# SEAWATER PRODUCTS FOR NASAL LAVAGES. COMPARISION AND LITERATURE REVIEW

PRODUCTOS DE AGUA DE MAR PARA LAVADOS NASALES. COMPARACIÓN Y REVISIÓN BIBLIOGRÁFICA

Irene López Barea (1)<sup>1,a</sup>, Luis Molini Cabrera (1)<sup>2,b</sup>, Manuel Enrique García Falcón (1)<sup>2,c</sup>, Cristóbal Coronel Rodríguez (1)<sup>3,d</sup>

# ABSTRACT

**Introduction:** There is a wide range of seawater products for nasal lavages. Their efficacy and superiority over conventional saline solutions are not well established. **Objectives:** The aim of this study was to analyse the best-selling seawater products, as well as reviewing the most recent literature regarding nasal lavages. **Methods:** A comparative study of composition, administration mode, age indicated for its use, price and bibliography provided on the web of the seawater products usually available in pharmacies was performed. Analysis of the bibliography provided and review of the scientific evidence regarding nasal lavages with saline solutions or seawater. **Results:** 44 products from 11 manufacturers were analysed. The concentration of sodium chloride varies from 0.9% to 2.5%. The most frequent mode of application is spray. The addition of plants, salts and other components is common. Only two brands provide bibliographic references on their website. According to the literature reviewed, both saline solutions and seawater seem especially useful in the treatment of upper respiratory tract infections and allergic rhinitis. **Conclusions:** There is no solid scientific evidence regarding the benefits of nasal lavages. With the current evidence it is not possible to recommend seawater over conventional saline or to establish the optimal concentration of the solution or the most convenient mode of administration. The addition of elements to seawater solutions is not justified enough.

Keywords: Nasal lavage; Seawater; Nasal sprays, Drug publicity, Evidence-based medicine. (Source: MESH-NLM)

## RESUMEN

Introducción: Existe una amplia gama de productos de agua de mar para lavados nasales. Su eficacia y superioridad respecto a las soluciones salinas convencionales no están bien establecidas. **Objetivos:** El objetivo de esta revisión fue analizar los productos de agua de mar más vendidos, así como revisar la bibliografía más reciente respecto a los lavados nasales. **Métodos:** Se realizó un estudio comparativo de la composición, el modo de administración, la edad indicada para su uso, los precios de venta y las citas aportadas en la web de productos de agua de mar habitualmente disponibles en farmacia; análisis de la bibliografía aportada, y revisión de la evidencia científica en relación a los lavados nasales con soluciones salinas o agua de mar. **Resultados:** Se analizaron 44 productos de 11 fabricantes. La concentración de cloruro sódico varía del 0,9% al 2,5%. El modo de aplicación más frecuente es en spray. Es común la adición de plantas, sales y otros componentes. Sólo dos marcas aportan referencias bibliográficas en su página web. Según la bibliografía revisada, tanto el suero salino como el agua de mar parecen especialmente útiles en el tratamiento de las infecciones de tracto respiratorio superior y de la rinitis alérgica. **Conclusiones:** Se concluye que no existe evidencia científica sólida respecto a los beneficios de los lavados nasales. Con la evidencia actual no es posible recomendar el agua de mar sobre el suero salino convencional ni establecer la concentración óptima de la solución ni el modo de administración más conveniente. La adición de elementos a las soluciones de agua de mar no está suficientemente justificada.

Palabras clave: Lavado nasal (proceso), agua de mar, rociadores nasales, publicidad de medicamentos, medicina basada en la evidencia. (Fuente: DeCS-BIREME)

- <sup>1</sup> Hospital Universitario Virgen del Rocío (Sevilla).
- <sup>2</sup> Ejercicio privado.
- <sup>3</sup> Centro de Salud Amante Laffón (Sevilla).
- <sup>a</sup> Graduated in Medicine. Internal Medicine Resident of Pediatrics and its specific areas.
- <sup>b</sup> Bachelor of Pharmacy.
- <sup>c</sup> Graduated in Human Nutrition and Dietetics.
- <sup>d</sup> Doctor en Medicina. Pediatra de Atención Primaria.

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### INTRODUCTION

In Primary Care centers, it is common to receive advertising about multiple seawater products for nasal lavages, which differ from each other in the way and strength of administration, in the concentration of sodium chloride (NaCl) in their composition, and the added elements, to which different properties are attributed. However, this usually lacks bibliographical citations that support them. Although the usefulness of nasal lavages with saline solution is supported by the scientific literature (1,2), studies on the efficacy of seawater and its comparison with the application of traditional saline solution are scarcer<sup>(3,5)</sup>. The present work intends to comparatively analyze the main characteristics and the references provided on the web of the best-selling seawater products on the market. Likewise, it reviews the most recent bibliography to conclude on the justification or not of the use of these products.

