Healing of wounds created in the nasal mucosa following endoscopic sinus surgery can be affected by different nasal packing materials

Cowin A • McIntosh D • Wormald PJ

Abstract

Chronic sinusitis is a very common condition requiring surgery if medical treatment fails. In fact, diseases relating to the nose and paranasal sinuses are one of the most common health care complaints in Australia and the USA (18 per cent). Although a proportion of these infections respond well to medical treatment, there remain a significant number of patients who develop chronic sinusitis requiring surgery.

After endoscopic sinus surgery (ESS) it is common practice to place nasal packing material in the operated area to prevent adhesions from forming. Although many different packs have been used clinically, there is little evidence of their effects on the repair of the nasal mucosa or on the formation of adhesions. This paper examines a sheep model developed for ESS which shows that different packing materials can affect the re-epithelialisation of wounds created in the nasal mucosa. The incorporation of bioactive agents into these packing materials could offer significant advantages in the healing of the nasal mucosa and may also help to reduce adhesions from forming. Improved healing would lead to reduced numbers of patients with recurrent chronic sinusitis.

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Introduction

The epithelium of the nasal cavity and nasal sinuses consists of a pseudostratified ciliated respiratory epithelium [1]. This epithelium protects against exogenous agents through its action as a physical barrier and a mechanical clearing system [2]. The clearing system functions through the action of cilia which trap exogenous materials and push mucus towards the back of the nose and throat where it is swallowed [3].

Allison Cowin*
Child Health Research Institute
King William Road, North Adelaide, SA 5006
CRC for Tissue Growth and Repair

David McIntosh

Peter-John Wormald
Dept of Surgery
The University of Adelaide
The Queen Elizabeth Hospital, Woodville SA
CRC for Tissue Growth and Repair.

* Please address all correspondence to Allison Cowin

Failure of this protective mechanism may occur as a result of damage or destruction of the epithelium or the cilia – this results in pooling of mucus, with the potentially pathogenic exogenous material becoming trapped and leading to further damage to the adjacent epithelium. The reasons for the initial failure of this mechanism are diverse in nature and include congenital defects, allergy, infection by viruses, bacteria, fungi or parasites, physical trauma caused by nose-picking, surgery or accident, and chemical trauma caused by smoking or noxious gases [4]. These can lead to diseases of the nasal cavity and nasal sinuses and are one of the most common health care complaint in Australia and the USA (18 per cent) [5].

Although a proportion of these infections respond well to medical treatment, there remain a significant number of patients who develop chronic sinusitis requiring surgery. Currently the accepted form of sinus surgery is endoscopic sinus surgery (ESS) [6]. The ESS surgical technique is a common procedure and accounts for more than 50 per cent of all ENT operations performed [7]. ESS involves opening the natural openings of the nasal sinuses to restore aeration and mucociliary drainage of the sinuses. In ESS, the majority of surgery is performed between the middle turbinate and the lateral nasal wall. These two surfaces are in relatively close

proximity and, consequently, one of the most frequent complications of ESS is the development of post-operative adhesions. Adhesions may cause closure of the ostia, prevent normal aeration of the sinuses and may block the normal mucociliary drainage pathways of the sinuses, causing a recurrence of chronic sinusitis. Hence, studies performed have aimed to provide a therapeutic treatment to enhance the regeneration of nasal cavity and nasal sinus epithelial tissue damage, prevent adhesion formation and prevent further infection following surgery.

To prevent post-operative bleeding and adhesions after nasal or sinus surgery, it is common practice to place nasal or sinus packing material in the operated area [8, 9]. Many different materials are used, including polyvinyl acetate sponges and ribbon gauze. However, these have the disadvantage of having to be removed at some time in the post-operative period, thus re-opening the wound and possibly contributing to poor healing. Patients have also described this as the worst aspect of their treatment [10]. This is backed up by our study which has shown that packing the nasal cavity post ESS with certain non-dissolvable packing materials (then left *in situ* for a certain time period post-ESS) can result in a significant loss of ciliated epithelium compared to unpacked controls [9].

The introduction of dissolvable packing materials have the benefit of not requiring post-operative removal. These dissolvable packing materials are based on the extracellular matrix protein called hyaluronic acid. Hyaluronic acid is a naturally occurring extracellular matrix glycosaminoglycan. It facilitates cell migration, impedes the passage of bacteria and, in foetal wounds, high levels of hyaluronic acid promote healing of wounds without scar tissue formation [11].

