

Effects of topical hyaluronic acid (Sepragel®/Hylan B) on mucosal healing after endoscopic sinus surgery

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Abstract

Objective: To investigate the effects of hyaluronic acid (HA) (Sepragel® Hylan B; Genzyme Co., Cambridge, MA, USA) on the mucosal healing of patients who undergone functional endoscopic sinus surgery (FESS) for chronic rhinosinusitis and/or nasal polyposis.

Methods: A total of thirty-six patients were included in the study. Patients had received topical administration of HA soaked sponges to the middle meatus on one side of their nasal cavities intra-operatively at the end of the procedures. Other side of the middle meatus was free of any treatment or packing to create a control group. Postoperative endoscopic examination was performed at the 1st, 4th and 12th weeks in order to score mucosal findings regarding synechia, mucosal hypertrophy and polyp formation on both sides. Mucosal findings were scored from 0 to 3 points (0: lesion free, 1: mild, 2: moderate, 3: severe).

Results: Average scores of the mucosal cavities were compared and it was found to be significantly low for the HA administered mucosa ($p<0.05$). Synechia formation and mucosal hypertrophy at the 1st, 4th and 12th weeks were significantly low for the Hylan B group compared to the control group ($p<0.05$ for both findings).

Conclusion: Topical HA has preventive effects on synechia formation and mucosal hypertrophy.

Keywords: Functional endoscopic sinus surgery, hyaluronic acid, chronic rhinosinusitis, nasal polyposis, synechia.

Özet: Topikal hyaluronik asidin (Sepragel®/Hylan B) endoskopik sinüs cerrahisi sonrası mukozal iyileşme üzerindeki etkisi

Amaç: Çalışmanın amacı kronik rinosinüzit ve/veya nazal polip tedavisi için fonksiyonel endoskopik sinüs cerrahisi (FESS) uygulanan hastalarda hyaluronik asidin (HA) (Sepragel® Hylan B; Genzyme Co., Cambridge, MA, ABD) mukozal iyileşme üzerine etkisini araştırmaktır.

Yöntem: Çalışmaya toplam 36 hasta dahil edildi. Cerrahi prosedürler hastaların bir taraf orta meatuslarına HA emdirilmiş spongel'in lokal uygulanması ile sonlandırıldı. HA uygulanmayan diğer nazal kavitelere herhangi bir tedavi ya da tampon uygulaması yapılmadı ve çalışmanın kontrol grubu olarak takipleri yapıldı. Her iki nazal kavite mukozal sineşi, hipertrofi ve nazal polip oluşumu yönünden postoperatif 1., 4. ve 12. haftalarda endoskopik muayene ile incelendi. Mukozal bulgulara muayene sonrası 0 ile 3 arasında puan verildi (0: lezyon yok, 1: hafif derece lezyon, 2: orta derece lezyon, 3: şiddetli derece lezyon).

Bulgular: Her iki taraf nazal kavite ortalama puanları karşılaştırıldı ve puan mukozasına HA uygulanan nazal kavitede istatistiksel olarak anlamlı derecede düşük bulundu ($p<0.05$). Sineşi oluşumu ve mukozal hipertrofi bulguları, 1., 4. ve 12. haftalarda HA grubunda kontrol grubundan istatistiksel olarak anlamlı derecede düşük bulundu ($p<0.05$).

Sonuç: Topikal hyaluronik asit uygulaması sineşi ve mukozal hipertrofinin üzerine önleyici etkilere sahipti.

Anahtar sözcükler: Fonksiyonel endoskopik sinüs cerrahisi, hyaluronik asit, kronik rinosinüzit, nazal polip, sineşi.

Surgical management of chronic rhinosinusitis and nasal polyposis has evolved and become an inevitable end point for the treatment of cases which are resistant to medical interventions.^[1] Related to the technical advances, blinded conventional surgical methods such as intranasal ethmoidectomy have been replaced with image-guided endoscopic and

more functional methods.^[2] Functional endoscopic sinus surgery (FESS) is a set of minimally invasive techniques in which paranasal air cells and ostia are opened under direct visualization.^[3] As all other surgical procedures, FESS is not a complication-free surgery. From minor to major, various complications such as minor bleeding, periorbital edema,

