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Efficacy and safety of a hypertonic nasal wash solution containing sea algae extracts in patients that underwent surgical correction of a deviated nasal septum and radiofrequency turbinate volume reduction

S. LASKARIS[1], S. GEORGIOU[2], C. CINGI[3], K. ALEVIZOPOULOS[2]

[1]Department of Otolaryngology and Head and Neck Surgery, Metaxas Cancer Hospital, Piraeus, Greece
[2]Research and Development Department, Gerolymatos International S.A., Athens, Greece
[3]Department of Otorhinolaryngology, Medical Faculty, Eskisehir Osmangazi University, Eskisehir, Turkey

Abstract. – OBJECTIVE: The objective of this study was to evaluate efficacy and safety of a Hypertonic Seawater Solution (2.3% NaCl) containing brown and blue-green Algae (HSS-A) in comparison to Isotonic Saline Solution (ISS) regarding the improvement of nasal breathing in patients that have undergone surgical correction of a deviated nasal septum and radiofrequency turbinate volume reduction.

PATIENTS AND METHODS: A total of 101 individuals were enrolled in the study (HSS-A: 57; ISS: 44). Nasal breathing was evaluated using a Peak Nasal Inspiratory Flow (PNIF) measurement device at four timepoints: prior to surgical intervention (up to 30 days pre-surgery) and at the 2nd, 10th and 20th postoperative days. On the 20th postoperative day, patients also answered a Nasal Surgical Questionnaire (NSQ) evaluating breathing ability and overall satisfaction from the use of both nasal sprays.

RESULTS: No significant differences were observed in PNIF measurements between groups at different points. On the 20th postoperative day, NSQ analysis showed that ISS-treated patients had more frequently moderate nasal bleeding compared to the HSS-A group (85.7% *vs.* 14.3%, *p*=0.038). No other statistically significant differences were observed between groups. When NSQ parameters were evaluated in a binary mode, a trend for reduced crusting scores was seen in the HSS-A group (15.9% *vs.* 35.5% in ISS, *p*=0.053). No safety concerns were reported throughout the study.

CONCLUSIONS: In patients that have undergone surgical correction of a deviated nasal septum and radiofrequency turbinate volume reduction, PNIF values did not differ significantly in patients receiving HSS-A and ISS solutions. Nasal bleeding was more frequent in ISS patients versus HSS-A. Overall, both solutions provided symptomatic relief and use satisfaction in the absence of side effects.

Key Words:
Saline Nasal Spray, Septoplasty, Submucosal turbinoplasty, Undaria pinnatifida, Spirulina platensis.

Introduction

Causes for chronic nasal obstruction can be divided into mucosal causes or anatomical abnormalities. One of the most frequent reasons related to anatomical abnormalities is the deviated septum which may also be accompanied by hypertrophy of the inferior turbinates. Accordingly, septoplasty or turbinoplasty performed with the intention of improving nasal breathing are the most common operations undertaken by ENT specialists.

In patients who have hypertrophy of the inferior turbinate only, it may be appropriate to first attempt medical treatment. However, in cases where this fails to resolve the issue, surgical reduction of the turbinate may be the only viable option. This procedure may be performed in conjunction with straightening of the septum, or on its own[1,2].

Recently, the principal focus of surgery has moved on to increasing patients' quality of life. This focus has meant that reducing patient recovery time and decreasing postoperative discomfort have become key concerns for surgical practitioners.

When the flow of air through the nose is impeded, nasal breathing becomes more difficult. The narrowest portion of the nasal airway is the nasal valve. A number of conditions potentially impede the passage of air through the nose by

Corresponding Author: Konstantinos Alevizopoulos Ph.D; e-mail: kalevizo@gerolymatos-int.com

increasing resistance within the nasal airway. The normal physiological processes involved in breathing may also narrow the airway, as occurs in the nasal cycle. Air does not pass through both sides of the nasal cavity at the same rate, as the nasal cycle ensures that first the passage on one side, then the other, becomes congested in the region of the frontal margin of the inferior concha and the nasal septum, then becomes decongested once more[3]. This asymmetric, alternating flow of nasal air has a periodicity of between 2 and 4 hours and is termed the "nasal cycle"[4].

