

Role of Topical Mytomycin C Application in Improving Outcome of Functional Endoscopic Sinus Surgery

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ABSTRACT

Background: functional endoscopic sinus surgery, (FESS), is a minimally invasive surgical procedure that opens up the paranasal sinus ostia with an endoscope. Endoscopic sinus surgery is seen as the standard treatment in chronic rhinosinusitis and Sinonasal polyposis.

Objective: it was to assess the efficacy of intra and postoperative topical application of Mitomycin C after endoscopic sinus surgery in reducing adhesions and scar formation and improving outcome of FESS.

Patients and Methods: this study included 60 cases (24 female (40%) and 36 male (60%) ranging in age from 18 to 50 years) with mean 34 bilateral chronic rhinosinusitis with or without sinonasal polyposis undergoing functional endoscopic sinus surgery. Every patient in this study had been submitted for full history taking, general examination, full ENT examination routine preoperative laboratory investigations and computerized tomography study on the nose and paranasal sinuses. Functional endoscopic sinus surgery had been done for all patients.

Results: In our study, bilateral nasal obstruction was presented in 46 patients (76.6%), anterior nasal discharge was presented in 22 patients (36.6%), posterior nasal discharge was presented in 18 patients (30%), headache was presented in 40 patients (66.6%) and facial pain was presented in 12 patients (20%). Endoscopic assessment of the patients 2 months after F.E.S.S revealed that the adhesions presented in 32 sides (26.7%) mainly occurred on the control side 25 (41.7%) while the Mitomycin C side showed minimal adhesions 7 (11.7%) with significant P value (0.04).

Conclusion: Topical application of MMC at end of FESS has beneficial role in prevention of adhesion formation and synechiae without any side effects/complications.

Keywords: Mitomycin C, Functional Endoscopic Sinus Surgery.

INTRODUCTION

Endoscopic sinus surgery is one of the most common operations. Using the endoscope, sinus surgery can be performed by the nose and at the outpatient clinic. However, sinus surgery is used as a last resort, and most patients do not understand what sinuses do or even what sinuses do. Sinus is a bony air cavity surrounding the nose. It relieves the echo head and the sound of one voice and can help protect the skull against sharp shock. If pockets are disabled, they can become infected. However, most of the "sinus" problems seen in many patients are actually problems in the main nasal passages caused by smoking or allergies. Sinus is normal even if the patient is suffering from symptoms of obstruction of the nose, pressure and obstruction of the airway. The only proven method of diagnosis of sinus disease is X-ray or CT scan ⁽¹⁾.

In FESS, after mucosal infiltration of 2% carbocaine with epinephrine, uncinectomy and middle antrostomy were performed without partial resection of middle turbinate when possible. Standard endoscopic anterior ethmoidectomy was made, opening the agger nasi and the ethmoidal bulla. When the posterior ethmoid was not involved by disease, surgical procedure is ended at this point.

In case of CT opacification of the posterior ethmoid and/or sphenoid sinus, a posterior ethmoidectomy and/or sphenoidotomy was performed ⁽²⁾.

Synechia and ostial constriction are common in the wake of FESS with incidence of 1 to 36%. This is assumed to result from the proximity of two or more rough mucous surfaces to each other during wound healing. Although not all synksia formation requires treatment, total bone stenosis and obstruction of critical tracts of flow may lead to surgical failure and the need for revision therapy ⁽³⁾.

The mitomycins are a family of aziridine-containing natural products isolated from *Streptomyces caespitosus* or *Streptomyces lavendulae*. Mitomycin C (MMC) has been used to reduce the stenosis and scar formation after surgery; many ophthalmologic and otorhinolaryngologic studies have showed its favorable effect⁽⁴⁾.

Mitomycin C has been used topically rather than intravenously in several areas. Mitomycin C is used to generate mitotically inactive feeder cells used in cell culture systems, such as mitotically

inactive fibroblast used in embryonic stem cell (ESC) systems ⁽⁵⁾.

It has been shown to maintain the patency of maxillary anrostomies in rabbits while preserving mucociliary function. Studies showed that topical Mitomycin C applied to the middle meatus for 5 minutes at a concentration of 0.5 mg/ml results in fewer adhesions than the control side and causes no adverse effects ⁽⁶⁾.

Harugop *et al.*⁽⁷⁾ stated that Chronic Rhino Sinusitis(CRS) patients have remarkable improvement in their symptoms after FESS. Topical application of Mitomycin-C at the conclusion of FESS has a role in prevention of adhesion formation.

The aim of this study is to assess the efficacy of intra and postoperative topical application of Mitomycin C after endoscopic sinus surgery in reducing adhesions and scar formation and improving outcome of FESS.

PATIENTS AND METHODS

A prospective study was carried out on 60 cases with bilateral chronic rhinosinusitis with or without sinonasal polyposis undergoing functional endoscopic sinus surgery in the Otorhinolaryngology department, Al-Azhar University Hospitals. **The study was approved by Medical Ethical Committee. All patients were informed and a written consent was obtained from all patients.** This study included 60 cases with bilateral chronic rhinosinusitis with or without sinonasal polyposis undergoing functional endoscopic sinus surgery we consider the right nasal cavity of all patients as a control side (group 1) and the left nasal cavity as a study side group (2).

