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Histopathological changes of nasal mucosa after nasal packing with Merocel

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Abstract

Objective. To determine histopathological changes in nasal mucosa associated with duration of nasal packing with Merocel tampons.

Methods. This study included 24 healthy rabbits, 6 rabbits per group. In group A, no tampon was applied. In group B, Merocel nasal tampons were applied and removed after 24 hours. In group C, the tampons were removed after 48 hours. In group D, the tampons were removed after 5 days. Specimens were obtained from the septum of each rabbit, including cartilage. Histopathological examination was performed.

Results. Significant differences were observed in terms of inflammatory infiltration and loss of cilia between groups A and B. Significant differences were also observed in terms of inflammatory infiltration, haematoma, cilia loss, epithelium dysplasia and cartilage degeneration between groups B and C. There were significant differences in terms of cilia loss, epithelium dysplasia and subepithelial fibrosis between groups C and D. Cartilage degeneration was mild in one animal in group B and in two animals in group C, and was moderate in four animals in group C.

Conclusion. It is recommended that Merocel nasal tampons are removed within 48 hours to preserve nasal mucosal function. Keeping the pack longer may cause cartilage degeneration and other complications.

Introduction

Nasal packs are widely used in the practice of otorhinolaryngology, most frequently in epistaxis interventions. It is reported that 7–14 per cent of adults experience nose bleeding at one point in their life. When bleeding cannot be stopped with conservative methods (such as digital pressure or cold compress application), anterior nasal tampons play an important role.[1] Nasal packs are also used following septoplasty, septorhinoplasty, and turbinate or endoscopic sinus surgery. Packing is used either to stop the bleeding or to help with settlement of the mucoperichondrial flaps after surgery. Furthermore, packing is used to prevent intranasal adhesion and synechia by keeping the septum and the lateral nasal wall apart.[2,3]

However, commonly used packing materials have some potential risks and complications, including mucosal damage, infection, septal perforation, allergy, dislocation, aspiration, fibrin accumulation, lowering of partial arterial oxygen pressure, granuloma and spherulocytosis.[3,4]

A wide variety of materials may be used in the production of nasal packing materials. Merocel (Medtronic Xomed, Jacksonville, Florida, USA) is one of the most widely used types of packing. Merocel is a non-absorbable dehydrated sponge composed of hydroxylated polyvinyl acetate. When absorbed with normal saline, it swells to fill up the nasal cavity and starts compressing vessels.[2,3,5–8]

Although packings are frequently used in ENT practice, there is no consensus on how long nasal packing can remain safe without causing injury to the nasal structures.[2,8] Nasal packs may cause damage by pressing on the nasal mucosa.

This study aimed to investigate histopathological changes associated with the duration of Merocel tampon use in a rabbit model. The analyses were performed in a rabbit model given that it is not possible to examine septum cartilage and mucosa histopathologically after nasal pack use in humans.

Materials and methods

This experimental study was approved by the Experimental Animal Ethics Committee (approval code: 2020/A28). The study comprised a total of 24 healthy male New Zealand rabbits with normal anterior rhinoscopic examination findings. Rabbits initially weighing 3000–5000 g at 20–42 weeks of age (mean age of 33 weeks) were included in the study. The anaesthetic used was a combination of ketamine hydrochloride (80 mg/kg) and xylazine hydrochloride (2 mg/kg) administered intramuscularly. A dose of 10 mg/kg metamizole (intramuscularly) was administered to all groups to minimise pain.