#### **METHODS**

In selecting the products, efforts were made to ensure that they were for sale in pharmacies and that they were usually available in pharmaceutical distributors. Name, laboratory, percentage of NaCl in their composition were collected from all of them if specified (0.9% was considered in "isotonic" solutions), components added to seawater, formats (amount in ml), form of administration (spray, irrigation, nasal drops), age of use according to manufacturer, sale price and number of bibliographic citations provided on their website. All literature provided by manufacturers was considered and reviewed, regardless of their year of publication or methodology. Subsequently, the available scientific evidence available was reviewed, proceeding to search Pubmed for meta-analyses, reviews, and randomized controlled clinical trials published in the last five years, as of November 16, 2021, according to the indicated strategy (Table 1) and paying special attention to those studies focused on the pediatric population.

### Table 1. Search strategy in Pubmed.

General search strategy: - Last five years. * - Meta-analyses, reviews, systematic reviews and randomized controlled clinical trials. *In the case of publications on seawater ((seawater[title] AND nasal[title]) OR "seawater solution*"[title]) a second search was carried out extending the temporal space (15 years)	"nasal saline"[title] OR "saline nasal"[title] OR "saline irrigation"[title] OR "nasal irrigation"[title] OR (seawater[title] AND nasal[title]) OR "seawater solution*"[title]
Search strategy for each component: -A search for each component. - To expand results without limiting by date of publication or by type of study.	nasal[title] AND aloe nasal[title] AND chamomile nasal[title] AND eucalipto nasal[title] AND eucalipto nasal[title] AND mint nasal[title] AND ("Allium cepa" OR onion) nasal[title] AND ("Allium cepa" OR onion) nasal[title] AND sabadilla nasal[title] AND sabadilla nasal[title] AND (copper OR cuprum) nasal[title] AND (copper OR cuprum) nasal[title] AND (ferrum OR iron) nasal[title] AND (ferrum OR iron) nasal[title] AND manganeso nasal[title] AND manganeso nasal[title] AND dexpanthenol nasal[title] AND dexpanthenol

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Given the scarcity of studies with seawater (seawater), the temporal space in this case was extended to the last 15 years. In a second stage, a specific search was carried out on the different components added to seawater, which due to lack of results was extended without limiting the date of publication or type of study.

## RESULTS Product review:

Eleven pharmaceutical brands were analyzed, totaling 44 products (Table 2).

Table 2. Seawater products for nasal application are commonly available in pharmacies. % NaCl: percentage
of sodium chloride in the solution or, failing that, tonicity.

Product (pharmaceutical	% NaCl  )		Formats (ml)	Mode of administration (spray, irrigation, drops)	Age of use	Number of bibliographic citations on your website
STERIMAR (Reig Jofre)						13
Hygiene and well-being	0,9%	-	50 100	Spray	> 3 years old	
Hygiene and well-being baby	0,9%	-	50 100	Spray	0-3 years old	
Allergy	0,9%	Manganese	100	Spray	All ages	
CARE+ (Stada)						0
Sea water normal intensity	0,9%	-	125	Spray	> 6 years old	
Sea Water with Chamomile and Aloe Vera. Strong intensity. hypertonic	Hypertonic	Chamomile and aloe vera extracts	125	Spray	Adults	
Nasal spray with sea water	0,9%	Dexpantenol	20	Spray	All ages	
RHINOMER (GSK)	)					0
Extra soft baby	0,9%	-	115	Spray	> 15 days	
Force 1	0,9%	-	135	Spray	> 1 year old	
Force 2	0,9%	-	135	Spray	> 2 years old	
Force 3	0,9%	-	135	Spray	> 6 years old	
Aloe Vera	0,9%	Aloe vera powder	100	Spray	> 2 years old	
Intense Eucalyptus	2,2%	Eucalyptus essentia oil and wild mint concentrate	20	Spray	> 6 years old	

RINASTEL (Almira	all)					0
Xilitol	0,9%	Xilitol	100	Spray	> 3 months	
Aloe Vera & camomila	2-2,5%	Aloe vera aqueous extracts, chamomile aqueous extracts		Spray	> 3 years old	
Eucalyptus	2-2,5%	Aqueous extracts of eucalyptus, aqueous extracts of mint	125	Spray	> 3 years old	
Baby	0,9%	Xilitol	125	Spray	> 3 months	
SINOMARIN (Concordia)						5
Babys	2,3%	-	24 single dose of 5 ml	Drops	All ages	
Mini	2,3%	-	30	Spray	> 6 months	
Kids	2,3%	-	100	Spray	> 6 months	
Adults	2,3%	-	125	Spray	> 6 years	
ORL	2,3%	-	200	Spray	> 6 months	
NASALMER (Omega pharma)						0
Hypertonic nasal spray	2,2%	-	125	Spray	> 12 years old	
Junior hypertonic nasal spray	2,2%	-	125	Spray	> 2 years old	
Babies hypertonic nasal spray	Hypertonic	-	125	Spray	>15 days	
Single dose babies	Hypertonic		40 single dose of 5 ml	Drops	-	
RHINOLAYA (Inebios)						0

