www.jcimcr.org

JCIMCR OPEN ACCESS Journal of Clinical Images and Medical Case Reports

ISSN 2766-7820

Short Commentary

Open Access, Volume 5

Real world efficacy, safety and performance evaluation of a hypertonic seawater solution comprising algal extracts and dexpanthenol in patients with allergic rhinitis

Stella Georgiou[1]; Petranka Andonova[2]; Vesna Dzambazovska[2]; Vesna Fidanoska Jovicikj[2]; Julija Ivanovski[2]; Emilija Manasievski[2]; Sevil Merdzanovska[3]; Luljijeta Mustafa Ramadani[2]; Aleksandra Pili[3]; Galapce Saljamovska[3]; Olga Smilevska Spasova[2]; Ana Tasevska Rajkovikj[2]; Persida Tofiloska Poposka[2]; Mira Toskovska[3]; Andrijana Ugrinovska Pandeva[2]; Konstantinos Alevizopoulos[1]*

[1]Research & Development Department, Gerolymatos International S.A, Attica, Greece.

[2]Public Health Institute of Pulmonary Diseases in Children-Kozle, Skopje, North Macedonia.

[3]Public Health Institute for Prevention, Treatment and Rehabilitation of Chronic Respiratory, Non-Specific and Allergic Diseases, Oteshevo, North Macedonia.

***Corresponding Author:**

Konstantinos Alevizopoulos

Research & Development Department, Gerolymatos International S.A, Attica, Greece.

Tel: +41-787527002;

Email: kalevizo@gerolymatos-int.com

Received: Jun 07, 2024

Accepted: Jun 24, 2024

Published: Jul 01, 2024

Archived: www.jcimcr.org

DOI: www.doi.org/10.52768/2766-7820/3147

Abstract

To obtain real world data on the efficacy, safety and performance of a Hypertonic Seawater Solution comprising Algal Extracts and Dexpanthenol (HSSAll) indicated for Allergic Rhinitis (AR), we have conducted a user survey study in a total of 300 adult and pediatric patients recruited in 2 hospital centers over a period of 9 months. The study assessed a series of quantitative and qualitative parameters, namely changes of several sinonasal and Quality-of-Life (QoL) symptom scores after HSSAll use, time to symptom relief, use of prescribed medication, product usability and satisfaction, consumer use and recommendation intentions as well as product safety and performance. Our results showed significant alleviation of sinonasal and QoL symptoms in both populations ($p<0.001$ for each symptom score). Symptom relief manifested predominantly within 30 minutes or less after HSSAll use in 70.1% of the total population; overall, symptoms improved gradually within the first three days of product use. 96.6% of the patients utilizing HSSAll adjunct to prescribed medication considered the combined treatment highly efficacious. Moreover, combined treatment allowed for a reduction of medicated product intake in 82.2% of the total population. Satisfaction on the usability and efficacy of the device exceeded 95%, and the overwhelming majority of respondents expressed their readiness to endorse HSSAll to peers (97.2%) or re-use it in the future (95.2%). No significant safety signals or technical concerns were identified during the study. These findings support the usefulness of HSSAll in managing sinonasal and QoL symptoms in AR patients.

Keywords: Nasal spray; User survey; Hypertonic sea water solutions; Sea algae; Sinonasal symptoms; Quality of life symptoms.

Abbreviations: AR: Allergic Rhinitis; ARS/CRS: Allergic/Chronic Rhinosinusitis; ENT: Ear Nose and Throat; HSS All: Nasal Spray with Hypertonic Seawater Solution Enriched with Algal Extracts; Qol: Quality of Life.

Citation: Georgiou S, Andonova P, Dzambazovska V, Jovicikj VF, Ivanovski J, et al. Real world efficacy, safety and performance evaluation of a hypertonic seawater solution comprising algal extracts and dexpanthenol in patients with allergic rhinitis. J Clin Images Med Case Rep. 2024; 5(7): 3147.

Introduction

Allergic Rhinitis (AR) is a prevalent condition affecting 10-20% of the adult population globally [1]. It is characterized by an IgE-mediated immune response against allergens, leading to symptoms such as rhinorrhea, nasal obstruction, itching, and sneezing. Ocular symptoms are also common in AR, especially with outdoor allergens. AR includes two main clinical entities: seasonal and perennial. Symptoms can be intermittent or persistent, with seasonal AR triggered by outdoor allergens and non-specific irritants exacerbating symptoms. It is a multidimensional disease and affects the quality of life, productivity and performance at work, thus making treatment imperative. It also has a profound impact on an individual's physical, social, and emotional well-being as well as quality of life (QoL). AR may contribute to rhinosinusitis, sharing similar symptoms with Allergic Rhinosinusitis (ARS) and Chronic Rhinosinusitis (CRS) [1,2].

