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Original article

Clinical Efficacy of Hyaluronic Acid on Nasal Mucociliary Clearance after Septoplasty

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Abstract:

Background: Nasal septal deviation disrupts nasal functioning mainly by obstruction, but it also impairs mucociliary clearance by increasing mucus secretion, compromising normal ciliary movements, and causing airway epithelium damage. This study aimed to study the effect of hyaluronic acid in accelerating nasal mucosa recovery after septoplasty. **Methods:** This comparative interventional study included 40 subjects who underwent septoplasty. The patients were assigned into two equal groups: Control group; each patient was subjected to alkaline nasal wash after septoplasty 3 times per day for 15 days. Study group; each patient was subjected to sodium hyaluronate spray after septoplasty 3 times per day for 15 days. Results: Study cases had significantly lower saccharin test results at day 15 ($p<0.001$) and day 30 ($p=0.04$). According to postoperative endoscopic examination findings at day 15, the study group proved to show statistical significant endoscopic findings than the control group ($p<0.05$). **Conclusion:** Sodium hyaluronate spray showed promising results in enhancing nasal mucosa recovery post-septoplasty. Its use led to improved saccharin test outcomes and reduced postoperative endoscopic findings compared to alkaline nasal wash.

Keywords: Hyaluronic Acid; Nasal Mucociliary, Clearance; Septoplasty.

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Introduction

Any impairment of normal cilia function or mucus composition acts as a critical disturbance in nasal mucociliary clearance. Many pathologic conditions- both congenital and acquired- can precipitate an alteration of mucociliary activity or can prompt stasis of secretions [(1)].

Nasal septal deviation disrupts nasal functioning mainly by obstruction, but it also impairs mucociliary clearance by increasing mucus secretion, compromising normal ciliary movements, and causing airway epithelium damage. Patients with septal deviation show a prolonged mucociliary transit time compared with healthy controls [(2)].

Septoplasty can resolve obstruction, but it has been shown to impair mucociliary clearance in the immediate postoperative period because of the mechanical trauma to nasal mucosa caused by surgery [(3)].

Hyaluronan is a glycosaminoglycan consisting of disaccharide chains formed from glucuronic acid and N-acetylglucosamine. It is a structural component of the extracellular matrix in the interstitial and connective tissues and, in addition, it plays an important biologic role in the respiratory system [(4)].

The purpose of this study was to study the effect of hyaluronic acid in accelerating nasal mucosa recovery after septoplasty.

Patients and methods

Saccharin test

Aim: - determine mucociliary clearance time .

Steps: - 5 mg Saccharin behind mucocutanous junction under observation.

Normal clearance: - Saccharin passes to nasopharynx and patients reports a sweet taste.

Transit time between applying of Saccharin and sweet taste is recorded.

Done both concave and convex side.

Percautions :-

- No anesthesia
- Sitting position

This comparative interventional study included 40 subjects who underwent septoplasty who presented in outpatient clinic of Benha University Hospitals with the inclusion criteria and accept to participate- were included in the study. Study was conducted during the period from June 2023 to September 2023.

Full ethical approval was granted by the research ethics committee of Benha University. Voluntary written informed consent was obtained from each participant.

Ethical Approval Code: Ms49-12-2021

Inclusion criteria were patients aged above 17 years and below 40 years old and deviated septum.

Exclusion criteria were patients aged below 17 years and above 40 years old, with uncontrolled systemic disease or coagulopathy, deviated septum patients with tumors, who presented with nasal polyposis or asthma and patient requiring additional nasal surgery.

Grouping: The patients were assigned randomly by sealed envelopes into two equal groups: **Control group**: Each patient was subjected to alkaline nasal wash after septoplasty 3 times per day for 15 days. **Study group**: Each patient was subjected to sodium hyaluronate spray after septoplasty 3 times per day for 15 days.