The application of exogenous hyaluronic acid has been assessed on dermal repair as a possible means of improving the wound healing process [12]. Hyaluronic acid has also been advocated for use in ophthalmology, in abdominal and pelvic surgery as a means of reducing adhesion formation, and in orthopaedic surgery as a means of increasing the intra-articular fluid present in osteoarthritic joints [13]. The results of our study have shown that addition of dissolvable nasal packs to wounded nasal epithelium provides some improvement in the rate of reepithelialisation of wounds but has little effect on reciliation of the wounded areas [14].

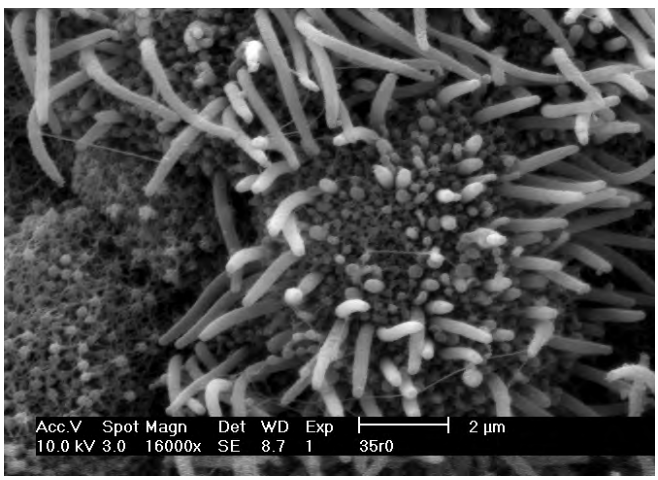
While re-epithelialisation is of great importance in the healing of nasal epithelium, re-ciliation of the epithelium remains vitally important to the nasal cavity's ability to maintain its health. An example of regenerating cilia on the surface of the nasal mucosa is shown in Figure 1. The return of cilia to the epithelium allows the mucous in the nose and sinuses to be moved continuously to the naso-pharynx and this allows the mucosa in the nose and sinuses to rid it of allergens, bacteria and other inhaled materials. Failure of re-ciliation leads to mucous stasis, secondary infection and chronically unhealthy mucosa.

Any improvement on the rate of epithelialisation and reciliation of the mucosa would therefore have direct benefits to patients. Not only would the patient feel relief from symptoms sooner but also the potential formation of adhesions, a common complication, would be reduced. Adhesions can form when two non-epithelialised opposing mucosal surfaces touch; therefore, if the rate of re-epithelialisation of the wounded area is increased, adhesion formation would be minimised. Additionally, the likelihood of further injury to the unhealed surfaces by noxious agents, bacteria and fungi not being cleared in the usual manner would also be reduced, so the chance of the patient developing further problems in the sinuses would also be minimised. There is therefore still a requirement for a method of treatment which accelerates the healing and improves the quality of healing of nasal cavity and sinus epithelial tissue.

An animal model of ESS

The requirement to examine the effect of nasal packing on the mucosa has led to the development of sheep as an animal model for ESS. In the literature, sheep have been shown to develop a similar spectrum of diseases to humans (including sinusitis, nasal polyposis and allergic rhinitis). In addition, the nasal cavity is suitable for nasal endoscopy and surgery [9, 15].

Figure 1. Scanning electron micrograph of the nasal epithelium showing regeneration of cilia on the wounded surface.



In fact, sheep provide the first reliable animal model of chronic sinusitis – almost all sheep sinuses are infested with the oestrus ova parasite unless they are dipped twice a year to prevent this. Thus studies have been performed to assess the healing in normal sheep and in sheep that have chronic sinusitis.

Our studies have shown that standard ESS techniques and instruments can be used in sheep, thereby duplicating the operative conditions and healing process of humans undergoing ESS [9]. The effect of pre-operative nasal packing on the nasal epithelium has also been documented [15]. The healing process of sheep nasal mucosa after full and partial thickness injury has been studied in detail and it was observed that re-epithelialisation of the nasal mucosa was an extremely slow process with only 65 per cent of the mucosa being re-epithelialised 84 days post wounding (Figure 2). Additionally, investigations showed that only 33 per cent of the normal wounded nasal mucosa had undergone re-ciliation after 84 days [16]. This indicates that there is room for significant improvement in the healing process.