AR management involves patient education to avoid known allergens, pharmacological medications and non-pharmacological treatments. Oral/intranasal antihistamines or decongestants, or intranasal corticosteroids are effective pharmaceutical interventions [1-4]. While these treatments are proven to be effective, non-pharmacological approaches like nasal saline irrigation have been employed to alleviate nasal symptoms, potentially reducing patient-reported disease severity across both adult and pediatric populations. In patients with AR, nasal irrigation remains a valuable adjunctive treatment option [2,4-8] that could be highly beneficial for patients reluctant to continue long-term steroid therapy.

Nasal irrigation constitutes a simple, safe and inexpensive procedure. It involves flushing the nasal cavity with saline solution, facilitating the removal of encrusted material and supporting mucosal healing. Irrigation with saline solutions helps moisturize the nasal cavity, promotes mucociliary clearance, and removes allergens and inflammatory mediators [9]. It has been reported to alleviate symptoms and improve patient-reported allergic rhinitis severity in both children [10-12] and adults [2,13-14]. Saline irrigation has shown benefits not only in AR but also in related conditions like rhinosinusitis. Isotonic and hypertonic saline solutions are commonly used, with hypertonic saline offering greater efficacy [1,2,6,7].

This user survey aimed to investigate the user satisfaction and clinical efficacy of HSSAll, a hypertonic (2.3% NaCl) seawater nasal spray containing sea algae and dexpanthenol, in ameliorating sinonasal symptoms and enhancing quality of life among children and adults afflicted with AR.

Material and methods

Nasal spray

HSSAll (Sinomarin® Plus Algae Allergy Relief, 30 mL, Gerolymatos International S.A) is a hypertonic (2.3% NaCl) seawater solution enriched with two algal extracts (Undaria pinnatifida and Spirulina platensis) and dexpanthenol. HSSAll relieves AR symptoms including blocked nose, sinus pressure, runny nose and sneezing, cleansing the nasal cavities and eliminating mucus and mucus-trapped allergens that may worsen AR symptoms. HSSAll can be used adjunctively to medicated treatments.

Users and survey design

This prospective user survey study involved patients who sought assistance for ENT symptoms during hospital visits to Oteshevo and Kozle Hospitals in North Macedonia. The recruitment took place in the period between March and November 2023. Patients were advised to engage in nasal rinsing daily with HSSAll as sole treatment or added to the prescribed medication according to its label. Upon patient consent, each patient was provided with the nasal spray and a questionnaire to be completed before the initial and after the final use.

The survey questionnaire was drafted to gather data on the effectiveness, safety, and performance of the device. Initially collecting patient demographic data (age and gender) and data on the ENT condition for which the spray was utilized, the questionnaire specifically assessed the severity of sinonasal and quality of life symptoms before and after product use. Furthermore, it assessed usage patterns (including frequency and co-administration with medication), time to symptom relief, overall evaluation and satisfaction and intention for future purchase. Finally, it evaluated safety and performance of the device based on the incidence of adverse events and/or device malfunctions reported by participants during product use. Overall, the questionnaire used Likert scales for grading of responses or response formats that encompassed options such as yes/no, multiple-choice, free-text, and multiple selections.

Statistical analysis

Data was analyzed using R version 4.3.2. All tests were two-sided, and the significance level was set at α=5%. Statistical analysis was based on descriptive statistics and was performed overall and by age group (≥18 years, <18 years). Descriptive statistics are presented as numbers (with percentages), means, and standard errors. Each item was described as categorical variable by absolute and relative frequencies before and after treatment. A shift table was used to present the change after treatment for each item. Improvement, no change or worsening of each item was presented in a frequency table. Percentages were based on the total number of patients. Missing categories were considered for the calculation of the summary percentages. Average score was calculated for each item based on the following rating scale: 0-6: Not troubled - Extremely troubled. Overall summaries of each score were based on the number of patients with non-missing data, mean, standard deviation, median, minimum and maximum before and after treatment. Comparisons between the two time points were assessed by paired samples t-test.

Results

Overall, 300 users participated in this prospective user survey. After excluding participants providing invalid answers, answers from 248 participants (each of whom answered all survey questions) were retained. The mean age of the entire cohort was 22.6±1.4 years, including 58.8% males and 41.1% females. Of them, 162 (65.3%) of users were children (<18 years) of 8.6±0.2 years and 64.2%/35.8% males/females; 86 (34.7%) of users were adults (≥18 years) of 49.1±1.7 years and 47.7%/51.2% males/females. Allergic rhinitis was the predominant disease (96.8%) the users suffered from in the total