A number of pathological conditions may be superimposed on top of the nasal cycle which then hinder the proper passage of air through the nose. Such conditions include rhinitis (of allergic or non-allergic type), nasal polyp formations, excessive nasal secretions or anatomical alterations, such as a septum that deviates from the midline. When this occurs, sleep apnoea may develop, with harmful consequences for patient health. Surgical intervention then becomes necessary to ensure the nose has sufficient patency for normal breathing. Following surgery, various medications or procedures are used to cleanse the nasal cavity and ensure the patient fully recovers.

There are objective clinical criteria available for diagnosis, quantification and treatment of nasal obstruction, including several methods of assessing nasal obstruction, transmittance, air flow and resistance. A thorough medical history is key to assessing nasal obstruction, in particular any history of symptoms indicative of rhinitis, namely nasal blockage, discharge, pruritus or sneezing. The time course of these symptoms should also be ascertained. Following the history, the physical examination involves a thorough evaluation of the nasal cavity. The physical examinations start with inspection of external part of the nose, where any deviation from the midline may provide an anatomical explanation for nasal obstruction. The examination then proceeds to the nasal interior. Although anterior rhinoscopy is rapidly performed, it is limited in its ability to reveal the entire nasal cavity and thus nasal endoscopy is required for a comprehensive and detailed evaluation. Nasal endoscopy is superior to anterior rhinoscopy, and may be undertaken with a rigid or flexible endoscope, with its own source of illumination. Generally speaking, patients tolerate the rigid endoscope better than the flexible endoscope and the images obtained are also superior. If a narrow calibre (<2.7 mm) device is used, this has the notable advantage that the patient does not need to be anaesthetised first[5].

Objective measurement of nasal air flow is helpful when set alongside the subjective impression of the degree to which nasal breathing is obstructed. The flow through the nose may be assessed by quantifying Peak Nasal Inspiratory Flow (PNIF)[6] or rhinomanometrically[7]. Nasal permeability can be calculated from the partial or total volume of the nasal cavity. The measurements required for volume estimation are obtained from computed tomographic or magnetic resonance imaging scans or by acoustic rhinometry (AR).

PNIF during inhalation may be measured using a portable flow meter[8]. Overall, PNIF measurements represent a reliable surrogate for nasal airflow[7] and are well tolerated by patients[9,10]. Moreover, they have low costs, are rapid, easy to perform and do not require computerised data analysis, allowing healthcare professionals to obtain a measurement of nasal air flow immediately[11]. PNIF is measured consecutively three times, with the highest value obtained being taken to represent the true value[6].

Questionnaires collecting data directly by patients are an effective way to assess the outcomes of surgical interventions. One questionnaire which is suitable for evaluating the outcome of ENT surgical interventions and has been validated in literature is the Nasal Surgical Questionnaire (NSQ). The NSQ reliably assesses nasal symptoms in patients and may be useful for both short- and long-term prospective studies of septoplasty[12].

Nasal douching with hypertonic saline/seawater solutions is a well-known postoperative practice facilitating relief of symptoms and recovery from endonasal surgery[13,14]. Although saline nasal lavage is a widely used application in treating sinonasal diseases, many research studies[15] showed that hypertonic saline has more advantages over isotonic saline for mucociliary clearance. Especially hypertonic saline is much more effective when mucosal edema is due to infection or surgical trauma.

In this study, we sought to determine the efficacy and safety of a hypertonic seawater solution containing brown and blue-green algae in comparison to isotonic saline solution in improving air flow, nasal breathing and symptom relief in patients following septoplasty and radiofrequency turbinate volume reduction.

Patients and Methods

This study was a single centre, open label, prospective parallel group, phase IV trial of non-interventional design. The study was conducted from September 2019 to April 2021 at ORL Athens Clinic, Greece. It conformed to the requirements of the Declaration of Helsinki. Ethical approval was granted by the clinic's Institutional Review Board. Before acceptance into the study, all patients were informed about the study and provided their consent to participate.