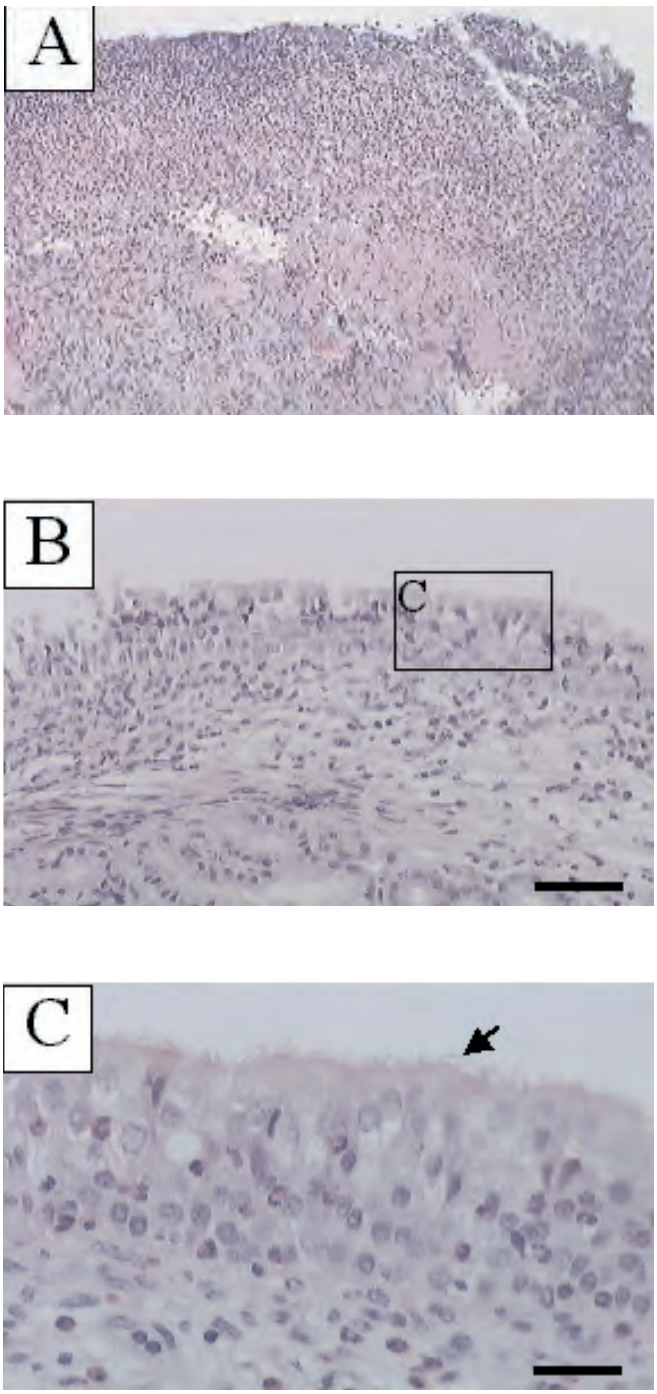
Three factors have emerged from our studies. Firstly, the healing of the nasal mucosa after surgery takes considerably longer than was previously thought. This delay in the healing process provides a unique opportunity to manipulate the process and attempt to both speed up healing and also prevent adhesion formation. Secondly, packing the nasal cavity with non-dissolvable packing material reduces the rate of healing and degree of ciliation of the nasal mucosa following ESS. Finally, our studies have revealed that packing with dissolvable packing materials does not adversely affect the rate of healing – these are therefore a potential delivery vehicle for bioactive agents which could be slowly released over time to influence the healing of the mucosal surfaces.

Growth factors and epithelial wound repair

Growth factors are potential bioactive agents that could be incorporated into dissolvable nasal packs to influence wound repair. It is well known that growth factors play a major role in the wound repair process as they attract inflammatory cells and fibroblasts into the wounded area, promote proliferation of fibroblasts, epithelial and endothelial cells, and stimulate angiogenesis and wound epithelialisation. They have a significant effect on the production and degradation of the extracellular matrix and can influence the synthesis of cytokines and growth factors by neighbouring cells [17].