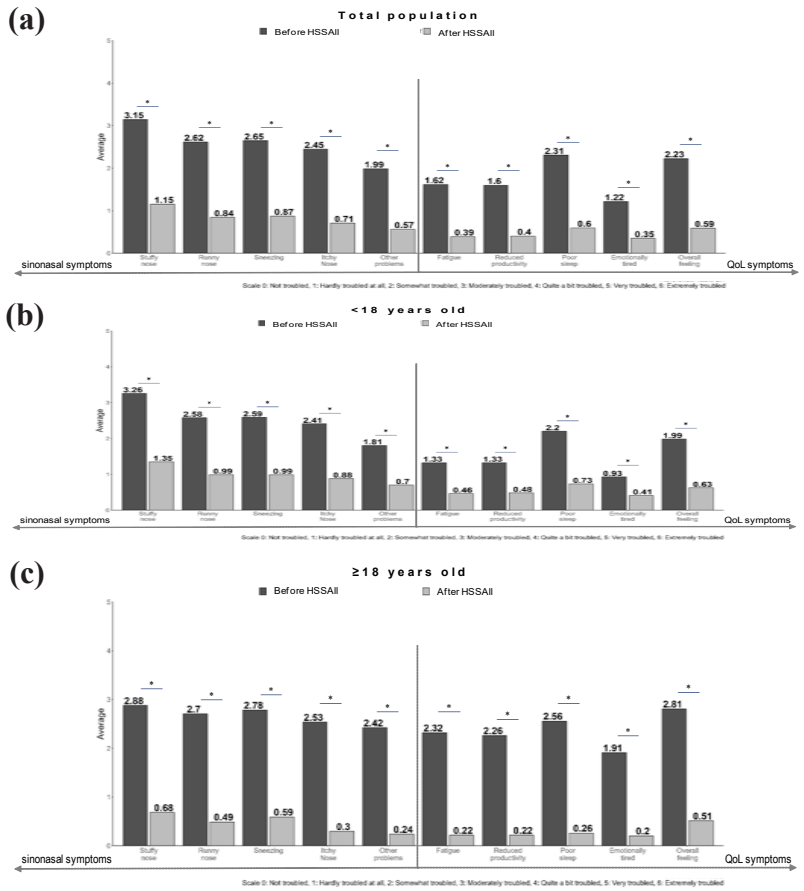

Figure 1: Average of each question response for sinonasal and quality of life symptoms for the total **(a)**, children **(b)**, and adult **(c)** populations.

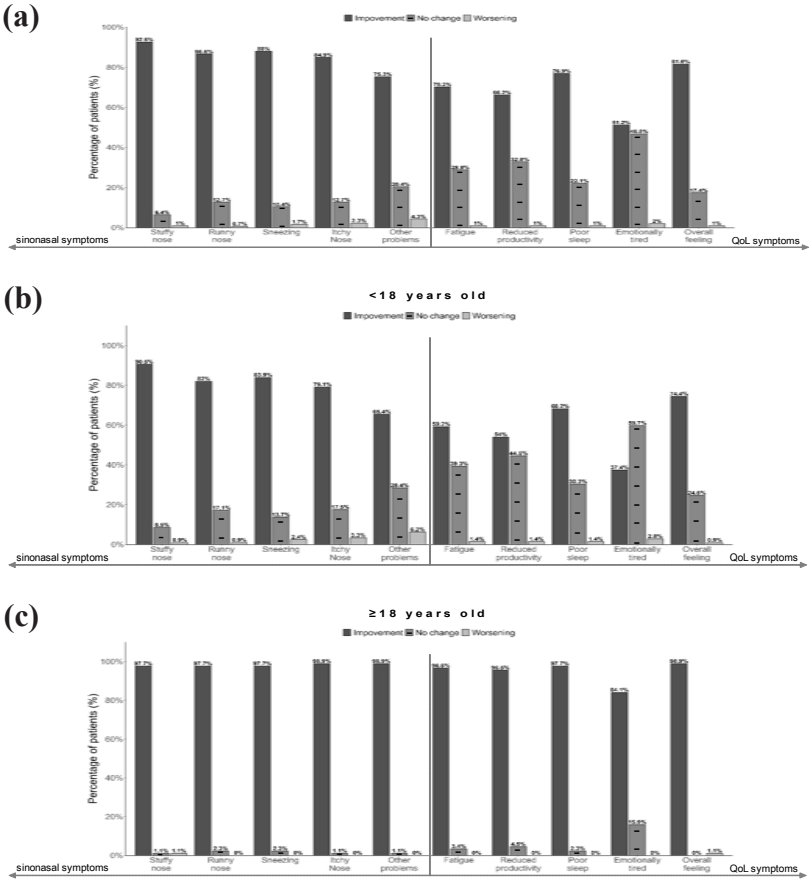

Figure 2: Frequency of shift changes of responses for sinonasal and quality of life symptoms for the total **(a)**, children **(b)**, and adult **(c)** populations.

