Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2022 Jan 13; 10(A):153-157.
https://doi.org/10.3889/oamjms.2022.8164
eISSN: 1857-9655
Category: *A - Basic Sciences*
Section: *Microbiology*

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

Riccardo Nocini[1], Michele Di Cosola[2], Angela Pia Cazzolla[2], Stefania Cantore[3,4], Francesca Castellaneta[5]*, Michele Covelli[6]

[1]Department of Surgical Sciences, Dentistry, Gynecology and Pediatric, University of Verona, Verona, Italy; [2]Department of Clinical and Experimental Medicine, Università degli Studi di Foggia, Foggia, Italy; [3]Faculty of Dentistry, University of Medicine, Tirana, Tirana, Albania; [4]Department of Interdisciplinary of Medicine, University of Bari Aldo Moro, Bari, Italy; [5]School of Medicine, University of Bari Aldo Moro, Bari, Italy; [6]Interuniversity Research Center "Population, Environment and Health - CIRPAS, University of Bari Aldo Moro, Bari, Italy

Edited by: Slavica Hristomanova-Mitkovska
Citation: Nocini R, Di Cosola M, Cazzolla AP, Cantore S, Castellaneta F, Covelli M. 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. Open-Access Maced J Med Sci. 2022 Jan 13; 10(A):153-157. https://doi.org/10.3889/oamjms.2022.8164
Keywords: Chronic rhinosinusitis; Nasal irrigation; Sea salt; Natural enzymes and lysozyme
***Correspondence:** Dr. Francesca Castellaneta, School of Medicine, University of Bari Aldo Moro, Bari, Italy. E-mail: fra_c@live.com
Received: 04-Dec-2021
Revised: 30-Dec-2021
Accepted: 03-Jan-2022

Funding: This research did not receive any financial support
Competing Interest: The authors have declared that no competing interest exists

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.

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 Nasalzyme 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) Nasalzyme 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 ±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 form 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.

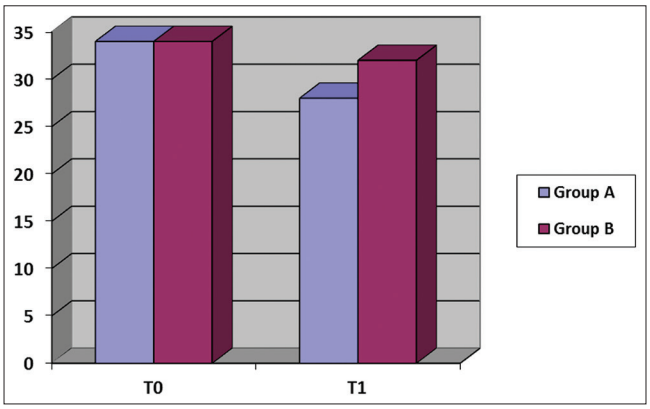

Figure 1: Sinus headache and/or facial pressure in Group A versus Group B. Test group (a) shown form T0 to T1, a reduction of 17,65% for the symptoms

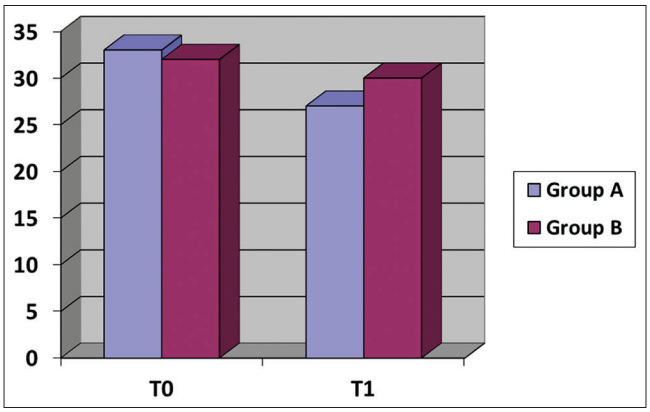

Figure 2: Congestion and/or nasal discharge in Group A versus Group B. Test group (a) shown form T0 to T1, a reduction of 18.18%, for the symptoms

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) Nasalzyme 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) Nasalzyme Gentle Formula to be an effective adjunctive treatment for symptoms associated with chronic sinonasal symptoms.

