

Role of mitomycin C in reducing adhesion formation following endoscopic sinus surgery

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Abstract

Objective: To study the role of mitomycin C in reducing adhesion formation following endoscopic sinus surgery.

Study design: Prospective, randomized, controlled trial.

Setting: Tertiary care referral centre.

Patients: Thirty patients were selected suffering long-term problems with bilateral chronic rhinosinusitis, with no relief obtained from medical therapy. Patients requiring revision sinus surgery or having acute upper respiratory tract infection were excluded.

Interventions: Diagnostic nasal endoscopies and non-contrast computerized tomography of nose and paranasal sinuses were undertaken and, following confirmation of the diagnosis, functional endoscopic sinus surgery (FESS) was carried out bilaterally using the Messerklinger technique. On completion of the surgery, a cotton wick soaked in mitomycin C was placed in one or other side of the nose in the middle meatus. Follow up was for three months and patients were assessed for subjective and objective improvement in their symptoms.

Results: Post-operatively, of the 11 (36.6 per cent) patients complaining of persistent nasal obstruction, nine had complaints limited to the control side only ($p = 0.005$). Out of the nine (30 per cent) patients complaining of recurrent nasal discharge, eight had complaints on the control side and only one reported discharge from both sides ($p = 0.006$).

Conclusion: Mitomycin C may be topically applied in post-operative FESS cases to reduce adhesion formation and hence the need for revision surgery.

Key words: Paranasal Sinusitis; Endoscopy; Mitomycin; Postoperative Complications

Introduction

Chronic sinusitis produces long-term inflammation of the mucous lining of the sinuses. Functional endoscopic sinus surgery (FESS), as described by Messerklinger, has been fully accepted for treating chronic sinus disease, with the assumption that restoration of sinus ventilation and correction of mucous apposition will allow restoration of the mucociliary clearance system. One problem the surgeon often encounters is that of post-operative adhesion occurring between the middle turbinate and the lateral nasal wall in the region of the ethmoid sinuses.^{1,2} If severe, the recurrence of symptoms is often due to these synechiae, and further surgery may be required to restore normal function. Various surgical approaches, as well as the use of systemic drugs³ and site-specific barriers,^{1,4} have been used to minimize inflammation and injury during surgery so as to reduce the risk of adhesion formation.

Mitomycin C is an antibiotic-antineoplastic agent isolated from *Streptomyces caespitosus*. It acts as an alkylating agent by selectively inhibiting deoxyribonucleic acid (DNA) synthesis and cross-linking DNA. At higher concentrations, cellular ribonucleic acid and protein synthesis are also suppressed. Mitomycin C has been used for many years in oncology and has been shown to have an antiproliferative action on human fibroblasts.⁵ In ophthalmological practice, it has been used following surgery for pterygium, glaucoma filtration and dacryocystorhinostomy,⁶ and experiments on rats have shown that a topical application prevents myringotomy closure.⁷ Recently, it has also been found to be useful in preventing laryngotracheal stenosis in dogs.⁸

The purpose of this study was to determine whether mitomycin C could be used to prevent the closure of maxillary sinus antrostomies^{9–11} and to prevent frontal recess stenosis while promoting

drainage of the ethmoidal and sphenoid sinus by preventing post-operative scarring.

Material and methods

Prior to commencement, ethical committee approval of the trial was obtained from the local hospital authorities. The study was conducted on 30 eligible patients with long-term bilateral nasal discharge and headache who were proven on radiological examination to have chronic sinusitis. In each instance, there had been no relief with medical therapy. We specifically excluded patients requiring revision surgery and those with systemic illnesses, such as cystic fibrosis, immunodeficiency, abnormalities of cilia transport, diabetes mellitus, tuberculosis and bleeding diatheses.

All patients were comprehensively examined and routine haematological and urine tests were undertaken. Diagnostic nasal endoscopy was first performed under local anaesthesia and coronal computed tomography scans were then performed in each instance.

