

# Nasal Irrigation with Hypertonic Seawater Solutions of 2.3% NaCl: A Safe and Effective Treatment Modality for Optimal Symptom Management in ENT Diseases

Evdokia Protopapadakis, Stella Georgiou and Konstantinos Alevizopoulos\*

Gerolymatos International SA, Research & Development Department, Kryoneri, Greece

\*Corresponding author: Konstantinos Alevizopoulos PhD, Gerolymatos International SA, Research & Development Department, 13 Asklipiou street, 14568, Kryoneri, Attica, Greece

Received: December 12, 2023

Published: April 26, 2024

## Abstract

The nasal mucosa, a critical defense against airborne pathogens, relies on effective Mucociliary Clearance (MCC). Nasal Saline Irrigation (NSI) is a simple procedure for cleansing and moisturizing nasal passages. It mechanically washes out mucus, secretory aggregation, inhaled agents, and inflammatory mediators from the nose, thus promoting MCC and helping reduce mucosal edema. NSI, recommended as an adjunct therapy for sinonasal diseases and after endoscopic sinus surgery, is typically performed with isotonic or hypertonic solutions. Several clinical studies have proven the superiority of hypertonic solutions based on their osmotic decongestion and mechanical cleansing actions. In particular, hypertonic seawater solutions of 2.3% NaCl (2.3%HSS), have extensively been validated in clinical trials involving healthy subjects, patients with ENT diseases or at the postoperative setting. In healthy individuals, these solutions resulted in increased MCC. In ENT disease management, 2.3%HSS, alone or enriched with additional natural ingredients, offered sinonasal symptom relief both as a stand-alone therapy or adjunctively, in combination with standard treatments, across different age groups. In patients with upper respiratory infections, these solutions reduced viral load and were more effective than isotonic solutions. Finally, when used in combination with medication, they have demonstrated quicker symptom relief versus medication alone, while resulting in reduced medication intake. In the post-surgery setting, 2.3%HSS with or without natural extracts, demonstrated superior efficacy over isotonic solutions, while offering accelerated postoperative recovery, and reduced symptoms. These data support the use of 2.3%HSS in nasal symptom management in ENT diseases.

**Keywords:** Nasal irrigation; Hypertonic seawater solutions; 2.3% NaCl; ENT diseases; Nasal symptom management

## Introduction

The nasal cavity is the first line of defense against airborne pathogens and particles such as pollutants, dust, aeroallergens, and infectious agents. Trapped into the mucosal layer, the inhaled agents are transported towards the pharynx and swallowed via the process of mucociliary clearance which is characterized by the rhythmic beating of cilia in cells lining the surface epithelium of the airways [1]. However, lack of appropriate clearance due to barrier dysfunction and pro-inflammatory responses induced by inhaled agents can disrupt normal functioning of the nose, resulting in bothersome nasal symptoms [2].

Nasal irrigation is a simple and effective technique used to cleanse and moisturize the nasal passages. It typically involves rinsing the nasal cavity with a saline solution, using a nasal spray, squeeze bottle, a neti pot or bulb syringe. This process helps flush out mucus, allergens, infectious agents and pollutants, reducing congestion and alleviating nasal symptoms [3,4].

Nasal irrigation is typically performed with two types of solutions [3,4]:

- I) Isotonic saline solutions: these solutions are based on buffered or non-buffered solutions comprising approximately 0.9% NaCl. Isotonic solutions may also include seawater solutions diluted to a final concentration of 0.9% NaCl (undiluted seawater is about 3.1-3.5% NaCl) or iso-osmolar solutions i.e., seawater solutions with a final concentration of 0.9% NaCl generated by electrodialysis to remove excess NaCl present in seawater (while maintaining other seawater ingredients intact).
- II) Hypertonic saline solutions: these solutions are similar to isotonic solutions but comprise a NaCl content superior to 0.9%, typically between 2-3% NaCl. As above, these solutions can be generated either by dilution of seawater or via selective electrodialysis of seawater to the desired % NaCl in the final solution.