The study group consisted of adult patients, both male and female, who underwent septoplasty with or without radiofrequency turbinate volume reduction. For acceptance, patients had to have an activated partial thromboplastin time (APTT) and international normalised ratio (INR) within the normal range. The exclusion criteria were a medical history of arterial hypertension or diabetes mellitus which remained uncontrolled despite medical treatment, pregnancy, previous participation in another clinical trial or having previously undergone the same surgical operation. A flow chart for the study is shown in Table I.

Patient enrolment occurred up to 30 days prior to surgery. The patients were then randomly allocated to two different treatment groups. In Group A, the treatment offered was nasal rinsing with an isotonic solution containing 0.9% NaCl (ISS; NasaMist® NeilMed Pharmaceuticals, Inc.). In Group B, the treatment available was a hypertonic (2.3% NaCl) seawater solution containing brown algae (*Undaria pinnatifida*) and blue-green algae (*Spirulina platensis*) (HSS-A; Sinomarin® Plus Algae ENT, Gerolymatos International SA, Athens, Greece).

The enrolment period lasted for 6 months. All patients had follow-up lasting a maximum of 53 days. The follow-up period consisted of the 30 days prior to surgery, the day of surgery itself and at 10 (±1) and 20 (±2) days post-surgery. Data collection had no effect on patient treatment, which proceeded according to the usual clinical practice.

Patient data were recorded in study files. No information regarding imaging results or other tests which did not form part of the study protocol was included in these files.

The flow of air through the nose during inhalation was quantified using a peak nasal inspiratory flow (PNIF) measurement device (GM Instruments) to provide an objective value. PNIF was measured consecutively three times, with the highest value obtained being taken to represent the true value[4,14]. PNIF values were measured before surgery and during post-surgical recovery at 2, 10 and 20 days after surgery in order to assess the efficacy and safety of the two rinsing solutions used in the study.

The nasal surgical questionnaire (NSQ)[12] was filled by the study participants on the 20th postoperative day. Patients were asked to mark their sense of obstruction during day, night, and exercise in 10 cm visual analogue scales (VAS) with markings of 0 = completely open and 10 = completely obstructed at either end. They further recorded their perception of improvement of nasal breathing (in a 5-option scale i.e., Worse/Non-Improved/Partially Improved/Significantly Improved/Completely Improved) as well as the feeling of crusting, bleeding, sneezing, presence of nasal secretions and feeling of pain post-surgery

Table I. Study flow chart.

	Preoperatively (day -30 to day 0)	Follow up visit day 2 and day 10 (±1) postoperatively	Follow up visit day 20 (±2) postoperatively
Signed informed consent form	x		
Eligibility criteria	x		
Age, Sex, Weight	x		
Medical History/comorbidities	x		
Smoking history	x		
Imaging evaluation	x		
PNIF results	x	x	x
Concomitant medication	x	x	x
Surgical complications		x	x
Adverse events	x	x	x
NSQ questionnaire			x
Satisfaction questionnaire			x

(in 4-option scales, i.e., None/Mild/Moderate/Severe). The questionnaire was completed prior to any other activity involved in follow-up. Patients also used the visual analogue scale (VAS) to indicate their overall satisfaction with the outcome of surgery (10 denotes patient's complete satisfaction). The results of the questionnaires were then subjected to semi-quantitative statistical analysis.

Statistical Analysis

Descriptive statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). The analysis was performed on all continuous variables in each study group. The categorical variables were presented in tables showing the absolute frequencies for each study group. Estimates of PNIF changes from baseline for each group and mean differences at each time point post-septoplasty were derived from the model as least squares means (LSMs). For two-sided statistical comparisons, a *p*-value not higher than 0.05 was considered to indicate statistical significance.

Results

101 individuals were enrolled in the study, consisting of 69 male patients and 32 female patients. The mean ages were 38.3 ± 11.7 and 35.9 ± 10.2 years for HSS-A and ISS groups, respectively. The ratio of male to female was 39:18 for HSS-A and 30:14 for ISS group. In both groups, the majority of patients (69.3%) were non-smokers. For those who did smoke, the median number of pack/years was 7.75. Only 5 individuals (5%) reported a co-morbid condition. The vast majority of the study participants (n=99) underwent septoplasty with radiofrequency turbinate volume reduction, with only 2 individuals undergoing septoplasty alone. Regarding baseline characteristics, no significant difference ($p>0.05$) was observed between HSS-A and ISS groups (Table II), indicating that the groups were well-balanced in terms of background factors. HSS-A solution was offered to 57 individuals (56.4%), while 44 patients (43.6%) were provided with ISS. All the recruited participants completed all four study visits.