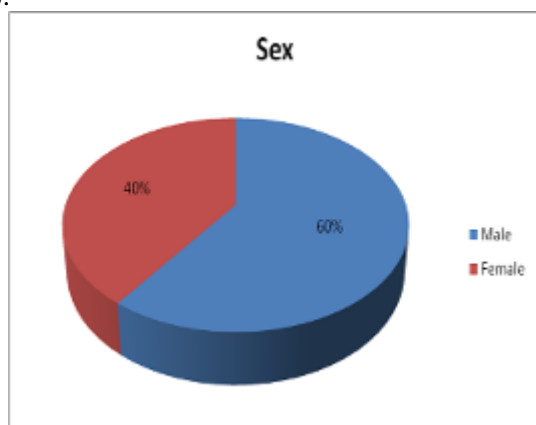


Figure (1): Sex distribution in the study group.

Inclusion criteria:

- History of chronic sinusitis, despite appropriate medical therapy (antibiotic, oral decongestant with antihistaminic, anti-

inflammatory and mucolytic). A chronic state was deemed to exist when symptoms persisted beyond 3 months or there were at least 6 episodes per year of recurrent acute sinusitis, each lasting at least 10 days⁽⁸⁾.

- Evidence of chronic sinusitis with or without nasal polyposis.
- Persistent changes of maxillary sinus with or without anterior ethmoid air cells on CT scanning of the paranasal sinuses 4 weeks after medical therapy without intervening acute infection so not to demonstrate diffusely swollen mucous membrane.

Exclusion criteria:

- History of sino nasal trauma.
- History of previous sino nasal surgery.
- Acute upper respiratory tract infections.
- Patients with unilateral sinusitis such as maxillary sinusitis of dental origin.
- Patients whom had underlying systemic disease such as; cysticfibrosis, immune deficiency and ciliary movement disorder.
- Patients with chronic specific inflammatory disease such as rhinoscleroma, T.B, syphilis.
- Patients with concha bulosa.
- History of bleeding disorders.
- Patients with complicated sinusitis.



Figure (1): Nasal endoscopy of the left side showing a small polyp and pus in the middle meatus



Figure (2): Nasal endoscopy showing left sinonasal polypi

Methods

Full history taking:

- **Personal history** of age, sex and special habits of medical importance.
- **Main complaint:** In the form of nasal obstruction, nasal discharge, headache or facial pain, diminution or loss of smell.
- **History of present illness:** onset, course and duration, severity and whether nasal discharge was anterior, posterior or both. The colour and character of the discharge and also asked about chronic illness in the form of presence of a systemic disease or immunologic disorder e.g. D.M, hypertension, chronic hepatic or renal disease and TB.
- **Past history:** having a previous nasal surgery, trauma or granuloma.

General examination:

General examination including; vital signs, body built, decubitus, mental function, chest and heart examination.

Full ENT examination:

Including anterior rhinoscopy and endoscopic examination.

Investigations:

- 1- Routine preoperative laboratory investigations (e.g. complete blood picture, coagulation profile, liver function tests, kidney function tests and blood sugar level).
- 2- Computerized tomography study on the nose and paranasal sinuses: Coronal view CT scan on the nose and paranasal sinuses had been done with bone window and without contrast. Prior to CT scanning, most patients received a full course of medical treatment 2 weeks to dry up the nasal cavity.



Figure (3): Coronal view CT scan of PNS with complete opacity of both maxillary sinus and anterior ethmoid sinuses (Diffuse sinonasal polyposis) with Lund- MacKay score = 20.

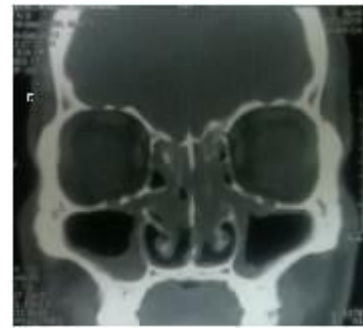


Figure (4): Coronal view CT scan of PNS with mucosal thickening of both maxillary sinus, with opacity of anterior ethmoid sinuses bilaterally with Lund- MacKay score = 17.

Operative procedure:

All surgeries were done by one surgeon to avoid bias and under general anesthesia. After injecting appropriate topical decongestive, the procedure were performed by Messerklinger technique.

The amount and location of sinus disease determine the extent of sinus surgery performed for each patient; however, every patient in the study group underwent middle meatal antrostomy and anterior ethmoidectomy.

When septal deviation limits access to the middle meatus, an endoscopic septoplasty was performed. The opening of the maxillary sinus was performed with conventional instrumentation .In all cases we preserved the middle turbinate keeping its mucosa as intact as possible

We considered the right nasal cavity of all patients as control side and the left one as study side. At the completion of the procedure, a piece of cotton soaked in 1 ml of MMC in a concentration of 0.5 mg/ml was placed in left middle meatus and another piece soaked in saline was placed in the right side. After a period of 5 minutes, the cotton pieces were removed and the nasal cavity was irrigated with 30 ml of sterile normal saline. This methodology was useful to avoid bias as each patient served as his or her own control .At the end of the procedure, both nasal cavities were tamponaded with Merocel packing. This packing was removed the morning after surgery. All patients were discharged with a 10-days course of oral antibiotics, nasal steroids for 4 weeks and instructions for saline irrigation of the nose for up to 2 months.