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lsotonic spray	0,9%	Himalayan salt, potassium chloride and copper gluconate	100	Spray	No data	
Fort	2,3%	Himalayan salt, potassium chloride and copper gluconate	50	Spray	> 6 months	
Protect	0,9%	Himalayan salt, Allium cepa, Sabadilla officinalis, manganese gluconate	50	Spray	All ages	
Kids	0,9%	Himalayan salt, Matricaria chamomilla, Ferrum phos, Cuprum gluconatum	50	Spray	Children	
NEBUMAR (Teva)						0
Nasal hygiene	0,9%	-	100	Spray	> 6 years old	
Nasal congestion	Hipertónica	-	100	Spray	> 6 years old	
Baby	0,9%	-	100	Spray	> 9 months	
NESIRA (Acofarma)						0
lsotonic and sterile sea water for children	0,9%	-	100	Spray	Children	
Isotonic and sterile seawater adults	0,9%	-	125	Spray	>6 years old	
Nasal congestion	Hipertónica	-	20	Spray	>1 year old	
PHARMEXMER (Pharmex)						0
Hypertonic spray	2,1%	-	100	Spray	> 6 years old	

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lsotonic spray	0,9%	-	100	Spray	> 6 years old	
Baby Comfort Isotonic	0,9%	-	100	Spray	> 6 months	
Kids Comfort Hypertonic	2,1%	-	100	Spray	> 2 years old	
Aloe and Chamomile	Hypertonic	Aloe vera, chamomile	100	Spray	> 2 years old	
Sparkling	0,9%	Carbon dioxide (0.4%)	100	Spray	> 2 years old	
RESPIMAR (Cinfa	)					0
Cleansing and hydration	0,9%	Aloe vera, chamomile	120	Spray	> 6 years old	
Decongestant	2,5%	Aloe vera, chamomile, menthol, polyethylene glycol	120	Spray	> 6 years old	
Pediatric	0,9%	Aloe vera, chamomile	120	Spray	> 0 months	

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The NaCl concentration varies from 0.9% to 2.5% in the most hypertonic solutions, the latter presenting a range between 2 and 2.5%. The solutions without added components differ from each other by their tonicity, by the way or force of application or by the size of the container or applicator. Those with greater force of application or tonicity are usually indicated in older patients. The most common mode of application is spray, although two of the brands also offer single-dose vials for application in drops in younger children. Regarding the added elements, the use of herbs or plants is frequent, mainly chamomile/chamomile and aloe vera.

The addition of other salts (manganese, iron, copper, or potassium) is also common. Lastly, some add other components, such as xylitol (also known as birch sugar) and dexpanthenol (provitamin B5), or show that obtaining seawater in certain geographical locations is an additional value. It was not possible to obtain objective or comparable data regarding the price of the products since, as they are available free of charge, both the laboratory sale price and the sale price to the public are variable. Bibliographic citations were only found on the web pages of two products. Sterimar<sup>®</sup> provides 13 citations, obtaining access to seven of the cited documents. Of the remaining six, three of them are publications from 1989 in Cahiers d'oto-laryngologie y Gazette Médicale; uno es una publicación en Review of Paediatry del año 1999; one is a 1999 Review of Paediatry publication; another shows an incomplete reference that prevents its location, and the last is a review on the nonpharmacological-treatment-of-nasal congestion in pediatrics published in 2 014 in Minerva Pediatrics. Except for the latter, which could not be accessed because they did not have a subscription to the magazine, no other references were found other than those provided by the product's own website.

The seven publications reviewed include a randomized controlled clinical trial <sup>(6)</sup>, an intervention with evaluation by telephone survey<sup>(7)</sup>, a descriptive-analytic observational study with the same type of evaluation <sup>(8)</sup> and four in vitro studies <sup>(9-12)</sup>. In the first trial, Grasso et al.<sup>(6)</sup> studied the efficacy of Sterimar Mn<sup>®</sup> (with manganese salts) for preventing exacerbations of

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allergic rhinitis in 60 patients over 18 years old. The control group receives "standard treatment" and the experimental group, in addition, four daily puffs of Sterimar Mn<sup>®</sup>.

After five months of treatment, the experimental group shows a statistically significant decrease in the number of exacerbations compared to the previous year (from 10.7 to 6.3 episodes vs. 9.5 to 9.3 episodes in the group control) and an improvement in quality of life measured according to the visual analogue scale between the third and fifth month of starting the study (in the experimental group, improvement of +0.2 points vs. in the control group, +0.67 points). The second cited study is an observational, cross-sectional, and multicenter study financed by Reig Jofre S.A., Sanabria Brassart et al. <sup>(7)</sup> surveyed 1 350 patients of all ages with various medical conditions to whom their attending physician recommended nasal lavages with seawater in regimens variables according to clinical criteria. Patients report improvement in symptoms compared to previous similar episodes. The following is an observational study that assesses adherence and tolerance of nasal washes with physiological saline solution (PSS) in the pediatric population. Jeffe et al. <sup>(8)</sup> select 61 patients (2-16 years) who are prescribed these rinses for nasal congestion and rhinorrhea in different pathologies, showing that the majority of children (93%) tolerate nasal rinses even though their parents (78%) initially think otherwise. The remaining studies are in vitro (9-12).