Analysis of Clinical Efficacy

PNIF values increased continuously after surgery for both HSS-A and ISS groups at each time point post-surgery (Table III, PNIF values). No statistically significant difference was recorded between the study groups at any stage in follow-up compared to baseline. However, the post-septoplasty increase in PNIF – is probably due to the surgical restoration of nasal septum and turbinate reduction as well as decrease of edema and crusting. Therefore further improvement by nasal washes may be difficult to achieve.

The primary endpoint used in this study was the difference in PNIF measured at the 20th postoperative day compared to the preoperative PNIF measurement (baseline). In agreement with this, both study groups had markedly improved PNIF values postoperatively. However, no statistically significant difference between study groups was noted (Table IV). Analogously, no statistical difference between study groups regarding PNIF was also noted at the 2nd and 10th postoperative days (Table IV). Figure 1 shows the change in PNIF for both study groups over time postoperatively.

A further (secondary) measure of efficacy used in this study was the subjective evaluation of nasal air flow at the 20th post operational day. This endpoint was assessed by means of a questionnaire, which asked about the following items: the patient's perception of any improvement in nasal breathing, the presence of crusting postoperatively, nasal bleeding, sneezing, nasal secretions and nasal pain. Nasal bleeding differed significantly between groups, with the group administered postoperatively HSS-A experiencing lower levels of this complication ($p=0.038$, Table V). There was also a lower level of nasal crusting, secretions and sneezing in the same group but the difference was not significant at the statistical level. The other parameters did not differ significantly between the two groups (see Table V).

When the same parameters were treated as binary data (i.e., symptom present or absent), statistical analysis again revealed no unequivocally significant differences (Table VI), although an apparent trend towards significance was observed ($p=0.053$). According to this trend, there appears to be a lower incidence of nasal crusting in the group administered HSS-A.

Difficulty in nasal breathing following surgery was also assessed. As can be seen in Table VII, the level of difficulty was similar in both study groups, not only for normal breathing but also when sleeping or exercising. No statistically significant differences were observed.

Table II. Baseline clinical characteristics of the study population per study group.

	HSS-A (N=57)		ISS (N=44)		Total (N=101)		*p*-value
Sex, n %							
Male	39	68%	30	68.2%	69	68.3%	1
Female	18	32%	14	31.8%	32	31.7%	
Age (years)							
n	57		44		101		0.278
mean	38.3		35.9		37.2		
median	37.0		35.5		36.0		
SD	11.68		10.16		11.06		
min	19		18		18		
max	66		58		66		
Weight, (kg)							
n	57		44		101		0.858
mean	77.0		77.5		77.2		
median	80.0		78.0		78.0		
SD	15.05		13.45		14.31		
min	49		51		49		
max	115		110		115		
Smoking, n %							
No	40	70%	30	68.2%	70	69.3%	1
Yes	17	30%	14	31.8%	31	30.7%	
Pack/years							
n	17		13		30		0.324
mean	14.703		9.115		12.280		
median	8.000		7.500		7.750		
SD	20.534		8.725		16.495		
min	1.25		0.50		0.50		
max	86.00		25.50		86.00		
Comorbidities, n %							
No	54	95%	42	95.5%	96	95.0%	1
Yes	3	5%	2	4.5%	5	5.0%	
Any imaging exam available, n %							
No	42	74%	33	75.0%	75	74.3%	1
Yes	15	26%	11	25.0%	26	25.7%	
Computed tomography available, n %							
No	45	79%	38	86.4%	83	82.2%	0.482
Yes	12	21%	6	13.6%	18	17.8%	
X-Ray available, n %							
No	54	95%	41	93.2%	95	94.1%	1
Yes	3	5%	3	6.8%	6	5.9%	
Magnetic Resonance Image available, n %							
No	57	100%	43	97.7%	100	99.0%	na
Yes	0	0%	1	2.3%	1	1.0%	
Endoscopy available, n %							
No	51	90%	42	95.5%	93	92.1%	0.46
Yes	6	11%	2	4.5%	8	7.9%	
Type of Surgery, n %							
A	56	98%	43	97.7%	99	98.0%	1
B	1	2%	1	2.3%	2	2.0%	

Table III. Descriptive data of PNIF per study group at each time point post-surgery.