Table 1: User survey demographics information.

Variable			
	Total population	**Children (<18 years)**	**Adults (≥18 years)**
Number of users [count (%)]	248 (100%)	162 (65.3%)	86 (34.7%)
Age (mean ± SE)	22.6±1.4	8.6±0.2	49.1±1.7
Sex (male/female)	145/102 (58.8% / 41.1%)*	104/58 (64.2% / 35.8%)	41/44 (47.7% / 51.2%)*
Condition			
Allergic rhinitis	240 (96.8%)	154 (95.1%)	86 (100.0%)
Nasopharyngitis	2 (0.8%)	2 (1.2%)	0
Sinusitis	1 (0.4%)	1 (0.6%)	0
AR & bronchiolitis	1 (0.4%)	1 (0.6%)	0
AR & bronchitis	1 (0.4%)	1 (0.6%)	0
AR & chronic rhinosinusitis	1 (0.4%)	1 (0.6%)	0
AR & nasopharyngitis	1 (0.4%)	1 (0.6%)	0
AR & asthma	1 (0.4%)	1 (0.6%)	0
Use frequency (number of users)			
>3 times/day	80	68	12
1-3 times/day	159	85	74
Prior to the medication	88	55	33
Between medicated doses	40	31	9
I did not pay attention	9	9	0
Other	0	0	0

*One adult patient did not provide gender data. **SE:** Standard error of means; **AR:** Allergic Rhinitis.

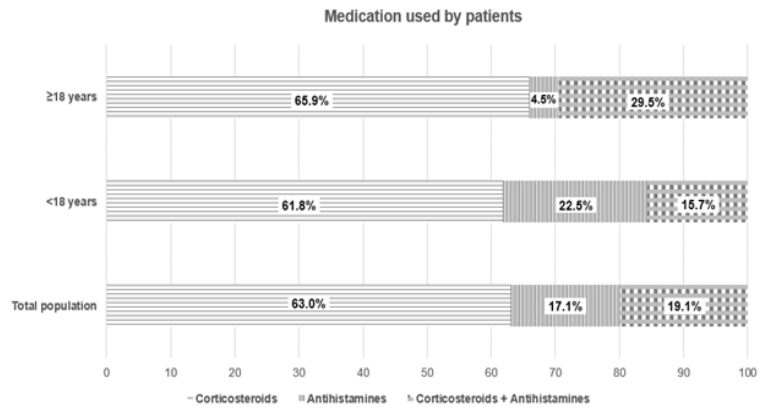

Figure 3: Type of medication used by patients in the study.

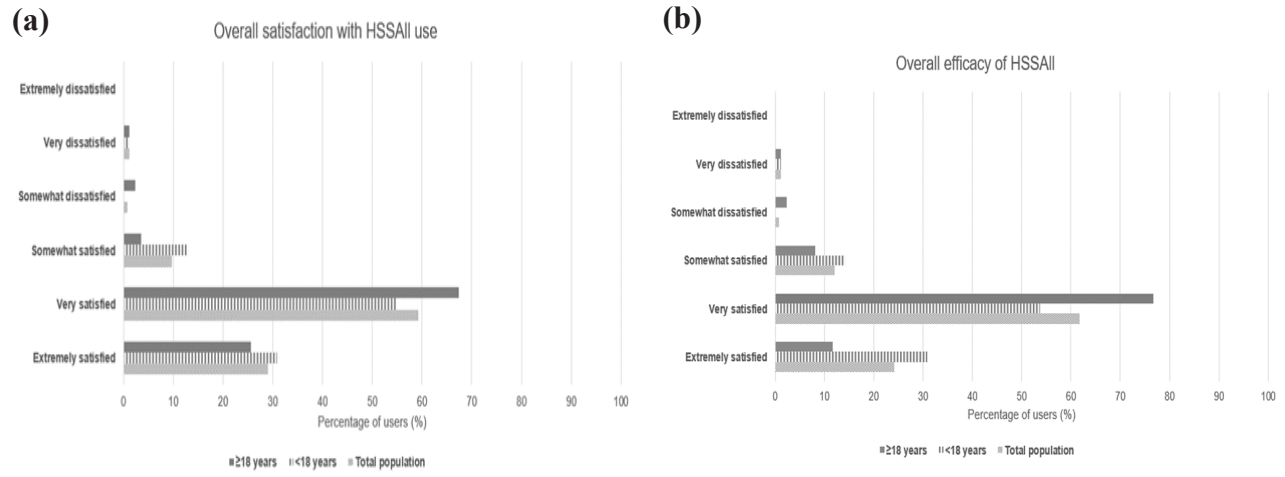

Figure 4: Users' satisfaction **(a)** and efficacy **(b)** following HSSAII use.

Table 2: Time to symptom relief (%).