Figure (5): Mitomycin C 10 mg

Postoperative care:

The patient returned for frequent post-operative care until the area was completely healed. Postoperative care was done weekly in the first month then every two weeks in the second two months. The MMC application was repeated in the same side of the nose four weeks postoperatively under local anaesthesia and with the use of an endoscope. The contralateral side received again a cottonoid soaked with normal saline.

Meticulous post-operative nasal endoscopy performed in out-patient clinic for inspection of the surgical site at each post-operative visit to endorse the outcome of the surgery. The area was cleaned of crusts, wound secretions and granulation tissue. Any adhesions between the MT and the lateral nasal wall were divided. This was important to avoid post-operative synechia and scarring. The recently created ostium was assessed and cleaned if necessary. The ostium was examined for any evidence of stenosis or discharge.

Following surgery, patients were seen in outpatient clinic for evaluation 3 months after surgery i.e. after complete healing. The outcome of surgery was evaluated subjectively and objectively.

The evaluation included:

- 1- **Subjective evaluation:** According to **Kennedy *et al.***⁽⁹⁾, symptoms were assessed concerning the degree of improvement (cured, improved, unchanged or worsened). The outcome was classified as cured if there was no more symptoms, and as improved if symptoms of the disease become better after surgery. When the symptoms remained the same, the outcome was classified as unchanged. It was classified as worsened when the symptoms become more than before surgery.
- 2- **Objective evaluation:** It was done by nasal endoscopy. Systematic nasal endoscopy was performed using 0 and 30 degree 4mm endoscope. It was done to inspect the surgical area (middle Turbinate, middle Meatus and maxillary ostium). The middle turbinate was examined for its presence. The middle meatus was evaluated as regard presence of polyps, discharge, edema, adhesions, and crusting. The maxillary ostium was

examined for its patency and size. The images seen through the endoscope were captured by the use of a camera.

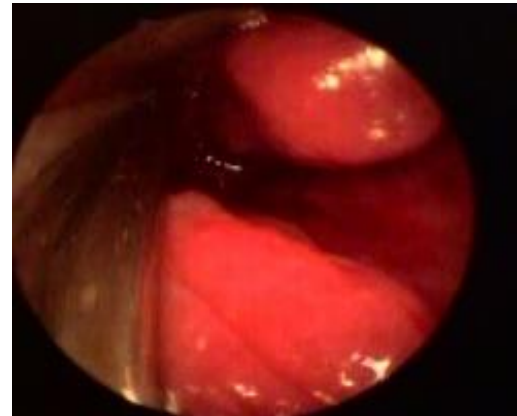


Figure (6): Intraoperative application of Mitomycin C pack in middle meatus

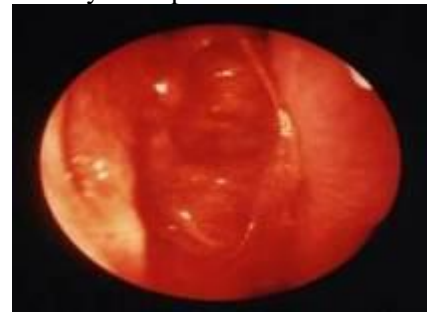


Figure (7): Endonasal endoscopic evaluation after middle meatal antrostomy, left side showing healthy, clean middle meatus, healthy lateral nasal wall, and healthy lateral surface of middle turbinate after one month.

Statistical analysis

Data were entered checked and analyzed using Epi-Info version 6 and SPP for Windows version 8.

X² (chi-squared) (test of significance) was used for difference between qualitative variable.

The threshold of significance was fixed at 5% level (p-value). The results were considered:

- Significant when the probability of error is less than 5% (p < 0.05).
- Non-significant when the probability of error is more than 5% (p > 0.05).
- Highly significant when the probability of error is less than 0.1% (p < 0.001).

RESULTS

This study was conducted on 60 patients, 24 female (40%) and 36 male (60%) ranging in age from 18 to 50 with mean 34 years with bilateral chronic rhinosinusitis with or without sinonasal polyposis. functional endoscopic sinus surgery had been done for all patients (figure 8).

Figure (9) shows the presenting clinical symptoms in patients of our study as bilateral nasal obstruction which presented in 46 patients (76.6%), anterior nasal discharge presented in 22 patients (36.6%), posterior nasal discharge presented in 18 patients (30.0%), headache presented in 40 patients (66.6%) and facial pain presented in 12 patients (20.0%).

Figure (10) shows the pre-operative endoscopic findings in study group which are: congested nasal mucosa presented in 25 patients (41.6%), polypi presented in 23 patients (38.3%) mucopurulent nasal discharge presented in 38 patient (63.3%), enlarged MT presented in 18 patients (30 %) and enlarged IT presented in 9 (15 %).

Figure (11) shows pre-operative C.T finding in patients of our study: Maxillary sinusitis presented in 60 patients (100%), these patients have mucosal thickening, partial or complete opacifications. Anterior ethmoiditis presented in 18 patients (30 %), Post ethmoiditis presented in 10 patients (16.6), Frontal sinusitis presented in 10 patients (16.6) and sphenoiditis presented in 4 patients (6.7). All patients have obliterated osteometal complex.