They compare different solutions (saline and seawater in different concentrations) regarding their effects on the healthy or injured epithelium. Their conclusions can be summarized as follows: hypertonic solutions caused cytotoxicity, affected the barrier function and reduced cilia beating, damage that did not occur with isotonic solutions<sup>(9)</sup>. Compared with conventional PSS, isotonic seawater promoted faster tissue re-epithelialization after mechanical injury<sup>(10)</sup>; being both isotonic, diluted seawater, compared to electrodialyzed, had a more sustained effect on tissue recovery after hypotonic stress<sup>(11)</sup>. A last study<sup>(12)</sup> specifically evaluated Sterimar Stop & Protect Cold and Flu <sup>®</sup> (2.3% hypertonic seawater with hyaluronic acid, eucalyptus oil, copper and manganese salts), not observing cytotoxic or proinflammatory effects and also observing a improvement of mucociliary clearance with respect to untreated tissues and better recovery capacity with respect to the use of PSS. Sinomarin<sup>®</sup>, for its part, collects five citations. One of them, entitled "Utility of the hypertonic solution (Sinomarin<sup>®</sup>) in rhinology," was published in the Revista Oficial de la Sociedad Francesa de Otorrinolaringología in 1998 and is not found on the Internet. Of the rest, 3 are randomized controlled clinical trials published in 1998 <sup>(13)</sup>, 2002 (13), 2003 <sup>(15)</sup>, and the last one could be classified as a narrative review <sup>(16)</sup>.

In the latter, published in Otolaryngologic Clinics of North America (1996), the author exposes the change in management of chronic sinusitis (from an eminently surgical treatment to conservative management) and the usefulness of nasal lavages with saline solution in this pathology. , alleging an unpublished communication of his own and an experimental study also of his own authorship (17). Since Sinomarin® products are all hypertonic (NaCl 2.3%), the referred studies focus on justifying this characteristic. Shoseyov et al.<sup>(13)</sup> comparan la aplicación en gotas de SSI versus compare the application of SSI drops versus hypertonic saline solution (HSS) (3.5%) for the treatment of chronic sinusitis in 30 pediatric patients (3-16 years). After four weeks of treatment, HSS statistically significantly improved the runny nose and cough, as well as the radiological image of the sinuses. The PSS only significantly improved the runny nose. Using validated scales, Rabago et al.<sup>(14)</sup> studied the long-term effect (six months) of daily nasal lavage with HSS on guality of life and symptom control in 76 adult patients with recurrent sinusitis. Improvement was observed in all the scales in the experimental group with respect to the control (without nasal washings), as well as a reduction in the use of antibiotics.

Finally, Garavello et al.<sup>(15)</sup> included 20 pediatric patients with seasonal allergic rhinitis (6-12 years), in whom they evaluated the efficacy of nasal irrigation with HSS (3%) versus no irrigation for the control of symptoms and

educing the use of antihistamines. He found statistically significant differences in both aspects from the third week of treatment.

# GENERAL REVIEW A. SEA WATER VERSUS SALINE SOLUTIONS:

Most experimental studies on nasal lavages use conventional saline solutions (not seawater). However, the available evidence in pediatrics can be summarized in the following systematic reviews: Cabaillot et al.<sup>(1)</sup> analyze the efficacy of isotonic solution lavages in upper respiratory tract infections, observing improvement in nasal symptoms, faster resolution of the episode, decrease in the incidence of complications and relapses and less consumption of additional medication (especially antibiotics) compared to therapeutic abstention. In treating allergic rhinitis in the pediatric age group, Wang et al.<sup>(2)</sup> observe that patients who receive nasal lavages with saline solution show statistically significant clinical improvement compared to therapeutic abstention.

No significant differences were observed compared to the use of nasal corticosteroids or when comparing the usual treatment alone (nasal corticosteroids or oral antihistamines) with the addition of lavages as adjuvant treatment. Finally, Gallant et al.<sup>(18)</sup> propose a systematic review of nasal washes in children under 18 years of age for the treatment of rhinosinusitis (acute or chronic), but finally only one study on acute rhinosinusitis meets the inclusion criteria. This compares the use of highdose amoxicillin + SSI washes versus placebo + lavados con placebo + SSI washes, finding no significant difference between the two groups.

As a conclusion of the different reviews, there is great heterogeneity between studies and difficulty for the objective assessment of clinical improvement, so higher quality studies are desirable to obtain more robust evidence <sup>(1,2,18)</sup>. Studies aimed at proving the efficacy of seawater are much scarcer. Chen et al. <sup>(3)</sup> studied the treatment of allergic rhinitis in children, noting that the combination of isotonic seawater spray and intranasal fluticasone showed better clinical and cytological results (decrease in the eosinophil count in nasal secretion) than each. One of them in isolation. The clinical improvement persisted even after reducing the dose of corticosteroids, making seawater a good adjuvant treatment. For their part, Slapak et al.<sup>(4)</sup> intend to study the efficacy of seawater both in the treatment and in preventing complications and recurrences of the common cold or flu in children from six to ten years of age.

