is effective for 7 days<sup>[5]</sup>. All cases were subjected to Functional endoscopic sinus surgery, Misserklinger technique under hypotensive general and in group (A) at the end of the surgical procedure a cotton pledges (2.0-cm2) of 0.5 mg/ml MMC solution were placed at middle meatus for 5 mins. Postoperatively, nasal pads soaked with 1ml mitomycin c (0.5mg/ml) was applied and removed after 2 days.

Statistical analysis: Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

- 1. P-value < 0.05 was considered significant.
- 2. P-value < 0.001 was considered as highly significant.
- 3. P-value > 0.05 was considered insignificant.

## **RESULTS:**

Table (1): Number of cases

		No	%
No of cases	e MMC	25	50%
	e out MMC	25	50%

This table showed the number of the patients which was fifty (50) patients subdivided into two groups: Group A which was 25 patients using Mitomycin c and Group B which was 25 patients without using Mitomycin c.

Table 2: Demographic data

		No	%
Sex	Male	17	34.0%
	Female	33	66.0%
Age	Mean± SD	35.1	5±2.15
	Range	20	0-64

According to the demographic data, this table showed that 33 females that represented 66% and 17 males that represented 34% participate in this study and their mean of age was  $35.15\pm2.15$  with the range (20-64).

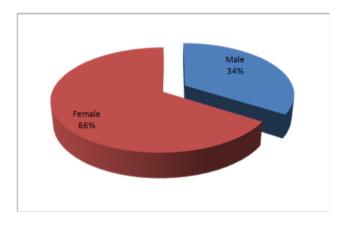


Table 3: Gender in studied groups

		e MMC		e out MMC		Chi square test	
		No	%	No	%	$X^2$	P value
Condon	Female	18	72.0%	15	60.0%	0.002	0.370
Gender	Male	7	28.0%	10	40.0%	0.802	0.370

As regard to gender, in group A (e MMC) the number of females were 18 that represented 72% and the number of males were 7 that represented 28%. In group B (e out MMC) the number of females were 15that represented 60% and the number of males were 10 that represented 40%.

Table 4: Pathology that require FESS:

	MMC		Control group		Chi square test	
	No	%	No	%	$X^2$	P value
Left side nasal mass	2	8.0%	3	12.0%		
Right side nasal mass	5	20.0%	3	12.0%	0.727	0.695
Right side nasal mass	18	72.0%	19	76.0%		

According to the pathology, both groups showing that the most common pathology was bilateral nasal polyp with the percentage of 72% in (MMC) and 76% in (e out MMC) with no significant difference between the two groups.

**Table 5:** Follow up (After 2 weeks)

	M	MC	Control group		
	No %		No	%	
Left side nasal crustation	0	0%	2	8.0%	
Right side nasal crustation	0	0%	1	4.0%	
Bilateral nasal crustation	0	0%	6	24.0%	

As regard to follow up after 2 weeks, the group using MMC showing no crustration while the group without using MMC showing crustration with the highest percentage of bilateral nasal crustration (24%).

Table 6: Follow up (After 3<sup>rd</sup> months)

	MMC		Control group	
	No %		No	%
Left side nasal synechia	0	0%	2	8.0%
Right side nasal synechia	0	0%	1	4.0%
Bilateral nasal synechia	0	0%	3	12.0%

In the follow up after three months, the group using MMC showing no synechia while the group without using MMC showing synechia with the highest percentage of bilateral nasal crustration (12%).

**Table 7:** Follow up (After 6<sup>th</sup> months)

	MMC		Contr	ol group	Chi square test	
	No	%	No	%	$X^2$	P value
Left side nasal mass	2	8.0%	3	12.0%		
Right side nasal mass	5	20.0%	3	12.0%	0.727	0.695
Right side nasal mass	18	72.0%	19	76.0%		

In the follow up after 6 months, the group using MMC showing no synechia except two cases (8%) showing bilateral nasal synechia while the group without using MMC showing synechia with the highest percentage of bilateral nasal crustration (16%).

#### **DISCUSSION**

FESS has been shown to be effective in treating patients who do not respond to medical therapy in around 85% cases. Even though there is a marked improvement in the technique of FESS, recurrence of the disease is a major issue. Failure of FESS has been reported to be close to  $20\%^{[3]}$ .

Synechia is reported to be the leading cause of failure of FESS in around 10–40%. Along with possible residual disease, synechia formation was regarded as an important cause of recurrence or failure of FESS<sup>[2]</sup>.

Mitomycin-C (MMC) is an alkylating antineoplastic antibiotic that prevents replication of fibroblasts and epithelial cells, in otolaryngology MMC is currently under inquiry for the prevention of

laryngotrachealstenosis, and as an adjunct to FESS to prevent closure of the maxillary sinus antrostomy<sup>[6]</sup>. The aim of this study was to assess the effect of mitomycin c in preventing synechia formation and ostial stenosis following endoscopic nasal surgery.

This study included fifty patients that divided into two groups, group A that using mitomycin c and group B without using mitomycin c. The statistical analysis revealed that 33 females that represented 66% and 17 males that represented 34% participate in this study and their mean of age was 35.15±2.15 with the range (20-64). In group A (e MMC) the number of females were 18 that represented 72% and the number of males were 7 that represented 28%. In group B (e out MMC) the number of females were 15 that represented 60% and the number of males were 10 that represented 40%.

Results shown above indicate that although MMC reduced postoperative adhesions but the difference wasn't statistically significant and had no effect in reducing formation of granulation tissue, polypoidhypertrophied mucosa. No difference was also found in the side of topical MMC application. This matched the study done by Baradaranfar *et al.*<sup>[7]</sup> that showed reduction of adhesion after using of MMC but without significant difference.