Table (1) shows subjective assessment of patients 3 months after F.E.S.S : nasal obstruction presented in only 10 patients on the study side (16.7%) and 29 patients on control side (48.4%) with significant P value (0.01) also anterior nasal discharge presented in only 6 patients on study side (10%) and 34 patients on control side (56.7%) with significant P value (0.02).

Table (2) shows the endoscopic assessment of the patients 1 months after F.E.S.S: the adhesions presented in 33 sides (28.3%), 20 (33.3%) occurred in the control side while the Mitomycin C side showed 13 (23.3%) with insignificant P value (0.4). The crusts presented in 9 study sides and in 14 control sides with insignificant P value (0.52). Unhealthy mucosa presented in 10 study sides and in 12 control sides with insignificant P value (0.74). Maxillary ostium

restenosis presented in 25 sides (21.7%) mainly occurred on control side cases 20 (33.3%) while the Mitomycin c side showed cases 5 (8.3%) with insignificant P value (0.1).

Table (3) shows endoscopic assessment of the patients 2 months after F.E.S.S: the adhesions presented in 32 sides (26.7%) mainly occurred on the control side 25 (41.7%) while the Mitomycin c side showed minimal adhesions 7 (11.7%) with significant P value (0.04). The crusts presented in 9 study sides and in 13 control sides with insignificant P value (0.11). Unhealthy mucosa presented in 6 study sides and in 15 control sides with insignificant P value (0.3). Maxillary ostium restenosis presented in 34 sides (28.3%) mainly occurred on control side (50%) while the Mitomycin c side showed (6.7%) with highly significant P value (0.001).

Table (4) shows endoscopic assessment of the patients 3 months after F.E.S.S: the adhesions presented in 34 sides (28.3%) mainly occurred on the control side 27(45%) while the Mitomycin c side showed minimal adhesions 7 (11.7%) with significant P value (0.02). The crusts presented in 7 study sides and in 15 control sides with insignificant P value 0.2. Unhealthy mucosa presented in 8 study sides and in 17 control sides with insignificant P value 0.2. Maxillary ostium restenosis presented in 34 sides (28.3%) mainly occurred on control side (50%) while the Mitomycin C side showed (6.7%) with highly significant P value (0.001).

Figure (12) shows locations of adhesions in patients of our study: We had overall 34 adhesions 27 of them at control side and 7 of them at mitomycin c side with significant P value (0.02).

Table (5) shows the relation between adhesions and recurrence of rhinosinusitis symptoms: adhesions presented in 34 sides (28.3%) 27 (79.4%) of them had recurrence of rhinosinusitis symptoms while no adhesions presented in 86 sides (71.7%) mostly on mitomycin c sides only 7 (20.5%) of them had recurrence of these symptoms with significant P value (0.001).

