A study on role of topical application of mitomycin c postoperatively in reducing adhesions/synechiae after FESS in patients with chronic rhinosinusitis: A Randomized controlled trial

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ABSTRACT

Introduction: Synechiae formation is a common and undesired complication after functional endoscopic sinus surgery. Mitomycin-c, known for its anti-proliferative and anti-fibroblastic properties holds potential for reducing synechiae and scar tissue formation following endoscopic sinus surgery. This study aims to evaluate the efficacy of topically applied mitomycin-c postoperatively in minimising adhesions and nasal obstruction symptoms using the Lund-Kennedy Endoscopic Scoring and Nasal Obstruction Symptom Evaluation (NOSE) scores.

Materials And Methods: This double-blind randomised study assessed topical mitomycin-c's efficacy in reducing adhesions post-FESS in 50 chronic rhino-sinusitis patients. Participants who were selected based on Lund-Mackay CT scores underwent functional endoscopic sinus surgery (FESS). The mitomycin-c and saline-soaked nasal packs were placed in middle meatuses either of one in each nasal cavity. Postoperative care included antibiotics, analgesics and saline douching. Outcomes were evaluated at 1, 4 and 12 weeks using the NOSE (nasal obstruction symptom evaluation) questionnaire and Lund-Kennedy scoring to determine mitomycin-c's impact on nasal obstruction and synechiae formation.

Results: The results indicated statistically significant variation between mitomycin-c and control sides in terms of symptoms and endoscopic findings in the first week postoperatively. By the fourth week, the clinical pictures of both sides were nearly identical.

Discussion: Data suggested that low-dose mitomycin-c significantly reduces adhesions and improves nasal symptoms in the early postoperative period for chronic rhinosinusitis patients. These results align with previous research, supporting mitomycin-c as a valuable adjunctive therapy in sinus surgery. Future studies are recommended to explore varying dosages and application methods for potential differences in outcomes.

KEYWORDS:
Mitomycin-c, Synechiae, Lund Kennedy score, FESS, NOSE score

INTRODUCTION

Endoscopic sinus surgery is widely regarded as the preferred treatment for chronic sinus disease. This approach is favoured because it preserves mucosa of sinus, restores ventilation and drainage through sinus ostia and effectively alleviates the pathology.[1] But, synechiae are one of the most common and undesired complications following FESS. Addressing synechiae is crucial as they can obstruct nasal airflow, block ostia, impair mucociliary function and hinder the delivery of topical medications.[2]

Post-surgical care aims to facilitate rapid healing and regrowth of healthy sinus lining by reducing inflammation, preventing infections, improving symptoms, restoring ciliary function, and preventing early complications. Currently, the use of compressible devices to irrigate the nasal passages with a significant volume of saline is standard practice. Performing nasal debridement in the office provides several benefits. However, repeated nasal endo-cleaning and debridement can be a painful procedure and may cause discomfort for patients postoperatively.

Mitomycin-c derived from Streptomyces caespitosus serves as a multifaceted compound with antibiotic, anti-proliferative and antineoplastic properties. Acting as an alkylating agent, it selectively impedes DNA synthesis and disrupts DNA base-pairs contributing to its therapeutic mechanism.[4] By inhibiting protein synthesis, mitomycin-c is known to effectively suppress fibroblast proliferation, reduces fibrosis and decreases vascularity both in vitro and in vivo. Its ability to influence wound healing has led to its application in ophthalmic surgeries where its effects on rapidly dividing cells is particularly beneficial.[5] This same wound-healing effect makes it suitable for application in procedures like FESS as well. It is thus hypothesised that topical application of mitomycin-c postoperatively following FESS can thereby be helpful in reducing crusting/synechiae formation by its anti-fibroblastic, anti-proliferative action and hence minimises the formation of scar tissue post-surgery.