All studied cases were subjected to the following: Detailed history taking, including Personal history, complaint & its duration, duration and progression of symptoms, history of sensitivity to drugs, medical history, past surgical history, and family history. **Physical examination: General examination including [**Vital signs, signs of Pallor, Cyanosis, Jaundice, and Lymph node enlargement] and local examination [External inspection, nasal septum inspection, anterior rhinoscopy, septal deviation assessment, nasal mucosa color and moisture, digital examination, assessment of turbinates, nasal endoscopy], and CT nose and pns (coronal, axial).

External Inspection: visually inspecting the external nose for any asymmetry, deformities, or signs of trauma. Any obvious deviations or irregularities in the nasal shape.

Nasal Septum Inspection: sing a nasal speculum and a light source, inspection the nasal septum for any visible deviations. Presence of any septal spurs or sharp edges.

Anterior Rhinoscopy: Looking for signs of mucosal inflammation, crusting, or discharge.

Septal Deviation Assessment: the patient was asked to breathe in and out through each nostril separately. Observe the nasal airflow and check for any blockages or restrictions. If there is a preference for breathing through one nostril.

Nasal Mucosa Color and Moisture: Assess the color and moisture of the nasal mucosa. Pale, bluish, or excessively dry mucosa may indicate issues.

Assessment of Turbinates: Evaluation of the size and position of the inferior turbinates. swelling or hypertrophy of turbinates- can contribute to nasal congestion.

Nasal Endoscopy Local Anesthesia (Optional): Administer a topical nasal decongestant or anesthetic. Gently insert the endoscope into the nasal cavity, usually through the inferior meatus. Navigate through the nasal passages, visualizing the structures along the way. Examine the nasal septum for deviations, spurs, or irregularities. Assess the condition of the nasal mucosa, looking for signs of inflammation, crusting, or abnormalities. Visualize the inferior, middle, and superior turbinates to assess their size and position. Evaluate for any signs of turbinate hypertrophy. Observe the nasal airflow during patient breathing for any areas of obstruction or constriction caused by septal deviation. Examine the nasal mucosa for signs of inflammation, such as redness or swelling. Chronic inflammation may be associated with septal deviation.

CT nose and pns (coronal, axial)

The patient is usually positioned supine on the CT table. The head is immobilized in a neutral position to ensure accurate imaging. Instruct the patient to hold their breath during image acquisition to minimize motion artifacts.

For high-resolution imaging, a slice thickness of 1 to 1.5 mm is commonly used. The kVp (kilovoltage peak) and mA (milliamperes) settings depend on the CT scanner and the specific protocol used. 130 KV and 150 mA/sec were used. Adjust the FOV based on the region of interest. A FOV of 14-18 cm is often suitable for imaging the nose and paranasal sinuses.

Window widths were about 1300: 2000 and window levels about –80: –200. Scan time was 1.5 sec. Acquire both coronal and axial images for a comprehensive evaluation.

All patients were subjected to septoplasty by the same Surgeon:

Procedures were carried out under general anesthetic with a cuffed endotracheal tube in order to avoid blood aspiration or swallowing. At the start of the procedure, a five-minute pack soaked in adrenaline in saline solution (1: 200,000) was introduced into the nostril. The patients were positioned supine on the surgical table, with the head end lifted. both nasal cavities were packed using merocel packs at the end of operation in both techniques.

Submucosal infiltration of the nasal septum was done. An incision was performed directly on deviated part then a mucoperichondrial flap was dissected at the proper cleavage plane to minimize bleeding, using a Cottle elevator in the right hand and endoscope in the left hand.

The septal cartilage was then incised posterior to the mucosal incision. The dissection of the contralateral mucoperichondrial flap was then performed. In cases of spur only, the incision was done directly over the spur using a sickle knife under endoscopic vision especially for posterior spurs.

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After removal of the merocele, packing on the first postoperative day, the control arm was treated with alka misr, washing 2 times per day for 15 days, and the experimental arm received sodium hyaluronate ,3% neublizing solution (3ml dilute in 2ml of saline solutions 2 times per day for 15 days).