Kim *et al.* (2009) study included 20 patients with bilateral chronic rhinosinusitis resistant to treatment, the effects of mitomycin C was evaluated on anterostomy size and were found to be effective only in the first month after surgery. But after six months (long term) follow up, MMC has no effect in reducing incidence of narrowing or obstruction of antrostomy. This finding is congruent with our results as after 3 weeks the MMC groups showed no crustration nor synechia but after 6 months, synechia started to reappear in the MMC group<sup>[11]</sup>.

Venkatraman *et al.* (2012) in his prospective, randomized controlled trial that involved 50 patients with chronic bilateral rhinosinusitis found that the routine use of topical MMC at the end of endoscopic surgery reduce the incidence of synechiae and also improve patients' symptoms score in the early post-operative period. This partially agrees with our result<sup>[9]</sup>.

Anil *et al.* (2014) in a prospective hospital based interventional study, 42 patients diagnosed to have chronic rhino sinusitis (CRS) underwent FESS and found that 3.1% cases showed adhesions so Topical application of MMC at the conclusion of FESS/ESS has a role in prevention of adhesion formation and this also agrees with our study<sup>[12]</sup>.

The study by Yamaoka et al (2012) showed a reduction in synechiaformation. Ramalingam et al

(2018) in his study under the mitomycin C group 38.7% had synechia after 3 months, while 61.22% of patients were synechia free as compared with 21.43%<sup>[8]</sup>.

Studies by Venkatraman *et al* (2011) and Singh *et al* (2011) determined the role of MMC in preventing synechiae formation and ostial stenosis following endoscopic sinus surgery. They showed decreased incidence of adhesions, improvement in symptoms and decreasedadverse tissue reactions (like discharge, polypoidal mucosa, crusting) after topical MMC application and more the concentration of MMC, better the results<sup>[9,10]</sup>.

#### **CONCLUSION**

The results of this study demonstrate that the topical use of MMC is beneficial in decreasing adhesion formation after endoscopic nasal surgery. It also proved to be safe as regards local or general complications. Anyhow, MMC begins to have a wide range of application in the field of rhinology and in the future, it will play an important role after endoscopic sinus surgery based on further researches like our study.

#### **CONFLICT OF INTEREST**

There are no conflicts of interest.

### REFERENCES

- Weber RK, Hosemann W. Comprehensive review on endonasal endoscopic sinus surgery. GMS Curr Top Otorhinolaryngol Head Neck Surg. 2015;14:Doc08. Published 2015 Dec 22. doi:10.3205/cto000123
- Bewick J, Egro FM, Masterson L, Javer AR, Philpott CM. Anatomic findings in revision endoscopic sinus surgery: Case series and review of contributory factors. Allergy Rhinol (Providence). 2016;7(3): 151–157. doi:10.2500/ar.2016.7.0173
- Ramalingam N, Parida PK, Saxena SK, Surianarayanan G. Comparison of triamcinolone and mitomycin C nasal pack in functional endoscopic sinus surgery: a randomized, clinical trial. Egypt J Otolaryngol 2018;34:242-7
- Ahmed A. Sadek, Osama G. Abdel-Naby and Mostafa M. Talaat. 2019. Mitomycin-C Prevents Post-

- Operative Adhesions after Endoscopic Nasal Surgery. ISSN: 2090-0740, July 2019Vol.20, No.2
- 5. Parul Singh and Abhishek Singh. Mitomycin-C Use in Ophthalmology. IOSR Journal of Pharmacy 2013; Volume 3, Issue 1, PP 12-14.
- Mohammed A. El Dabaa, Atef A. El Maraghy, Mohammed A. Yones, et al., 2019. Role of Topical Mytomycin C Application in Improving Outcome of Functional Endoscopic Sinus Surgery. The Egyptian Journal of Hospital Medicine (January 2019) Vol. 74 (8), Page 1891-1901
- Baradaranfar, Mohammad-Hossein & Khadem, Jalal & Zahir, Shokooh & Kouhi, Ali & Dadgarnia, Mohammad & Baradarnfar, Amin. (2011). Prevention of Adhesion after Endoscopic Sinus Surgery: Role of Mitomycin C. ActamedicaIranica. 49. 131-5.
- Yamaoka WY, Gregório LC. The use of mitomycin-C to reduce synechia in middle meatus in sinus surgery: preliminary results. Braz J Otorhinolaryngol 2012; 78:44–50.
- 9. Venkatraman V, Balasubramanian D, Gopalkrishnan S *et al.* (2011): Topical Mitomycin C in Functional endoscopic sinus surgery. Eur Arch Otorhinolaryngol., 269(7):1791-4.
- Singh T, Lade H and Natesh V(2011):Role of mitomycin C in prevention of post-operative adhesions after endoscopic sinus surgery: A prospective study. Indian J Otolaryngol Head Neck Surg.,63 (3): 249–254.
- Netto, M. V., Mohan, R. R., Sinha, S., Sharma, A., Gupta, P. C., & Wilson, S. E. (2006). Effect of prophylactic and therapeutic mitomycin C on corneal apoptosis, cellular proliferation, haze, and long-term keratocyte density in rabbits. Journal of Refractive Surgery, 22(6), 562-574.
- 12. Harugop, Anil, *et al.* "Effectiveness of mitomycin-c for prevention of adhesion formation after functional endoscopic sinus surgery (FESS/ESS) in cases of chronic rhinosinusitis: a prospective hospital based interventional study." Journal of Evidence based Medicine and Healthcare 1.15 (2014): 1901-1908.