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Review

Nasal irrigation: From empiricism to evidence-based medicine. A review

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ABSTRACT

Nasal irrigation plays a non-negligible role in the treatment of numerous sinonasal pathologies and postoperative care. There is, however, a wide variety of protocols. The present review of the evidence-based literature sought objective arguments for optimization and efficacy. It emerged that large-volume low-pressure nasal douche optimizes the distribution and cleansing power of the irrigation solution in the nasal cavity. Ionic composition and pH also influence mucociliary clearance and epithelium trophicity. Seawater is less rich in sodium ions and richer in bicarbonates, potassium, calcium and magnesium than is isotonic normal saline, while alkaline pH and elevated calcium concentration optimized ciliary motility in vitro. Bicarbonates reduce secretion viscosity. Potassium and magnesium promote healing and limit local inflammation. These results show that the efficacy of nasal irrigation is multifactorial. Large-volume low-pressure nasal irrigation using undiluted seawater seems, in the present state of knowledge, to be the most effective protocol.

1. Introduction

Several national and international consensus conferences now recommend nasal irrigation as adjuvant treatment in numerous sinonasal pathologies [1–6]. It provides mechanical cleansing of mucus, crust, cell debris and various air contaminants (pathogens, allergens, airborne particles, etc.). It enhances mucociliary clearance [7,8] and reduces the mucus contact time of airborne elements. It reduces local concentrations of pro-inflammatory mediators [9–11] and humidifies the nasal mucosa, notably postoperatively and in many chronic sinonasal pathologies.

A recent meta-analysis of 10 controlled trials taken from a review of 11,500 studies included more than 400 allergic rhinitis patients [7]. Regular saline irrigation in adults and children improved nasal symptomatology in 35% of cases and quality of life in 30%. Mucociliary clearance on saccharine test was increased by about 30%. The impact on medical drug consumption was harder to quantify; moreover, the included population was small for such a common treatment, and methods and administration times varied greatly, limiting the scientific value of the study [7].

The heterogeneity of the literature makes it difficult to get any clear idea concerning the various solutions and means of administration. Irrigation solution composition would seem to be an important issue: chronic patients sometimes report improvement with sea bathing, and some studies suggest that irrigation solutions taken from certain seas provide better functional improvement [12,13].

The present article comprises a literature review and update on the various solutions and means of administration available.

1.1. Means of irrigation

To the best of our knowledge, there is no consensus regarding means of irrigation. A study of the cavity distribution of 40 mL of radio-opaque substance in healthy subjects reported benefit with positive pressure irrigation versus negative pressure administration (by sniffing) or nebulization: nasal cavity and sinus distribution was more exhaustive [14]. Wormald et al., using 5 mL Tc99m-labeled irrigation solution, found better nasal cavity and sinus distribution with douche administration than nebulization or sprays [15].

We found no studies, comparative or not, in the literature focusing on syringe administration, despite this being the most widespread method. Several studies reported greater efficacy with large-volume irrigation [16,17]. A recent study compared 26 nasal

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Table 1
Composition (mg/L) of physiological saline, electrodialyzed seawater and Ringer's lactate [40,48].

	Physiological saline	Seawater (Physiomer®) [40,48]	Ringer's lactate (source: Vidal® dictionary 2014)
Sodium	3500	2400–2600	3000
Chloride	5500	5400–6300	3900
Magnesium		1100–1500	
Calcium		280–390	120
Potassium		44–62	150
Sulfates		2755	
Lactates			2500
Iron		6	
Zinc		27–90	
Selenium		38	
Copper		13–40	
pH	4.5–7	8	6–7.5

irrigation devices available on the German market [18], testing them on a resin nasal cavity model based on normal non-congested cadaver nostrils. Irrigation volumes ranged from 30 to 500 mL, for a mean 200–250 mL. The greater the irrigation volume, the larger the cavity area covered by the irrigation: large-volume irrigation reaches a larger proportion of the nasal cavities. Depending on volume and device, application time ranged between 6 and 54 s, and output between 3.9 and 27.2 mL/s. Only compression systems delivering ≥120 mbar pressure reached the entire nasal cavity. The authors added that tight fit between nozzle and nostril and the possibility of inserting the nozzle into the vestibule and orienting it 45° upward optimized cavity coverage and minimized loss of irrigation solution [18]. It also appeared that good ergonomics, irrigation quality and microbial safety were associated with devices that were transparent, equipped with an anti-reflux nozzle, in high-quality supple and compressible plastic, with ≥5 mL/s output or ≥120 mbar administration pressure, that could be taken apart and washed by hand or in a dishwasher, and were adapted for microwave ovens.

Clinically, a prospective single-blind randomized study compared postoperative efficacy between two commercially available nasal irrigation devices; in 31 endonasal surgery patients, large-volume low-pressure irrigation was associated with better postoperative nasal cavity cleansing on the Lund-Mackay postoperative endoscopy score than low-volume high-pressure irrigation [19].