	HSS-A	ISS	*p-value*
Pre-operatively			
n	57	44	
mean	63.5	65.0	0.788
median	65.0	70.0	
SD	28.98	25.10	
min	10	20	
max	130	120	
2nd postoperative day			
n	57	44	
mean	75.3	76.2	
median	80.0	80.0	
SD	40.12	33.72	
min	10	10	
max	160	170	
10th postoperative day			
n	57	44	
mean	96.5	94.1	
median	95.0	100.0	
SD	39.69	37.45	
min	30	30	
max	200	190	
20th postoperative day			
n	57	44	
mean	120.2	116.8	
median	120.0	120.0	
SD	36.48	35.62	
min	60	50	
max	220	200	

SD: Standard Deviation.

Table IV. Change in PNIF between study groups at 2nd, 10th and 20th post operational day.

	n	Within treatment LSM (SE)	Comparison	Between treatments LSM (SE)	*p*-value
2nd postoperative day					
HSS-A	57	11.7 (3.89)	*vs.* ISS	0.3 (5.29)	0.962
ISS	44	11.5 (4.27)			
10th postoperative day					
HSS-A	57	32.9 (4.38)	*vs.* ISS	3.5 (6.10)	0.566
ISS	44	29.4 (4.84)			
20th postoperative day					
HSS-A	57	56.7 (4.15)	*vs.* ISS	4.6 (5.73)	0.428
ISS	44	52.1 (4.58)			

LSM= Least Square Means. SE= Standard Error.

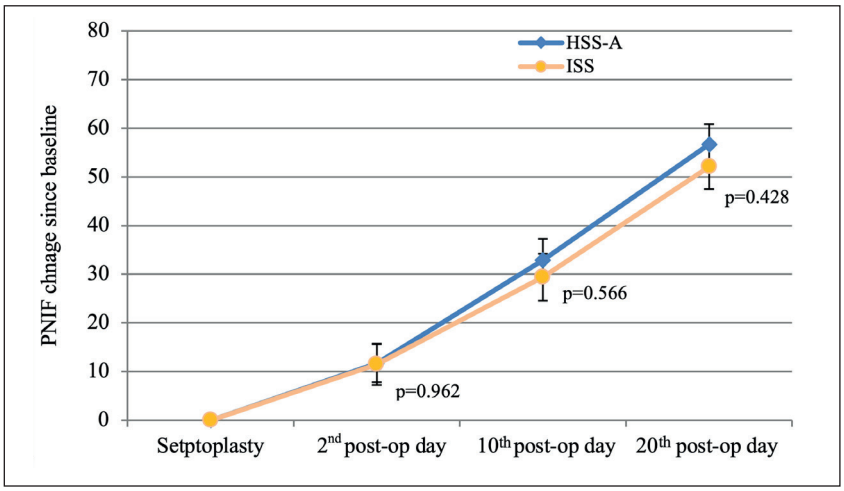

Figure 1. Change in PNIF values postoperatively in comparison to baseline visit ("Septoplasty").

Table V. Evaluation of nasal breathing per study group at 20th postoperative day.

