





Efficacy of a Non-addictive Nasal Irrigation Based on Sea Salt Enriched with Natural Enzymes among Patients with Sinusitis: An *In Vivo*, Randomized, Controlled Trial

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Abstract

BACKGROUND: Chronic rhinosinusitis (CRS) is a common condition that is defined as inflammation of the nose and paranasal sinuses. Nasal irrigation plays an important role in the treatment of CRS. Evidence from basic research favors hypertonic saline over isotonic saline for mucociliary clearance, but evidence from clinical studies is controversial.

AIM: This study aims to investigate the hypothesis that the use of daily nasal irrigation based on sea salt, enriched with natural enzymes and lysozyme, may be useful in patients with CRS.

PATIENT AND METHODS: Patients (30 men and 30 women) 18–55 years old (mean age 41 ± 3 y.o.), with two episodes of acute sinusitis or one episode of chronic sinusitis per year for 2 consecutive years, were enrolled stratified by sex and age and randomly divided into two groups supplementation: Group A (test) and Group B (control/placebo). Moreover, an exit questionnaire was asked to Group A subjects to report whether their sinus-related quality of life has gotten worse, stayed the same, or improved (scale from 0 to ±100%).

RESULTS: The result showed that in the test group (A) from T0 to T1, a reduction of 17.65% for the symptoms related headache and/or facial pressure and a reduction of the 18.18%, for the symptoms relates to congestion and/or nasal discharge. On the other hand, the control group (B) shown less difference between T0 and T1.

CONCLUSIONS: This study strengthens the argument that the tested formulation is a safe, well-tolerated, long-term therapy that patients with chronic sinonasal complaints can and will use at home with minimal training and follow-up.

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Introduction

Chronic rhinosinusitis (CRS) is one of the most common nasal inflammatory disorders, affecting 5–12% of adult populations worldwide [1], [2]. Based on this background, a survey was conducted in five Italian cities enrolling 4999 adult subjects (2923 males and 2076 females; mean age 35 years), equally distributed along Italy. The outcomes reflected the situation that may occur in clinical practice. The rough prevalence was about 20%, including both acute and CRS. The winter is the most common season for overall rhinosinusitis occurrence [2]. Several pathogenic factors have been attributed to the development of CRS, including the presence of biofilms, changes of mucociliary clearance, remodeling of tissue, and immune factors [3], [4], [5], [6].

As CRS identifies several cofactors supporting their pathogenesis, the therapeutic approaches could be different. Steroid compounds, such as budesonide

or mometasone, are commonly added to saline irrigations for control of inflammatory mediators in CRS [7], [8], [9]. In recent times, topical therapies have come out as an alternative release method for localized, high concentration medication with less side effects [2].

Several randomized controlled trials examining saline nasal irrigation (SNI) suggest that it is a safe, effective, and tolerable therapy for rhinosinusitis and sinus symptoms [10], [11], [12], [13], [14], [15]. SNI is usually performed with saline or other solutions and improves the mucosal function of the nasal cavity due to direct mucosal cleansing.

Researchers have hypothesized an active role of lysozyme in CRS pathogenesis, suggesting a therapeutic effect in patients affected by CRS [4]. Moreover, patients with CRS have been treated with Dead Sea salt irrigations, showing promising results for symptoms reduction [5].

With these premises, we hypothesized that the use of daily nasal irrigation based on sea salt, enriched with natural enzymes and lysozyme, may be useful in patients with CRS.

The aim of this study was to evaluate if the use of a daily nasal irrigation formulation, containing sea salt, and enriched with lysozyme (H2Ocean Nasalzyne Gentle Formula, USA), in participants with CRS, would be effective compared to the control group.

Patients and Methods

Participants

Subjects from the first visit and specialist otolaryngology clinic with histories of frequent sinusitis were randomized to the experimental and control groups. Subjects (totally 60) were enrolled for a study period of 100 days/4 months. Exclusion criteria included pregnancy, smoking habits, and nasal polyps and/or nasal deviation.

Participants were too informed about sinus disease and its treatment. Nasal irrigation theory and technique were explicated. Written and verbal informed consent was obtained from each participant. The Institutional Ethics Committee of the Faculty of Medical Sciences (Albania) approved the application to conduct the clinical trial in the faculty, Protocol Identification: INTL_ALITCOOP/DentPath/2020_SLK. Participants randomly received an educational intervention that included a brief discussion of rhinosinusitis, a demonstration of product use, to facilitate each participant's skill. All participants were supervised frequently with validated questionnaires.

Experimental design

Participants were stratified by sex and age and randomly divided into two groups supplementation:

1. Group A – Test group: H2Ocean (USA) Nasalzyne Gentle Formula (4 irrigations daily) or
2. Group B – Control group: Placebo (physiological solution) were administered for 10 weeks (100 days/4 months).

Clinical examination

Clinical outcomes were assessed with several methods in both the test and control groups: (a) Compliance with nasal irrigation, recorded in a daily diary and (b) the presence or absence of sinus symptoms in a scale from 1 to 3 were (1) was absence; (2) presence; and (3) high presence of symptoms and (headache and/or facial pressure; congestion; and/or nasal discharge). The above items were assessed for 100 days/4 months.

Moreover, an exit questionnaire was asked to Group A subjects to report whether their sinus-related quality of life (QOL) has gotten worse, stayed the same, or improved (scale from 0 to $\pm 100\%$).

Statistical analyses

Pre- and post-assessed changes in total scores at each follow-up point compared with scores at the beginning of the study. Researchers analyzed two samples on score changes from the baseline (T0) of 100 days/4 months (T1) to test differences in percentage of group status.