Our objective here is to evaluate the effectiveness of topically applied mitomycin-c in reducing adhesions/synechiae and reducing Nasal Obstruction symptoms using Lund-Kennedy endoscopic scoring and Nasal obstruction symptom

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Inclusion criteria	Exclusion criteria
Age from 18-65 years	Age below 18 and above 65 years
No h/o previous FESS/Nose surgeries	H/o previous FESS/Nose surgeries
Bilateral chronic rhino sinusitis with symptoms refractory to medical treatment (Antibiotics and corticosteroid) given for at least for 3 months.	Acute upper respiratory tract infection, Unilateral Sino nasal disease
Patients with complete osteomeatal unit occlusion on non-contrast CT PNS with ≤2 grades of variation between both nasal cavities on the Lund-Mackay CT scoring and a minimum score of 4 on each side	Uncontrolled diabetes, uncontrolled hypertension, immune compromised status, ciliary motility disorders, cystic fibrosis, known autoimmune disorders.
	Sino nasal tumours, Mass, Malignancy, Gross DNS

evaluation score (NOSE) postoperatively after FESS. The focus of this study is to reduce the repeated need for hospital visits for nasal debridement post-surgery. This goal underscores the purpose of this research to ensure a seamless postoperative recovery.

MATERIALS AND METHODS

This is a prospective, comparative, double-blinded randomised controlled study that involved patients diagnosed with bilateral chronic rhino sinusitis presented to the Otorhinolaryngology outpatient department.

Following approval from the Institutional Ethics Committee (IEC-129/06/2023/IEC/SMCH), the study was commenced for a duration of 12 months (June 2023- June 2024).

The sample size was calculated with a power of 90% and a 5% alpha error, resulting in 44 participants. To accommodate a 10% attrition rate, the study required 48 samples, rounded up to 50.

Sample size: 50

Fifty participants with bilateral chronic rhino sinusitis who met the study's inclusion and exclusion criteria were chosen to participate. All participants provided informed consent and received detailed information about the planned procedure, post-operative application of mitomycin-c, expected outcomes and potential side effects. Preoperative non-contrast computed-tomography paranasal sinus (CT PNS) was conducted and participants were selected based on Lund-Mackay CT scoring system, ensuring a difference of ≤2 between both sides and minimum score of 4 on each side.

One hundred lots were prepared with fifty labelled "right" and fifty labelled "left". Participants randomly selected a labelled lot ("right" or "left"), determining the intervention side. Both the investigator and the patients were blinded to the selected lot ensuring the study was conducted in a double-blinded manner.

All participants completed a preoperative NOSE (nasal obstruction symptom evaluation) questionnaire and underwent direct rigid nasal endoscopy. FESS with Messerklinger technique under general anaesthesia employing an approach based on the severity and specific anatomical involvement.

After completing FESS, a half Ivalon nasal pack soaked with 1 ml (0.1 mg/ml) mitomycin-c was placed in one middle meatus, half Ivalon pack soaked in 1 ml saline was placed in the other middle meatus. A full saline-soaked Ivalon pack was placed in each nasal cavity followed by dressing. Postoperative care included intravenous antibiotics and analgesics. Bilateral nasal packs were removed on postoperative day 1, nasal douching started on day 2 and diagnostic nasal endoscopy with endo-cleaning was performed on day 3. Patients were discharged the same day with oral antibiotics, analgesics and instructions to continue saline nasal douching three times daily until the next review. All participants were reviewed at 1, 4 and 12 weeks postoperatively. Nasal obstruction symptoms were evaluated in the first week using the NOSE questionnaire. Endoscopic findings scored with Lund-Kennedy scoring (Table I) system at 1st and 4th weeks. Comparing the findings between nasal cavities helped predict mitomycin-c's effectiveness in improving nasal obstruction symptoms and reducing crusting/synechiae formation after FESS.

NOSE questionnaire includes scoring of symptoms like nasal congestion/stuffiness, nasal block, breathing difficulty, nasal obstruction during exertion, trouble sleeping scores as 0 (no symptom),1 (mild), 2 (moderate), 3 (fairly bad), and 4 (severe).

Statistical Analysis: Statistical analysis was conducted using IBM SPSS Statistics version 19. Descriptive statistics such as mean (standard deviation)/median (interquartile range)/median (range) and frequencies (percentages) were used for quantitative and qualitative data, respectively. A paired t-test was applied to compare Lund-Mackay scores between right and left sides of the nose pre-operatively. A $p<0.05$ was considered as significant. Wilcoxon signed-rank test was used to compare the outcome measurements between the interventional and control sides.