While the control group received standard treatment (symptomatic and antibiotics according to medical indication), the experimental group also received nasal lavages with isotonic seawater (with different modes of administration in different subgroups), which they maintained for 12 weeks. In the acute phase, the group that received seawater showed statistically significant differences in terms of greater improvement in rhinorrhea and nasal obstruction, subjective improvement in general condition, and less use of nasal decongestants and mucolytics.

At longer follow-up (up to 12 weeks), continued use of douches reduced sick days, school absences, and complications, as well as the use of antipyretics, nasal decongestants, mucolytics, and antibiotics, suggesting a preventive role for these pathologies. There were no differences between the various seawater subgroups, although spray application was better tolerated than irrigation. Only one study was found that compared the efficacy of saline and seawater. Köksal et al. <sup>(5)</sup>, in a controlled clinical trial in children under two years of age with upper respiratory tract infection, compare the efficacy of SSI versus 2.3% seawater administered as nasal drops for nasal obstruction, without finding statistically significant differences between both intervention groups.

### **B. DIFFERENT CONCETRATIONS:**

The already commented review by Wang et al.<sup>(2)</sup> shows evidence in favor of HSS compared to ISS in treating allergic rhinitis in children, which should not exceed a 3% NaCl concentration to avoid local irritation or other adverse effects.



For their part, Kanjanawasee et al. <sup>(19)</sup> carried out a systematic review of this topic, including trials with multiple pathologies. Observes evidence in favor of HSS over SSI, suggesting greater efficacy in the following subgroups: rhinitis (versus rhinosinusitis), under 18 years of age, with "high volumes" of solution and "high pressure" application devices, and with NaCl <5% HSS more frequently produced local irritation, although no major adverse effects were reported.

### C. MODES OF ADMINISTRATION:

In the studies reviewed, both Cabaillot et al.<sup>(1)</sup> and Slapak et al.<sup>(4)</sup> observe that spray application is better tolerated and equally effective than irrigation in treating upper respiratory tract infections.

#### D. ELEMENTS ADDED TO SEAWATER:

The search for components added to seawater did not return any results regarding the following elements: aloe vera, mint, Allium cepa (onion), sabadilla, potassium chloride, iron, and manganese. On the other hand, Sterimar Mn <sup>®</sup> and Sterimar Stop & Protect Cold and Flu<sup>®</sup> (with copper and manganese salts, eucalyptus extract and hyaluronic acid) were evaluated in the bibliography provided by this brand <sup>(6,12)</sup>, although by the design of both studies it is not possible to know what part of the observed effect is due to the "added elements" and not only to seawater. Several interesting studies were found about xylitol, dexpanthenol and hyaluronic acid: Xylitol is a glycitol that, by promoting the concentration of nitric oxide (NO) in epithelial tissue, has an antimicrobial and anti-inflammatory effect. Among the studies reviewed, a clinical trial conducted in adult patients with chronic rhinosinusitis stands out (20).

The group that received xylitol nasal irrigations had statistically significant differences in the improvement of clinical parameters and in the increase in NO concentration in the sinus epithelium compared with the baseline situation and the control group (irrigations with SSI). On the other hand, according to Silva et al.<sup>(21)</sup> irrigations with xylitol can also be beneficial in the postoperative period of endoscopic endonasal surgery. Dexpanthenol (provitamin B5) is known for its antioxidant effect, cell proliferation promoter, and

epithelium protector. Tantilipikorn et al. <sup>(22)</sup> observed a significant improvement in mucociliary clearance and rhinorrhea with the application of dexpanthenol (compared to SSI) in the postoperative period of chronic rhinosinusitis. However, more than in monotherapy, it seems to be of interest in combination with alphaagonists.

In patients with nasal congestion (due to allergic rhinitis or after nasal surgery), Jagade et al.<sup>(23)</sup> obtained better symptomatic control, less rebound effect, and better medication tolerance in the group treated with dexpanthenol + alpha-antagonist nasal drops. in combination than in those patients who only received alpha-antagonists. Mösges et al. (24) add that this synergism leads to earlier healing in patients with acute rhinitis. Hyaluronic acid is a high molecular weight glycosaminoglycan present in the respiratory mucosa. Its fragmentation gives rise to smaller molecules that act as proinflammatory mediators. On the contrary, the high molecular weight hyaluronic acid suppresses the immune and inflammatory response and contributes to cell proliferation <sup>(25)</sup>. SFurthermore, its intranasal application decreases the number of neutrophils in the mucosa compared to the use of SSI, in addition to being well tolerated and without adverse effects (25-26). However, the data regarding its efficacy compared to SSI are not conclusive: while some studies (25-26) show a statistically significant (although clinically modest) greater symptomatic improvement in the group treated with hyaluronic acid, others (27) do not differences were found between both groups.

### DISCUSSION

The bibliographical references provided by pharmaceutical companies are scarce. They do not justify the wide range of products offered or the preference of seawater over conventional saline solution for nasal lavages.