Comparing the efficacy of different solutions, several clinical studies and/or meta-analyses have pointed to a functional superiority of hypertonic versus isotonic solutions in various

conditions including rhinitis/rhinosinusitis or after endoscopic sinus surgery (ESS) [5-9]. This superiority is attributed to both osmotic decongestion and mechanical wash properties of hypertonic solutions as a result of the high ionic strength and the cleansing force of the irrigation solution, respectively. On the contrary, isotonic solutions only bear mechanical wash properties [3,4]. From a safety perspective, only minor side effects have been reported when using both solutions (e.g., irritation, mild bleeding, etc.). However, there is tendency for an increased incidence of minor side effects of hypertonic solutions when their hypertonicity exceeds 3% NaCl [5].

Among different hypertonic solutions used in practice, hypertonic seawater solutions of 2.3% NaCl (2.3%HSS), are among the best validated irrigation solutions as based on their efficacy and safety profile revealed in several clinical trials. Below, we will summarize the clinical findings on these solutions.

### Healthy subjects

Two clinical trials conducted in healthy subjects have shown that 2.3%HSS increased mucociliary clearance and improved nasal function [10,11]. It was further shown that 2.3%HSS was more effective than isotonic solutions in healthy volunteers [10]. 2.3%HSS thereby offers an effective treatment approach to improve mucociliary clearance, facilitating removal of accumulated mucus, crusts, and entrapped particles and pathogens.

### Patients with ENT diseases

2.3%HSS either alone or enriched with additional natural ingredients like algal and herbal extracts, have demonstrated through numerous scientific publications, excellent clinical efficacy, safety, tolerance, and user satisfaction. Overall, it was shown, that use of 2.3%HSS can provide sinonasal symptom relief either as a stand-alone therapy or adjunctively, in combination with standard treatments, in all age populations.

Specifically, cleansing the nasal cavity with 2.3%HSS was shown to be efficacious in various types of rhinitis and/or sinusitis of acute, chronic, allergic or non-allergic etiology. Importantly, 2.3%HSS was highly effective in reducing nasal congestion and other symptoms affecting patient quality of life. These actions are attributed to both mechanical and osmotic properties of the 2.3% NaCl hypertonic seawater solution which increases mucociliary clearance, reduces local edema and offers superior efficacy in comparison to controls or isotonic solutions [12,13]. Combined with standard medication, 2.3%HSS products offered additional benefits versus standard treatment alone in clinical trials conducted in adult and pediatric patients. Finally, use of 2.3%HSS allowed patients to achieve optimal disease management, increasing symptom-free days, while simultaneously reducing medication intake [14-17].

Specifically, in infants and young children diagnosed with acute rhinosinusitis of bacterial or viral origin like the common cold and flu, hypertonic seawater solutions of 2.3% NaCl were safe and efficacious [13]. When used as an add-on therapy to medication, 2.3%HSS was superior to medication alone [15]. In young children and adolescents suffering from allergic rhinitis, 2.3%HSS enriched with algal extracts and dexpantenol, resulted in a significant increase in symptom-free days coupled with reduced medication consumption [16]. In this study, 2.3%HSS combination treatment resulted in better ocular, nasal, asthma, and overall allergic symptom score reduction versus medication alone [16].

In adult patients suffering from intermittent or permanent nasal obstruction due to several types of rhinitis, 2.3%HSS monotherapy was effective and well tolerated, leading to significant improvement in obstruction as well as sneezing and rhinorrhea [18]. Similar to results in pediatric populations, 2.3%HSS combination therapy was superior to medication in adult rhinitis patients [14]. Moreover, 2.3%HSS was superior to isotonic treatment in improving mucociliary clearance in chronic rhinitis patients [12]. Tolerance and product satisfaction were also high for the majority of users suffering from ENT diseases who used 2.3%HSS products together with medication [17,19]. Finally, in a recent study conducted with 2.3%HSS enriched with algal and herbal extracts in hospitalized COVID-19 patients, the product, given as an add-on treatment to standard anti-viral medication, contributed significantly to overall symptom improvement and decreased viral load in the nasal cavity [20]. The same solution was also able to reduce viral load and increase the number of patients testing negative for COVID-19 at hospital discharge in a separate clinical study conducted in COVID-19 patients [21]. In conclusion, 2.3%HSS products have shown favorable clinical efficacy and tolerability in ENT disease symptom management. Use in combination with prescribed medication allows optimal disease management and reduction of medication intake.