In various studies using the Lund-Mackay score on sinus CT scans and the Modified Lund-Kennedy naso-endoscopic score has proven beneficial for categorizing the severity and prognosis of extensive sinus disease.[13] It is said that there exists a noteworthy correlation between these scores, highlighting their utility in clinical practice. The Nasal Obstruction Symptom Evaluation Score (NOSE) is widely recognised for its reliability and ease of use in studying nasal obstruction outcomes among adults. Its effectiveness in

outcome studies underscores its value in clinical assessments and treatment evaluations for nasal obstruction.[14]

Studies stated that there is no clinically significant association between the Lund Mackay and SNOT-22 scores suggesting the need of distinct measures to assess symptom severity and disease impact in chronic rhinosinusitis patients.[15] Various methods have been employed in previous studies to investigate the efficacy of mitomycin c in sinus surgery. In one study participants were divided into two groups where one received a wick with 1 ml of mitomycin-c (0.4 mg/ml), while other received a saline-soaked wick intraoperatively. Facial pain, nasal block, nasal discharge, hyposmia and SNOT-20 scores were evaluated using the Wilcoxon matched pairs test. Post-surgery, conventional nasal packing with steroid and antibiotic ointment was utilized.[8]

RESULTS

Fifty participants were enrolled in the study. Mean age was 33.28 years (standard deviation (SD)=10.144). Ages ranged from 19 to 63 years. The age distribution showed that the majority of the study population were under 30 years, highlighting a predominantly younger age group. Out of 50 participants 15 were female and 35 were male.

The mean Lund Mackey Score was 8.28 (SD=1.196) for the right side and 8.14 (SD=1.069) for the left side. The p-value of 0.431 suggests that there is no statistically significant difference between the scores, suggesting a similar extent of sinus disease on both sides at baseline.

Pre-operative NOSE scores

The mean scores were as follows: nasal congestion/stuffiness 1.84 (SD 0.681), nasal block 1.34 (SD 0.479), breathing difficulty 1.42 (SD 0.609), obstruction during exertion 1.64 (SD 0.693), and trouble sleeping 1.56 (SD 0.577). The total NOSE score had a mean of 7.80 (SD 1.629).

Post-operative NOSE scores

Post-intervention scores showed a significant difference: nasal congestion/stuffiness mean 0.12 (SD 0.328), nasal block mean 0.18(SD 0.388), breathing difficulty mean 0.02(SD 0.141), nasal obstruction during exertion mean 0.16(SD 0.373) and trouble sleeping mean 0.12(SD 0.328). The total NOSE score had a mean of 0.60 (SD 0.782).

The comparison between pre- and post-operative scores shows significant improvement across all variables. Pre-operative scores indicated moderate to severe symptoms with means from 1.34 to 7.80.Post-intervention scores showed a dramatic reduction, with means ranging from 0.02 to 0.60, indicating minimal to negligible symptoms.

This clear contrast highlights the effectiveness of the intervention and underscores the importance of functional endoscopic sinus surgery in enhancing patient outcomes. The substantial decrease in mean scores and reduced standard deviations post-surgery indicates significant improvement in nasal symptoms/before surgery, the Total NOSE scores for both the interventional and control sides were similar with medians of 7.5 and 8, respectively (p=0.251), indicating no significant difference between them. However, by postoperative week 1, the Total NOSE score significantly dropped on the interventional side, in comparison to control side($p<0.001$) suggesting the significant positive impact of intervention in reducing nasal symptoms post-surgery (Table II).

In postoperative week 1, on the control side 84% had no polyps (score 0), 16% had polyps within middle meatus (score 1). 46% reported no discharge (score 0), 44% had thin and clear discharge (score 1) and 10% had thick and mucopurulent discharge (score 2). 20% had no oedema (score 0), 70% had mild oedema (score 1) and 10% had moderate oedema (score 2). 42% had no scarring (score 0), 50% had mild scarring (score 1) and 8% had moderate scarring (score 2) 20% had no cresting (score 0), 60% had mild cresting (score 1) and 20% had moderate cresting (score 2).

Whereas on mitomycin-c side, 98% had no polyps (score 0), 2% had small polyps within middle meatus (score 1). 60% had no discharge (score 0), 38% had mild clear discharge (score 1), and 2% had mucopurulent discharge (score 2). 74% had no oedema (score 0), 26% had mild oedema (score 1). 84% had no scarring (score 0), 16% had mild scarring (score 1). 76% had no cresting (score 0) and 24% had mild cresting (score 1).