1.2. In vitro *data*

1.2.1. Composition of commercially available solutions

It is important to be aware of the fact that the exact composition of the various products and recipes could not be found in the literature, except for Physiomer®[1] and Ringer's lactate. Table 1 and Fig. 1 show the chemical compositions of the various nasal irrigation solutions. There are several "recipes" for "home-made" saline, with or without buffer, that patients can make up themselves at home, using water, salt and, in some cases, sodium bicarbonate. Unlike normal saline (NaCl 0.9%), composition and sterility are neither controllable, reproducible or reliable. Home-made solutions using "sea" salt contain only chloride ions and sodium.

There are also commercially available products consisting of seawater diluted to one-third in distilled water (e.g., Stérimar®[2], Marimer®[3], Vicks®[4]) to obtain an isotonic solution.

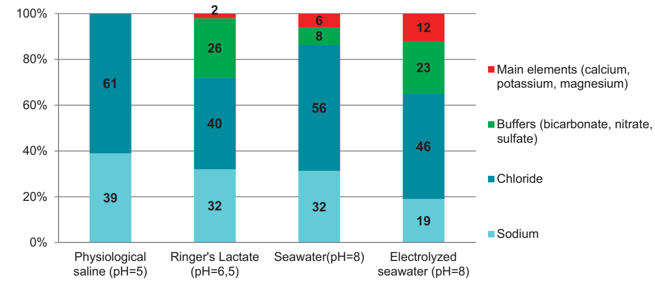

Fig. 1. Physical and chemical characteristics of various isotonic saline solutions versus seawater (biochemical analyses provided by Laboratoire de la Mer®).

Although these are marketed as "seawater", the one-third dilution conserves only part of the naturally present minerals, which are themselves proportionally diluted (http://www.sterimar.com/en/nasal-family-solutions.php). Another product consists of electrodialyzed seawater (Physiomer®), providing an isotonic solution with reliable osmolarity, while conserving high concentrations of the main seawater ions (https://register.epo.org/application?lng=en&number=EP98460042). Its composition is known and can be compared to physiological saline and Ringer's lactate (Table 1). Products obtained by this procedure are, like Ringer's lactate, rich in calcium, potassium and magnesium ions and buffering (bicarbonates), with low sodium ion content (Table 1). Like seawater, they have slightly alkaline pH (controlled pH close to 8), while normal saline is acidic, with pH varying from 4.5 to 7.

1.2.2. Role of the various components

It is now agreed that, *in vitro*, these ions show non-negligible action on epithelial cells. Sodium ions can inhibit hair-cell calcium flow, thus reducing ciliary beat frequency [20]. Magnesium ions reduce local inflammation by reducing mediator secretion [21] and degranulation [22] in cells implicated in allergy. Paradoxically, they increase IL-8 secretion by nasal epithelial cells [23]. Finally, magnesium and zinc can reduce respiratory mucosa cell apoptosis during inflammatory processes [24]. Calcium is involved in regulating ciliary beat frequency and synchronization, via various ciliated cell surface receptors [25], in all of which acetylcholine and serotonin act as messengers by increasing cell calcium intake [25]. Airflow also stimulates cell calcium intake and ciliary beat via shear-stress-induced mechanotransduction [25]. Potassium promotes respiratory epithelium repair via the EGF/EGFR pathway [26,27]. Bicarbonate ions, as well as acting as buffer, efficiently reduce mucus viscosity, thus facilitating elimination by ciliated cell movement [28].

1.2.3. Role of pH and tonicity

In vitro, solutions with pH <7 or >10 reduced tracheal mucosa ciliary beat frequency in rats and chicken embryos [29]. In humans, solutions with acidic pH likewise reduced ciliary beat frequency, while slightly alkaline solutions enhanced it [30,31]. *In vivo*, on the other hand, in humans, pH impact on mucociliary clearance is more difficult to ascertain. England et al. found no statistical correlation between pH and mucociliary clearance in 56 healthy non-smokers [32]. More recently, Chusakul et al. reported clear improvement in symptoms with alkaline isotonic solutions in allergic rhinitis; mucociliary clearance, on the other hand, was unaffected whatever the pH, in a range from 6.2 to 8.4 [33]. However, change in mucociliary clearance seems not to depend exclusively on pH: *in vitro*, in chicken embryo tracheal explants, hypertonic (1.5%) and hypotonic (0.45%) irrigation both reduced ciliary beat frequency as compared to physiological (0.9%) saline [29]. Beat arrest was irreversible with a 14% solution, and hypertonicity triggered mucus hypersecretion

[1] Laboratoire de la Mer®, ZAC La Madeleine, avenue du Général-Patton, Saint-Malo, France.
[2] Laboratoires Fumouze, SOFIBEL, Church & Dwight Group, New York, USA.
[3] Laboratoire Gilbert, Batteur Group, Hérouville Saint-Clair, France.
[4] Procter and Gamble Pharmaceuticals France, Asnière-sur-Seine, France.