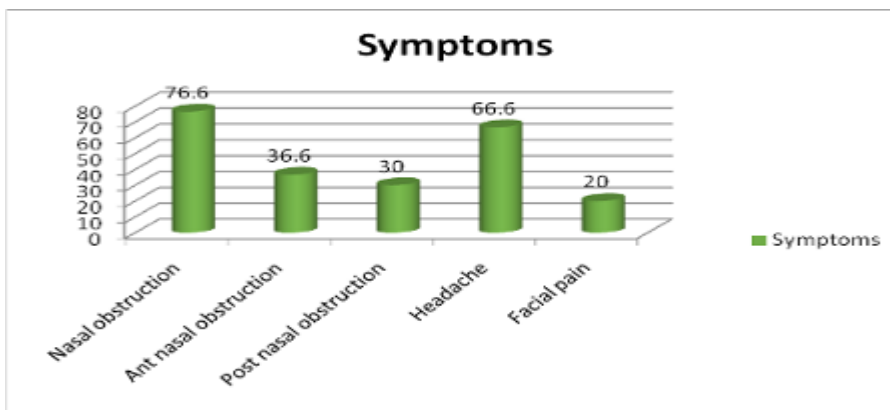


Figure (9): Clinical presenting symptoms in our study

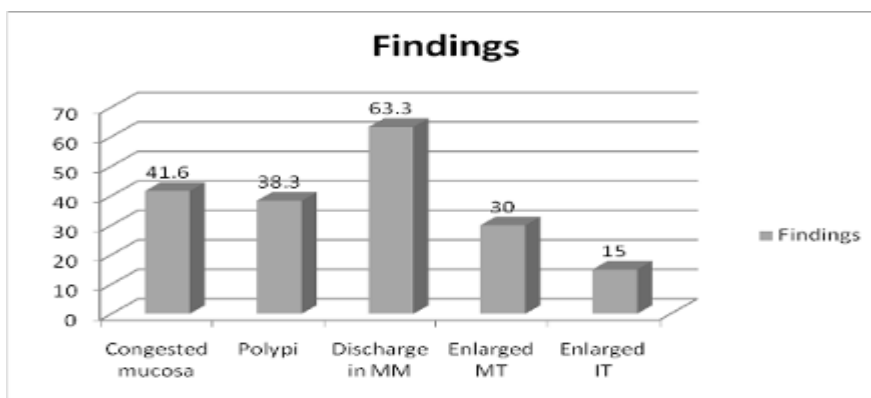


Figure (10): Pre-operative endoscopic finding

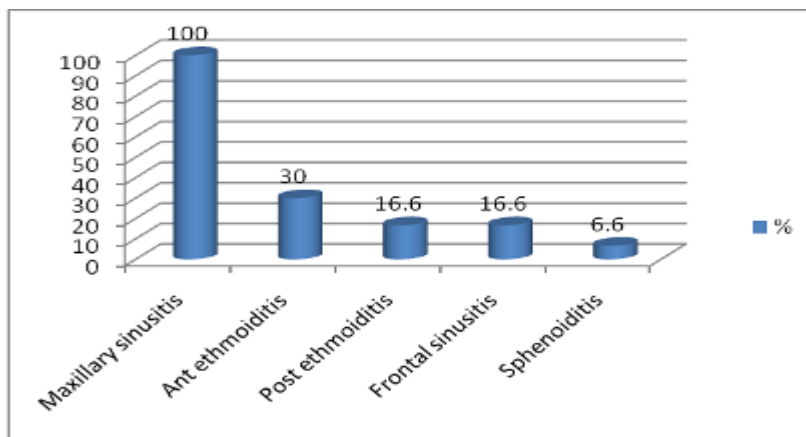


Figure (11): Pre-operative C.T finding in patients of our study

Table (1): Subjective assessment of the patients 3 months after F.E.S.S

Symptoms		Study(n=60)		Control (n=60)		Total		X2 test	P value
		No	%	No	%	No	%		
Nasal obstruction	+VE	10	16.7	29	48.4	19	31.7	6.24	0.01 S
	-VE	50	83.3	31	51.7	41	68.3		
Ant nasal discharge	+VE	6	10.0	26	43.4	15	25.0	5.69	0.02 S
	-VE	54	90.0	34	56.7	45	75.0		

Table (2): Endoscopic assessment of the patients one month after F.E.S.S

Findings		Study side (n=60)		Control side (n=60)		Total		X2 test	P value
		No	%	No	%	No	%		
Adhesion	+VE	13	21.7	20	33.3	33	28.3	0.739	0.4 NS
	-VE	47	78.3	40	66.7	87	71.7		
Crusts	+VE	9	15	14	23.3	23	20	0.417	0.52 NS
	-VE	51	85	46	76.7	97	80		
Unhealthy mucosa	+VE	10	16.7	12	20.0	22	18.3	0.111	0.74 NS
	-VE	50	83.3	48	80.0	98	81.7		
Maxillary Ostium restenosis	+VE	5	8.3	20	33.3	25	21.7	3.535	0.1 NS
	-VE	55	91.7	40	66.7	95	78.3		

Table (3): Endoscopic assessment of the patients 2 months after F.E.S.S

Findings		Study side (n=60)		Control side (n=60)		Total		X2 test	P value
		No	%	No	%	No	%		
Adhesion	+VE	7	11.7	25	41.7	32	26.7	4.176	0.04 S
	-VE	53	88.3	35	58.3	88	73.3		
Crusts	+VE	9	15	13	21.7	22	18.3	0.111	0.52 NS
	-VE	51	85	47	78.3	98	81.7		
Unhealthy mucosa	+VE	6	10.0	15	25	21	16.7	1.08	0.3 NS
	-VE	54	90.0	45	75.0	99	83.3		
Maxillary Ostium restenosis	+VE	4	6.7	30	50.0	34	28.3	11.82	0.001 HS
	-VE	56	93.3	30	50.0	86	71.7		

Table (4): Endoscopic assessment of the patients 3 months after F.E.S.S

Findings		Study side (n=60)		Control side (n=60)		Total		X2 test	P value
		No	%	No	%	No	%		
Adhesion	+VE	7	11.7	27	45	34	28.3	5.25	0.02 S
	-VE	53	88.3	33	55	86	71.7		
Crusts	+VE	7	11.7	15	25	22	13.3	0.73	0.2 NS
	-VE	53	88.3	45	75	98	86.7		
Unhealthy mucosa	+VE	8	13.3	17	28.3	25	18.3	0.94	0.2 NS
	-VE	52	86.7	43	71.7	95	81.7		
Maxillary Ostium restenosis	+VE	4	6.7	30	50.0	34	28.3	11.82	0.001 HS
	-VE	56	93.3	30	50.0	86	71.7		

Table (5): Relation between adhesions and recurrence of rhinosinusitis symptoms

Recurrent symptoms of Rhinosinitis	Adhesions		No adhesions		Total		Z test	P value
	No	%	No	%	No	%		
Present	13	76.5	4	23.5	17	100.0	1.73	0.042 S
Absent	4	9.30	39	90.70	43	100.0	13.4	0.001 HS
Total	17	28.3	43	71.7	60	100.0	4.47	0.001 HS

