

ORIGINAL ARTICLE

Comparison of Mitomycin-C with Normal Saline in preventing Synechiae formation in patients undergoing Endoscopic Sinus Surgery



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ABSTRACT

Background: Chronic rhinosinusitis (CRS) is a prevalent condition affecting 5% to 12% of the population, often necessitating endoscopic sinus surgery (ESS) for treatment. Postoperative synechiae formation is a common complication of ESS, potentially leading to recurrent infections and impaired healing. Mitomycin-C (MMC), an antineoplastic agent known for its anti-fibrotic properties, has been proposed as a preventive agent against synechiae formation. .

Objective: This study aimed to evaluate the efficacy of MMC in reducing postoperative synechiae formation compared to normal saline

Methods: This prospective randomized control trail study was conducted at Ahmed Medical Center Rawalpindi over a six-month period, including 60 patients with CRS or nasal polyps. Patients were randomly assigned to two groups: Group A (MMC; n=30) received a topical MMC solution applied to the middle meatus after ESS, and Group B (normal saline; n=30) received normal saline. Synechiae formation was assessed four weeks postoperatively. Data were analyzed using SPSS version 26, with chi-square tests employed for statistical analysis.

Results: Postoperative synechiae occurred in 2/30 (6.7%) of the Mitomycin-C group versus 3/30 (10%) of the saline group (RR=0.67, 95% CI 0.12–3.71, p=0.64) was observed in 8.3% of the study population. In Group A, 2 patients (6.7%) developed synechiae, compared to 3 patients (10%) in Group B. The difference in synechiae formation between the groups was not statistically significant (p = 0.64).

Conclusion: Although MMC slightly reduced synechiae formation compared to normal saline, the difference was not statistically significant. This suggests that MMC may not provide a substantial advantage in preventing synechiae in routine ESS. Further research with larger sample sizes and varying MMC concentrations is necessary to clarify its role in synechiae prevention.

Keywords: Endoscopic sinus surgery; Mitomycin-C; Synechiae; Chronic rhinosinusitis

INTRODUCTION: Chronic rhinosinusitis (CRS) is a frequently encountered condition affecting the sinonasal region, with an estimated prevalence of 5% to 12% [1]. It often necessitates referral to an ear, nose, and throat (ENT) specialist for further evaluation and treatment. Endoscopic sinus surgery (ESS) is a widely accepted and commonly performed procedure for treating chronic rhinosinusitis (CRS) and other sinonasal pathologies[2,3]. Although ESS has significantly advanced the treatment of sinus diseases, one of the frequent post-operative complications is the formation of synechiae, or adhesions, within the nasal cavity[4]. Synechiae can obstruct the normal drainage pathways of the sinuses, leading to recurrent infections, impaired healing, and reduced surgical outcomes[5]. Consequently, the prevention of synechiae formation is a critical aspect of post-operative care following ESS.

The development of adhesions is among the most frequent complications following nasal surgeries. Previous research has highlighted that it is the most prevalent complication after functional endoscopic sinus surgery, with an incidence rate ranging from 10% to 40%[2]. Several approaches have been employed to minimize synechiae formation, including mechanical spacers, topical corticosteroids, and saline irrigation[7]. However, one agent that has gained attention for its anti-fibrotic properties is Mitomycin-C (MMC), an antineoplastic antibiotic known for its ability to inhibit fibroblast proliferation and scar formation[8]. MMC has been used in various surgical fields to reduce scar formation, such as in ophthalmic surgery and airway procedures, and its potential application in sinus surgery presents a promising avenue for investigation.

The comparison of Mitomycin-C and normal saline in preventing synechiae formation in patients undergoing endoscopic sinus surgery (ESS) is crucial. While normal saline irrigation is routinely employed post-operatively to maintain nasal hygiene and prevent crusting, it does not possess any direct anti-fibrotic properties. In contrast, Mitomycin-C has shown promising results in both experimental and clinical studies for its ability to reduce fibrosis and prevent adhesions. This prospective randomized trial aims to compare the efficacy of topical Mitomycin-C versus normal saline in preventing postoperative synechiae formation after endoscopic sinus surgery.

METHODS: This comparative prospective randomized controlled trial was conducted in the ENT Department Ahmed Medical Center Rawalpindi. The study lasted over a period of six months starting from (March 9, 2024 to September 9, 2024). A total of 60 patients were included and the sample size calculated using the WHO calculator, maintaining a significance level of 5% and power of the study of 80%. Patients were randomly allocated (1:1) to Mitomycin-C or saline groups using a computer-generated sequence and sealed envelopes, ensuring allocation concealment. Group assignments were determined by a computer-generated random sequence, and group allocation was concealed in opaque envelopes. Group A consisted of 30 patients in whom mitomycin-C (MMC) solution was applied topically to the middle meatus after endoscopic sinus surgery (ESS), while Group B included 30 patients who received normal saline in the same manner, serving as the control group. Consecutive sampling was adopted for patient selection.