Surgery was performed under local anaesthetic infiltration with 2 per cent xylocaine with 1 in 200 000 adrenaline. A standard technique, as described by Messerklinger, was followed in all cases and, on completion of the surgery, a cotton plug soaked in 1 ml mitomycin C (0.4 mg/ml) was placed in either the right or left middle meatus for four minutes, with a similar cotton dressing soaked in saline in the contralateral side. The side selected for treatment was randomized. On removal of the cotton dressing, the cavities were irrigated and a pack of Merocel applied for a period of four days. Antibiotics (amoxicillin–cloxacillin) and anti-inflammatory/analgesic (ibuprofen–paracetamol) drugs were given post-operatively.

Patients were examined at weekly intervals for a month and then monthly up to three months after surgery, depending on the perceived clinical need to clean debris and depending upon the extent of the patient's disease. Post-operatively, the patients were assessed for improvement in their symptoms; an observer, blinded to the technique used, also carried out an objective assessment. Synechiae were noted if present and the patency of the maxillary sinus antrastomies was assessed in all cases.

Results

Of the 30 patients selected, 20 (66.6 per cent) were men and 10 (33.3 per cent) women. Maximum number i.e. 13 (43.3 per cent) patients were of age group 30–40, followed by 10 (33.3 per cent) of age group 20–30. Pre-operative endoscopy recorded bilateral blockage of the osteomeatal complex; this and other anatomical variants and pathologies are listed in Table I.

Nine (30 per cent) of the patients who had been treated complained of recurrent nasal discharge post-operatively, and the majority i.e. 8 (27 per cent) of these patients had residual pathology and a complaint emanating from the controlled side that had been treated with saline. Only one case had an

TABLE I
PRE-OPERATIVE ENDOSCOPIC FINDINGS

Finding	Patients	
	<i>n</i>	%
Blocked osteomeatal complex	30	100
Inferior turbinate hypertrophy	16	53
Deviated nasal septum	9	30
Polyps	7	23
Paradoxical middle turbinate	6	20
Medial projecting uncinata	8	27
Concha bullosa	5	17

ongoing complaint of discharge from both sides of the nose. Thus the results are statistically significant ($p = 0.006$).

In eleven cases (37 per cent), there was an ongoing complaint of nasal obstruction subsequent to surgery; in these cases, nine had a problem limited to the control side only and two complained of obstruction on both sides ($p = 0.005$). Endoscopic examination revealed the complications as listed in Table II.

Discussion

Post-operatively, raw areas lying in close proximity tend to heal with regenerating epithelium and fibrous tissue growing between them. After endoscopic sinus surgery, such adhesions can lead to re-obstruction of the sinus ostium and recurrent sinus infection. Stammberger observed synechiae of varying sizes between the head of the middle turbinate and the lateral wall in 8 per cent (43/500) of his patients at the time of follow up.¹² He divided the synechiae, excised any excessive scar tissue and placed a small piece of Silastic in the nose, but he concluded that recurrence of synechiae could not always be prevented. Ramadan evaluated causes of surgical failure at the time of revision surgery and found adhesions in 29 cases (56 per cent), with the most common cause of failure being adhesions in the ethmoid area (30.7 per cent) and maxillary sinus ostium stenosis (27 per cent).²

To avoid these complications, Weymuller suggested prolonged packing of the operative site such that the middle turbinate was medialized towards the nasal septum.¹ However, this may result in airway obstruction and diminished olfaction. As a result, Brennan described a device made of medical grade polyurethane which isolated the middle turbinate from both the nasal septum and the lateral nasal wall. This 'boomerang turbinate glove' was used in 234 successive intranasal sinus surgical procedures for a period of 10–14 days, with no major adhesions observed.⁴

In an animal study in rabbits, Ingrams *et al.* reported the result of using sponges soaked with mitomycin C in concentrations of 0.04, 0.4 and 1 mg/ml, placed for five minutes at the site of the middle meatal antrastomy.¹⁰ They found that antrastomies in the control and 0.04 mg/ml treatment groups tended to close by one week post-operatively,

TABLE II
POST-OPERATIVE ENDOSCOPIC FINDINGS*

Finding*	Mitomycin C side [n (%)]	Control side [n (%)]	p [†]
Synechia/adhesions	1 (3)	11 (37)	0.001
Crusting	0	3 (10)	0.24
Polypoid mucosa	1 (3)	3 (10)	0.60
Granulations	0	1 (3)	0.94
Discharge	2 (7)	9 (30)	0.02

*Middle meatus endoscopic view; †chi-square

but that they remained open for four weeks in the group treated with mitomycin C 0.4 mg/ml and for 12 weeks in the 1.0 mg/ml group. This trial suggests that a delay in fibrosis allows re-epithelialization to take place before scar tissue forms, thus increasing the success rate of FESS.