Results

Sixty patients (30 men and 30 women) aged between 18 and 55 years old (mean age 41 ± 3 y.o.), with two episodes of acute sinusitis or one episode of chronic sinusitis per year for 2 consecutive years, were enrolled. All 100% of participants consented to participate in the outcomes study. There were no significant baseline differences in QOL scores or sinus-related medical histories in T0 participants. Participants also expressed agreement in their perception that at-home use of the tested product reduced the number of meeting to their physician.

Participants acknowledged each element of the instruction strategy used in the preliminary meeting as significant in their use of the products. Because therapy is novel for most patients, participants also noted several at-home strategies that facilitated regular use, which included incorporating the nasal irrigation time into an already existing daily hygiene routine and placing the products in convenient and accessible locations.

In the test group (A) shown from T0 to T1, a reduction of 17.65% for the symptoms related headache and/or facial pressure and a reduction of the 18.18%, for the symptoms relates to congestion and/or nasal discharge. On the other hand, the placebo group (B) shown less difference between T0 and T1 (Figures 1 and 2).

All Group "A" participants also confirmed positive long-term effects of the tested product on sinus-related QOL and noted a sense of satisfaction linked with the reduction of their sinus symptoms.

Discussion

Given the importance of the concept of disease control, from a clinical as well as from a

research perspective, there still remains a need for a gold standard to assess disease control in CRS [4]. The primary goal of any treatment, especially in chronic diseases, is to achieve and maintain clinical control, which can be defined as a disease state in which the patient does not have symptoms, or the symptoms are not impacting QOL.

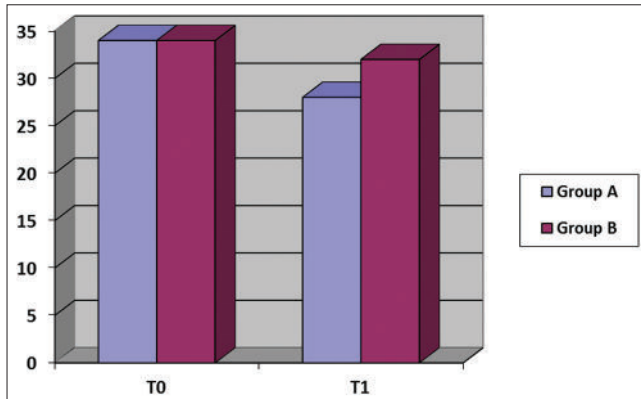


Figure 1: Sinus headache and/or facial pressure in Group A versus Group B. Test group (a) shown from T0 to T1, a reduction of 17,65% for the symptoms

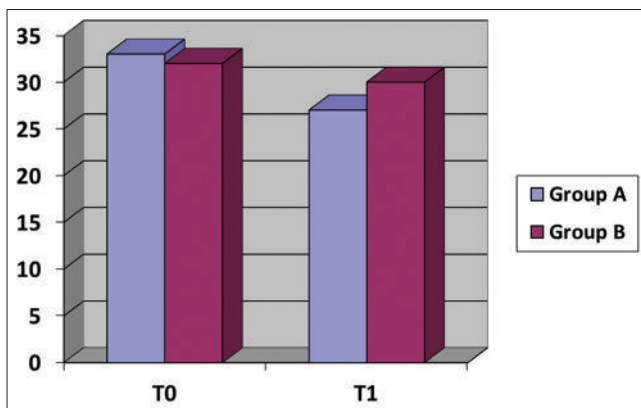


Figure 2: Congestion and/or nasal discharge in Group A versus Group B. Test group (a) shown from T0 to T1, a reduction of 18,18%, for the symptoms

Topical nasal rinses take advantage of this secretory lining in multiple ways. First, nasal rinses physically disrupt the viscous surface layer, removing the mucus and its associated particulate matter [16], [17], [18], [19], [20], [21], [22]. In addition, the presence of nasal saline is hypothesized to function by thinning mucous, improving mucociliary clearance, decreasing edema, and reducing antigen load in the nasal and sinus cavities. Although its use in CRS is nearly universal, significant variety exists with regard to delivery volume, delivery pressure, frequency of use, duration of use, composition, and hygiene recommendations [22], [23], [24], [25], [26], [27], [28]. There were several studies assessing QOL in CRS patients.

Among participants with CRS, we found an interesting improvement, in decreased overall

sinus symptom severity, no adverse effects, and high participant satisfaction. These results were consistent with other reports of QOL improvement using SNI over a short period of time [9], [10], [11], [12], [13].

The current study is limited by its relatively small sample size, and the participants' potential bias toward using the tested product, because they already used in the past SNI medications.

The primary concern without irrigation randomization or a matched control group is the generalizability of our sample. The duration of symptoms of our participants varied.

Opening the nasal passage with the aid of a simple device was highly effective in relieving symptoms regardless of which solution was used. The differences found between the control group and Groups A and B have shown that washing the nose with physiological saline or sea salt to clear the nose in acute upper respiratory tract infections has utility in the improvement of symptoms. Sea salt, enriched with natural enzymes and lysozyme, may be added to standard treatment protocols.

These issues require further study in a larger patient population including identified subgroups, such as patients with chronic rhinitis alone, patients with polypoid change, and patients who have had previous sinonasal surgery.

Conclusions

Use of the tested formulation was regular, well-tolerated, and met with participant satisfaction.

This study strengthens the argument that H2Ocean (USA) Nasalzime Gentle Formula is a safe, well-tolerated, long-term therapy that patients with chronic sinonasal complaints may use at home with minimal training after due consultation with their physician.

Clinicians may consider H2Ocean (USA) Nasalzime Gentle Formula to be an effective adjunctive treatment for symptoms associated with chronic sinonasal symptoms.

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