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cerebrospinal fluid rhinorrhoea and orbital injury may occur during or after the surgery.^[4,5] The main goal of FESS is to eradicate diseased mucosa, restore sinus ventilation and maintain a healthy normal functioning mucosal ciliary activity.^[6] Unfortunately, after the extirpation process, denuded edematous mucosal surfaces proximate and unfavorable synechia formation may occur. Uncontrolled synechia formation of the middle meatus or frontal recess area may result with recurrent disease or iatrogenic sinonasal pathologies. In order to inhibit the risky approximation of highly adhesive raw surfaces, modifications in surgical methods or systemic and topical administrations of chemical agents such as corticosteroids have been proposed.^[7]

Recently, physicians have been tried to adapt viscoelastic biomaterials between denuded surfaces in body cavities to prevent fibrin formation and fibroblast ingrowth.^[8] As an example of these biomaterials, hyaluronic acid (HA) is a natural polysaccharide (glycosaminoglycan composed of repeated disaccharides of D-glucuronic acid and N-acetyl-glucosamine) in the extracellular matrix of living organism, such as connective and epithelial tissues.^[9] HA has important bioactivities, such as decreased adhesion formation and increased epithelial regeneration and it has various clinical applications from dry eye syndrome to wound healing.^[10,11]

In the present study, we aimed to investigate the effects of HA on the mucosal healing of patients undergone endoscopic sinus surgery for chronic sinusitis with or without nasal polyposis.

Materials and Methods

Study design

Ethical committee of the hospital has approved the study and all patients had given written consent. Twenty-one male and 15 female adult patients with chronic sinusitis with or without polyposis who are resistant to medical therapy and required FESS (bilateral ethmoidectomy without middle turbinectomy, with or without antrostomy and with or without nasal septoplasty, and with or without frontal sinusotomy) were recruited to this study. None of the patients had previous nasal or endoscopic sinus surgery. Patients were asked about any food hypersensitivity and none had declared chicken hypersensitivity (Sepragel® is derived from rooster material).

Surgical procedures and follow-up

All procedures were performed under general anesthesia by the senior author of this study. At the end of the procedures,

one side of the ethmoid cavities was filled with approximately 6 to 12 mL “Hylan B”. Sepragel® sinus (Genzyme Co., Cambridge, MA, USA) is a sterile, non-pyrogenic, transparent, viscoelastic gel composed of cross-linked molecules of hyaluronan. Hyaluronan is a bioabsorbable material that functions to fill a cavity to keep mucosal surfaces separate during the healing process. Other side of the middle meatus was free of any treatment or packing. Patients received postoperative oral antibiotic (second generation cephalosporin) for 10 days. Topical nasal steroids were not administered. Patients were also instructed not to take any medication (included over the counter drugs) unless approved by the senior author of the study.

Outcome parameters

The physicians performed postoperative endoscopic controls of the cavities at the 1st, 4th and 12th weeks after the procedures. During the examination, cavity was refilled with Sepragel®, based on the amount of remaining Hylan B in the cavity. Cavities were scored in terms of the presence and degree of “synechia, mucosal hypertrophy and polyp formation” shown in Table 1. Examiner graded the pathology from 0 to 3 points. “0” indicates “no visible lesion”, “1” indicates “mild lesion”, “2” indicates “moderate lesion” and “3” indicates “severe lesion”. Each patient was graded with a minimum “0”, maximum “9” total points and grading was repeated at the 1st, 4th and 12th weeks.

Statistical analysis

Statistical analysis was performed with “SPSS 15.0 (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL, USA) for Windows XP”. Median values of the total scores of groups (Hylan B group and control group) were compared using Wilcoxon Signed Ranks statistical analysis. $p < 0.05$ was considered statistically significant.

Results

Of the 36 patients, 21 were male and 15 were female with a mean age of 41.64 ± 3.26 (range: 22 to 62) years. Of the 36

Table 1. Endoscopic evaluation of nasal cavity.

Endoscopic examination	Score
No visible lesion	0
Mild lesion	1
Moderate lesion	2
Severe lesion	3

patients, 20 had chronic rhinosinusitis without nasal polyposis and 16 had nasal polyposis. All patients had bilateral endoscopic anterior and posterior ethmoidectomy. Five patients had simultaneous septoplasty with ethmoidectomy.