On week 1 notable differences were observed in polyp between mitomycin-c and control sides ($p=0.020$), suggesting a notable impact of the intervention on polyp formation early after surgery. Similarly, variables like discharge ($p=0.054$), oedema ($p<0.001$), scarring ($p<0.001$), and cresting ($p<0.001$) showed significant differences. These findings indicated that mitomycin-c side exhibited less discharge, oedema, scarring and cresting compared to the control side during this initial period. The median Total Kennedy score for the mitomycin-c side was 1, while the control side had a median score of 4. The p-value for this comparison is <0.001, indicating a highly significant difference with the interventional group showing much lower scores suggesting better outcomes.

By postoperative week 4, 86% had no polyps (score 0), 14% had minor polyps (score 1). 64% had no discharge (score 0), and 36% had mild clear discharge (score 1). 68% had no oedema (score 0), and 32% had mild oedema (score 1). 92% had no scarring (score 0), and 8% had mild scarring (score 1). 80% had no cresting (score 0) and 20% had mild cresting (score 1).

On the mitomycin-c side100% had no polyps (score 0). 78% had no discharge (score 0), 20% had mild watery discharge (score 1) and 2% had mucopurulent discharge (score 2). 98% had no oedema (score 0) and 2% had mild oedema (score 1). 98% had no scarring (score 0) and 2% had mild scarring (score 1). 94% had no cresting (score 0) and 6% had mild cresting (score 1).

On week 4, the differences in polyp remained significant ($p=0.008$). However, the significance levels for discharge ($p=0.083$), oedema ($p=0.180$), scarring ($p<0.001$) and cresting ($p=0.180$) decreased or became non-significant, suggesting

Table I: Lund-Kennedy endoscopic scoring system

Charecteristics	Score definition
Nasal polyps	0 = none; 1=confined to middle meatus; 2=beyond middle meatus
Discharge	0 = none; 1=clear and thin; 2=thick and purulent
oedema	0=absent; 1=mild; 2=severe
Scarring	0=absent; 1=mild; 2=severe
Crusting	0=absent; 1=mild; 2=severe

Table II: Pre-operative and post-operative week 1 Average Nasal Obstruction Symptom Evaluation (NOSE) scores.

Variables	NOSE score	Interventional Side	Control Side	p-value
Nasal congestion/stuffiness	Pre-op Nose score	2(1,4)	2(1,4)	0.173
	POD 1st week Nose score	0(0,1)	1(0,2)	<0.001
	p-value	<0.001	<0.001	
Nasal Block	Pre-op Nose score	1(1,2)	2(1,3)	0.016
	POD 1st week Nose score	0(0,1)	1(0,2)	<0.001
	p-value	<0.001	<0.001	
Breathing difficulty	Pre-op Nose score	1(1,3)	1(1,3)	0.583
	POD 1st week Nose score	0(0,1)	0(0,1)	0.059
	p-value	<0.001	<0.001	
Nasal obstruction	Pre-op Nose score	2(1.3)	1(1,3)	0.251
	POD 1st week Nose score	0(0,1)	0(0,1)	0.527
	p-value	<0.001	<0.001	
Trouble sleeping	Pre-op Nose score	2(1,3)	1.5(1,4)	0.828
	POD 1st week Nose score	0(0,1)	0(0,2)	0.074
	p-value	<0.001	<0.001	
Total Median (IQR)	Pre-op Nose score	7.5(7,9)	8(7,9)	0.251
	POD 1st week Nose score	0(0,1)	2(1,3)	<0.001
	p-value	<0.001	<0.001	

Table III: Mean Lund Kennedy endoscopic scores on week 1 and 4 postoperatively

Variables	Lund Kennedy	Interventional Side	Control Side	p-value
POLYP	POD 1st week	0(0,1)	0(0,1)	0.02
	POD 4th week	0(0,0)	0(0,1)	0.008
	p-value	0.317	0.317	
DISCHARGE	POD 1st week	0(0,2)	1(0,2)	0.054
	POD 4th week	0(0,2)	0(0,1)	0.083
	p-value	0.003	0.003	
EDEMA	POD 1st week	0(0,1)	1(0,2)	<0.001
	POD 4th week	0(0,1)	0(0,1)	<0.001
	p-value	0.001	<0.001	
SCARRING	POD 1st week	0(0,1)	1(0,2)	<0.001
	POD 4th week	0(0,1)	0(0,1)	0.18
	p-value	0.008	<0.001	
CRESTING	POD 1st week	0(0,1)	1(0,2)	<0.001
	POD 4th week	0(0,1)	0(0,1)	0.008
	p-value	0.003	<0.001	
Total Kennedy score Median (IQR)	POD 1st week	1(1,1)	4(2,4)	<0.001
	POD 4th week	0(0,1)	1(1,2)	<0.001
	p-value	<0.001	<0.001	