References

1. Santacroce L, Charitos IA, Ballini A, Inchingolo F, Luperto P, De Nitto E, *et al*. The human respiratory system and its microbiome at a glimpse. Biology (Basel). 2020;9(10):E318. https://doi.org/10.3390/biology9100318
   PMid:33019595
2. Passali D, Damiani V, Passali GC, Cassano P, Piemonte M,

Ciprandi G. The impact of rhinosinusitis in clinical practice: An Italian survey. Acta Biomed. 2020;91(1-S):28-35. https://doi.org/10.23750/abm.v91i1-S.9247

PMid:32073558

3. Tan NC, Psaltis AJ. Latest developments on topical therapies in chronic rhinosinusitis. Curr Opin Otolaryngol Head Neck Surg. 2020;28(1):25-30. https://doi.org/10.1097/MOO.0000000000000598

PMid:31789928

4. Woods CM, Lee VS, Hussey DJ, Irandoust S, Ooi EH, Tan LW, *et al*. Lysozyme expression is increased in the sinus mucosa of patients with chronic rhinosinusitis. Rhinology. 2012;50(2):147-56.

5. Giudice G, Cutrignelli DA, Sportelli P, Limongelli L, Tempesta A, Di Gioia G, *et al*. Rhinocerebral mucormycosis with orosinusal involvement: Diagnostic and surgical treatment guidelines. Endocr Metab Immune Disord Drug Targets. 2016;16(4):264-9. https://doi.org/10.2174/1871530316666161223145055

PMid:28017141

6. Cazzolla AP, Cosola MD, Ballini A, Santacroce L, Lovero R, Testa NF, *et al*. The association between nutritional alterations and oral lesions in a pediatric population: An epidemiological study. Biomed Res Int. 2021;2021:9992451. https://doi.org/10.1155/2021/9992451

PMid:34746317

7. Di Cosola M, Ballini A, Zhurakivska K, Ceccarello A, Nocini R, Malcangi A, *et al*. Retrospective analysis of clinical and radiologic data regarding zygomatic implant rehabilitation with a long-term follow-up. Int J Environ Res Public Health. 2021;18(24):12963. https://doi.org/10.3390/ijerph182412963

PMid:34948572

8. Charitos IA, Castellaneta F, Santacroce L, Bottalico L. Historical anecdotes and breakthroughs of histamine: From discovery to date. Endocr Metab Immune Disord Drug Targets. 2021;21(5):801-14. https://doi.org/10.2174/1871530320666200729150124

PMid:32727338

9. Lin SY, Baugher KM, Brown DJ, Ishman SL. Effects of nasal saline lavage on pediatric sinusitis symptoms and disease-specific quality of life: A case series of 10 patients. Ear Nose Throat J. 2015;94(2):E13-8. https://doi.org/10.1177/014556131509400212

PMid:25651352

10. Santacroce L, Sardaro N, Topi S, Pettini F, Bottalico L, Cantore S, *et al*. The pivotal role of oral microbiota in health and disease. J Biol Regul Homeost Agents. 2020;34(2):733-7. https://doi.org/10.23812/20-127-L-45

PMid:32492992

11. Kanjanawasee D, Seresirikachorn K, Chitsuthipakorn W, Snidvongs K. Hypertonic saline versus isotonic saline nasal irrigation: Systematic review and meta-analysis. Am J Rhinol Allergy. 2018;32(4):269-79. https://doi.org/10.1177/1945892418773566

PMid:29774747

12. Zahedi FD, Asmi NH, Husain S, Gendeh BS. Identification of nasal irrigation bottle contamination in post sinonasal surgery. Indian J Otolaryngol Head Neck Surg. 2019;71(Suppl 3):1837-42. https://doi.org/10.1007/s12070-017-1219-x

PMid:31763256

13. Ballini A, Dipalma G, Isacco CG, Boccellino M, Di Domenico M, Santacroce L, *et al*. Oral microbiota and immune system crosstalk: A translational research. Biology (Basel). 2020;9(6):E131. https://doi.org/10.3390/biology9060131

PMid:32560235

14. Ballini A, Scacco S, Boccellino M, Santacroce L, Arrigoni R. Microbiota and obesity: Where are we now? Biology (Basel). 2020;9(12):E415. https://doi.org/10.3390/biology9120415

PMid:33255588

15. Signorini L, Ballini A, Arrigoni R, De Leonardis F, Saini R, Cantore S, *et al*. Evaluation of a nutraceutical product with probiotics, vitamin d, plus banaba leaf extracts (*Lagerstroemia speciosa*) in glycemic control. Endocr Metab Immune Disord Drug Targets. 2020;21(7):1356-65. https://doi.org/10.2174/1871530320666201109115415