Main Article

Dr M Tan takes responsibility for the integrity of the content of the paper

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Table 1. Scores for inflammatory markers of histopathological evaluation

Group*	Inflammatory infiltration	Haematoma	Mucosal oedema	Cilia loss in respiratory epithelium	Epithelial dysplasia-metaplasia	Subepithelial fibrosis	Cartilage damage
A – control, no tampon							
– 1	0	0	0	0	0	0	0
– 2	0	0	0	0	0	0	0
– 3	0	0	0	0	0	0	0
– 4	0	0	0	0	0	0	0
– 5	0	0	0	0	0	0	0
– 6	0	0	0	0	0	0	0
B – tampon removed after 24 hours							
– 1	1	0	0	1	0	0	0
– 2	1	1	0	1	0	0	0
– 3	0	0	1	1	1	0	1
– 4	2	0	0	1	0	0	0
– 5	1	0	0	1	1	0	0
– 6	1	0	1	0	0	0	0
C – tampon removed after 48 hours							
– 1	2	1	2	3	2	1	2
– 2	3	2	1	2	1	0	1
– 3	2	2	1	2	2	0	1
– 4	3	1	0	2	1	1	1
– 5	3	2	1	3	1	1	2
– 6	2	1	1	2	2	0	1
D – tampon removed after 5 days							
– 1	2	1	0	2	3	2	2
– 2	2	0	1	2	2	2	3
– 3	3	0	0	3	2	1	2
– 4	2	1	0	2	2	2	1
– 5	2	0	1	3	3	3	3
– 6	2	2	0	3	3	2	1

*Digits in 'Group' column represent animal numbers. Data represent scores for each rabbit specimen, in each group: 0 = none, 1 = mild, 2 = moderate and 3 = severe

The animals were randomly divided into four equal groups. Merocel tampons were prepared from the 8 cm classic Merocel tampons, with dimensions of 20 × 5 × 5 mm, and applied bilaterally. After placement, the tampons were injected with 1 cc physiological saline solution to achieve expansion. In group A (control group, $n = 6$), no tampon was applied. In group B ($n = 6$), tampons were applied and removed after 24 hours. In group C ($n = 6$), tampons were applied and removed after 48 hours. In group D ($n = 6$), tampons were applied and removed after 5 days.

Specimens were taken on the first day in the control group. In groups B, C and D, the tampon was removed and the specimens were taken after 1, 2 and 5 days of tampon placement, respectively. The lateral wall of the nasal cavity was dissected unilaterally under sterile conditions, and approximately 1 × 1 cm full-thickness specimen was obtained from the septum of each rabbit, including the cartilage. Once the bleeding was under control, the incisions were closed properly. The rabbits were delivered alive to the animal laboratory.

The biopsy specimen was fixed in a 10 per cent neutral formalin solution, and a routine tissue follow up was performed. The specimen was then embedded in paraffin and cut into sections of 6 µm thickness. Haematoxylin and eosin stained sections were evaluated under a Nikon Optiphot-2 light microscope and with the Nikon DS-L3 image analysis system (Tokyo, Japan), and photographs were taken.

The specimens were scored in terms of: inflammatory infiltration, haematoma, mucosal oedema, loss of cilia in respiratory epithelium, epithelial dysplasia-metaplasia, subepithelial fibrosis and cartilage degeneration. The scores for each parameter were determined as follows: none = 0, mild = 1, moderate = 2 and severe = 3. The maximum total score per rabbit was 21 (Table 1).

The SPSS® for Windows version 17 statistical software program was used for statistical analysis. The measurable variables are expressed as mean ± standard error. The chi-square test was used to compare the groups. A value of $p < 0.05$ was considered statistically significant.

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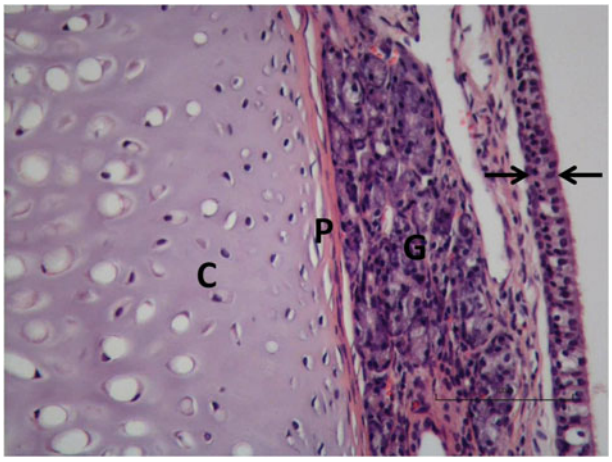

Fig. 1. Haematoxylin and eosin stain of group A (control group, no tampon), highlighting respiratory epithelium (arrows), gland structures (G) in lamina propria, cartilage perichondrium (P), and cartilage (C). Measuring scale = 100 μm.