The study included patients of both genders, aged 15 to 45 years, diagnosed with bilateral allergic nasal polyps, recurrent nasal polyps, or chronic rhinosinusitis that had persisted for more than three months despite conservative treatment. The exclusion criteria consist of patients with pregnancy, or bleeding disorders. Ethical approval was granted by the Health Education Research foundation committee under letter no: (HERF/Research/REC/No-2024-03 dated 04-03-26) and written informed consent were obtained from patients. Postoperatively, antibiotics, nasal decongestants, saline douches, and medications were administered. Synechiae formation was assessed at 4 weeks postoperatively via anterior rhinoscopy (binary outcome: yes/no) by otorhinolaryngologist.

Data were analyzed with SPSS version 26, with quantitative variables presented as mean $\pm$ SD and qualitative data as frequencies and percentages. As the data was qualitative in nature a chi-square tests were used to compare synechiae formation between groups. A p-value <0.05 was considered significant. Data were analyzed with SPSS v.26. Quantitative variables are presented as mean $\pm$ SD. Categorical variables are summarized as counts (%) and compared between groups using the chi-square test or Fisher's exact test (when expected counts <5). Odds ratios (OR) and 95% confidence intervals (CI) were calculated to quantify treatment effects. A two-sided P-value <0.05 was considered statistically significant.

Table 1: Demographic Characteristics of Participants in the MMC and Saline Groups

Characteristic	Group A (MMC, n=30)	Group B (Saline, n=30)	P-value
Age, mean $\pm$ SD (years)	30.2 $\pm$ 8.1	29.7 $\pm$ 7.5	0.78*
Male, n (%)	19 (63.3%)	16 (53.3%)	–
Female, n (%)	11 (36.7%)	14 (46.7%)	–

*Student's t-test.

RESULTS: The patients' ages ranged from 15 to 45 year. "Mean patient age was 30.2 $\pm$ 8.1 years in Group A and 29.7 $\pm$ 7.5 years in Group B (p=0.78, Student's t-test), indicating no significant age

difference.” Out of this study participants 58% were male and 42% were females. They were further divided in two groups A and B. In Group A (Mitomycin-C), there were 19 male patients (63.3%) and 11 female patients (36.7%), while Group B (Normal Saline) consisted of 16 male patients (53.3%) and 14 female patients (Table 1).

Patients were followed clinically and endoscopically at 1 week, 4 week and 3 months postoperatively to monitor for synechia formation and each side for the nasal cavity. Postoperative synechia formation was observed in 5 patients (8.3%) at the 4-week follow-up. A comparison was made between the two treatment groups: Group A, which received mitomycin-C, and Group B, which received normal saline. In Group A, 2 patients (6.7%) developed synechia, while in Group B, 3 patients (10%) experienced the same complication. Despite the variation in treatment modalities, the difference in synechia formation between the two groups was not statistically significant. Postoperative synechia occurred in 2/30 (6.7%) of the Mitomycin-C group and 3/30 (10%) of the saline group; the relative risk (RR) of synechia with MMC was 0.67 (95% CI 0.12–3.71), with no statistically significant difference ($P=0.640$).” Synechia in 2/30 vs. 3/30 patients ($RR=0.67$, 95% CI 0.12–3.71; $p=0.64$), indicating that the use of mitomycin-C did not result in a substantial reduction in postoperative synechia compared to normal saline (Table 2).

Table 2: Comparative analysis of two groups one received Mitomycin while the other received Normal Saline.

Nasal Synechia		No. of Patients	p-Value
Group A (n=30)	Yes	2	0.64
	No	28	
Group B (n=30)	Yes	3	
	No	27	

DISCUSSION: The present study aimed to evaluate the efficacy of Mitomycin-C (MMC) in reducing postoperative nasal synechia formation in patients undergoing nasal surgery, comparing it to a control group treated with normal saline. Synechia formation is a frequent complication in nasal surgeries, potentially leading to discomfort, airway obstruction, and the need for additional interventions. Several methods, including topical agents like MMC, have been investigated to reduce this risk.

In this study, 60 patients were divided into two groups: Group A received MMC, and Group B was treated with normal saline. Although the incidence of synechia formation was lower in Group A (6.7%) than in Group B (10%), the difference was not statistically significant ($p = 0.64$). This lack of statistical significance suggests that MMC did not offer a substantial advantage in preventing postoperative synechia formation compared to normal saline. Consequently, the routine use of MMC in nasal surgeries solely for synechia prevention may not be justified.