Improvement in minutes	Total population	<18 years	≥18 years
Improvement in <5 min	74 (29.8%)	45 (27.8%)	29 (33.7%)
Improvement in <30 min	100 (40.3%)	71 (43.8%)	29 (33.7%)
Improvement in >30 min	66 (26.6%)	41 (25.3%)	25 (29.1%)
No improvement	7 (2.8%)	4 (2.5%)	3 (3.5%)
NA	1 (0.4%)	1 (0.6%)	0
sum	**248 (100.0%)**	**162 (100.0%)**	**86 (100.0%)**

Improvement in days	Total population	<18 years	≥18 years
1st day of use	68 (27.4%)	43 (26.5%)	24 (27.9%)
2nd day of use	56 (22.6%)	37 (22.8%)	20 (23.3%)
3rd day of use	68 (27.4%)	36 (22.2%)	32 (37.2%)
After 5 days	32 (12.9%)	26 (16.0%)	6 (7.0%)
After 7 days	14 (5.6%)	13 (8.0%)	1 (1.2%)
I saw no improvement	9 (3.6%)	6 (3.7%)	3 (3.5%)
NA	1 (0.4%)	1 (0.6%)	0
sum	***248 (100.0%)***	***162 (100.0%)***	***86 (100.0%)***

NA: Non-Applicable data (the patient provided no answer to this question); min: minutes.

Table 3: HSSAll use with prescribed medication: Efficacy and customers perception.

	Prescribed medication given		
	Total population	***<18 years***	***≥18 years***
	Count (%)	Count (%)	Count (%)
Yes	146 (58.9%)	102 (63.0%)	44 (51.2%)
No	100 (40.3%)	58 (35.8%)	42 (48.8%)
NA	2 (0.8%)	2 (1.2%)	0
sum	***242 (100.0%)***	***166 (100.0%)***	***86 (100.0%)***

Participants using prescribed medication

Overall efficacy of the combined treatment				***Reduction of prescribed medication intake***				***Willingness to use the nasal spray alone, without medication***			
	Total population	***<18 years***	***≥18 years***		***Total population***	***<18 years***	***≥18 years***		***Total population***	**<18 years**	**≥18 years**
	Count (%)	Count (%)	Count (%)		Count (%)	Count (%)	Count (%)		Count (%)	Count (%)	Count (%)
Extremely good	44 (30.1%)	31 (30.4%)	13 (29.5%)	*Absolutely yes*	44 (30.1%)	27 (26.5%)	17 (38.6%)	*Absolutely yes*	46 (32.2%)	41 (40.2%)	5 (11.4%)
Very good	74 (50.7%)	49 (48.0%)	25 (56.8%)	*Yes*	51 (34.9%)	33 (32.4%)	18 (40.9%)	*Yes*	30 (20.8%)	19 (18.6%)	11 (25.0%)
Good	23 (15.8%)	18 (17.6%)	5 (11.4%)	*May be yes*	34 (23.3%)	26 (25.5%)	8 (18.2%)	*May be yes*	44 (29.5%)	19 (18.6)	25 (56.8%)
Total positive	***141 (96.6%)***	***98 (96.1%)***	***43 (97.7%)***	***Total positive***	***129 (88.4%)***	***86 (84.3%)***	***43 (97.7%)***	***Total positive***	***120 (82.2%)***	***82 (77.5%)***	***41 (91.3%)***
Bad	4 (2.7%)	3 (2.9%)	1 (2.3%)	*May be Not*	6 (4.1%)	6 (5.9%)	0	*May be Not*	14 (9.6%)	12 (11.8)	2 (4.5%)
Very bad	0.0	0	0	*Not*	11 (7.5%)	10 (9.8%)	1 (2.3%)	*Not*	12 (8.2%)	11 (10.8%)	1 (2.3%)
Extremely bad	0.0	0	0	*Absolutely not*	0	0	0	*Absolutely not*	0	0	0
Total negative	***4 (2.7%)***	***3 (2.9%)***	***1 (2.3%)***	***Total negative***	***17 (11.6%)***	***16 (15.7%)***	***1 (2.3%)***	***Total negative***	***26 (17.8%)***	***23 (21.9%)***	***3 (6.8%)***
NA	1 (0.7%)	1 (1.0%)	0	*NA*	0	0	0	*NA*	0	0	0
Sum	***146 (100.0%)***	***102 (100.0%)***	***44 (100.0%)***	***Sum***	***146 (100.0%)***	***102 (100.0%)***	***44 (100.0%)***	***Sum***	***146 (100.0%)***	***102 (100.0%)***	***44 (100.0%)***

NA: Non-Applicable data (the patient provided no answer to this question).

Table 4: Consumer intentions following HSSAll use.