Post -operative care and follow up: We performed the saccharin transit time to all patients preoperatively and at 15, 30 days post operatively.

Post-operative endoscopic nasal examination at 15 to 30 days after the surgery to assess: Adhesion, Crustation, Edema, Discharge.

Oral antibiotics applied for 5 days postoperatively: 1 gm single dose of intravenous cefazolin intraoperatively and 1000 mg oral amoxicillin–clavulanate and 500 mg oral paracetamol- were administrated.

Statistical analysis

The collected data was revised, coded, and tabulated using Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Shapiro-Wilk test was used to assess normality of data. Mean, standard deviation (± SD), median, and range- were used for numerical data. Frequency and percentage were used for non-numerical data. The student t test was used to examine the relationship between two numerical parametric variables. Wilcoxon Test was used to assess the statistical significance of the difference of non-parametric variable between two times period. Mann Whitney Test (U test) was used to assess the statistical significance of the difference of a non-parametric variable between two study groups. Chi-Square test was used to examine the relationship between two qualitative variables. A p value is considered significant if <0.05 at confidence interval 95%.

Results

According to demographic data of the studied groups, no significant differences in age or gender between the two groups. There were no significant differences in the distribution of nasal obstruction, headache, discharge, epistaxis, smell disorders and ear complaint between the two groups. There were no significant differences between study cases and controls in the duration of surgery or blood loss. Additionally, all cases and controls received nasal packing during surgery, Table (1).

Study cases had significantly lower saccharin test results at day 15 ($p<0.001$) and day 30 ($p=0.04$). However, there were no significant differences between study cases and controls in the preoperative scores. Same group comparison of saccharin test in study cases revealed significant lower saccharin test results in day 15 and day 30 compared to pre operation (both p value <0.001). A significant lower saccharin test results in day 30 compared to pre-operation in control group as well as significant lower result in day 30 compared to day 15 (both p <0.001). At concave side, cases had significantly lower saccharin test scores at day 15 ($p<0.001$) and at day 30 ($p=0.03$). There were no significant differences between the two groups in the pre-operative scores or at day 30. Same group comparison of saccharin test in study cases revealed significant lower saccharin test results in day 15 and day 30 compared to pre-operation (both p value <0.001). A significantly lower saccharin test results in day15 and day 30 compared to pre-operation in control group as well as significantly lower result in day 30 compared to day 15, Table (2).

According to postoperative endoscopic examination findings at day 15- in the study group- 2 out of 20 individuals (10%) had positive findings for adhesion, while in the control group, 8 out of 20 individuals (40%) had positive findings. For crustation, 3 individuals (15%) in the study group had positive findings, while in

the control group, 8 individuals (40%) had positive findings. Regarding edema, 8 individuals (40%) in the study group had positive findings, whereas in the control group, 17 individuals (85%) had positive findings. For discharge, 3 individuals (15%) in the study group had positive findings, while in the control group, 8 individuals (40%) had positive findings. A significant higher distribution of all post-operative endoscopic examination findings in control group compared to study group ($p<0.05$ in all findings), Table (3).

According to the post-operative endoscopic examination findings at day 30, the study group and control group exhibited distinct results. In the study group, 1 out of 20 individuals (5%) had positive findings for adhesion, while in the control group, 5 out of 20 individuals (25%) had positive findings. For crustation, 1 individual (5%) in the study group had positive findings, while in the control group, 5 individuals (25%) had positive findings. Regarding edema, 2 individuals (10%) in the study group had positive findings, whereas in the control group, 13 individuals (65%) had positive findings. Lastly, for discharge, 1 individual (5%) in the study group had positive findings, while in the control group, 5 individuals (25%) had positive findings, Table (4).