	HSS-A (N=57)		ISS (N=44)		Total (N=101)		*p*-value
	n	%	n	%	n	%	
Nasal breathing is:							
Completely improved	27	47.40%	18	40.90%	45	44.60%	0.774
Significantly improved	27	47.40%	24	54.50%	51	50.50%	
Partially improved	3	5.30%	2	4.50%	5	5.00%	
Do you feel crusts at nasal breathing?							
None	20	35.10%	7	15.90%	27	26.70%	0.167
Mild	27	47.40%	27	61.40%	54	53.50%	
Moderate	9	15.80%	8	18.20%	17	16.80%	
Severe	1	1.80%	2	4.50%	3	3.00%	
Do you have nasal bleeding?							
No	37	64.90%	21	47.70%	58	57.40%	0.038
Mild	19	33.30%	17	38.60%	36	35.60%	
Moderate	1	1.80%	6	13.60%	7	6.90%	
Do you sneeze?							
No	37	64.90%	22	50.00%	59	58.40%	0.191
Mild	16	28.10%	20	45.50%	36	35.60%	
Moderate	4	7.00%	2	4.50%	6	5.90%	
Do you have nasal secretions?							
No	23	40.40%	12	27.30%	35	34.70%	0.181
Mild	21	36.80%	23	52.30%	44	43.60%	
Moderate	11	19.30%	5	11.40%	16	15.80%	
Severe	2	3.50%	4	9.10%	6	5.90%	
Do you feel pain in the nose?							
No	35	61.40%	24	54.50%	59	58.40%	0.784
Mild	21	36.80%	19	43.20%	40	39.60%	
Moderate	1	1.80%	1	2.30%	2	2.00%	

Table VI. Evaluation of nasal breathing per study group at 20th postoperative day. Binary analysis (symptom present/absent) was used.

	HSS-A (N=57)		ISS (N=44)		Total (N=101)		*p*-value
	n	%	n	%	n	%	
Nasal breathing is:							
Completely improved	27	47.40%	18	40.90%	45	44.60%	0.656
Significantly/partially improved	30	52.60%	26	59.1	56	55.40%	
Do you feel crusts at nasal breathing?							
No	20	35.10%	7	15.90%	27	26.70%	0.053
Yes	37	64.90%	37	0.841	74	73.30%	
Do you have nasal bleeding?							
No	37	64.90%	21	47.70%	58	57.40%	0.126
Yes	20	35.10%	23	0.523	43	42.60%	
Do you sneeze?							
No	37	64.90%	22	50.00%	59	58.40%	0.192
Yes	20	35.10%	22	50.00%	42	41.60%	
Do you have nasal secretions?							
No	23	40.40%	12	27.30%	35	34.70%	0.247
Yes	34	59.60%	32	72.70%	66	65.30%	
Do you feel pain in the nose?							
No	35	61.40%	24	54.50%	59	58.40%	0.624
Yes	22	38.60%	20	45.50%	42	41.60%	

Table VII. Difficulty in nasal breathing per study group. Value 10 denotes complete nasal obstruction; Value 1 denotes completely open nasal breathing.

		n	Mean	SD	Median	Min	Max	*p*-value
Level of difficulty								
Normal breathing								
	HSS-A	57	3.8	3.38	2	1	10	0.781
	ISS	44	3.6	2.81	3	1	10	
Sleeping at night								
	HSS-A	57	4	3.32	2	1	10	0.831
	ISS	44	3.9	2.67	3	1	10	
During exercise								
	HSS-A	57	4.2	3.27	3	1	10	0.888
	ISS	44	4.1	2.59	3	1	10	

Table VIII. Relief of symptoms at the postoperative period by the use of over-the-counter nasal sprays per study group. Value 10 denotes complete patient's satisfaction. Value 1 denotes patient's dissatisfaction.

		n	Mean	SD	Median	Min	Max	*p*-value
Relief by postoperative treatment								
Normal breathing								
	HSS-A	57	8.1	2.25	9	1	10	0.765
	ISS	44	8	1.73	8	1	10	
Sleeping at night								
	HSS-A	57	8	2.06	9	1	10	0.919
	ISS	44	8	1.84	8	1	10	
During exercise								
	HSS-A	57	7.9	2.19	9	1	10	0.703
	ISS	44	7.8	1.66	8	1	10	

Postoperative use of both HSS-A and ISS was associated with symptom relief (Table VIII). The users were highly satisfied rating both solutions with 8 out of 10 for relief of symptoms following surgery, not only for ordinary breathing but also when sleeping or exercising (Table IX).