	Willingness to recommend HSS to peers			Willingness to purchase HSS in the future		
	Total population	**<18 years**	**≥18 years**	**Total population**	**<18 years**	**≥18 years**
	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)
Absolutely yes	128 (51.6%)	92 (55.4%)	36 (43.9%)	120 (48.4%)	95 (57.2%)	25 (30.5%)
Yes	90 (36.3%)	49 (29.5%)	41 (50.0%)	95 (38.3%)	45 (27.1%)	50 (61.0%)
Maybe yes	23 (9.3%)	19 (11.4%)	4 (4.9%)	21 (8.5%)	19 (11.4%)	2 (2.4%)
Total positive	**241 (97.2%)**	**160 (96.3%)**	**81 (98.8%)**	**236 (95.2%)**	**159 (95.7%)**	**77 (93.9%)**
Maybe not	3 (1.2%)	3 (1.8%)	0	6 (2.4%)	3 (1.8%)	3 (3.7%)
Not	3 (1.2%)	2 (1.2%)	1 (1.2%)	3 (1.2%)	3 (1.8%)	0
Absolutely not	0	0	0	1 (0.4%)	0	1 (1.2%)
Total negative	**6 (2.4%)**	**5 (3.0%)**	**1 (1.2%)**	**10 (4.0%)**	**6 (3.6%)**	**4 (4.9%)**
NA	1 (0.4%)	1 (0.6%)	0	2 (0.8%)	1 (0.6%)	1 (1.2%)
sum	**248 (100.0%)**	**166 (100.0%)**	**82 (100.0%)**	**248 (100.0%)**	**166 (100.0%)**	**82 (100.0%)**

NA: Non-Applicable data (the patient provided no answer to this question)

population and 95.1% in the children population. All the adult participants (100.0%) suffered from allergic rhinitis. Within the children group, and apart from allergic rhinitis, 1.2% of children presented with nasopharyngitis, 0.6% with sinusitis, while the remaining 3% combined allergic rhinitis with other conditions (bronchiolitis, bronchitis, chronic rhinosinusitis, nasopharyngitis, and asthma; each condition represented at 0.6%). The most frequent use of the nasal spray was 1-3 times daily in all three populations; use of >3 times per day or prior to medication was also common (Table 1).

Nasal spray efficacy

In all groups, individuals noted substantial alleviation of all nasal and QoL symptoms evaluated after using HSSAll nasal spray (Figure 1a-c). Nasal congestion, rhinorrhea, sneezing, pruritus, and other nasal problems were significantly reduced ($P<0.001$ for each symptom score). Likewise, fatigue, compromised productivity, sleep deprivation, emotional fatigue, and overall feeling was markedly improved after HSSAll use ($P<0.001$ for each symptom score). Notably, the most troublesome symptom in the total population and the two subpopulations was nasal obstruction for which the symptom score declined from 3.15 to 1.15 for the total population, from 3.26 to 1.35 in the <18 years group, and from 2.88 to 0.68 in the adults group (Figure 1a-c).

The percentage of patients indicating positive, negative, or neutral shifts in symptom scores is depicted in Figure 2. Marked symptom improvements were noted in the total and adult populations for every nasal and QoL symptom checked. 92.6% of the entire cohort felt relief from congested nose as well as 90.5% of the minors. 98.9% of the adults experienced improvements in other nasal problems and in their overall feeling. The only symptom for which no noticeable difference had been observed was emotional fatigue among the children who used nasal sprays (Figure 2a-c).

Quick symptom relief allows patients to resume their daily activities with minimal disruption. In this study, the majority of patients in all groups perceived fast symptom resolution (40.3/29.8%, 43.8/27.8%, 33.7/33.7% for <30 min/<5 min relief for the total, children and adult populations, respectively). Only 26.6%, 25.3% and 29.1% experienced prolonged time (beyond 30 min) to symptoms recovery in the same groups. All populations reported that symptoms subsided already in the 1st day of spray use (27.4%, 26.5% and 27.9% of the total, children and adult populations, respectively) with similar percentages reporting symptom relief during the 2nd or the 3rd day. Compared to adults and the entire population, more children felt better in the 3rd day of use versus the 1st and 2nd days (Table 2).

Users were encouraged to use HSSAll added to their medication treatment. The combinatorial scheme was followed by 58.9%, 63.0% and 51.2% of patients in the total, children and adult populations, respectively (Table 3). Corticosteroids were the predominant medication used by 65.9% of adults, 63.0% of the entire population and 61.8% of children (Figure 3). When questioned, the overall efficacy of this combination was judged as good/very good/extremely good by the vast majority of the adult population (97.7%). Similarly, 96.6% and 96.1% of the total and children populations, respectively, shared this opinion. 97.7% of the adults reduced the overall medicated product intake upon using HSSAll. This percentage reached 88.4% and 84.3% in the total and children populations, respectively. 91.3% of adults, 77.5% of children and 82.2% of the total population contemplated utilizing HSSAll as a standalone intervention, foregoing the need for medication (Table 3).