PMid:33167849

16. Muzio LL, Ballini A, Cantore S, Bottalico L, Charitos IA, Ambrosino M, *et al*. Overview of *Candida albicans* and human papillomavirus (HPV) infection agents and their biomolecular mechanisms in promoting oral cancer in pediatric patients. Biomed Res Int. 2021;2021:7312611. https://doi.org/10.1155/2021/7312611

PMid:34765678

17. Crincoli V, Cazzolla AP, Di Comite M, Lo Muzio L, Ciavarella D, Dioguardi M, *et al*. Evaluation of Vitamin D (25OHD), bone alkaline phosphatase (BALP), serum calcium, serum phosphorus, ionized calcium in patients with mandibular third molar impaction. An observational study. Nutrients. 2021;13(6):1938. https://doi.org/10.3390/nu13061938

PMid:34200107

18. Charitos IA, Ballini A, Cantore S, Boccellino M, Di Domenico M, Borsani E, *et al*. Stem cells: A historical review about biological, religious, and ethical issues. Stem Cells Int. 2021;2021:9978837. https://doi.org/10.1155/2021/9978837

19. Santacroce L, Di Cosola M, Bottalico L, Topi S, Charitos IA, Ballini A, *et al*. Focus on HPV infection and the molecular mechanisms of oral carcinogenesis. Viruses. 2021;13(4):559. https://doi.org/10.3390/v13040559

PMid:33810374

20. Di Cosola M, Cazzolla AP, Charitos IA, Ballini A, Inchingolo F, Santacroce L. *Candida albicans* and oral carcinogenesis. A brief review. J Fungi (Basel). 2021;7(6):476. https://doi.org/10.3390/jof7060476

PMid:34204731

21. Man A, Ciurea CN, Pasaroiu D, Savin AI, Toma F, Sular F, *et al*. New perspectives on the nutritional factors influencing growth rate of *Candida albicans* in diabetics. An *in vitro* study. Mem Inst Oswaldo Cruz. 2017;112(9):587-92. https://doi.org/10.1590/0074-02760170098

PMid:28902283

22. Di Cosola M, Ambrosino M, Limongelli L, Favia G, Santarelli A, Cortelazzi, R, *et al*. Cocaine-induced midline destructive lesions (CIMDL): A real challenge in diagnosis. Int J Environ Res Public Health. 2021;18(15):7831. https://doi.org/10.3390/ijerph18157831

PMid:34360121

23. Grassi FR, Pappalettere C, Di Comite M, Corsalini M, Mori G, Ballini A, *et al*. Effect of different irrigating solutions and endodontic sealers on bond strength of the dentin-post interface with and without defects. Int J Med Sci. 2012;9(8):642-54. https://doi.org/10.7150/ijms.4998

PMid:23055816

24. Campanella V, Syed J, Santacroce L, Saini R, Ballini A, Inchingolo F. Oral probiotics influence oral and respiratory tract infections in pediatric population: A randomized double-blinded placebo-controlled pilot study. Eur Rev Med Pharmacol Sci. 2018;22(22):8034-41. https://doi.org/10.26355/eurrev_201811_16433

PMid:30536353

25. Santacroce L, Inchingolo F, Topi S, Del Prete R, Di Cosola M, Charitos IA, *et al*. Potential beneficial role of probiotics on

the outcome of COVID-19 patients: An evolving perspective. Diabetes Metab Syndr. 2021;15(1):295-301. https://doi.org/10.1016/j.dsx.2020.12.040
PMid:33484986

26. Ballini A, Di Cosola M, Saini R, Benincasa C, Aiello E, Marrelli B, *et al*. Comparison of manual nylon bristled versus thermoplastic elastomer toothbrushes in terms of cleaning efficacy and biological potential role on gingival health. Appl Sci. 2021;11:7180.
27. Di Cosola M, Cantore S, Balzanelli MG, Isacco CG, Nguyen KC, Saini R, *et al*. Dental-derived stem cells and biowaste biomaterials: What's next in bone regenerative medicine applications. Biocell. 2022;46(4):923-9.
28. Posa F, Colaianni G, Di Cosola M, Dicarlo M, Gaccione F, Colucci S, *et al*. the myokine irisin promotes osteogenic differentiation of dental bud-derived MSCs. Biology (Basel). 2021;10(4):295. https://doi.org/10.3390/biology10040295
PMid:33916859