Treatment of wounds with exogenous growth factors has been clearly shown to accelerate the wound healing process [18]. Currently the effects of these bioactive dissolvable nasal

Figure 2. Effect of wounding on re-epithelialisation of nasal mucosa following ESS. Haematoxylin and Eosin stained sections of sheep nasal mucosa are shown at 7 and 84 days post wounding (A and B respectively). No re-epithelialisation can be observed at 7 days post wounding (A). Even at 84 days post wounding, complete re-epithelialisation is not observed (B). The arrow points to cilia on the epithelium (C). Magnification bar in B refers to both A and B and = 100μm. Magnification bar in C = 50μm.



packs on the rate of re-epithelialisation and reciliation of the nasal mucosa following ESS in the sheep models are being investigated.

Conclusion

Hopefully these studies will lead to improvements in the clinical treatment of patients with chronic sinusitis. Improving the rate of healing should reduce the number of adhesions formed post surgery, thereby preventing the recurrence of the chronic sinusitis condition.

References

1. Biedlingmaier J & Trifillis A. Comparison of CT scan and electron microscopic findings on endoscopically harvested middle turbinates. Otolaryngology – Head & Neck Surgery 1998; **118(2)**:165-173.
2. Torkkelli T, Rautianen M & Nuutinen J. Ciliary ultrastructure and mucociliary transport in upper respiratory tract infections. Am J Rhinology 1994; **8(5)**:211-215.
3. Ginzel A & Illum P. Nasal mucociliary clearance in patients with septal deviation. Rhinology 1980; **18**:177-181.
4. Al-Rawi M, Edelstein DR & Erlandson RA. Changes in nasal epithelium in patients with severe chronic sinusitis: a clinicopathologic and electron microscopic study. Laryngoscope 1998; **108**:1816-1823.
5. Jones NS. Statements of clinical effectiveness: rhinosinositis. British Association of Otolaryngologists, Head & Neck Surgeons 1998: 21-31.
6. Albert D. Nasal obstruction and rhinorrhoea in infants and individuals. In: Adams D & Cinnamond M. Scott-Brown's Otolaryngology. London: Butterworths 1997; **6(17)**:1-17.
7. Kennedy D, Zinreich S, Rosenbaum A & Johns M. Functional endoscopic sinus surgery: theory and diagnostic evaluation. Arch Otolaryngology 1985; **111**:576-582.
8. Brennan L. Minimising post-operative care and adhesions following endoscopic sinus surgery. ENT Journal 1996; **75(1)**:45-48.
9. Shaw LC-K, Dymock RB, Cowin AJ & Wormald P-J. The effect of packing on the nasal mucosa of sheep. J Laryngol & Otolaryngol 2000; **114(7)**:506-9.
10. Garth R & Brightwell AP. A comparison of packing materials used in nasal surgery. J Laryngol Otol 1994; **108(7)**:564-566.
11. Clark R. Wound repair. Overview and general considerations. In: Raf C. The Molecular and Cellular Biology of Wound Repair. New York: Plennum Press 1996, Ch 1.
12. Davidson JM, Nanney LB, Bradley KN, Whitsett JS, Aquino AM, Beccaro M & Rastrelli A. Hyalvronate derivatives and their application to wound healing: preliminary observations. Clin. Mater 1991; **8(1-2)**:171-7.
13. Burns J, Skinner K, Colt J, Sheidlin A, Bronson R, Yaacobi Y & Goldberg EP. Prevention of tissue injury and postsurgical adhesions by precoating tissues with hyaluronic acid solutions. J Surg Res 1995; **59(6)**:644-652.
14. McIntosh D, Cowin A, Adams D, Rayner T & Wormald P-J. The effect of a dissolvable hyaluronic acid based pack on the healing of the nasal mucosa of sheep. Am J Rhinol 2002; **16(2)**:85-90.
15. Shaw CL, Cowin AJ & Wormald PJ. Standardization of the sheep as a suitable animal model for studying endoscopic sinus surgery. Aust J. Otolaryngol 2001b; **4(1)**:23-26.
16. Shaw LC-K, Cowin AJ & Wormald P-J. A study of the normal temporal healing pattern and the mucociliary transport after endoscopic partial and full-thickness removal of nasal mucosa in sheep. Immunol & Cell Biol 2001a; **79(2)**:145-148.
17. Greenhalgh DG. The role of growth factors in wound healing. Journal of Trauma: Injury Infection and Critical Care 1996; **41(1)**:159-167.
18. Mustoe TA, Pierce GF, Thomason A, Gramates P, Sporn MB & Deuel TF. Accelerated healing of incisional wounds in rats induced by transforming growth factor-β. Science 1987; **237**:1333-1336.