### Patients undergoing ESS

Endoscopic sinus surgery (ESS) is often accompanied by adverse effects on nasal mucosa physiology and function resulting in the formation of crusts, nasal blockage, and other sinonasal symptoms, worsening the quality of post-operative life of patients. Irrigation solutions are strongly recommended and employed to reduce these adverse effects as part of postoperative treatments [22-25]. 2.3%HSS used either alone or enriched with additional herbal and algal ingredients have proven effective in providing sinonasal symptomatic relief post-surgery.

Specifically, in patients who have undergone septoplasty, post-operative nasal rinsing with 2.3%HSS improved nasal airway airflow and patency. Irrigation with 2.3%HSS was shown to be advantageous for both mucociliary clearance and postoperative decongestion, thereby improving nasal breathing and minimizing the risk of postoperative infections [22]. In another cohort of patients following septoplasty and concha radiofrequency, patients experienced less nasal crusting, dryness, and obstruction while receiving 2.3%HSS compared to saline or tap water controls [23]. Patients after septoplasty and radiofrequency turbinate volume reduction rinsing their noses with 2.3%HSS enriched with algal extracts reported less nasal bleeding and less crust formation compared to their counterparts who used saline. These results support the preferential use of 2.3%HSS products in patients with an increased predisposition to post-surgical hemorrhage [26].

Sinonasal symptoms were reduced in patients after ESS following nasal rinsing with 2.3%HSS according to both endoscopic findings and patients' evaluations. 2.3%HSS proved effective for symptom management in patients with aspirin-induced chronic rhinosinusitis which is a hard-to-control severe progressive disease. Patients using 2.3%HSS felt less discomfort and lower nasal obstruction, facial pain/pressure, headache and trouble sleeping, nasal mucosal edema, nasal secretions, and crusting compared to the group using saline [24]. Relief of the aforementioned symptoms was also perceived in subjects with uncontrolled chronic rhinosinusitis receiving ESS, in the postoperative period [27].

In another study, patients who underwent ESS for nasal polypsis and performed nasal douching with 2.3% HSS enriched with algal extracts, reported lower nasal symptom and endoscopic finding scores than isotonic controls. In the same study, 2.3% HSS, enriched with algal extracts, was more effective than isotonic control in modifying levels of the inflammatory marker IL-8 and repair-related markers, TGF- $\alpha$  and EGF, suggesting optimal nasal mucosa reparation after ESS [28].

Conclusively, 2.3% HSS accelerated postoperative recovery, reduced symptoms like nasal bleeding, crusting and congestion, ensured nasal mucosa moistening, and improved patient satisfaction with surgical outcome, while demonstrating superior efficacy over isotonic irrigation solutions. Data from clinical studies in post-surgery patients support the high safety profile of 2.3% HSS products.

## Conclusion

Hypertonic irrigation solutions have been widely used to provide symptomatic relief in patients with ENT diseases. Among different solutions used, hypertonic seawater solutions of 2.3% NaCl were shown to be particularly effective, simultaneously offering a high level of safety. Used either alone or in combination with prescribed medication, these solutions are a versatile tool to be used in clinical practice for optimal disease management.

**Conflicts of Interest/Competing Interests:** The authors are employees of Gerolyntos International SA, a company commercializing nasal irrigation solutions.