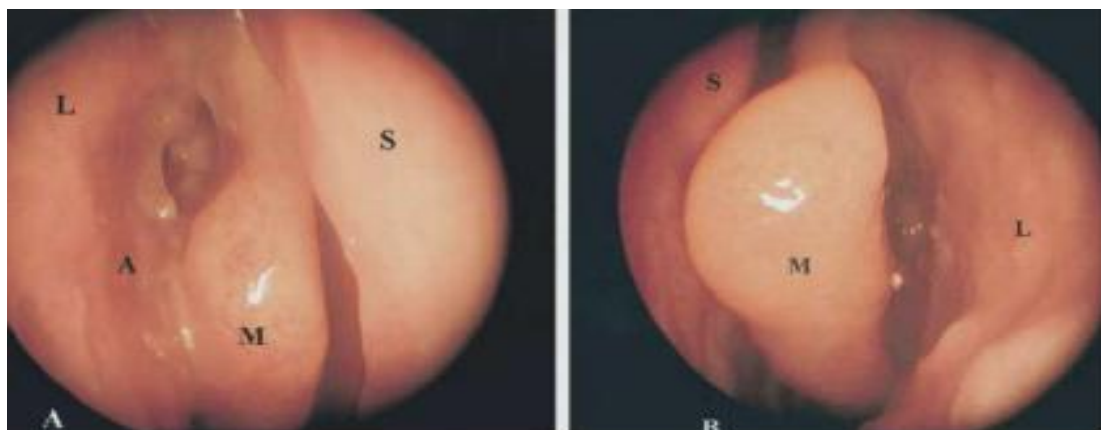


Figure (13): Endoscopic view of the control, *right side (A)* and the Mitomycin C–treated, *left side (B)* 3 months after sinus surgery. An adhesion (A) is noted in the right middle meatus (L, lateral nasal wall; S, septum; M, middle turbinate).

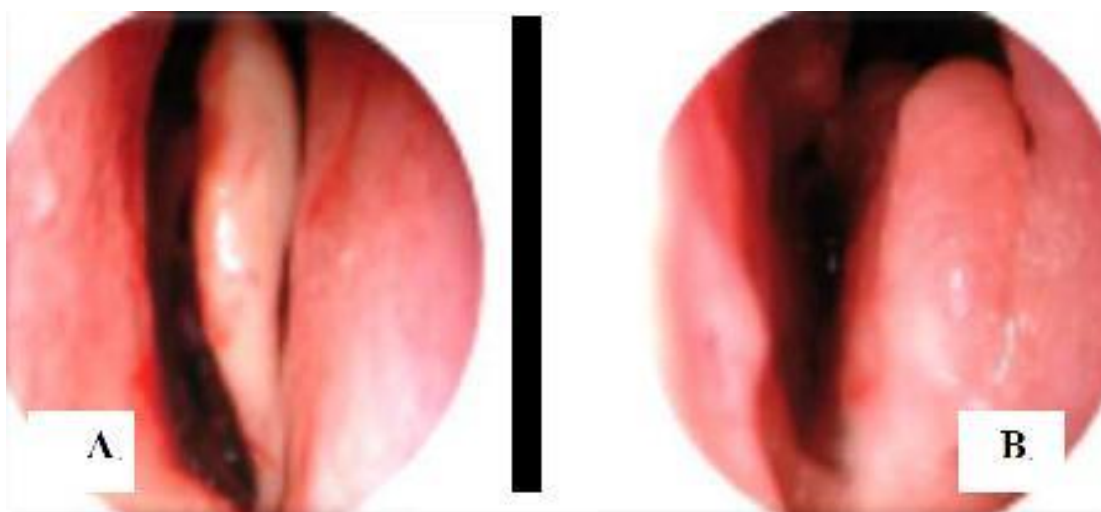


Figure (14): Endoscopic view of the study side (*left side*)

(A) No adhesions are noted in the left middle meatus one month after surgery.

(B) Adhesions presented 3months later on in the same side.

DISCUSSION

Sinusitis is one of the most common health care problems in the world, and there is evidence that it is becoming more prevalent and the incidence of infection. Functional laparoscopic sinus surgery (FESS) was accepted as Messerklinger as the choice of treatment method for chronic sinus disease. Although there is progress in surgical devices and technique, postoperative adhesions, the formation of synechia continues to occur between 1-27%. The occurrence of adhesions requiring surgical intervention is 1-2% ⁽¹⁰⁾.

Synechia formation and ostial stenosis are common following FESS with a reported incidence of 1–36%. Prevention of formation of adhesions and synechia begins in the operating room. Meticulous removal of bone splinters and avoiding mucosal stripping will help to avoid stenosis and synechia. Also the use of the modern microdebriders preserves

the mucosa and minimizes the presence of bone fragments and remnant tissues⁽¹¹⁾.

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 laryngotracheal stenosis, and as an adjunct to FESS to prevent closure of the maxillary sinus antrostomy⁽¹²⁾.

Konstantinidis *et al.*⁽¹³⁾ assessed the efficacy of MMC using a two-stage application procedure allowing a more prolonged effect on the mucosa of the middle meatus. Wound healing in the postoperative period after endoscopic sinus surgery is a prolonged and complex process mediated by several cell types. Although this period can be long and stenosis has been reported years after surgery, the first 6-8 weeks up to 3 months are the most important.

They worked at the end of endoscopic surgery for chronic rhinosinuitis and four weeks postoperatively 30 patients received a pledget soaked with 1ml of mitomycin C (0.5 mg/ml) in the middle meatus for 5 minutes while a pledget soaked in saline was placed in the contralateral side. Patients were assessed at least 6 months postoperatively by a blinded observer for the presence of synechiae and antrostomy stenosis. Medical records were reviewed for episodes of recurrent sinusitis.