When compared to previous studies, our findings align with some similar trends. Several studies have shown a reduction in synechia formation with MMC, indicating its potential to reduce postoperative adhesions[9,10,11]. However, synechia incidence varied across studies, including our own. For instance, Konstantinidis et al.[10] reported that MMC effectively prevented adhesions and restenosis, but our study recorded a higher synechia rate of 38.7% in the MMC group. This discrepancy may be due to the lower MMC dose (0.5 mg/ml) and shorter follow-up period in our study. Such conflicting results are consistent with earlier research that questioned MMC's clinical efficacy in reducing synechia. While MMC's fibroblast-inhibiting properties suggest theoretical benefits, real-world evidence remains inconsistent.

Mitomycin-C is an alkylating agent that inhibits fibroblast proliferation and has been applied in various surgical procedures to minimize scar tissue formation and adhesion development. In ophthalmic surgeries, particularly pterygium excision, MMC has demonstrated clear benefits in reducing postoperative fibrosis[12]. However, its success in nasal surgeries has been more inconsistent. Some studies have reported reductions in synechia

formation with MMC use, but others have found no significant differences compared to control groups[13,14,16]. This inconsistency could be related to variations in surgical techniques, MMC concentrations, and patient characteristics. For example, while Konstantinidis et al.[10] emphasized MMC's efficacy in preventing adhesions and restenosis, our study noted a higher synechiae incidence, likely due to the lower MMC dose and shorter follow-up duration. This discrepancy highlights the influence of study design, dosage, and follow-up periods on the inconsistent outcomes of MMC in synechiae prevention. Although MMC theoretically inhibits fibroblasts and reduces scarring, its effectiveness in real-world settings varies.

In addition to MMC, postoperative irrigation solutions also play a crucial role in recovery. Kurtaran et al.[17] found that hypertonic 2.3% sea water was the most effective irrigation solution for reducing dryness, swelling, adhesions, and nasal obstruction after nasal septum surgery with conchoplasty. In contrast, a smaller study on 0.9% sodium chloride with sodium hyaluronate nebulizations post-FESS showed no significant reduction in adhesions but demonstrated improvements in cilia motility, mucosal healing, and nasal patency[18,19]. Comparing these approaches, MMC targets fibroblast inhibition to prevent synechiae, while hypertonic saline solutions and sodium hyaluronate focus on enhancing mucosal healing and function. These differences underscore the importance of individualized treatment plans that consider the patient's condition, type of surgery, and postoperative care protocol to optimize outcomes. Larger studies are necessary to establish the definitive roles of these interventions.

Moreover, the safety profile of MMC should not be overlooked. While it has been shown to be safe in low concentrations, concerns about potential side effects such as delayed wound healing and mucosal atrophy persist[15]. The findings of this study reinforce the notion that the routine use of MMC in nasal surgeries may not be warranted unless there are clear indications based on individual patient risk factors for synechiae formation. Our study was limited by its small size and single-center design, which may affect generalizability. Additionally, while follow-up was short-term, longer follow-up would better assess synechiae recurrence. "Our study's modest sample size (n=60) and the low incidence of synechiae (only 5 total events) limit the power to detect anything but a large effect. As highlighted by Sullivan et al., P-values are confounded by sample size, so the lack of statistical significance here may reflect limited power rather than true equivalence. We therefore interpret our negative finding cautiously and recommend larger trials to more precisely estimate MMC's effect. Overall, the analysis is simple and generally appropriate, but including discussion of sample size limitations would improve the manuscript.

Future studies with larger sample sizes, longer follow-up periods, and varying concentrations of MMC are needed to draw more conclusive results regarding its role in synechiae prevention. Additionally, the exploration of alternative agents and techniques to minimize postoperative synechiae remains a critical area of research.

CONCLUSION: This study found that while Mitomycin-C (MMC) may reduce the incidence of postoperative synechiae formation in nasal surgery patients compared to normal saline, the difference was not statistically significant. This suggests that MMC does not provide a substantial advantage in preventing synechiae in routine nasal surgeries. The findings align with other studies that have shown conflicting results regarding MMC's efficacy, likely due to variations in dosage, surgical techniques, and follow-up durations.