that while the intervention initially had a strong impact on these outcomes, the differences diminished over time. The median Total Kennedy score for the mitomycin-c side further decreased to 0, whereas the control side had a median score of 1. The p-value remains <0.001, indicating that the significant difference between the groups persisted with the interventional group continuing to show better outcomes(Table III). While the statistical difference is notable, clinically the distinction between the groups is minimal by the fourth week. Both groups generally experienced similar healing processes, leading to comparable clinical outcomes.

During the 12th-week follow-up endoscopy, two participants out of 50 developed synechiae on the control side: one between the middle and inferior turbinates, and the other between the middle turbinate and lateral wall. No adverse effects were observed up to 12 weeks post operatively.

DISCUSSION

Unlike the previous studies we employed an extended protocol using low dose mitomycin c post operatively where the nasal packing was soaked with the medication, aiming to maximise its efficacy in supporting wound healing. Our

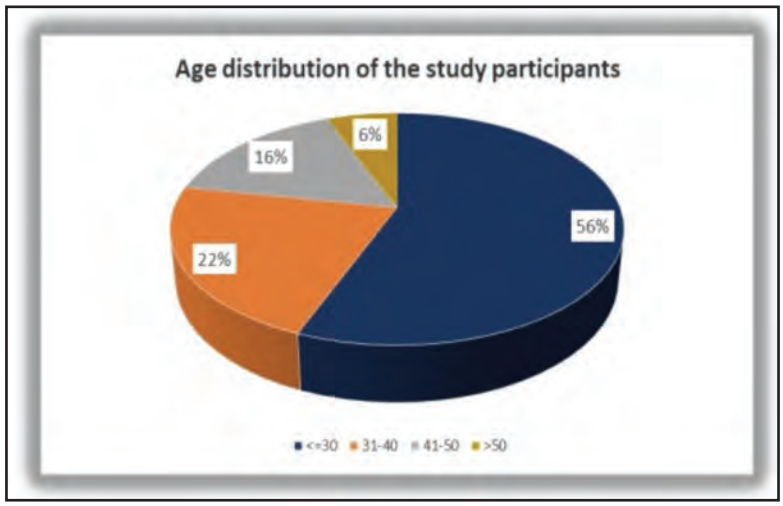

Fig. 1: Age distribution of study participants (N=50)

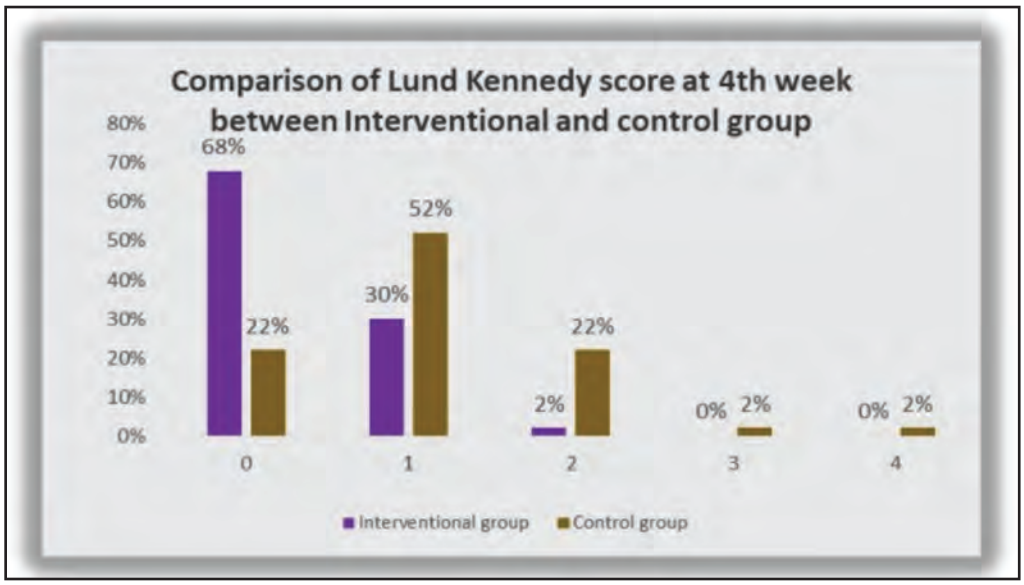

Fig. 2: Comparison of total Lund Kennedy scores between mitomycin-c and control sides on post-operative week 4 (N=50)