Most web pages do not include a bibliography, and those that make present serious objections: the age of the publications included (practically half are ten or more years old)<sup>(8,13,14,16,17)</sup>; the use of studies that, due to their design, are not adequate to assess efficacy <sup>(7,8)</sup>; expose works with conventional saline solutions as a defense of their seawater products (they do not





show superiority of these over those)<sup>(8,13-15)</sup>; the omission of comparison groups of interest: no comparison is established between isotonic and hypertonic solutions <sup>(14,15)</sup> or between a product with several added elements and the basal solution without these elements <sup>(6,12)</sup>; the allusion to in vitro studies for the defense of isotonic solutions, with the limits that these present: they do not reproduce the conditions of the epithelium in vivo or its usual exposure in clinical practice to the studied product <sup>(9-12)</sup>, and the interpretation of statistical significance outside of clinical significance <sup>(6)</sup>.

The first question to consider is whether there is a superiority of seawater over the use of cheaper saline solution in the efficacy of nasal lavages. Obtaining quality evidence from systematic reviews is difficult due to the great heterogeneity of existing studies (in terms of pathology, concentration of solutions, modes and guidelines of administration...) and the difficulty in objectively assessing their results (impossibility of blinding the patient, the non-use of validated scales...) <sup>(1,2,18)</sup>. The search only found one comparative study between saline and seawater<sup>(5)</sup> in which no significant differences were observed between the two intervention groups. Therefore, with the current scientific evidence, it does not seem possible to recommend one solution over another, requiring more and higher quality studies on the efficacy of both treatments.

The second question concerns the use of different concentrations of NaCl. Although the review by Kanjanawasee et al.<sup>(19)</sup> advocates the superiority of HSS over PSS, there is an important limitation in their conclusions due to the great heterogeneity of the studies included in terms of the characteristics of the patients and the intervention. therapy. Although he attempts to bridge this heterogeneity with a subgroup analysis, these remain highly heterogeneous. Nor does it seem, then, a resolved issue.

A third matter of interest would be the mode of administration. Again, the studies are heterogeneous, and comparisons between modes of application are scarce. Both Cabaillot et al.<sup>(1)</sup> and Slapak et al.<sup>(4)</sup> observe that, in upper respiratory tract infections, spray application is better tolerated and equally effective than irrigation.

**Contributions to the authorship:** CCR has participated in the conception and design of the article, the contribution of study material, the critical review of the article and the approval of the final version. ILB has participated, in addition to the above, in the data collection and interpretation of the results. MEGF has experience in data collection, its analysis and performance, and the article's writing. LMC has participated in the contribution of study material. MEGF and LMC have also participated in the critical review of the article and in the approval of the final version.

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Finally, regarding the additional elements to seawater, only certain scientific evidence was found in favor of xylitol (as symptomatic treatment in chronic rhinosinusitis and in the postoperative period of endoscopic endonasal surgery)<sup>(20,21)</sup> and dexpanthenol (mainly in combination with alpha-agonists for nasal congestion in allergic rhinitis and after endonasal surgery, with improvement of symptoms and less rebound effect) (22-24), obtaining contradictory results with respect to hyaluronic acid (25-27). Although other elements, such as chamomile and aloe vera, have studied and recognized benefits in clinical practice, no studies were found on their specific application in nasal washes. Among the limitations of the study is the fact that there are difficulties in extracting solid scientific evidence regarding the benefits of nasal lavages with seawater. In addition to the impossibility of carrying out blind studies for the patient and the non-use of validated scales, it is difficult to objectively assess its effect. Something similar found in other reviews on the matter<sup>(28-30)</sup>.

#### CONCLUSIONS

Both saline solution and seawater seem especially useful for improving symptoms, reducing the incidence of complications, and reducing the use of other medications in upper respiratory tract infections. Likewise, they could have a role in treating allergic rhinitis in children. With the current evidence, it does not seem possible to recommend one solution over another (saline solution or seawater). Nor can we establish the optimal concentration of the solution and the most convenient mode of administration. The addition of elements to seawater solutions is not sufficiently justified with the currently available literature.

-Both saline solution and seawater seem especially useful for improving symptoms, reducing the incidence of complications, and reducing the use of other medications in upper respiratory tract infections. -Likewise, they could have a role in treating allergic rhinitis in children.

-With the current evidence, it does not seem possible to recommend one solution over another (saline solution or seawater). Nor can we establish the optimal concentration of the solution and the most convenient mode of administration.

-The addition of elements to seawater solutions is not sufficiently justified with the currently available literature.