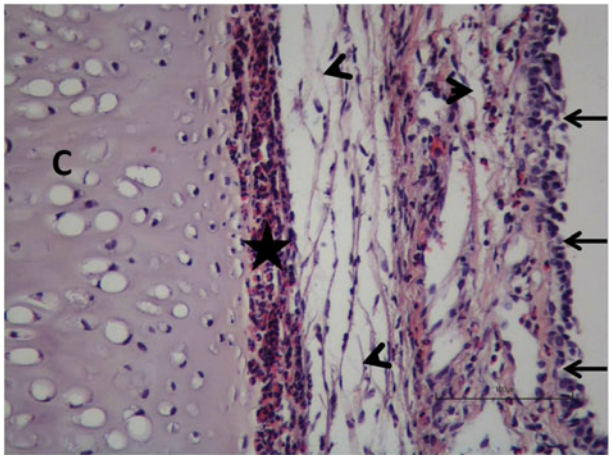

Fig. 3. Haematoxylin and eosin stain of group C (tampon removed after 48 hours), illustrating degeneration and dysplasia changes in the respiratory epithelium (arrows), mucosal oedema (arrowheads), intense inflammatory infiltration (star) in the cartilage perichondrium (star), and cartilage (C). Measuring scale = 100 μm.

Results

Group A

In the control group (no tampon), respiratory epithelium, mucosa and cartilage tissues were observed as having normal histological structure on the sections (Figure 1).

Group B

When tampons were applied and removed after 24 hours, cilia loss, degeneration and dysplastic changes were observed locally in the respiratory epithelial cells, whereas inflammatory infiltration and mucosal oedema were seen in the subepithelial area. The mucous glands displayed patches of irregularity and degeneration, with minimal degenerative changes observed in the cartilage matrix (Figure 2).

Group C

When tampons were applied and removed after 48 hours, cilia loss, degeneration, dysplastic and metaplastic changes were observed extensively in the respiratory epithelial cells. Additionally, there was extensive inflammatory infiltration and oedema in the subepithelial area and perichondrium of the cartilage. In some areas, advanced cartilage degeneration and basophilic granulation in the cartilage matrix were also observed (Figure 3).

Group D

When tampons were applied and removed after 5 days, there was widespread degeneration, dysplastic change, diffuse inflammatory infiltration in the mucosa, extravascular erythrocytes, subepithelial oedema and fibrosis in the respiratory epithelium. Moreover, goblet cell hyperplasia was detected partly in the dysplastic epithelium. Intense inflammatory infiltration was observed in the perichondrium of the cartilage, which extended into the cartilage matrix at certain points (Figure 4).

Statistical findings

Statistically significant differences were found between groups A and B in the terms of inflammatory infiltration ($p = 0.015$) and loss of cilia ($p = 0.08$). Between groups B and C, statistically significant differences were found in inflammatory infiltration

