



Mitomycin C For the Treatment of Chronic Rhinosinusitis Adhesion Formation Following Functional Endoscopic Sinus Surgery

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ABSTRACT

BACKGROUND:

Endoscopy can be used in a variety of ways to treat patients with sinonasal symptoms and is crucial to the preoperative and postoperative care of patients. In the last 20 years, fibre optic technology has made significant advancements in our understanding of how to investigate the nasal cavity. Nasal endoscopy can be performed with both rigid and flexible endoscopes, however rigid endoscopes have the advantage of a larger field of view, better clarity, and the capacity to utilise an additional hand for apparatus. A flexible endoscope may be able to provide better visibility of the maxillary sinus floor or the lateral recess in the frontal sinus in some circumstances, especially in postoperative patients. In the context of benign sinus disease, FESS has provided the requirements for sinus imaging. Endoscopic sinus surgeons should have a precise understanding of both normal and aberrant anatomy in order to perform sinus surgery as effectively and securely as possible.

AIM: The purpose of this study is to determine whether mitomycin-C can prevent adhesions from forming during functional endoscopic sinus surgery (FESS) in patients with chronic rhinosinusitis (CRS). to contrast group A's with group B's symptomatic improvement following FESS.

MATERIAL AND METHOD:

The current study used a "clinical trial-static group comparison" study design, which is a style of research that includes patients from two groups. Before beginning the trial, the groups were similar in the majority of fundamental aspects; one group received a novel kind of treatment, while the other received a more conventional one. Both groups' results were compared at the end of the study period, and any differences resulting from the new treatment were documented. 100 patients make up the current trial, 50 of whom are in Group A (Interventional-MMC) and 50 of whom are in Group B. (Control-Saline). According to the parameters of the study's design, the groups were comparable in terms of age, sex, symptoms, pre-operative CT score, and pre-operative endoscopic grading.

RESULTS:

However, there was a statistically significant difference between groups A and B regarding the overall symptom score from pre- to post-operative. In terms of improvement in facial pain from pre-operative to post-operative, there was a statistically significant difference between groups A and B. In terms of nasal blockage from pre-operative to post-operative, there was a statistically significant difference between groups A and B. In terms of nasal discharge from pre-operative to post-operative, there was no statistically significant difference between groups A and B. In terms of hyposmia from pre-operative to post-operative, there was no statistically significant difference between group A and group B.

CONCLUSION:

To sum up, the topical use of MMC following FESS was beneficial and played a clear effect in lowering the incidence of postoperative adhesion development. The severity of postoperative adhesions was decreased by topical MMC administration. After applying MMC, it was discovered that the rate of adhesion development had drastically decreased compared to the estimate.

KEYWORDS: Chronic Rhino-Sinusitis, Nasal polyps, functional endoscopic sinus surgery, quality of life, Mitomycin-C, Dacryocystorhinostomy.

INTRODUCTION

Early in the 16th century in Bologna, anatomist and surgeon Berenger del Carpi gave the first definitive proof of the paranasal sinuses' (PNS) existence. Since the time of Hippocrates in 5BC, the existence of sinus infections and potential treatments have likely been known.¹ With a lifetime frequency of about 15%, chronic rhino-sinusitis (CRS) is a clinical illness that is exceedingly prevalent.² Up to 30 million Americans may have CRS, and more than 200,000 sinus surgeries are carried out each year.³ According to the Integrated Health Interview Series for 1997–2006, 55.8% of sinusitis patients spend more than \$500 a year on medical care, which is more than those with chronic illnesses do. According to survey data from 2006, people with sinusitis miss an average of 5.67 working days each year owing to illness, compared to 3.74 days for people without sinusitis.^{4,5}

About 134 million people in India suffer from sinusitis, which can cause headaches, fever, nasal blockage, and congestion. According to the National Institute of Allergy and Infectious Diseases (NIAID), chronic rhinosinusitis affects 1 in 8 Indians and is more common than diabetes, asthma, or coronary heart disease.^{6,7} Recent research reveals that the clinical and pathological subgroups of CRS without polyposis and CRS with polyposis may be different.⁸ Although it is generally agreed that classifying CRS based on whether nasal polyps are present or absent is important from both a clinical and research perspective, the precise impact of NP on treatment outcomes is not clearly described in the literature.⁹ Functional endoscopic sinus surgery (FESS), developed by Messerklinger, has been acknowledged as the gold standard for treating chronic sinusitis since it preserves the mucosal lining of the sinuses, aids in sinus ventilation and drainage through natural apertures, and removes pathology.^{10,11} Patients may have significant advantages in terms of reduced symptom severity and enhanced quality of life.¹²