Table (1): Demographic data, pre-operative nasal manifestations and operative data among the studied groups

		Study group n=20	**Control group n=20**	**p**
Age		41.2±12.3	41.3±11.4	0.968
Gender	Female	10(50%)	9(45%)	0.618
	Male	10(50%)	11(55%)	
Pre-operative nasal manifestations				
Nasal obstruction		20(100%)	20(100%)	1.000
Headache		9(45%)	7(35%)	0.371
Post nasal discharge		13(65%)	13(65%)	1.000
Epistaxis		4(20%)	5(25%)	0.527
Smell disorders		5(25%)	4(20%)	0.618
Ear complaint		5(25%)	4(20%)	0.618
Operative data				
Duration of surgery		55.3±6.6	55±7.4	0.688
Blood loss (ml)		71.5±6.9	74.3±9.6	0.450
Nasal packing		20(100%)	20(100%)	1.000

Data are presented as Mean ±SD or frequency (%)

Table (2): Saccharin test at convex side and concave side among studied groups at different time points

	Study group	**Control group**	**p**
Convex side	n=20	n=20	
Pre-operation (min)	11.1±1.6	11.4±1.9	0.210
Day 15 (min)	6.9±1.2	10.6±2.3	<0.001*
Day 30 (min)	6.9±1.6	7.8±1.4	0.04*
Pairwise comparison	p1 <0.001*, p2 <0.001*, p3=0.970	p1=0.218, p2<0.001*, p3=0.001*	
Concave side			
Pre-operation	14.8±2.2	14.7±2.2	0.514
Day 15	9.6±2.1	12.4±1.6	<0.001*
Day 30	9.2±2	9.8±1.8	0.03*
Pairwise comparison	p1 <0.001*, p2 <0.001*, p3=0.351	p1=0.001*, p2<0.001*, p3=0.001*	

Data are presented as Mean ±SD, P1 difference between pre-operation and day 15; P2 difference between pre-operation and day 30; P3 difference between day 15 and day 30, *: statistically significant as P value <0.05

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Table (3): Post-operative endoscopic examination 15 days among studied groups

	Study group n=20	**Control group** n=20	**p**
Adhesion	2(10%)	8(40%)	0.004*
Crustation	3(15%)	8(40%)	0.033*
Edema	8(40%)	17(85%)	<0.001*
Discharge	3(15%)	8(40%)	0.001*

Data are presented as frequency (%), *: statistically significant as P value <0.05

Table (4): Post-operative endoscopic examination 30 days among studied groups

	Study group n=20	**Control group** n=20	**p**
Adhesion	1(5%)	5(25%)	0.021*
Crustation	1(5%)	5(25%)	0.021*
Edema	2(10%)	13(65%)	<0.001*
Discharge	1(5%)	5(25%)	0.021*

Data are presented as frequency (%), *: statistically significant as P value <0.05.

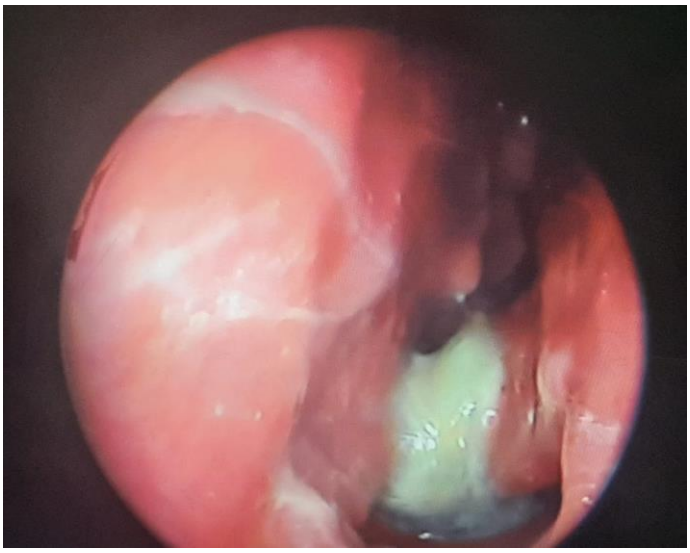

Figure (1): Nasal crustation & discharge after septoplasty without application of hyaluronic acid.