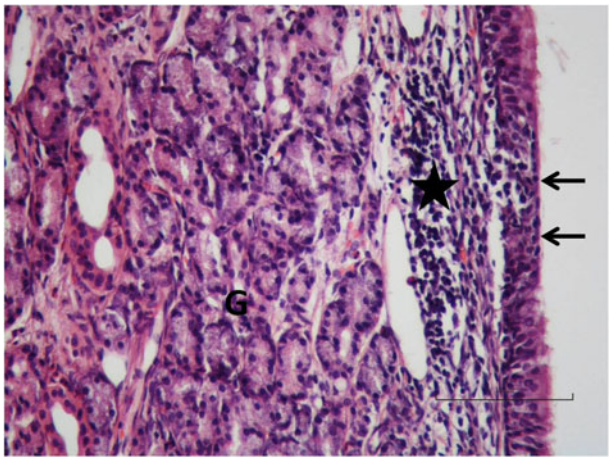

Fig. 2. Haematoxylin and eosin stain of group B (tampon removed after 24 hours), showing loss of cilia and metaplastic change in the respiratory epithelial cells (arrows), inflammatory infiltration (star) in the subepithelial area, and gland structures in the lamina propria (G). Measuring scale = 100 μm.

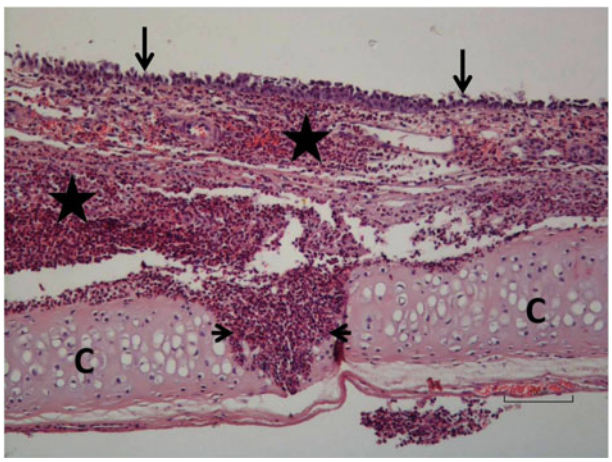

Fig. 4. Haematoxylin and eosin stain of group D (tampon removed after 5 days), demonstrating degeneration in the respiratory epithelium (long arrows), intense inflammatory infiltration (stars) in the mucosa, cartilage degeneration (short arrows), and cartilage (C). Measuring scale = 100 μm.

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($p = 0.033$), haematoma ($p = 0.015$), cilia loss ($p = 0.002$), epithelium dysplasia ($p = 0.037$) and cartilage degeneration ($p = 0.026$). Furthermore, statistically significant differences were found between groups C and D in terms of epithelium dysplasia ($p = 0.03$) and subepithelial fibrosis ($p = 0.03$).

Discussion

Various nasal packing types are used in ENT practice to stop bleeding, prevent synechia and haematoma, and support mucoperichondrial flaps, both after endonasal surgery and in epistaxis management. However, nasal pack use carries risks of infection, synechia, perforation, and pain or bleeding during pack removal.[3,9]

A wide variety of materials are used in nasal packing. The two main classes of packing materials are absorbable and non-absorbable. Examples of non-absorbable packing materials are polyvinyl alcohol sponges, Vaseline® gauze strips, cotton gauze strips, alginate, Telfa™, cellulose Tabotamp® and Rapid Rhino (ArthroCare UK, Glenfield, UK). Examples of absorbable packing materials include gelatine (e.g. Gelfilm®, Gelfoam®), bovine gelatine plus thrombin (Floseal®), NasoPore (Polyganics, Groningen, Netherlands) and MeroGel (Medtronic Xomed Surgical Products, Jacksonville, Florida, USA).[10,11] The selection of materials is based on accessibility, cost, personal preference and experience.

This study examined the changes in nasal mucosa associated with the use of an inexpensive and frequently used, non-absorbable and removable nasal packing material over time. Despite common usage, there is no consensus regarding the safe duration of nasal packing placement in the nasal structures.[12,13] It is accepted that nasal pack use can cause changes in the nasal mucosa. The duration and type of packing are acknowledged as being determining factors for histopathological changes of the nasal mucosa.