Due to a reduction in sinus ventilation and mucus outflow, postoperative adhesions of the middle meatus may result in lingering symptoms (postnasal drip, etc.). One to two percent of adhesions require surgical treatment. Adhesions develop between the two wounded surfaces after sinonasal surgery as a result of the formation of fibrous tissue and regenerated epithelium when these surfaces are in close contact. Anatomical barriers have had only sporadic success in preventing the establishment of such adhesions.^{13,14} After separating the adhesion, Stemberger utilised a silastic sheet and hypothesised that synechiae recurrence was not always avoidable. Brennan applied a Boomerang turbinate glove made of medical-grade polyurethane and observed no major adhesions but encountered foreign body reaction. Weymuller

medialized the middle turbinate by maintaining a prolonged pack on the operated site, which caused airway obstruction and decreased olfaction. After FESS had its own limits, numerous attempts were undertaken to prevent adhesion formation.¹⁵ In order to prevent adhesion formation following FESS, a material that can be applied quickly, is affordable, and has no application-related issues has been sought after for years. MMC has been tested in otolaryngological operations and appears to be a promising anti-scarring agent for use in ophthalmological procedures.¹⁶ After conducting a thorough literature search on the subject of MMC in FESS, the results only included 4 articles from around the world and 1 prospective research from India. Three of these articles, with positive findings, support the topical administration of MMC, whereas one study is against its usage. According to this perspective, there is discussion and scepticism about the involvement of topical MMC in the prevention of adhesion development following FESS, and additional research in this area is necessary to clarify this issue.

MATERIAL AND METHODS

The current study, was carried out in the Department of Surgery by using a "clinical trial-static group comparison" research method, which involves including individuals in two groups. Before beginning the trial, the groups were similar in the majority of fundamental aspects; one group received a novel kind of treatment, while the other received a more conventional one. Both groups' results were compared at the end of the study period, and any differences resulting from the new treatment will be documented.¹⁷

100 patients make up the current trial, 50 of whom are in Group A (Interventional-MMC) and 50 of whom are in Group B. (Control-Saline). According to the parameters of the study's design, the groups were comparable in terms of age, sex, symptoms, pre-operative CT score, and pre-operative endoscopic grading. The study comprised patients undergoing FESS who had endoscopic profiles of Chronic Rhino-Sinusitis (CRS), clinical pre-operative CT scans, and these diagnoses.

The study was carried out at a hospital, and all participants received consistent documentation of their clinical characteristics, any necessary surgery, and follow-up protocol in accordance with the standard operating procedure (SOP). The follow-up time ranges from three to twelve months. As per the protocol, the minimum follow-up is three months. The institutional ethical committee approved the study. All patients provided written, informed permission in the languages of Kannada, Marathi, and English about the procedure in accordance with the proforma and standard operating procedure (SOP) accepted by the institution's ethical committee.

Inclusion criteria:

- Patients with features suggestive of CRS with or without Nasal Polyposis (NP), willing to undergo a CT scan of paranasal sinuses (PNS) and FESS were included in the study.

Exclusion criteria:

- Patients with acute exacerbation of symptoms
- Established asthma and suspected cystic fibrosis
- Patients refusing to undergo CT scan PNS
- Patients with established or impending complications
- Patients refusing endoscopic surgery
- Patients with prior sinus surgeries were excluded from the study.

In Group A, there were 20 unilateral and 30 bilateral sides, for a total of 80 operational sides. The age range for this group ranged from 18 to 70 years. Similar to Group A, Group B had an age range of 18 to 70 years, 20 unilateral sides, and 30 bilateral sides, for a total of 80 operating sides. Light anterior nasal packing was performed after the procedure using ribbon gauze that had been soaked in steroid and antibiotic ointment. Next pack removal, all patients received oral antibiotics for two weeks, nasal saline rinses three times per day,

and topical steroid spray twice per day for three weeks in each nasal cavity before being released from the hospital the following day.