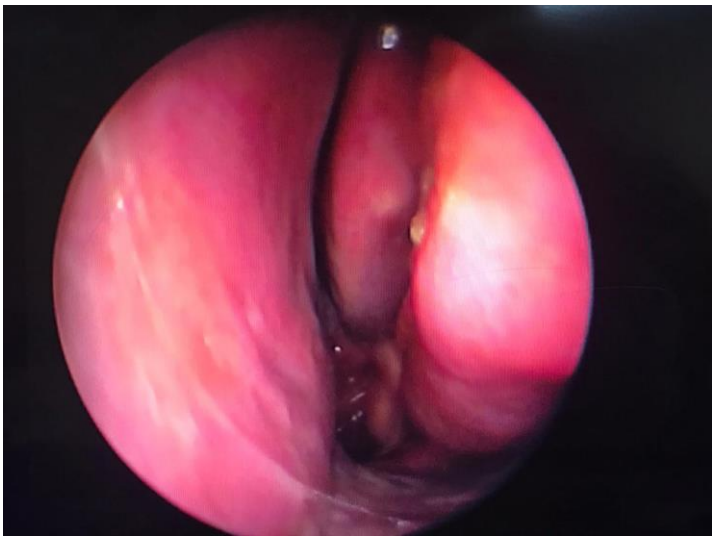

Figure (2): left nasal cavity after application of hyaluronic acid.

Discussion

Mechanism of action of hyaluronic acid: - 1st → passively, It is related to molecule itself

It increases viscoelasticity of extracellular material (ECM). So, it's well maintained, and its components (collagen and elastic fibers) are stable. Second(2nd) signaling molecule → immune modulation by binding to IL-8 which is released by endothelial & epithelial cells and fibroblast during inflammation, thus binding prevents unwanted immune response.

According to demographic data of the studied groups, the mean age of both study group and control- was similar, with study cases having a mean age of 41.2 years (SD=12.3) and control having a mean age of 41.3 years (SD=11.4). The gender distribution was also comparable, with 50% of cases being female and 45% of controls being female. Statistical tests showed no significant differences in age or gender between the two groups.

In the current study, according to preoperative nasal manifestations among studied groups, there were no significant differences in the distribution of nasal

obstruction, headache, discharge, epistaxis, smell disorders and ear complaint between the two groups.

Parallel to our findings, 36 patients were included, with grade II nasal polyposis undergoing functional endoscopic sinus surgery received intranasal sodium hyaluronate 9 mg twice daily or saline for 30 days commencing on the second day after surgery. Patient groups were well matched at clinical characteristics and no significant between-group differences were seen [(6)].

According to our study, study cases had significantly lower saccharin test results at day 15 ($p<0.001$) and day 30 ($p=0.04$). However, there were no significant differences between study cases and controls in the preoperative scores. Same group comparison of saccharin test in study cases revealed significant lower saccharin test results in day 15 and day 30 compared to pre-operation (both p value <0.001). A significant lower saccharin test results in day 30 compared to pre-operation in control group as well as significant lower result in day 30 compared to day 15 (both $p <0.001$).

According to our study, cases had significantly lower saccharin test scores at day 15 ($p<0.001$) and at day 30 ($p=0.03$) at concave side. There were no significant differences between the two groups in the pre-operative scores or on day 30. Same group comparison of saccharin test in study cases revealed significant lower saccharin test results in day 15 and day 30 compared to pre-operation (both p value <0.001). A significantly lower saccharin test results in day15 and day 30 compared to pre-operation in control group as well as significantly lower result in day 30 compared to day 15.