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Correspondence: Irene López Barea. Address: Hospital Infantil Virgen del Rocío. C/Luca de Tena s/n. C.P.: 41013. Sevilla (ESPAÑA). E-mail: ire.lopbar@gmail.com

#### REFERENCES

- Cabaillot A, Vorilhon P, Roca M, Boussageon R, Eschalier B, Pereirad B. Saline nasal irrigation for acute upper respiratory tract infections in infants and children: A systematic review and meta-analysis. Paediatr Respir Rev. 2020 Nov;36: 151–8. doi: https://doi.org/10.1016/j.prv.2019.11.003
- 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 Jul-Ago;48(4):360–7. doi: <u>https://doi.org/10.1016/j.aller.2020.01.002</u>
- Chen JR, Jin L, Li XY. The effectiveness of nasal saline irrigation (seawater) in treatment of allergic rhinitis in children. Int J Pediatr Otorhinolaryngol. 2014;78(7):1115–8. doi: https://doi.org/10.1016/j.ijporl.2014.04.026
- Šlapak I, Skoupá J, Strnad P, Horník P. Efficacy of isotonic nasal wash (seawater) in the treatment and prevention of rhinitis in children. Arch Otolaryngol Head Neck Surg. 2008 Ene;134(1):67–74. doi: <u>https://doi.org/10.1001/archoto.2007.19</u>
- Köksal T, Çizmeci MN, Bozkaya D, Kanburoğlu MK, Şahin Ş, Taş T, 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 Ene;46(4):1004–13. doi: https://doi.org/10.3906/sag-1507-18
- Grasso M, De Vincentiis M, Agolli G, Cilurzo F, Grasso R. The effectiveness of long-term course of Sterimar Mn nasal spray for treatment of the recurrence rates of acute allergic rhinitis in patients with chronic allergic rhinitis. Drug Des Devel Ther. 2018 Abr;12:705–9. doi: https://doi.org/10.2147/dddts145173
- Sanabria Brassart J, Armengot-Carceller M, Jiménez del Valle A, Bermejo Rodríguez R. Encuesta poblacional a usuarios de lavados nasales con agua de mar: seguimiento de la recomendación médica, hábitos de uso, percepción de beneficios y satisfacción global. Acta Pediatr Esp [Internet]. 2020 [última consulta el 17/08/2022];78(3-4):e74-e81. Disponible en: <u>https://www.actapediatrica.com/index.php/secciones/originales/1682encuesta-poblacional-a-usuarios-de-lavados-nasales-con-agua-de-mar-seguimientode-la-recomendacion-medica-habitos-de-uso-percepcion-de-beneficios-ysatisfaccion-global#.tvvUN3ZBzIV
  </u>
- Jeffe JS, Bhushan B, Schroeder JW. Nasal saline irrigation in children: A study of compliance and tolerance. Int J Pediatr Otorhinolaryngol. 2012 Mar;76(3):409–13. doi: https://doi.org/10.1016/j.ijporl.2011.12.022
- Jiao J, Yang J, Li J, Li Y, Zhang L. Hypertonic saline and seawater solutions damage sinonasal epithelial cell air-liquid interface cultures. Int Forum Allergy Rhinol. 2020 Ene;10(1):59–68.doi: https://doi.org/10.1002/alr.22459
- Huang S, Constant S, De Servi B, Meloni M, Saaid A, Culig J, et al. Is a diluted seawaterbased solution safe and effective on human nasal epithelium? Eur Arch Otorhinolaryngol. 2021 Ago;278(8):2837–42. doi: <u>https://doi.org/10.1007/s00405-020-06527-1</u>
- De Servi B, Meloni M, Saaid A, Culig J. In vitro comparison of safety and efficacy of diluted isotonic seawater and electrodialyzed seawater for nasal hygiene. Med Devices (Auckl). 2020 Dic;13:391–8. doi: <u>https://doi.org/10.2147/mder.s285593</u>
- Huang S, Constant S, De Servi B, Meloni M, Culig J, Bertini M, et al. In vitro safety and performance evaluation of a seawater solution enriched with copper, hyaluronic acid, and eucalyptus for nasal lavage. Med Devices (Auckl). 2019 Sep;12:399–410. doi: https://doi.org/10.2147/mders.209644
- Shoseyov D, Bibi H, Shai P, Shoseyov N, Shazberg G, Hurvitz H. Treatment with hypertonic saline versus normal saline nasal wash of pediatric chronic sinusitis. J Allergy Clin Immunol. 1998 May;101(5):602–5. doi: <u>https://doi.org/10.1016/s0091-6749(98)70166-6</u>
- 14. Rabago D, Zgierska A, Mundt M, Barrett B, Bobula J, Maberry R. Efficacy of daily hypertonic saline nasal irrigation among patients with sinusitis: A randomized controlled trial. J Fam Pract [Internet]. 2002 Dic [última consulta el 1 7 / 0 8 / 2 0 2 2 ]; 5 1 (1 2): 1 0 4 9 - 5 5. Disponible en: https://pubmed.ncbi.nlm.nih.gov/12540331/