main objective was to facilitate a smoother immediate postoperative recovery period, thereby enhancing patient satisfaction. Nasal pain is a common and bothersome issue arising from frequent endoscopic debridements post-surgery. During the repeat endo-cleaning in week 1, participants reported less discomfort on the interventional side compared to the control side, likely due to reduced need for debridement in the interventional side. Moreover, our findings in the first postoperative week revealed significant improvements in nasal obstruction symptoms as well.

Following upper airway surgery, the nasal and paranasal mucosal lining undergoes a well-coordinated recovery process involving inflammation, cellular proliferation, matrix formation, and remodelling governed by various growth factors and cytokines.[6]

Intranasal adhesions, also known as synechiae occur when the nasal mucosa heals improperly after injury or surgery. This abnormal healing process can cause the mucosal surfaces within the nasal cavity to stick together leading to the formation of fibrous bands. These adhesions can obstruct normal airflow and cause various symptoms such as nasal congestion, difficulty breathing and recurrent sinus infections.[7] Proper postoperative care and management are crucial to minimise the risk of developing intranasal adhesions. The frequently utilised nasal packing material following nasal endoscopic surgeries is polyvinyl acetate (known as Merocel or Ivalon). This material is usually coated or treated with a non-adhesive layer to facilitate its easy removal post-surgery and minimize potential damage.

Harugop et al.,[8] found that while mitomycin-c provided superior symptomatic relief for nasal obstruction and facial

pain, it did not significantly affect nasal discharge and hyposmia. Consistent with the previous study, our findings also indicated significant difference in congestion and nose block between the mitomycin-c side and the control side at week 1 postoperatively, with p<0.001. Furthermore, no significant differences in nasal discharge were observed between the interventional and control sides at both week 1 and week 4 postoperatively (p=0.054 and 0.083 respectively).These findings suggest that while mitomycin-c may offer certain symptomatic benefits but, its impact on other postoperative outcomes remains limited, aligning with the findings of Harugop et al.

Singh et al.[9] also reported the safety of mitomycin-c used topically when comparing various concentrations applied for five minutes. Their study concluded that mitomycin-c application post-endoscopic surgery improved symptoms such as nasal obstruction, hyposmia and reduced adhesion rates and middle meatal antrostomy closure rates. Although our study did not assess hyposmia, we compared other nasal symptoms and found no significant differences in breathing difficulty (p=0.059), nasal obstruction (p=0.527), or trouble sleeping (p=0.074).

Venkatraman et al.,[10] highlighted that during the 1st week when the patients were reviewed there was a notable decrease in the occurrence of synechiae and improvement in symptoms like nose block, discharge from the nose on the side where mitomycin-c was used as compared to the control side where normal saline was used. However, after three and six months these differences were no longer significant. In our study, we evaluated nasal discharge, oedema, scarring, cresting, and polyps as essential parameters for assessing synechiae formation. We found that while the difference was significant by week 1, it became less pronounced by week 4 aligning with the findings of the previous study. Although statistical significance was observed on week 4 (p<0.001) the median total Lund Kennedy scores on mitomycin-c side was 0(0,1) and control side was 1(1,2) showing not much of a difference clinically.

A newer study by Sulieman et al.,[11] further supports efficacy of intra and postoperative mitomycin-c application in decreasing the incidence of synechiae after FESS. Their findings indicated that mitomycin-c not only minimised adhesions but also promoted better mucosal healing over a three-month follow-up period.[1] ml of mitomycin-c (0.8 mg/ml) was applied in the middle nasal passage for five minutes, followed by another application three weeks afterwards.

Our findings align with Ramalingam et al.,[12] stating a significant reduction in crusting during the initial week after surgery and there were improvements noted in reducing discharge, oedema of mucosa, polyp formation, and keeping the ostia open.

LIMITATIONS

The follow-up period in this study was limited to 12 weeks. Extending the follow-up in future research may provide more comprehensive insights into the long-term effects of mitomycin-c in reducing synechiae and improving nasal obstruction post-FESS.