In the study which was conducted in a previously and provided evidence of a therapeutic effect of hyaluronic acid on nasal mucosa recovery after septoplasy, sixty-five patients underwent septoplasty. On postoperative day 1, patients were randomized to a control arm that was treated with mupirocin ointment or an experimental arm that received additional treatment with sodium hyaluronate solution. They noted that one month after surgery, a reduction of saccharin transit time (STT) was observed, when comparing preoperative control group values and, after 1-month, postoperative values in both sides ($p < 0.015$ and $p < 0.005$, convex and concave side, respectively). Our results show a significant reduction of the STT for both nasal sides as soon as 15 days after septoplasty in patients randomized to additional treatment [(7)].

Additionally, twenty-four eligible septoplasty patients were recruited. The patients were divided evenly into; group "A" used nasal saline wash (control group), and group "B" used hyaluronic acid. It was observed that mean of saccharine time test pre-operatively was (Rt. 11.1±7.1, Lt. 14.4±7.5) in group "A," and (Rt. 14.8±3.3, Lt. 13.2±5.0) in group "B," then increased on 10 days postoperatively to (Rt. 21.4±8.5, Lt. 23.7±10.2) in group "A," and (Rt. 23.8±4.3, Lt. 23.3±3.5) in group "B," but it remarkably reduced after 6 weeks post-operatively, being in group "B" (Rt. 7.5±5.1, Lt. 7.5±3.2), compared, to group "A" that, took a longer time "slower healing process" (Rt. 14.3±5.5, Lt 17.3±5.5) with P=0.0001. The Saccharine time comparison between the (convex side) and (concave side) in both groups was significant ($p= 0.041$), with total of 13/24 (54.2%) for concave side and 11/24 (45.8%) for the con-vex side, and the saccharine time of all patients was in the preoperative period in the convex side of the nasal cavity is slightly prolonged in the concave side, [(8)].

According to post-operative endoscopic examination findings at day 15, in the study group, 10% had positive findings for adhesion, while in the control group, 40% had positive findings. For crustation, 15% in the study group had positive findings, while in the control group, 40% had

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positive findings. Regarding edema, 40% in the study group had positive findings, whereas in the control group, 85% had positive findings. For discharge, 15% in the study group had positive findings, while in the control group, 40% had positive findings. The study group proved to show statistical significant endoscopic findings than the control group. ($p<0.05$).

According to the postoperative endoscopic examination findings at day 30, the study group and control group exhibited distinct results. In the study group, 5% had positive findings for adhesion, while in the control group, 25% had positive findings. For crustation, 5% in the study group had positive findings, while in the control group, 25% had positive findings. Regarding edema, 10% in the study group had positive findings, whereas in the control group, 65% had positive findings. Lastly, for discharge, 5% in the study group had positive findings, while in the control group, 25% had positive findings. The distribution of all post-operative endoscopic examination findings was significantly higher in the control group compared to the study group ($p<0.05$ for all findings).

It was concluded that a significantly lower incidence of exudate was seen in sodium hyaluronate recipients at 1 month compared with control. The median endoscopic rating scale was 0 (IQR0,1) in patients receiving sodium hyaluronate and 4 (IQR1,4) in control subjects at 1 month after surgery (RR9.84; 95% CI 1.41,68.47; $p = 0.000$). Sodium hyaluronate was well tolerated in patients following functional endoscopic sinus surgery. The use of intranasal sodium hyaluronate in patients undergoing functional endoscopic sinus surgery for nasal polyposis augmented the improvement in mucociliary clearance observed following this procedure and improved several clinical and endoscopic parameters [(6)].

A meta-analysis of adhesion formation frequency on endoscopy demonstrated a lower risk ratio in the hyaluronic acid intervention group (42 out of 283 cases) compared to the control group (81 out of 282) of 0.52 (95 per cent confidence interval = 0.37–0.72). Hyaluronic acid use was not associated with any significant adverse events [(9)].

Conclusion

Sodium hyaluronate spray showed promising results in enhancing nasal mucosa recovery post-septoplasty. Its use led to improved saccharin test outcomes and reduced post-operative endoscopic findings compared to alkaline nasal wash.

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Author contribution

Authors contributed equally in the study**.**

Conflicts of interest

No conflicts of interest

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