Consumer reviews and perspectives

Users were highly satisfied with HSSAll usability and efficacy in all three populations, with percentages of satisfaction (extremely/very/somewhat satisfied) exceeding 95% in all populations (Figure 4a-b). The overwhelming majority of respondents to the survey (97.2%, 96.3% and 98.8% of the total, children and adult populations, respectively) expressed their readiness to endorse HSSAll to peers. In agreement to this, 95.2%, 95.7%, and 93.9% of the total, children and adult populations, respectively, indicated their intention to procure HSSAll in the future (Table 4).

Surveillance of safety and technical quality of the nasal spray

The use of HSSAll nasal spray was deemed safe. Out of 248 respondents, 10 adults and 4 children reported 16 adverse events. Nine of them (56.3%) were related to the disease itself, two were related to the product (12.5%) and for five events, the users did not provide additional information (31.3%). The two events that were definitely attributed to the product were

reported by children; there was one case with nasal irritation and one case with nasal dryness. Both cases presented with mild intensity and subsided spontaneously. One technical complaint was recorded during the study; however the user did not specify the origin of the problem.

Discussion

Nasal saline douche, a longstanding natural remedy, has been endorsed as an effective treatment used in allergic rhinitis, chronic rhinosinusitis and upper respiratory tract infections. In addition, nasal irrigation is often recommended as an adjunct to pharmacological treatments for offering symptom relief and improved quality of life [2]. Several clinical studies suggest that hypertonic solutions are more efficacious than isotonic solutions [15]. Recently, a series of hypertonic (2.3% NaCl) products comprising seawater solutions, algae extracts, and other ingredients have been developed and tested in clinical trials [16-21]. These included HSSAll, a product dedicated to the treatment of allergic rhinitis. In a clinical study conducted in a pediatric population, HSSAll used together with standard anti-allergic medication versus standard medication alone was superior at improving AR symptoms and led to an overall increase of disease-free days and a reduction of prescribed medication used by patients [16]. To evaluate the efficacy, safety and performance of HSSAll in a real-world setting, we sought to perform a user survey study in a mixed population comprising both children and adults.

Our results support the use of HSSAll in both adults and children with allergic rhinitis. Both populations benefited from a notable alleviation of cardinal AR symptoms such as nasal obstruction, rhinorrhea, itching and sneezing after spraying with HSSAll. In addition, quality of life symptoms were also markedly improved and both adults and minors perceived reduction of fatigue, compromised productivity, sleep disturbances and emotional exhaustion after HSSAll use. When used in combination with medication, HSSAll was also deemed to be highly effective. More importantly, users were further able to lower medication consumption. These results were in agreement with clinical observations obtained with HSSAll in AR patients [16] and other clinical trials testing hypertonic saline sprays in AR [10-12,14,22].

Users of HSSAll experienced quick symptom relief shortly after spraying, with results evident in as less as 5 minutes in a portion of the patients; this property added to user satisfaction. Overall, it is crucial for a nasal spray to provide quick relief allowing users to perform daily activities with minimal disruption. In addition, rapid action can enhance the overall effectiveness and satisfaction with the product, making it more likely for patients to continue using it as part of their treatment regimen. In agreement with this, users reported high satisfaction with the product itself and its efficacy, both with and without medication. They were also very pleased with its performance, leading to an inclination towards using the medical device alone without medicated treatments. Their high satisfaction was additionally reflected in their recommendation of the nasal spray to others and their willingness for subsequent purchases. For what concerns the safety of the device, only a handful of minor adverse events were reported; these resolved quickly without additional intervention. These results confirm the high safety profile of HSSAll making it a favorable treatment option.

Overall, the abovementioned results support and strengthen the use of HSSAll as a non-pharmacological intervention approach for optimal relief of symptoms in patients with allergic rhinitis. These findings corroborate the results reported of other real-world studies conducted with the same hypertonic seawater solution with our without additional ingredients in patients with various ENT conditions [15,17,23].

Conclusion

Overall, use of HSSAll reduces signs and symptoms of allergic rhinitis in children and adults and limits the need for medicated treatments. Nasal spraying with HSSAll emerges as a promising complementary or stand-alone therapy for allergic rhinitis due to its well-tolerated nature, effectiveness, and ease of use.

Declarations

Conflicts of interest: No conflict of interest was declared by the authors.

