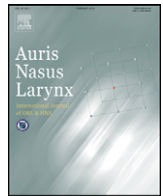




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The use of sodium hyaluronate-carboxymethylcellulose to prevent postoperative mastication pain from harvesting of temporalis fascia

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ABSTRACT

Objective: To evaluate the anti-adhesive and anti-inflammatory effects of sodium hyaluronate-carboxymethylcellulose (HA-CMC) in reducing postoperative pain after temporalis fascia harvest during tympanomastoid surgery.

Materials and methods: Between January and December 2009, 27 patients underwent tympanoplasty and open cavity mastoidectomy involving the harvesting of temporalis fasciae (more than 3×4 cm). At the end of surgery, patients were injected with 1.5 g HA-CMC or normal saline around the fascia harvest area. Beginning immediately postoperatively and for 2 months after surgery, patients scored their pain in the temporal area on a visual analogue scale (VAS).

Results: There were no significant postoperative complications, such as bleeding or hematoma, in either control group. VAS scores of both groups decreased over time and were negligible after 2 months. VAS scores of the HA-CMC and control groups differed significantly ($p < 0.001$ by repeated measures ANOVA for all VAS scores).

Conclusion: HA-CMC can decrease immediate postoperative pain arising from tissue adhesion and inflammation, thus reducing postoperative mastication pain.

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1. Introduction

During tympanomastoid surgery, the temporalis fascia is most commonly used for myringoplasty due to its large quantity, reduced blood supply, relative resistance to infection, and lower metabolic rate, and because no separate incision is required for harvest [1]. To harvest the temporalis fascia, a surgeon must dissect between the temporalis muscle and adjacent tissues. After incision and grafting of the fascia, the traumatized temporalis areas are electrocauterized to control bleeding, but are not otherwise manipulated. Many patients who undergo tympanoplasty accompanied by temporalis fascia harvest complain of dull pain in the ipsilateral temporal area during mastication or even while resting. However, these complaints are usually disregarded by the surgeon or even by patients because postoperative mastication pain is a minor complication compared with other complications such as facial palsy and postoperative wound infection.

We supposed that postoperative mastication pain may arise from direct injury to the temporalis muscle and/or from postoperative tissue adhesion. Adhesion formation is a complicated process.

Although its pathophysiology is understood, it has not yet been solved. Adhesions can result from mechanical tissue damage, tissue ischemia, or the presence of foreign materials. In addition, two areas of injury must be in contact with each other. Both fibrinogenesis and fibrinolysis are activated, with a distortion of the dynamic balance between these two processes leading to adhesion formation [2,3].

Sodium hyaluronate, a nonsulfated glycosaminoglycan polysaccharide, is known to be inert, safe and easy to use, and remains at a biological site over extended periods of time [4,5]. Chemically modified sodium hyaluronate-carboxymethylcellulose (HA-CMC) is a bioresorbable agent shown to greatly reduce the incidence and degree of postoperative adhesions in patients, including those undergoing radical debulking procedures during abdominal and gynecological surgeries [6,7]. We have therefore evaluated the anti-adhesive effects of HA-CMC in reducing postoperative mastication pain after large temporalis fascia harvest during tympanomastoidectomy.

2. Materials and methods

2.1. Patients

This prospective, single-blinded study was carried out on patients who underwent tympanoplasty with open cavity mastoidectomy from January to December 2009 in the Department of

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Otolaryngology, Asan Medical Center, Seoul, Republic of Korea. Total 27 patients (16 male and 11 female) underwent tympanoplasty and open cavity mastoidectomy and the mean age was 48.0 ± 13.7 years (from 26 to 69 years).

We performed open cavity mastoidectomy when (1) the matrix of cholesteatoma had grown so extensively, that it looked unable to be eradicated from canal wall up technique, (2) the mastoid cavity was so contracted that we decided to carry out open cavity mastoidectomy for complete removal of the remaining disease, (3) there was suspiciously large dehiscence over labyrinth such as facial nerve or lateral canal from CT scan, and (4) the patients had received tympanomastoidectomy previously with failure. In this study, patients were included if (1) a large area of temporalis fascia (more than 3×4 cm) was harvested for coverage of the cavity after open cavity mastoidectomy and meatoplasty, (2) they had no problems with mastication before surgery, (3) the ear was available for follow-up for a minimum period of 2 months. Patients were excluded if (1) their ears had undergone previous tympanomastoid surgery, (2) they could not express their extent of pain or dullness, and (3) they showed delayed healing or postoperative complications such as infection or hematoma.

The study protocol was approved by the institutional Review Board of the Asan Medical Center, and all patients provided written informed consent.

2.2. Harvesting fascia

Following general endotracheal anesthesia, four quadrants of each ear canal were injected with a solution of 1% lidocaine and 1:200,000 epinephrine. A #15 blade was used to fashion a postauricular incision approximately 5 mm behind the postauricular crease and bleeding was controlled with electrical cauterization.