**Grant Information:** The author(s) received no specific funding for this work.

## References

- Matsui H, Randell SH, Peretti SW, Davis CW, Boucher RC. Coordinated clearance of periciliary liquid and mucus from airway surfaces. *J Clin Invest*, 1998; 102(6): 1125-1131. doi: 10.1172/JCI2687. PMID: 9739046; PMCID: PMC509095.
- He Y, Fu Y, Wu Y, Zhu T, Li H. Pathogenesis and treatment of chronic rhinosinusitis from the perspective of sinonasal epithelial dysfunction. *Front Med (Lausanne)*, 2023; 10: 1139240. doi: 10.3389/fmed.2023.1139240. PMID: 37138733; PMCID: PMC10149833.
- Principi N, Esposito S. Nasal Irrigation: An Imprecisely Defined Medical Procedure. *Int J Environ Res Public Health*, 2017; 14(5): 516. doi: 10.3390/ijerph14050516. PMID: 28492494; PMCID: PMC5451967.
- Georgiou S, Alevizopoulos K. Nasal Irrigation in the COVID-19 Era. *Int J Clin Stud Med Case Rep*, 2021; 13(3): 1-8. doi: 10.46998/IJCMCR.2021.13.000314
- 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): 269-279. doi: 10.1177/1945892418773566. Epub 2018 May 18. PMID: 29774747.
- Li CL, Lin HC, Lin CY, Hsu TF. Effectiveness of Hypertonic Saline Nasal Irrigation for Alleviating Allergic Rhinitis in Children: A Systematic Review and Meta-Analysis. *J Clin Med*, 2019; 8(1): 64. doi: 10.3390/jcm8010064. PMID: 30634447; PMCID: PMC6352276.
- Liu L, Pan M, Li Y, Tan G, Yang Y. Efficacy of nasal irrigation with hypertonic saline on chronic rhinosinusitis: systematic review and meta-analysis. *Braz J Otorhinolaryngol*, 2020; 86(5): 639-646. doi: 10.1016/j.bjorl.2020.03.008. Epub 2020 May 16. PMID: 32534983; PMCID: PMC9422444.
- Wang Y, Jin L, Liu SX, Fan K, Qin ML, Yu SQ. Role of nasal saline irrigation in the treatment of allergic rhinitis in children and adults: A systematic analysis. *Allergol Immunopathol (Madr)*, 2020; 48(4): 360-367. doi: 10.1016/j.aller.2020.01.002. Epub 2020 Apr 21. PMID: 32331798.
- Yu JF, Zhang Y, Liu ZB, Wang J, Bai LP. 3% nebulized hypertonic saline versus normal saline for infants with acute bronchiolitis: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)*, 2022; 101(43): e31270. doi: 10.1097/MD.00000000000031270. PMID: 36316926; PMCID: PMC10662888.
- Lee SH, Song J, Lee SH, Hwang SJ, Lee HM. Effect of Hypertonic Seawater (Sinomarin®) on Mucociliary Clearance in Normal Subjects, 2003; 10(1): pp. 19–22.
- Bencova A, Vidan J, Rozborilova E, Kocan I. The impact of hypertonic saline inhalation on mucociliary clearance and nasal nitric oxide. *J Physiol Pharmacol*, 2012; 63(3): 309-313. PMID: 22791646.
- Liu Z, Wang H. The clinical research of 2.3% hypertonic salt water in the treatment of patients with chronic rhinitis. In *J Taishan Med College*, 2015: 35(7).
- Köksal T, Çizmecci MN, Bozkaya D, Kanburoglu MK, Sahin S, et al. Comparison between the use of saline and seawater for nasal obstruction in children under 2 years of age with acute upper respiratory infection. *Turk J Med Sci*, 2016; 46(4): 1004-1013. doi: 10.3906/sag-1507-18. PMID: 27513397.
- González GJA, Sanchez A, Mejia YR. A clinical study conducted in 2007 with Mexican patients: an investigational, prospective, longitudinal, comparative, multicentre, open-label study on the efficacy and tolerability of Sinomarin Spray for the treatment of rhinitis. *Journal of the Federation of Otolaryngological and Societies of the Mexican Republic (FESORMEX)*, 2008.
- Lu CY, Chen DH. [The curative effect observation of nasal irrigation by hypertonic saline in treatment of infant acute rhinosinusitis]. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2017; 31(17): 1367-1369. Chinese. doi: 10.13201/j.issn.1001-1781.2017.17.018. PMID: 29798234.
- Mitsias DI, Dimou MV, Lakoumentas J, Alevizopoulos K, Sousa-Pinto B, et al. Effect of nasal irrigation on allergic rhinitis control in children; complementarity between CARAT and MASK outcomes. *Clin Transl Allergy*, 2020; 10: 9. doi: 10.1186/s13601-020-00313-2. PMID: 32190296; PMCID: PMC7068957.
- Georgiou S, Alevizopoulos K. A Real-World User Survey Study Conducted with a Hypertonic Seawater Nasal Irrigation Solution Comprising Algal and Herbal Ingredients in Patients with E.N.T. Disorders. *Int J Clin Stud Med Case Reports*, 2022; 17(4): 1-4. DOI: 10.46998/IJCMCR.2021.17.000417.
- Freche C, Castillo L, De Corbiere S, Dessi P, Fontanel JP, et al. Usefulness of hypertonic sea water (Sinomarin®) in rhinology. *Revue Officielle de la Société Française de ORL*, 1998 ; 50(4).
- Georgiou S, Alevizopoulos K. A Real-World User Survey on the Effectiveness of a Hypertonic Seawater Nasal Spray as an Add-On to Pharmacological Treatment in Patients with ENT Diseases. *Int J Clin Stud Med Case Reports*, 2023; 25(4): 1-4. DOI: 10.46998/IJCMCR.2023.25.000618.
- Gangadi M, Georgiou S, Moschotzopoulou E, Antronikou T, Kainis E, Alevizopoulos K. Efficacy and safety of a hypertonic seawater nasal irrigation solution containing algal and herbal natural ingredients in patients with COVID-19. *Eur Rev Med Pharmacol Sci*, 2022; 26(2 Suppl): 112-123. doi: 10.26355/eurrev\_202212\_30495. PMID: 36524919.
- Pantazopoulos I, Chalkias A, Miziou A, Spanos M, Gerasileiou E, et al. A hypertonic seawater nasal irrigation solution containing algal and herbal natural ingredients reduces viral load and SARS-CoV-2 detection time in the nasal cavity. *J. Pers. Med*, 2023; 13: 1093.
- Kurtaran H, Ugur KS, Yilmaz CS, Kaya M, Yuksel A, Ark N, et al. The effect of different nasal irrigation solutions following septoplasty and concha radiofrequency: a prospective randomized study. *Braz J Otorhinolaryngol*, 2018; 84(2): 185-190. doi: 10.1016/j.bjorl.2017.01.005. Epub 2017 Feb 22. PMID: 28325622; PMCID: PMC9449243.