STATISTICAL ANALYSIS

Following data collection, the data were analyzed using SPSS-20 using the statistical techniques listed below: For numerical variables, the mean and standard deviation are used. Unpaired t-test: Applied to compare the mean scores of the two groups. Coupled t-test. used to assess meaningful change in each group at several time points. By Mann-Whitney U test: Used to compare two groups when the results are categorical. To compare the various time points in each group with the category result, use the Wilcoxon matched pairs test. Chi-square test: utilized to evaluate the relationship between two characteristics.

RESULT: -

After screening 300 sinusitis patients over the study period, the sample size for the study was determined. 100 patients in total were chosen based on both inclusion and exclusion criteria, and they were then split into two groups, each of which contained 50 patients and 80 operating sides.

Table 1: Patients of CRS with NP and CRS without NP

Group	CRS with NP	Percentage	CRS without NP	Percentage
Group-A	12	18.66%	35	81.33%
Group-B	13	24%	15	76%

In the present study out of 100 patients, 25 (21.33%) patients had manifested with nasal polyps, and 25 (78.66%) presented without nasal polyposis. In group-A out of 50, CRS with NP was 1,2 and CRS without NP were 35 patients. In group B, CRS with NP was 13, and CRS without NP was 15 patients

Table 2: Comparison of symptoms in Pre-op and Post-op scores between groups

	Group A	Group B
Pre-op	4.3 ± 1.36	6.2± 1.54
Post-op	1.4± 0.83	1.3± 0.66
Pre-post op difference	-4.5 ± 1.83	-4.7± 1.06

Preoperative mean symptoms scores for groups A (4.3± 1.36) and B (6.2± 1.54) were greater than postoperative scores for groups A (1.4± 0.83) and B (1.3± 0.66) in both groups. During the preoperative phase and the transition from the preoperative to the postoperative period, there was no statistically significant difference between group A and group B. This means that in terms of symptomology, both groups were comparable prior to surgery. Similar clinical results were seen in both groups.

Table 3: Comparison of two groups with pre- and post-operative symptom scores by Mann-Whitney U test

Variables	Time	Group A	Group B
Symptom Total score	Pre-op	5.42 ±2.46	6.21 ±74.19
	Post-op	1.75± 0.83	1.22 ±77.59
Facial pain/ pressure	Pre-op	1.66 ±1.2	2.32± 82.64
	Post-op	0.34 ±0.2	0.78± 85.55
Nasal Obstruction	Pre-op	2.41 ±1.21	2.63± 70.85
	Post-op	0.80± 0.3	0.88± 79.48
Nasal Discharge/ Ant / Post	Pre-op	1.69± 1.3	1.82± 71.94
	Post-op	0.48± 0.40	0.42 ±62.01
Hyposmia	Pre op	0.17 ±0.5	0.05 ±67.03
	Post-op	0.16 ±0.62	0.03 ±61.82

The difference in the total symptom score between groups A and B from pre- to post-operative was statistically significant, nonetheless. In terms of improvement in facial pain from pre-operative to post-operative, there was a statistically significant difference between groups A and B. In terms of nasal blockage from pre-operative to post-operative, there was a statistically significant difference between groups A and B. In terms of nasal discharge from pre-operative to post-operative, there was no statistically significant difference between groups A and B. In terms of hyposmia from pre-operative to post-operative, there was no statistically significant difference between group A and group B.

DISCUSSION

Patients between the age group of 18-70 years were included in the study. The selection of this age group was based on the knowledge that sinus pneumatization is known to occur throughout adolescence. In a study by **Chopra H et al (2006)**¹⁸ the mean age of presentation was 35 years with the age range of 5-65 years. In a study by **Chung J H et al (2002)**¹⁹ the age range was 21-75 years with a mean age of 44.5 years.

The various studies on CRS show variations in the sex distribution of patients. Some studies show male preponderance and few studies show female preponderance. Therefore, there is no consensus opinion about the sex-wise involvement of CRS but there is an inclination towards male preponderance as per the available literature. In a study by **Chung J H et al (2002)**¹⁹ there was an almost equal distribution of cases amongst sexes- 27 males and 28 females. In a study by **Baradaranfar MH et al(2010)**¹⁰ had more males (60.5%) and fewer female (40.5%) patients.