Regarding safety, only one adverse event in one patient was recorded over the course of the study. This involved a mild infection of the nasal cavity occurring postoperatively which was effectively treated with oral antibiotics. The adverse event was in the group receiving HSS-A. This event was deemed unrelated to the use of HSS-A. No adverse events of high severity were noted in either group.

Discussion

PNIF has found various applications in ENT practice. It has been employed to assess the efficacy of treatment for allergic rhinitis in both adult and child patients[16-20], in evaluating benefit from intranasal corticosteroids[21-23] and in assessing the outcome of surgical operations on the nose[24]. Accumulated data advocate the use of PNIF as a valuable, reliable, safe, rapid and objective measure of nasal obstruction[25].

Correcting deviation of the nasal septum by surgical means results in an improvement of between 47% and 98% in the degree of nasal obstruction[24,26-28]. The concept that remedying any septal irregularities will widen the airways bilaterally is straightforward, since the septum is a stable anatomical structure in the nasal cavity. The use of nasal washes postoperatively is a standard medical practice in patients who undergo surgical correction of nasal septal deviation. Decongestive solutions can accelerate postoperative recovery, reduce symptoms like nasal bleeding, sneezing and congestion, and improve patient satisfaction with surgical outcome[13,14]. In this clinical study, nasal rinses with a hypertonic seawater solution containing brown and blue-green algae or isotonic saline were offered, in order to ameliorate nasal symptoms and crusting in patients following septoplasty. HSS-A did not demonstrate superiority to normal saline in improving nasal air flow 20 days postoperatively. This could be due to the fact that the surgical repair is already very efficient in correcting septal defects in both groups, as expected. Additionally, it is highly possible that both solutions were equally effective in mechanically removing mucus and other secretions. Furthermore, in most of the subjective parameters examined by means of a patient questionnaire, the

Table IX. Overall satisfaction of patients per study group.

	n	Mean	SD	Median	Min	Max	*p*-value
HSS-A	57	1.5	0.68	1	1	4	0.107
ISS	44	1.8	0.69	2	1	3	

two nasal solutions used did not differ significantly. However, HSS-A did demonstrate superiority for nasal bleeding in comparison to normal saline solution. Despite not reaching statistical significance, treatment with HSS-A was associated with improvement in several symptoms following surgery including crusting and with an increased level of patient satisfaction.

One limitation of this study is the relatively small number of participants. Further research into the benefits of HSS-A is warranted. No safety signals have been detected for either solution.

Conclusions

Collectively, the findings from this study are limited by its non-interventional and non-randomized design, as well as the limited number of trial participants. However, data indicate that HSS-A is safe and efficacious as a postoperative rinsing solution for patients undergoing surgical correction of nasal septal deviation. The findings of this study support preferential use of HSS-A in patients with an increased predisposition to post-surgical haemorrhage.

Conflict of Interest

S. Georgiou and K. Alevizopoulos are employees of Gerolymatos International S.A., the company that developed the finished product tested in this study.

Funding

This study was sponsored by Gerolymatos International S.A. However, Gerolymatos International S.A. did not solicit this research project or protocols with the investigators or the institution. Gerolymatos International S.A. was not responsible for the management of the study, data processing and reporting.

Ethics Approval

Ethics approval was granted by the ORL Athens Clinic Institutional Review Board. It conformed to the requirements of the Declaration of Helsinki.

Informed Consent

Before acceptance into the study, all patients were informed about the study and provided their consent to participate.

Authors' Contributions

Conceptualization: S. Laskaris, K. Alevizopoulos; Methodology: S. Laskaris, K. Alevizopoulos; Data collection, processing, and analysis: S. Laskaris; Data interpretation: S. Laskaris, S. Georgiou, C. Cingi, K. Alevizopoulos; Literature review: S. Laskaris, S. Georgiou, C. Cingi, K. Alevizopoulos; Manuscript preparation, editing and final review: S. Laskaris, S. Georgiou, C. Cingi, K. Alevizopoulos.

ORCID ID

Spyridon Laskaris: 0000-0001-9197-0085
Stella Georgiou: 0000-0001-7619-6714
Cemal Cingi: 0000-0003-3934-5092
Konstantinos Alevizopoulos: 0000-0002-5197-3780

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