Results: Adhesions were observed in 8 patients. All adhesions rated as moderate to severe (4 patients) were observed in the control side ($p = 0.043$). Restenosis was observed in 2 sides treated with mitomycin C and in 9 control sides ($p = 0.032$). Recurrent symptoms of sinusitis occurred in three patients on the saline side they conclude that Mitomycin C is safe and effective in the prevention of severe adhesions and antrostomy stenosis when applied twice, during surgery and the early postoperative period.

Harugop *et al.*⁽⁷⁾ determined whether topical application of Mitomycin C after FESS decreases the incidence of postoperative adhesion formation in 42 patients (22 male, 20 female) between the ages 17 to 66. The mean age was 32.3 ± 11.95 years.

In our study, bilateral nasal obstruction was presented in 46 patients (76.6%), anterior nasal discharge was presented in 22 patients (36.6%), posterior nasal discharge was presented in 18 patients (30%), headache was presented in 40 patients (66.6%) and facial pain was presented in 12 patients (20%).

In the study done by **Harugop *et al.*⁽⁷⁾**, all 42 (100%) patients presented with nasal obstruction and in 40 patients it was of more severe nature (\geq grade 3). The other symptoms in order of frequency of presentation were - facial pain in 29 (69%), nasal discharge in 32 (76.1%) and smell disturbance in 8(19.4%) patients.

Our study showed subjective assessment of patients 3 months after F.E.S.S : nasal obstruction presented in only 10 patients on the study side (16.7%) and 29 patients on control side (48.4%) with significant P value (0.01) also ant nasal discharge presented in only 6 patients on study side (10%) and 34 patients on control side(56.7%) with significant Pvalue (0.02).

In the study done by **Harugop *et al.*⁽⁷⁾**, when assessed 3 month post-operatively, facial pain was relieved in 28(96.6%) of 29 patients, nasal obstruction was improved in 41(97.6%) of 42 cases and nasal discharge was improved in 28(87.5%) of 32 patients. Out of 8 cases of hyposmia, 4 cases had improvement in severity and 4 cases had no improvement.

The second application of MMC in our study was performed 4 weeks postoperatively. Intraoperative and postoperative use of topical Mitomycin C in concentration 0.4 and 0.8 mg/ml applied over 5 min have been shown to decrease adhesion formation in patients undergoing FESS. This study shows the effect of Mitomycin C in prevention of synechiae formation and closer of ostiomeatal complex. They found the more the concentration of MMC, the better the result.

In our study, a piece of cotton soaked in 1 ml of MMC in a concentration of 0.5 mg/ml was placed in left middle meatus and another piece soaked in saline was placed in the right side. After a period of 5 minutes, the cotton pieces were removed and the nasal cavity was irrigated with 30 ml of sterile normal saline.

This methodology was useful to avoid bias as each patient served as his or her own control. The MMC application was repeated in the same side of the nose four weeks postoperatively under local anaesthesia and with the use of an endoscope.

Rahal *et al.*⁽¹⁴⁾ showed a decrease in the incidence of stenosis of surgically created maxillary antrostomies in a rabbit model. Histological analysis in these studies also indicated decreased fibroblast proliferation but a rapid return of normal respiratory epithelium after topical Mitomycin C application. The latter study also showed a dose response effect with antrostomy closure by 1 week in 0.04-mg/mL group, 4 weeks in the 0.4-mg/mL group, and 12 weeks in the 1-mg/mL group.

In our study, the results were assessed depending on endoscopic evaluation rather than histological one.

Kim *et al.*⁽⁴⁾ performed a double blind randomized clinical trial on 38 patients with maxillary sinus mucocel, at the end of endoscopic antrostomy, they used topical MMC and concluded that topical MMC is useful in prevention of stricture of maxillary sinus.

We had overall 34 adhesions 27 of them at control side and 7 of them at mytomycin c side with significant Pvalue {0.02}

Harugop *et al.*⁽⁷⁾ Performed FEES on 23 patients bilaterally and 19 patients unilaterally thus making total of 65 sides of surgery. Out of these 65 procedures uncinectomy was done in 64(98.5%), middle meatus antrostomy with osteomeatal clearance was done in 62 (95.4%), total ethmoidectomy was done in 33 (50.7%), anterior ethmoidectomy was done in 15 (23.1%), frontal recess clearance in 18 (27.7%), sphenoid sinus clearance in 21 (32.3%). Additional procedures done were septoplasty in 19 patients and turbinoplasty/

partial resection of middle turbinate in 16 cases on each side.

The relation between adhesions and recurrence of rhinosinusitis symptoms revealed that adhesions were presented in 34 sides (28.3%) 27 (79.4%) of them had recurrence of rhinosinusitis symptoms while no adhesions presented in 86 sides (71.7%) mostly on mitomycin c sides only 7 (20.5%) of them had recurrence of these symptoms with significant P value (0.001).

Whether more applications of Mitomycin C will offer more benefit is controversial issue. **Darzi and Chowdri**⁽¹⁵⁾ had shown that other topical or injected drugs such as Triamcinolone and 5-fluorouracil have also been used presenting moderate symptomatic relief, but final results referring to scar reduction are not always satisfactory.

In our study, no systemic or local side effects from topical application of intranasal Mitomycin C were reported.

At the completion of sinonasal surgery when injured surfaces are in close proximity, the regenerating epithelium and fibrous tissue may grow between these surfaces creating an adhesion. Attempts to limit such adhesion formation with anatomical barriers have met with limited success⁽¹²⁾.