No operative or postoperative complication occurred and no side effects were observed related to Hylan B. Table 2 showed postoperative mucosal grading. Synechia formation at the 1st, 4th and 12th weeks was significantly less for the Hylan B group compared to the control group ($p < 0.05$). Mucosal hypertrophy at the 1st and 4th weeks was significantly less for the Hylan B group compared to the control group ($p < 0.05$). The degree of the polyp formation was not significant at the 12th week between the groups ($p > 0.05$). Statistical results are summarized in Table 3.

Discussion

Rhinologists are frequently experienced with the blockage of the middle meatus after endoscopic sinus surgery. Unfortunately, this is usually come out with the recurrent disease and revision procedures. Numerous methods with varying results have been proposed to deal with this issue.^[12] Medialization of the middle turbinate with transseptal suturing or iatrogenic adhesion creation, middle turbinate reductions (complete or partial), antrostomy stents and various spacers such as non-absorbable packing materials or Silastic® etc. have been tried in order to widen middle meatus and ethmoidectomy cavity.^[13,14] These measures share a common role to keep away the denuded mucosal surfaces of the lateral side of the middle turbinate and ethmoid cavity. In this study, we aimed to use Seprigel® sinus (Hylan B) with the same goal.

The Hylan B molecules fill the sinus cavity and act as a spacer without an inflammatory response and adverse reactions. As well as the spacer effect of the Hylan B, anti-inflammatory effect of the molecule is seems to be important to obtain our results. Because our short-term observations (at the 1st and 4th week) revealed that “mucosal hypertrophy and edema” at the 1st and 4th week was significantly less for the Hylan B group compared to the control group. In agreement with our observations, Kimmelman et al. showed that Hylan B applied cavities in their study group revealed significantly less mucosal edema especially at the 4th week.^[7] These findings may ascribe to the anti-inflammatory effects of Hylan B, which was already showed by previous in vitro and in vivo studies.^[15,16]

We also observed another important effect of Hylan B in our patients that it significantly reduces synechia formation in the area of middle meatus especially at the 1st, 4th

Table 2. Postoperative mucosal grading.

Grade	Synechia	Mucosal hypertrophy	Polyp formation
Grade 0	No	No	No
Grade 1	Mild	Edema	Mucosal hypertrophy
Grade 2	Moderate	Moderate mucosal hypertrophy	Mild polyposis
Grade 3	Total obstruction	Severe mucosal hypertrophy	Severe polyposis

Table 3. Median scores (1st week $p < 0.05$; 4th week $p < 0.05$; 12th week $p < 0.05$).

	1st week		4th week		12th week	
	Control	Hylan B	Control	Hylan B	Control	Hylan B
Synechia	0.31	0.15	0.43	0.09	0.26	0
Mucosal hypertrophia	1.08	0.61	1.17	0.44	0.56	0.42
Polyp formation	–	–	0.05	0.048	0.62	0.61

and 12th weeks compared to the control group. This was already observed in the study of Kimmelman et al.^[7] However, our observations are the results of much longer follow-up period and revealed that even at the postoperative 12th week, Hylan B has a significant protective effect on preventing synechia formation. Another important aspect of the follow-up procedure is long-term findings of nasal mucosa about the nasal polyp formation. Our results indicated that there is no significant difference between the groups about recurrence of the nasal polyps at the postoperative 12th week. Although Hylan B has been shown to be effective to reduce inflammation in various tissues, nasal polyp seems to have more complicated etiology that does not explain solely with inflammatory reaction.

Although Seprigel® is non-pyrogenic and sterile, the application of Hylan B to the ethmoid cavity has a potential of being infected. As well as Kimmelman et al., we did not experience any postoperative infectious complication in our study group. Additionally, no unfavorable side effect of Hylan B was observed both in our and Kimmelman's study.^[7] Various minor complications have been reported after the clinical application of HA.^[8] However, these reports were about the non-nasal application of the HA.^[17,18] According to our and literature findings, it is possible to accept intranasal application of HA as a safe procedure.

Conclusion

Outcomes of our study have demonstrated that topical HA is effective in preventing synechia formation on paranasal mucosa after endoscopic sinus surgery in long-term. While the preventive effect of HA on mucosal hypertrophy is significant in short-term, preventive effect is insignificant on the recurrence of nasal polyposis in long-term.

Conflict of Interest: No conflicts declared.

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