Once hemostasis was achieved, a small Paparella curved retractor was positioned to hold the auricle forward. The assistant placed a Cushing straight retractor under the upper part of the incision and pulled laterally, exposing the temporalis fascia. Before harvesting fascia, a greater than 3×4 cm sized incision was made on the temporalis fascia superiorly to the level of the linea temporalis and dissected the temporalis fascia free from the temporalis muscle using a periosteal elevator and Metzenbaum scissors. This tissue was then pressed between two slide glasses and placed on the back table in the open air for natural drying (Fig. 1). One senior surgeon carried out every surgery in this study. To avoid the selecting bias between HA-CMC and control group,

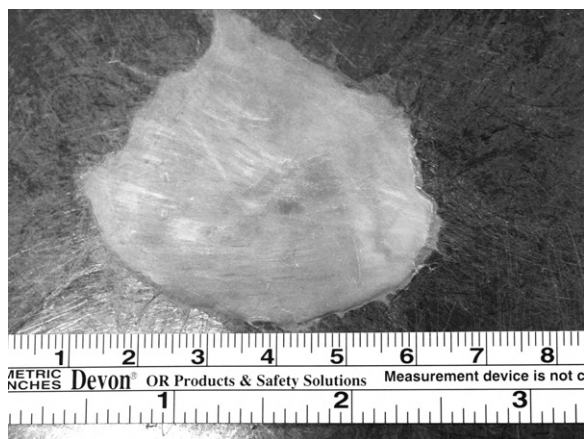


Fig. 1. Harvest of temporalis fascia during surgery. Large temporalis fascia (more than 3×4 cm) was harvested for grafting in tympanoplasty and open cavity mastoidectomy. After fascia harvest, bleeding was controlled with electrocauterization.

another surgeon prepared all temporalis muscle fascia in the same way before the senior surgeon started to operate.

2.3. Application of HA-CMC

At the end of the surgery, the temporalis fascia was inserted for myringoplasty and coverage of the mastoid denuded surface. After packing the ear canal with cotton wicks, we alternately assigned patients into HA-CMC group ($N = 14$) who received 1.5 g of HA-CMC (Guardix[®], Hanmi pharmaceutical co., Ltd., Seoul, Korea) and Control group ($N = 13$) who received the same volume of normal saline into the fascia harvest area before skin suture. For HA-CMC group, we applied HA-CMC (1.5 g) around the space where temporalis muscle fascia had been harvested. Since HA-CMC was viscoelastic solution prepared in a syringe, it was not difficult to deliver HA-CMC evenly on the harvested area.

Each patients did not know whether they had received HA-CMC or not during the operation under general anesthesia.

2.4. Evaluation of postoperative pain

Postoperative pain was evaluated using a visual analogue scale (VAS), with pain scored from “none (0)” to “very severe (10)”. Patients were instructed to mark the point on the line corresponding to their perception of current pain. VAS scores were recorded daily for 1 week, and at the end of weeks 2, 3, 4, and 8.

2.5. Statistics

R version 2.6.1 was used to analyze data and draw survival curves (R Development Core Team, Vienna, Austria, <http://www.R-project.org>). Values were presented as means \pm standard deviations. The analysis of variance (ANOVA) for repeated measures was used to compare VAS scores. Changes within and between groups were considered statistically significant when P values were <0.05 .

3. Results

There were no significant differences between the HA-CMC and control group in patient age, sex, and side of operation. None of the patients experienced any postoperative complications, such as hematoma, wound infection, or facial palsy (Table 1).

Beginning immediately after surgery, patients in both the HA-CMC and control groups complained of dull pain in the temporal area during mastication. This pain decreased over time and became negligible after 2 months. The initial VAS scores were 2.9 ± 1.7 in the HA-CMC group and 3.9 ± 3.2 in the control group, decreasing to 0.6 ± 0.9 and 0.6 ± 1.0 , respectively, 2 months after surgery. For those 2 months, however, VAS scores of the HACMC group differed significantly from those of the control group ($p < 0.001$ by repeated measure ANOVA for all VAS scores) (Fig. 2).

4. Discussion

The temporalis muscle is one of the masticator muscles, together with the masseter, medial and lateral pterygoid muscles.

Table 1

Patient demographics. There were no significant differences between the HA-CMC and control groups.