References

1. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, et al. European Position Paper on Rhinosinusitis and Nasal Polyps. Rhinology. 2020; 58(Suppl S29): 1-464. doi: 10.4193/Rhin20.600.
2. Head K, Snidvongs K, Glew S, Scadding G, Schilder AG, et al. Saline irrigation for allergic rhinitis. Cochrane Database Syst Rev. 2018; 6: CD012597.
3. Seidman MD, Gurgel RK, Lin SY, Schwartz SR, Baroody FM, et al. AAO-HNSF. Clinical practice guideline: Allergic rhinitis. Otolaryngol Head Neck Surg. 2015; 152(1 Suppl): S1-43. doi: 10.1177/0194599814561600.
4. Sur DK, Plesa ML. Treatment of Allergic Rhinitis. Am Fam Physician. 2015; 92(11): 985-92.
5. Ural A, Oktemer TK, Kizil Y, Ileri F, Uslu S. Impact of isotonic and hypertonic saline solutions on mucociliary activity in various nasal pathologies: clinical study. J Laryngol Otol. 2009; 123(5): 517-21. doi: 10.1017/S0022215108003964.
6. Hermelingmeier KE, Weber RK, Hellmich M, Heubach CP, Mösges R. Nasal irrigation as an adjunctive treatment in allergic rhinitis: a systematic review and meta-analysis. Am J Rhinol Allergy. 2012; 26(5): e119-25. doi: 10.2500/ajra.2012.26.3787.
7. Chong LY, Head K, Hopkins C, Philpott C, Glew S, et al. Saline irrigation for chronic rhinosinusitis. Cochrane Database Syst Rev. 2016; 4(4): CD011995. doi: 10.1002/14651858.CD011995.pub2.
8. 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.
9. 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.
10. Garavello W, Romagnoli M, Sordo L, Gaini R, Di Berardino C, et al. Hypersaline nasal irrigation in children with symptomatic seasonal allergic rhinitis: a randomized study. Pediatr Allergy Immunol. 2003; 14: 140-3.
11. Garavello W, Di Berardino F, Romagnoli M, Sambataro G, Gaini RM. Nasal rinsing with hypertonic solution: an adjunctive treatment for pediatric seasonal allergic rhinoconjunctivitis. Int Arch Allergy Immunol. 2005; 137(4): 310-4. doi: 10.1159/000086462.
12. Marchisio P, Varricchio A, Baggi E, Bianchini S, Capasso ME, et al. Hypertonic saline is more effective than normal saline in seasonal allergic rhinitis in children. Int J Immunopathol Pharmacol. 2012; 25(3): 721-30.

13. Tomooka LT, Murphy C, Davidson TM. Clinical study and literature review of nasal irrigation. Laryngoscope. 2000; 110(7): 1189-93. doi: 10.1097/00005537-200007000-00023.

14. Sansila K, Eiamprapai P, Sawangjit R. Effects of self-prepared hypertonic nasal saline irrigation in allergic rhinitis: A randomized controlled trial. Asian Pac J Allergy Immunol. 2020; 38(3): 200-207. doi: 10.12932/AP-090618-0331.

15. Protopapadakis E, Georgiou S, Alevizopoulos Nasal Irrigation with Hypertonic Seawater Solutions of 2.3% NaCl: A Safe and Effective Treatment Modality for Optimal Symptom Management in ENT Diseases. Int J Clin Med Case Rep. 2024; 36(2): 1-4. https://doi.org/10.46998/ijcmcr.2023.36.000885.

16. 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.

17. 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 Clinic Stud Medic Case Reports. 2022; 17(4): 1-4. DOI: 10.46998/IJCMCR.2021.17.000417.

18. 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 radiofrequency turbinate volume reduction. Eur Rev Med Pharmacol Sci. 2022; 26(2 Suppl): 38-48. doi: 10.26355/eurrev_202212_30481.

19. Gangadi M, Georgiou S, Moschotzopoulou E, Antronikou T, Kainis E, et al. 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.

20. Pantazopoulos I, Chalkias A, Miziou A, Spanos M, Gerovasileiou 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(7): 1093. doi: 10.3390/jpm13071093.

21. Perić A, Gaćeša D, Kovačević SV, Perić AV, Vojvodić D, et al. The effect of nasal douching by hypertonic 2.3 per cent sea water with algae extracts on the concentration of epidermal growth factor, transforming growth factor-α and interleukin-8 in nasal secretions of patients with nasal polyposis following endoscopic surgical treatment. J Laryngol Otol. 2024; 138(5): 520-526. doi: 10.1017/S0022215123001974.

22. Sinha ON, Deswal, M. Comparing hypertonic saline and xylometazoline in allergic rhinitis. International Journal of Research in Medical Sciences. 2017; 3(12): 3620-3623. https://doi.org/10.18203/2320-6012.ijrms20151411.

23. 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 Clinic Stud Medic Case Reports. 2023; 25(4): 1-4. DOI: 10.46998/IJC-MCR.2023.25.000618.