- Garavello W, Romagnoli M, Sordo L, Gaini RM, Di Berardino C, Angrisano A. Hypersaline nasal irrigation in children with symptomatic seasonal allergic rhinitis: A randomized study. Pediatr Allergy Immunol. 20
- Parson DS. Chronic sinusitis. A Medical or Surgical Disease? Otolaryngol Clin North Am. 1996 Feb;29(1):1–9.
- 17. Talbot AR, Herr TM, Parsons DS. Mucociliary Clearance and Buffered Hypertonic Saline Solution. Laryngoscope. 1997 Abr; 107(4):500–3. doi: https://doi.org/10.1097/00005537-199704000-00013/a>
- Gallant JN, Basem JI, Turner JH, Shannon CN, Virgin FW. Nasal saline irrigation in pediatric rhinosinusitis: A systematic review. Int J Pediatr Otorhinolaryngol. 2018 May:108:15562. doi:https://doi.org/10.1016/j.ijporl.2018.03.001
- 1Kanjanawasee D, Seresirikachorn K, Chitsuthipakorn W, Snidvongs K. Hypertonic Saline Versus Isotonic Saline Nasal Irrigation: Systematic Review and Meta-analysis. Am J Rhinol Allergy. 2018 Jul;32(4):269–79. doi: https://doi.org/10.1177/1945892418773566
- 20. Lin L, Tang X, Wei J, Dai F, Sun G. Xylitol nasal irrigation in the treatment of chronic rhinosinusitis. Am J Otolaryngol. 2017 Jul-Ago;38(4):383–9. doi: : https://doi.org/10.1016/j.amjoto.2017.03.006
- Da Silva CFFS, Da Silva FER, Pauna HF, Hurtado JGGM, Dos Santos MCJ. Symptom assessment after nasal irrigation with xylitol in the postoperative period of endonasal endoscopic surgery. Braz J Otorhinolaryngol. 2022 Mar-Abr;88(2):243-50. doi: https://doi.org/10.1016/j.bjorl.2020.05.023
- 22. Tantilipikom P, Tunsuriyawong P, Jareoncharsri P, Bedavanija A, Assanasen P, Bunnag C, et al. A randomized, prospective, double-blind study of the efficacy of dexpanthenol nasal spray on the postoperative treatment of patients with chronic rhinosinusitis after endoscopic sinus surgery. J Med Assoc Thai [Internet]. 2012 Ene [Ultima consulta el 17/08/2022];95(1):58–63. Disponible en: <u>https://pubmed.ncbi.nlm.nih.gov/22379743/</u>
- Jagade MV, Langade DG, Pophale RR, Prabhu A. Oxymetazoline plus dexpanthenol in nasal congestion. Indian J Otolaryngol Head Neck Surg. 2008 Dic;60(4):393–7. doi: <u>https://doi.org/10.1007/s12070-008-0125-7</u>
- Mösges R, Shah-Hosseini K, Hucke HP, Joisten MJ. Dexpanthenol: An Overview of its Contribution to Symptom Relief in Acute Rhinitis Treated with Decongestant Nasal Sprays. Adv Ther. 2017 Ago;34(8):1850–8. doi: <u>https://doi.org/10.1007/s12325-017-0581-0</u>
- 25. Ciofalo A, Zambetti G, Altissimi G, Fusconi M, Soldo P, Gelardi M, et al. Pathological and cytological changes of the nasal mucosa in acute rhinosinusitis: the role of hyaluronic acid as supportive therapy. Eur Rev Med Pharmacol Sci [Internet]. 2017 Oct [citado el 30 d e N o vi e m b r e d el 2 0 2 1]; 2 1 (19): 4411-8. D is p o n i b l e n : https://www.europeanreview.org/article/13515
- Gelardi M, Iannuzzi L, Quaranta N. Intranasal sodium hyaluronate on the nasal cytology of patients with allergic and nonallergic rhinitis. Int Forum Allergy Rhinol. 2013 Oct;3(10):807–13. doi: <u>https://doi.org/10.1002/alr.21193</u>
- 27. Savietto E, Marioni G, Maculan P, Pettorelli A, Scarpa B, Simoni E, et al. Effectiveness of micronized nasal irrigations with hyaluronic acid/isotonic saline solution in nonpolipoid chronic rhinosinusitis: A prospective, randomized, double-blind, controlled s tu dy. Am J Otolaryn g ol. 2020 Jul-Ag o;41(4):102502. doi: https://doi.org/10.1016/j.amjoto.2020.102502
- Martínez-Suárez V, Martínez-Hernández D, Zamorano-León JJ, Larrea-Cruz B, Pellegrini Belinchón FJ, Jiménez Del Valle Á, et al. Estudio delphi "lavados nasales con aguas de mar": Opinión, actitud y comportamiento médico sobre el uso de soluciones nasales de agua de mar. Pediatr Integral. 2017;21(8):559.e1-559. Disponible en: https://www.pediatriaintegral.es/wp-content/uploads/2017/xxi08/13/n8-559-e1-8\_Int-Esp.pdf
- Martínez-Serrano A, Martínez-Campos P, Seijoso-González L, Ruiz-Rojo H. Revisión narrativa de la técnica de los lavados nasales en pediatría. Enferm Clínica. 2021;31(3):189-94. doi: https://doi.org/10.1016/j.enfcli.2021.01.005
- Bastier P-L, Lechot A, Bordenave L, Durand M, de Gabory L. Nasal irrigation: From empiricism to evidence-based medicine. A review. European Annals of Otorhinolaryngology, Head and Neck Diseases. 2015;132(5):281–5. doi:10.1016/j.anorl.2015.08.001