	HA-CMC group ($n = 14$)	Control group ($n = 13$)	P -value
Age (years)	46 ± 11	53 ± 10	NS
Sex (Male:Female)	8:6	8:5	NS
Side (Right:Left)	9:5	8:5	NS
Postoperative complications	No	No	

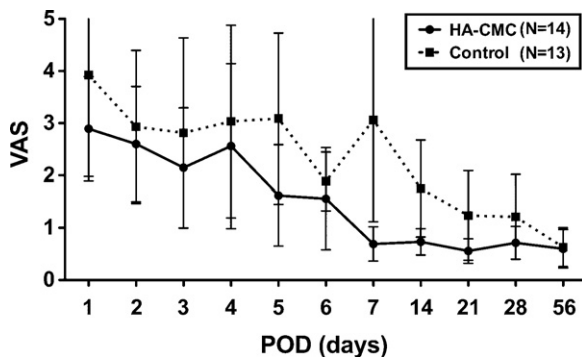


Fig. 2. Changes in visual analogue scale (VAS) of the HA-CMC and control groups. After surgery, patients in both the HA-CMC and control groups complained of dull pain in the temporal area during mastication. This pain decreased over time and was negligible after 2 months. VAS scores of the two groups differed significantly ($p < 0.001$ by repeated measures ANOVA for all VAS scores), indicating that HA-CMC played a role in preventing adhesion between the traumatized 34 temporalis muscle and adjacent soft tissues.

The temporalis muscle arises from the temporal fossa and the deep part of the temporal fascia, passing medial to the zygomatic arch and inserting into the coronoid process of the mandible. The temporal muscle is covered by the temporal fascia, also known as the temporal aponeurosis [8].

This is the first study to evaluate the anti-adhesive effect of HA-CMC in reducing postoperative mastication pain. We found that VAS scores of patients injected with HA-CMC significantly differed from those of the control group, suggesting that the anti-adhesive effects of HA-CMC prevented postoperative tissue adhesion between the traumatized temporalis fascia harvest site and adjacent tissues. In general, damage to the temporalis muscle and fascia causes muscle atrophy with disfigurement, contracture of the muscle with limited mouth opening, and pain. Bipolar coagulation is widely used in surgical hemostasis in tympanomastoidectomy, including temporalis fascia harvest. However, the incidence of adhesions after bipolar coagulation has rarely been studied. Adhesion formation begins with the formation of a fibrin matrix, typically occurring during coagulation in the presence of suppressed fibrinolysis [9]. In a study of wounds made by several coagulation methods, bipolar high-frequency coagulation was found to cause large zones of destruction, as assessed by macroscopic, microscopic, and ultrastructural cellular alterations [10].

During temporalis muscle fascia harvest, it is unavoidable to prevent injuries to the temporalis muscle or surrounding tissue from dissection and electro-cauterization, especially when approaching more anteriorly and superiorly to obtain large fascia. These injuries can cause posttraumatic adhesion and muscle contracture, inducing postoperative mastication pain. This pain is usually temporary, lasting only one or two months after tympanomastoidectomy. However, although a minor complaint, it can affect patient quality of life.

Subjects in HA-CMC group felt less uncomfortable than those in the control group even immediately after surgery, when tissue adhesion had not yet developed. In addition to its anti-adhesive effects, HA-CMC may have anti-inflammatory properties during the initial wound healing process after temporalis fascia harvest.

Hyaluronate is an anionic, non-sulfated glycosaminoglycan distributed widely throughout connective, epithelial, and neural tissues [11]. As one of the chief components of the extracellular matrix, hyaluronate contributes significantly to cell proliferation and migration, and may also be involved in the progression of some malignant tumors. Inflammation after surgical trauma leads to the generation of many biological factors, including growth factors, cytokines and eicosanoids, which are necessary for subsequent

wound healing steps by promoting the migration of inflammatory cells, fibroblasts and endothelial cells into the wound site [12]. During the early inflammatory phases of wound repair, the wounded tissue has high amounts of hyaluronate, due probably to increased synthesis [12]. Hyaluronate acts as a promoter of early inflammation, which is crucial for the entire wound healing process.

Hyaluronate may also function in the negative feedback loop of inflammatory activation through its specific interactions with the biological constituents of inflammation. $\text{TNF-}\alpha$, an important cytokine generated during inflammation, stimulates the expression of the hyaluronate-binding protein TSG-6 (TNF-stimulated gene 6) in fibroblasts and inflammatory cells. TSG-6 also forms a stable complex with the serum proteinase inhibitor $\text{I}\alpha\text{I}$ (Inter- α -inhibitor), having a synergistic effect on the latter's plasmin-inhibitory activity. Plasmin is involved in activating the proteolytic cascade of matrix metalloproteinases and other proteinases, leading to inflammatory tissue damage. Therefore, the TSG-6/ $\text{I}\alpha\text{I}$ complex, which may also be organized by binding to hyaluronate in the extracellular matrix, may serve as a potent negative feedback loop to moderate inflammation and stabilize granulation tissue as healing progresses [12,13].

5. Conclusion

Our results indicate that HA-CMC can decrease postoperative mastication pain resulting from large temporalis fascia harvest during tympanomastoidectomy. This reduction in pain may be due to the anti-adhesive and anti-inflammatory properties of HA-CMC. Additional studies are required to determine whether HA-CMC has similar effects in other types of otologic surgery, including myringoplasty and temporalis flap surgery.

Conflict of interest

None.

Acknowledgment

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