A study by **Tilakraj Singh et al (2011)**²⁰ showed middle meatal antrostomy and ethmoidectomy were commonly performed procedures (60 in each group). Next in order was sphenoidotomy (30 in one and 20 in another group). Frontal sinus surgery was done in the least number of patients (10 in each group). A study by **Nair S et al (2011)**²¹ showed that laminectomy and middle meatal antrostomy were the procedures done in all the cases. Other procedures were done according to disease involvement.

In CRS, the maxillary and ethmoid sinuses were frequently implicated, and middle meatal antrostomy with maxillary sinus clearing and ethmoidal clearance were the most frequently done surgeries, as shown by the comparison of the aforementioned studies with the current study. The frontal and sphenoid sinuses were the least impacted sinuses in CRS, as seen by the lower volume of frontal sinus and sphenoid sinus disease clearing procedures.

In a study by **Chopra H et al (2006)**¹⁸ showed septoplasty done in 11 patients. The middle turbinate concha bullosa and paradoxical curved middle turbinate

were found in 26% of patients, these may require canthoplasty or resection. A study by **Gupta M et al(2006)**¹⁷ showed deviated nasal septum in 30% of patients and paradoxical middle turbinate and concha bullosa in 37% of patients. These patients may require septoplasty or canthoplasty or resection. In a study by **Baradaranfar MH et al (2011)**¹⁰ showed 14 adhesions of which- 2 were type A, 7 were type B, 1 type C, and 4 were type D and out of these 14 adhesions 1 was severe and the rest 13 were mild, and without interfering in direction of sinus drainage. In comparison with the study by **Baradaranfar MH et al (2011)**¹⁰ our study had a smaller number of type B and C adhesions and more of type A adhesions and this could be attributed to the fact that **Baradaranfar MH et al (2011)**¹⁰ included revision cases also in their study but revision cases were excluded in the present study.

A study by **Gupta M et al (2006)**¹⁷ showed polypoidal mucosa in 10% of cases on the control side and 3% of cases on the MMC side. Similarly, the study by **Venkatraman V et al (2011)**²² showed decreased incidence of adverse tissue reactions like polypoidal mucosa on the MMC side as compared to normal saline. Thus, MMC has a role in reducing the incidence of polypoidal mucosa in the postoperative period after FESS as per the above two studies, however, the present study did not support this possible role of MMC.

A study by **Gupta M et al (2006)**¹⁷ showed the rate of discharge at 30% on the control side as compared to 7% on the MMC side. Similarly, the study by **Venkatraman V. et al (2011)**²² showed decreased incidence of adverse tissue reactions like discharge on the MMC side as compared to normal saline. Thus, MMC has a role in reducing the incidence of discharge in the postoperative period after FESS.

Netkovski J et al (2006)²³ in their study showed improvement in nasal obstruction in 87%, post nasal discharge in 74.3%, anterior nasal discharge in 70.5%, headache in 59.4%, and hyposmia in 58.7% of the patients. A study by Hemant **Chopra et al (2006)**¹⁸ showed improvement in all symptoms especially nasal obstruction (83%) and nasal discharge (86%). Overall, there was a marked improvement in symptoms after FESS in 70% of patients. A study by **Venkatraman V et al (2011)**²² observed statistically significant improvement in nasal obstruction and discharge on the MMC side as compared to saline sides.

A study by **Pynnonen et al (2009)**²⁴ and **Browne JP et al (2007)**²⁵ have shown that SNOT-20 is the most widely used quality-of-life instrument for sinonasal conditions and validation studies have supported dividing SNOT into four domains namely- rhinology, ear & facial, sleep and psychological domains. The two constructs (rhinology, ear & facial domains) address symptoms

and two others (sleep and psychological domains) address aspects of health-related quality of life.

CONCLUSION:

In conclusion, topical MMC treatment after FESS was beneficial and played a clear role in lowering the rate of postoperative adhesion development. The types of postoperative adhesions could be reduced with the topical MMC treatment. Following the application of MMC, a markedly greater reduction in adhesion development was observed than was predicted. In the immediate preoperative and postoperative periods, topical MMC applications. This requires more analysis.

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