23. Süslü N, Bajin MD, Süslü AE, Öğretmenoğlu O. Effects of buffered 2.3%, buffered 0.9%, and non-buffered 0.9% irrigation solutions on nasal mucosa after septoplasty. *Eur Arch Otorhinolaryngol*, 2009; 266(5): 685-689. doi: 10.1007/s00405-008-0807-5. Epub 2008 Sep 18. PMID: 18802718.
24. Perić A, Kovačević SV, Barać A, Gaćeša D, Perić AV, Jožin SM. Efficacy of hypertonic (2.3%) sea water in patients with aspirin-induced chronic rhinosinusitis following endoscopic sinus surgery. *Acta Otolaryngol*, 2019; 139(6): 529-535. doi: 10.1080/00016489.2019.1605454. Epub 2019 Apr 29. PMID: 31035841.
25. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology*, 2020; 58(Suppl S29): 1-464. doi: 10.4193/Rhin20.600. PMID: 32077450.
26. Laskaris S, Georgiou S, Cingi C, Alevizopoulos K. 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 radio-frequency turbinate volume reduction. *Eur Rev Med Pharmacol Sci*, 2022; 26(2 Suppl): 38-48. doi: 10.26355/eur-rev\_202212\_30481. PMID: 36524909.
27. Dawood MR, Mohammed ZS. Comparative study on the use of hypertonic saline vs. isotonic saline nasal irrigation following endoscopic sinus surgery. *Pol Otorrhino Rev*, 2022; 11(1): 14-20.
28. Perić A, Gaćeša D, Kovačević SV, Perić AV, Vojvodić D, et al. The effect of nasal douching by hypertonic 2.3% sea water with algae extracts on the concentration of epidermal growth factor, transforming growth factor- $\alpha$  and interleukin-8 in nasal secretions of patients with nasal polypsis following endoscopic surgical treatment. *J Laryngol Otol*, 2023; 1-26. doi:10.1017/S0022215123001974