In an experimental study, Genç *et al.* compared ribbon gauze packing and trans-septal sutures.[14] The packings were removed after 48 hours. The researchers' histopathological examination showed that mucosal damage and inflammation were significantly increased in both groups in comparison to the control group.[14] In our study, the extension of inflammation was significantly higher in group B (tampons removed after 24 hours) in comparison to the control group (group A, no tampon). Additionally, the mucosal damage and inflammation parameters were significantly greater in group C (tampons removed after 48 hours) and group D (tampons removed after 5 days) compared to group A. These results showed that, as the duration of nasal packing in situ increased, so did the inflammatory changes.

In another animal study, the Merocel tampon and glove finger tampon were applied for 48 hours, and loss of cilia was observed in both groups. Furthermore, in the Merocel group, lamina propria damage was observed in half of the animals, and cartilage degeneration was observed in one animal.[15] In our study, we evaluated both cilia loss and cartilage degeneration in all groups. Slight loss of cilia was observed in five animals after tampon removal in group B ($n = 6$). In group C ($n = 6$), moderate loss of cilia was observed in four animals, and severe loss of cilia was observed in two animals. In group D ($n = 6$), moderate loss of cilia was observed in three animals, and severe loss of cilia was observed in three animals. Cartilage degeneration was mild in only one animal in group B, whereas it was mild in two and moderate in four animals in group C, and mild in two, moderate in two and severe in two animals in group D.

In a different study utilising Merocel, the packing was positioned at the maxillary sinus of the rabbit, and biopsy was performed after two weeks. The biopsy specimens showed a disrupted mucociliary structure and fibrosis in the lamina propria.[16] In our study, subepithelial fibrosis was not observed in group B, and was mild in three animals in group C. In group D, subepithelial fibrosis was mild in one animal, moderate in four animals and severe in one animal. A statistically significant difference was found between groups C and D in terms of subepithelial fibrosis.

In a clinical study, nasal pack use duration was evaluated in patients who underwent septoplasty. The patients were divided into two groups according to pack use duration, whereby the packing was removed after 24 or 48 hours, respectively. The discomfort score was significantly lower in the second group; however, no statistically significant differences were found in terms of headache and bleeding.[12] In another study, nasal packs were removed after 12 hours and 24 hours in epistaxis patients. Headache and lacrimation were minimal in the 12-hour group, whereas no significant difference was found in terms of re-bleeding.[17] Another study used Merocel wrapped with Surgicel® cellulose based thrombogenic material, which was removed after 48 hours. Only 1 of the 25 patients had re-bleeding, and there were no additional complications.[18]

- Nasal packs are widely used in ENT practice
- There is no consensus regarding the duration of use for different nasal pack types
- A longer duration of nasal pack use can cause various problems
- After 48 hours, nasal pack use can damage nasal septum cartilage
- This paper describes the first histopathological study published in English on the effects of nasal pack use over time

The results of this study indicate that caution is needed when nasal packing tampons remain in place for longer than 48 hours. Sometimes, nasal packing may be needed for longer durations. This might not be necessary for epistaxis interventions, but it may be required after nasal surgery. Extra caution is advised where there is adhesion; it may be necessary to moisten the nasal packs when removing the tampons, and to perform nasal examination following pack removal.

Conclusion

There are no established guidelines or consensus regarding the timing of packing removal. A limited number of studies in the literature show histopathological changes in the nasal mucosa associated with the duration of nasal packing placement. In our study, histopathological changes were evaluated with a broad set of parameters in groups of different pack use duration. The results showed statistically significant differences in the histopathological findings of nasal mucosa depending on the duration of nasal packing placement. The results of this study suggest that nasal packing removal within 48 hours of placement could prevent histopathological changes in the nasal mucosa and complications. There are many materials available that can reduce damage to the mucosa; it would be preferable to use a nasal packing material such as the standard Merocel tampon for no longer than 48 hours if possible, considering both the anti-haematoma effects and patient discomfort.

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