The exclusion of patients with comorbidities such as uncontrolled diabetes, hypertension and autoimmune disorders ensures a homogenous study population. However, further research may be needed to explore the applicability of the findings to a broader, more medically complex population.

The primary outcome of this study was nasal obstruction, while other symptoms of chronic rhinosinusitis such as facial pain and olfactory function, were not extensively evaluated. Future studies could benefit from a more comprehensive assessment of patient symptoms.

While no significant adverse effects were observed during the 12-week follow-up, longer-term studies would be valuable in assessing the potential delayed effects of mitomycin-c, such as mucosal changes.

CONCLUSION

In conclusion, the postoperative topical application of low dose mitomycin-c appears to significantly reduce adhesions/synechiae and improve nasal symptoms in early postoperative period in patients with chronic rhinosinusitis. These findings are supported by previous research and highlight the potential of mitomycin-c as an effective adjunctive therapy in sinus surgery. This study employed a specific concentration and volume of mitomycin-c. However, exploring alternative dosages or application methods may reveal varied outcomes, suggesting the need for further investigation in future research comparing various doses and methods of application of mitomycin-c.

REFERENCES

1. Gupta M, Motwani G. Role of mitomycin C in reducing adhesion formation following endoscopic sinus surgery. J Laryngol Otol 2006; 120(11): 921-3.
2. Henriquez OA, Schlosser RJ, Mace JC, Smith TL, Soler ZM. Impact of synechiae after endoscopic sinus surgery on long-term outcomes in chronic rhinosinusitis. Laryngoscope 2013; 123(11): 2615-9.
3. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology 2020; 58(Suppl S29): 1-464.
4. Pratt WB, Ruddon RW, Ensminger WD, Maybaum J. The Anticancer Drugs. New York: Oxford University Press; 1994.
5. Arranz-Márquez E, Katsanos A, Kozobolis V, Konstas AG, Teus MA. A Critical Overview of the Biological Effects of Mitomycin C Application on the Cornea Following Refractive Surgery. Adv Ther 2019;3 6(4): 786-97.
6. Watelet JB, Bachert C, Gevaert P, Van Cauwenberge P. Wound healing of the nasal and paranasal mucosa: a review. Am J Rhinol 2002; 16(2): 77-84.
7. Stępiński MJ, Banaszewski J. Intranasal Synechiae as Complications of Rhinosurgical Treatment—A Review of Current Knowledge. J Clin Med 2023; 12(21): 6831.
8. Harugop AS, Mudhol RS, Kaku D, Vishnu H, Suhasini H. Subjective and Objective Outcome Evaluation of FESS with and without Mitomycin C: A Randomized Control Trial. Madridge J Otorhinolaryngol 2018; 3(1): 31-6.

9. Singh TD, Lade H, Natesh V. Role of Mitomycin-C in Prevention of Post Operative Adhesions After Endoscopic Sinus Surgery—A Prospective Study. Indian J Otolaryngol Head Neck Surg 2011; 63(3): 249-54.
10. Venkatraman V, Balasubramanian D, Gopalakrishnan S, Saxena SK, Shanmugasundaram N. Topical Mitomycin C in functional endoscopic sinus surgery. Eur Arch Otorhinolaryngol 2012; 269(7): 1791-4.
11. Sulieman YM, Mostafa I, Youssef Y. Efficacy of Mitomycin C in Prevention of Adhesions Formation after Functional Endoscopic Sinus Surgery. J Otolaryngol Rhinol 2023; 9(2): 139.
12. 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(4): 242-7.
13. Lund VJ, Kennedy DW. Staging for rhinosinusitis. Otolaryngol Head Neck Surg 1997; 117(3 Pt 2): S35-40.
14. Baba Caliaperoumal VB, GS D, Velayutham P, Krishnaswami B, Rama Krishnan KK, Savery N. Correlation of Clinical Symptoms With Nasal Endoscopy and Radiological Findings in the Diagnosis of Chronic Rhinosinusitis: A Prospective Observational Study. Cureus 2021; 13(7): e16591.
15. Hopkins C, Browne JP, Slack R, Lund V, Brown P. The Lund-Mackay staging system for chronic rhinosinusitis: How is it used and what does it predict? Otolaryngol Head Neck Surg 2007; 137(4): 555-61.