Baradaranfar et al.⁽¹⁶⁾ investigated the effect of MMC in reducing scar formation and adhesion in the nasal mucosa after endoscopic nasal surgery. This double blind randomized clinical trial study was performed on 37 patients with bilateral chronic rhinosinusitis. At the end of FESS, randomly impregnated mesh with MMC was placed in one side and another mesh impregnated with saline in the opposite side for 5 minutes. Patients were followed at least for three months. They showed that 32.4% had adhesions, among these 10.8% were on MMC side and 27% were on control side which shows the beneficial effect of MMC in prevention of adhesions. They concluded that MMC may be effective in reducing adhesions after FESS, but they failed to show any statistical difference.

Studies by **Venkatraman et al.**⁽¹⁷⁾ and **Singh et al.**⁽¹⁰⁾ determined the role of MMC in preventing synechia formation and ostial stenosis following endoscopic sinus surgery. They showed decreased incidence of adhesions, improvement in symptoms and decreased adverse tissue reactions (like discharge, polypoidal mucosa, crusting) after topical MMC application and more the concentration of MMC, better the results. They concluded that Mitomycin-C applied topically following endoscopic sinus surgery was helpful in improvement of symptoms like nasal obstruction and hyposmia as well as decreased adhesion rate and middle meatal

antrostomy closure rate. Topical application of Mitomycin-C was safe in a dose of 0.4–0.8 mg/ml applied over 5 min and offered significant improvement both subjectively and objectively.

On the other hand Yamaoka and Gregório⁽¹⁸⁾ assessed the effectiveness of mitomycin C in humans to prevent synechia after functional endoscopic sinus surgery in humans. Among 11 included studies, most studies used Mitomycin C dose of 0.4–0.5 mg/mL 1–5 mL in the middle meatus for 5 min duration. Eight studies reported synechiae with 281 and 281 nasal cavities received Mitomycin C and saline, respectively. For outcome of nasal synechiae, a multivariate meta-analysis suggested that mitomycin c was associated with a 66% (RR = 0.34, 95% CI: 0.18–0.65) lower risk of nasal synechiae with moderate heterogeneity (I² = 43%, 95% CI: 0–77%). Subgroup analyses by age and history of revision could reduce the degree of heterogeneity. Mitomycin C benefits were found in subgroups of age 40 years (RR = 0.27, 95% CI: 0.05–1.50) and patients without any history of revision (RR = 0.19, 95% CI: 0.06–0.58). Five studies with 134 and 140 nasal cavities for Mitomycin C and saline were included in pooling of maxillary sinus ostium stenosis. Mitomycin C was associated with 74% (RR = 0.26, 95% CI: 0.12–0.54) lower risk of maxillary sinus ostium stenosis when compared with saline with low heterogeneity (I² = 5%, 95% CI: 0–85%). There was no evidence of publication bias for both poolings. Conclusion: Applying Mitomycin C topically after endoscopic sinus surgery could reduce the risk of nasal synechiae and maxillary sinus ostium stenosis in short term by 66% and 74%, respectively. The treatment effects may be more beneficial in patients aged 40 years or younger or in patients without history of revision. However, the present study showed that a significant improvement was found at study side with p value (0.01).

They concluded that mitomycin C was not effective in preventing postoperative synechiae in patients submitted to functional endoscopic sinus surgery. However the present study showed that significant improvement was found in study side with P value (0.02).

Venkatraman et al.⁽¹⁹⁾ used mitomycin C to reduce post-operative complications following endoscopic sinus surgery in a prospective, randomized controlled trial involving 50 patients with chronic bilateral rhino sinusitis. On completion of the surgery, a cotton pledget soaked in Mitomycin C was placed in one nostril (test) and saline-soaked pledget (control) was placed in the other side of the nose, both in the middle meatus. The side of the nasal cavity receiving the topical Mitomycin C was

randomized. The patients were assessed periodically (first week, first month, third month and sixth month) for synechia formation and presence or absence of their symptoms. At the first week follow up, there was a statistically significant difference in the incidence of synechia between the saline and Mitomycin C side. Furthermore, there was a statistically significant improvement with regards to patient symptoms (nasal block and discharge) in the Mitomycin C side when compared to the saline side. At the third and sixth month, there was no difference between the two groups. The incidence of adverse tissue reaction (granulation, discharge, polypoidal mucosa and crusting) was less in the Mitomycin C side when compared to the saline side at the first month follow up. Topically applied Mitomycin C reduces the incidence of synechia in the immediate post-operative period in patients undergoing endoscopic sinus surgery. There is also an improvement in nasal obstruction and discharge with a reduction in the incidence of adverse tissue reaction in the early post-operative period. One of the limitations of the present study was the duration of the follow up long term (more than 6 months) is advised to evaluate the result of **Venkatraman et al.**⁽¹⁹⁾.

Harugop et al.⁽⁷⁾ concluded that Chronic Rhino Sinusitis (CRS) patients have remarkable improvement in their symptoms after FESS. Topical application of Mitomycin-C at the conclusion of FESS has a role in prevention of adhesion formation.

CONCLUSION

Topical application of MMC at end of FESS has beneficial role in prevention of adhesion formation and synechia without any side effects/complications. Further trials with good research methodology and long-term follow-up should be conducted to confirm our research.

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