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REFERENCES

1. 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. *The Egyptian Journal of Otolaryngology*. 2018 Oct;34:242-7. https://doi.org/10.4103/ejo.ejo_9_17
2. Sulieman YM, Ibrahim M, Youssef Y (2023) Efficacy of Mitomycin C in Prevention of Adhesions Formation after Functional Endoscopic Sinus Surgery. *J Otolaryngol Rhinol* 9:139. <https://doi.org/10.23937/2572-4193.1510139>
3. Flint PW, Haughey BH, Lund VJ, K Thomas Robbins, J Regan Thomas, et al. (2021) *Cummings Otolaryngology Head and neck surgery*. Elsevier. (7th edn), Philadelphia. <https://shop.elsevier.com/books/cummings-otolaryngology/flint/978-0-323-61179-4>
4. Hershil K, Eugene W, Kiao I, Sacks R, Singh N, et al. (2022) Peri-operative measures to prevent middle turbinate lateralization and adhesion formation in endoscopic sinus surgery -asystemic review of the literature *AJO* 5: 20.<https://doi.org/10.21037/ajo-22-6>

5. Smith ME, Elstad (2009) Mitomycin C and the endoscopic treatment of laryngotracheal stenosis. are two applications better than one? *Laryngoscope* 119: 272-283. <https://doi.org/10.1002/lary.20056>
6. Okkens WJ, Lund VJ, Hopkins C et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology*. 2020 Feb 20;58(Suppl S29):1-464. <https://doi.org/10.4193/Rhin20.600>
7. Khatri H, Wong E, Inthavong K, Sacks R, Singh N. Peri-operative measures to prevent middle turbinate lateralisation and adhesion formation in endoscopic sinus surgery: a systematic review of the literature. *Australian Journal of Otolaryngology*. 2022 Jul 1;5:1-7. <https://doi.org/10.21037/ajo-22-6>
8. AS Harugop, RS Maduhol, et al. (2017) Mitomycine-c as panacea for prevention of adhesion formation after functional endoscopic sinus surgery (fess/ess) in cases of chronic rhinosinusitis (crs). *Journal of Biomedical and Pharmaceutical Sciences* 4: 560-565. https://www.ejbps.com/ejbps/abstract_id/2750
9. 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. *The Egyptian Journal of Otolaryngology*. 2018 Oct;34:242-7. https://doi.org/10.4103/ejo.ejo_9_17
10. Konstantinidis I, Tsakiropoulou E, Vital I, Triaridis S, Vital V, Constantinidis J. Intra- and postoperative application of Mitomycin C in the middle meatus reduces adhesions and antrostomy stenosis after FESS. *Rhinology*. 2008 Jun 1;46(2):107. <https://pubmed.ncbi.nlm.nih.gov/18575010/>
11. Koshy RT, Gopalakrishnan S, Karthikeyan P. Topical Application of Mitomycin C in Functional Endoscopic Sinus Surgery. *Ann SBV* 2020;8(1):19–22. <https://doi.org/10.5005/jp-journals-10085-8106>
12. Kaufman SC, Insler MS, Ibrahim-Elzembely HA, Kaufman HE. Mitomycin C in ophthalmic surgery. *Surv Ophthalmol*. 1996;41(5):335-365. https://doi.org/10.4103/joco.joco_283_23
13. Mandal R, Ghosh S, Maiti M, Das S. Role of Mitomycin C in prevention of synechiae formation following functional endoscopic sinus surgery. *Indian J Otolaryngol Head Neck Surg*. 2011;63(2):146-150. <https://doi.org/10.1007/s12070-011-0145-6>
14. Cingi C, Eskizmir G, Cakli H, Ozudogru E. The efficacy of Mitomycin-C in preventing postoperative adhesion after endoscopic nasal surgery: A clinical study. *B-ENT*. 2008;4(4):241-244.
15. Moore EJ, Kern EB. Atrophic rhinitis: A review of 242 cases. *Am J Rhinol*. 2001;15(6):355-361. <https://doi.org/10.1177/194589240101500601>
16. El Dabaa MA, El Maraghy AA, Yones MA, Dawood YM, Megahed MA. Role of Topical Mytomycin C Application in Improving Outcome of Functional Endoscopic Sinus Surgery. *The Egyptian Journal of Hospital Medicine*. 2019 Jan 1;74(8):1891-901. <https://doi.org/10.21608/ejhm.2019.28873>
17. Kurtaran H., Ugur K.S., Yilmaz C.S., Kaya M., Yuksel A., Ark N., Gunduz M. The effect of different nasal irrigation solutions following septoplasty and concha radiofrequency: A prospective randomized study. *Braz. J. Otorhinolaryngol*. 2018;84:185–190. <https://doi.org/10.1016/j.bjorl.2017.01.005>
18. Stępiński MJ, Banaszewski J. Intranasal Synechiae as Complications of Rhinosurgical Treatment-A Review of Current Knowledge. *J Clin Med*. 2023 Oct 29;12(21):6831. doi: [10.3390/jcm12216831](https://doi.org/10.3390/jcm12216831)
19. Hwang J.C., Gill A.S., Squires L.D., Steele T.O. Sjögren's Syndrome Sequelae: Nasal Synechiae and Nasopharyngeal Stenosis. *Ear Nose Throat J*. 2021;100((Suppl. 10)):1095S–1097S. <https://doi.org/10.1177/0145561320936965>

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