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Research Paper

Healing of the nasal septal mucosa in an experimental rabbit model of mucosal injury

Kyu Young Choi [a], Sung Woo Cho [b], Jun-Jae Choi [b], Yu-Lian Zhang [b], Dae Woo Kim [b], Doo Hee Han [b], Hyun Jik Kim [b], Dong-Young Kim [b], Chae-Seo Rhee [b], Tae-Bin Won [b,*]

[a] *Department of Otorhinolaryngology-Head and Neck Surgery, Hallym University College of Medicine, Kangnam Sacred Heart Hospital, Seoul, 07441, South Korea*
[b] *Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University College of Medicine, Seoul National University Hospital, Seoul, 03080, South Korea*

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Abstract *Objective:* The aim of this study was to investigate the regeneration process of the nasal mucosa after a surgically created mucosal defect in the rabbit nasal septum, and to evaluate the effects of different interventions.
Methods: A 7 mm-diameter circular mucosal defect was made in the septum of forty New Zealand white rabbits. The rabbits were divided into four groups (ten rabbits in each group) according to the type of intervention; no treatment (control), silastic sheet (SS), hyaluronic acid (HA), and silastic sheet and hyaluronic acid (SS + HA) group. The diameter of the defect, mucosal thickness, epithelial thickness, and ciliated cell count were evaluated every week for five weeks.
Results: The average diameter of the defect in the control group were 5.1, 3.65, 1.2, 0.75, and 0.05 mm at postoperative 1, 2, 3, 4, and 5 weeks. In the SS group, the diameter decreased to 4.35, 2.1, 0.35, 0.15, and 0 mm at postoperative 1, 2, 3, 4, and 5 weeks, respectively, in which the mean diameter of the postoperative week 2 was significantly smaller compared to control (3.65 mm vs. 2.1 mm, $P = 0.039$). For the HA group and SS + HA group, the diameter of the defect did not show a significant difference from the control group during the five weeks. The mucosal thickness, epithelial thickness, and ciliated cell count of the regenerated mucosa were not significantly different among the groups.

* Corresponding author. Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University College of Medicine, Seoul National University Hospital, 101, Daehak-ro, Jongno-gu, Seoul, 03080, South Korea. Fax: +82 2 745 2387.
E-mail address: binent@hanmail.net (T.-B. Won).
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Conclusion: The regeneration process of the nasal septal mucosa was identified using a novel rabbit model. Mucosal regeneration can be accelerated by applying silastic sheets.

Introduction

Mucosa of the nasal septum can be injured in a number of rhinologic surgeries. With the recent advances in endoscopic skull base surgery and the use of the nasoseptal flap for reconstruction, the number and extent of iatrogenic injury to the septal mucosahas increased. However, a comprehensive understanding of the process involved in the healing of the septal mucosa is lacking and the factors that influence its regeneration have yet to be clarified.

The process of wound repair has been extensively studied in tissues such as the gingiva and the skin.[1] Although the healing process of the sinonasal cavity has been reported using different animal models,[2–6] there has been no studies evaluating wound healing after injury to the nasal septal mucosa.

Silastic sheet is commonly used after nasal surgery to promote mucosal healing. It is thought to accelerate the mucosal healing process by moistening and humidifying the wound.[7,8] Although there have been a number of reports on clinical outcome with a silastic sheet after septoplasty, the effect of this material on septal mucosa has not been clearly documented. Moreover, there are relatively few studies describing such effects at a histological level. Hyaluronic acid has shown to bring about a shorter epithelialization time in patients undergoing sinus surgery,[9] but its effect on promoting healing of the septal mucosa has not been proven.

The objective of this study was to investigate the regeneration process of the nasal mucosa in a surgically created defect in the rabbit nasal septum, and to evaluate the effects of different interventions that can promote mucosal wound healing.

Materials

Septal mucosa wound healing model in rabbit

The experiment was performed in the Seoul National University Hospital Biomedical Research Institute in Seoul, Korea. Approval from Institutional Animal Care and Use Committee in Seoul National University was obtained before initiation of the study (No. 13—0085). The study was conducted in accordance with the principles of the Helsinki Declaration on the use of laboratory animals. Forty adult New Zealand white rabbits with a mean body weight of 3,700 g (3000 to 4200 g) were used as experimental animals. They were randomly assigned to one of four groups; control group, silastic sheet group (SS), hyaluronic acid group (HA), and both silastic sheet and hyaluronic acid group (SS + HA).

Prior to surgery, each animal received an intramuscular injections consisting of Zoletil® 10 mg/kg (tiletamine 125 mg/ml, zolazepam 125 mg/ml) and Rumpun® (2% xylazine) at a ratio of 1:2 for general anesthesia. Areas over the nose (snout) were shaved and draped with povidone-iodine solution. After infiltration with a mixture of 1% lidocaine and 1:100,000 epinephrine, a 5 cm-long midline nasal dorsum skin incision was made through the periosteum with a #10 blade. The laterally-based periosteal flaps were raised bilaterally, fully exposing the nasal bone. Nasal osteotomy was performed in a rectangular shape using a 4 mm straight osteotome gaining access to the nasal septum. The septum was fully exposed by separating the upper lateral cartilages from the septum and performing bilateral partial inferior turbinectomy (Fig. 1A). A circular mucosal incision was made with a diameter of 7 mm on the concave side of the septum,[10] at an intersection point 3 mm below the septal roof and 3 mm caudal to the end of the middle turbinate, using a circular punch that we had manufactured (Fig. 1B). The mucosa of the circular lesion was elevated and stripped off together with the perichondrium using a blunt duckbill elevator, exposing the underlying septal cartilage (Fig. 1C). Bleeding control was achieved with bosmin-soaked gauze. Sixteen rabbits had the left septum used as the intervention side, while the right side was used in 24 rabbits.

For the control group, the elevated nasal bone was put back in place after the mucosal removal, followed by skin closure. For the SS group, a 1 cmX 1 cm square piece of a silastic sheet (Medtronic Xomed, Jacksonville, FL) was placed on the septum covering the defect, and anchored to the septum superiorly using a 5-0 Vicryl (Ethicon, Inc., Somerville, NJ) (Fig. 2A). For the HA group, a piece of MeroGel® (Ethicon, Inc., Somerville, NJ) was cut to a 1 cmX 1 cm-sized square piece and placed on the injured septum (Fig. 2B), then it was hydrated with 1 ml of sterile normal saline according to the manufacturer's instructions. Lastly, for the SS + HA group, the silastic sheet was applied over the HA (Fig. 2C). Intramuscular procaine penicillin (40,000 IU) was administered on a prophylactic basis for three consecutive days postoperatively, and fentanyl (0.02 mg/kg) was injected subcutaneously for pain control. All surgical procedures were performed by one investigator.

In order to evaluate the process of mucosal healing, two rabbits in each group were sacrificed using a phenobarbital overdose after 1, 2, 3, 4, and 5 weeks. The entire cartilaginous septum was harvested for evaluation.

Analysis of mucosal regeneration

Harvested septum was washed three times in phosphate buffered saline (Sigma—Aldrich, St. Louis, MO) and digital photographs of the wound site were obtained (Fig. 3A). Remaining blood clot, foreign body, and granulation tissue formed on the septum were all removed with gentle suction