In a clinical study by Chung *et al.*, adhesions were identified in a total of 16 of 55 post-operative patients, with significantly more adhesion formation on the untreated side.¹¹ We obtained similar results. In our study, we found adhesions of all grades (mild, moderate and severe), which were predominantly observed on the control side, occurred throughout the nasal cavity, and were both medial and lateral to the middle turbinate. Mitomycin C markedly reduced the rate of formation of such adhesions as well as reducing the prevalence of a complaint of post-operative nasal discharge. In like manner, we also noted less frequent mucosal hypertrophy and polypoid change after using mitomycin C. We observed no systemic or local adverse effects from topical intranasal mitomycin C application.

In conclusion, we would concur with previous research, which has suggested that topically applied mitomycin C prevents local complications in patients undergoing endoscopic sinus surgery, without exposing them to the risk of systemic toxicity.

- This was a prospective, randomized, controlled trial of the use of mitomycin C in preventing complications in patients having endoscopic sinus surgery
- Previous work has suggested that such treatment reduces post-operative complications and, in particular, reduces adhesion formation
- In this study, 30 cases of chronic rhinosinusitis were treated with functional endoscopic sinus surgery; mitomycin C was applied to one side and saline to the other in the immediate post-operative period
- Results suggest a lower prevalence of post-operative complications in those patients receiving mitomycin C

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References

- 1 Weymuller EA Jr. Complications of endoscopic sinus surgery. *Op Tech Otolaryngol Head Neck Surg* 1990;**1**: 149–52
- 2 Ramadan HH. Surgical causes of failure in endoscopic sinus surgery. *Laryngoscope* 1999;**109**:27–9
- 3 Thompson JN, Whawell SA. Pathogenesis and prevention of adhesion formation. *Br J Surg* 1995;**82**:3–5
- 4 Brennan LG. Minimizing postoperative care and adhesions following endoscopic sinus surgery. *Ear Nose Throat J* 1996;**75**:45–8
- 5 Khaw PT, Doyle JW, Sherwood MB, Grierson I, Schultz G, McGorray S. Prolonged localized tissue effects from 5-minute exposures to fluorouracil and mitomycin C. *Arch Ophthalmol* 1993;**111**:263–7
- 6 Kao SCS, Liao CL, Tseng JHS. Dacryocystorhinostomy with intraoperative mitomycin C. *Ophthalmology* 1996; **104**:86–91
- 7 Estrem SA, Van Leeuwen RN. Use of mitomycin C for maintaining myringotomy patency. *Otolaryngol Head Neck Surg* 2000;**122**:8–10
- 8 Eliashar R, Eliachar I, Esclamado R, Gramlich T, Strome M. Can topical mitomycin prevent laryngotracheal stenosis? *Laryngoscope* 1999;**109**:1594–1600
- 9 Rahal A, Peloquin L, Ahmarani C. Mitomycin C in sinus surgery: preliminary results in a rabbit model. *J Otolaryngol* 2001;**30**:1–5
- 10 Ingrams DR, Volk MS, Biesman BS, Pankratov MM, Shapshay SM. Sinus surgery: does mitomycin C reduce stenosis? *Laryngoscope* 1998;**108**:883–6
- 11 Chung JH, Cosenza MJ, Rahaber R, Metson RB. Mitomycin C for the prevention of adhesion formation after endoscopic sinus surgery: a randomized, controlled study. *Otolaryngol Head Neck Surg* 2002;**126**:468–74
- 12 Stammberger H. Endoscopic endonasal surgery – concepts in treatment of recurring rhinosinusitis, Part II. Surgical technique. *Otolaryngol Head Neck Surg* 1986; **94**:147–56

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Dr M Gupta takes responsibility for the integrity of the content of the paper.
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