



Treatment of allergic rhinitis by comparative administration of 3% hypertonic saline, normal saline and 0.5% diluted betadine saline

Dr. Amit Prakash

Senior Resident, Department of ENT, Darbhanga Medical College & Hospital, Darbhanga, Bihar, India

Abstract

Symptoms of allergic rhinitis may include nasal obstruction (blockage or congestion), rhinorrhoea (which can be anterior leading to nasal discharge, or posterior leading to post-nasal drip), nasal itching and sneezing. In addition to nasal symptoms, some people with allergic rhinitis also report eye symptoms (watering, redness, itching) and ear symptoms such as pain, pressure or feeling of fullness; however, aural (ear) symptoms have also been reported as an adverse effect of nasal saline irrigation. There is evidence that people with allergic rhinitis may experience decreased quality of life due to issues such as loss of sleep, secondary daytime fatigue, impaired school and work performance, decreased cognitive functioning and decreased long-term productivity. Hence based on above findings the present study was planned for Treatment of Allergic Rhinitis by Comparative Administration of 3% Hypertonic Saline, Normal Saline and 0.5% Diluted Betadine Saline.

The present study was planned in Darbhanga Medical College & Hospital, Darbhanga, Bihar, India. The study was conducted from March 2019 to Oct 2019. Total 30 patients of age 20 – 50 years age of both sexes were enrolled in the present study. The patients were divided in three study groups based on administration. The 10 patients in Group I were administered with the 0.9% Normal Saline. The 10 patients in Group II were administered with the 3% hypertonic saline. The remaining 10 patients in Group III were administered with the 0.5% diluted betadine saline. All cases were administered with the respective irrigation solution for three times as day in nostrils for 4 weeks period.

The data generated from the present study concludes that there was significant outcome following nasal irrigation, in all the three treatments but no significant differences between the treatments. All three modalities of treatment improve the quality of life. The diagnosis should be based on combination of proper history, physical examination, radiological investigation, endoscopic nasal evaluation & laboratory results. The complications of sinusitis must be dealt with urgently. If action is taken in time many irreversible conditions are avoided and patients have potential to recover and function independently as was the case with our patient.

Keywords: allergic rhinitis, povidone-iodine, diagnostic nasal endoscopy, etc

Introduction

Rhinitis, which occurs most commonly as allergic rhinitis, is an inflammation of the nasal membranes that is characterized by sneezing, nasal congestion, nasal itching, and rhinorrhea, in any combination^[1]. Although allergic rhinitis itself is not life-threatening (unless accompanied by severe asthma or anaphylaxis), morbidity from the condition can be significant.

Rhinitis is defined as inflammation of the nasal membranes^[2] and is characterized by a symptom complex that consists of any combination of the following: sneezing, nasal congestion, nasal itching, and rhinorrhea^[1]. The eyes, ears, sinuses, and throat can also be involved. Allergic rhinitis is the most common cause of rhinitis. It is an extremely common condition, affecting approximately 20% of the population.

Although allergic rhinitis is not a life-threatening condition, complications can occur and the condition can significantly impair quality of life^[3, 4], which leads to a number of indirect costs. The total direct and indirect cost of allergic rhinitis was recently estimated to be \$5.3 billion per year^[5]. A 2011 analysis determined that patients with allergic rhinitis averaged 3 additional office visits, 9 more prescriptions filled, and \$1500 in incremental healthcare costs in 1 year than similar patients without allergic rhinitis^[6].

Allergic rhinitis involves inflammation of the mucous membranes of the nose, eyes, eustachian tubes, middle ear, sinuses, and pharynx. The nose invariably is involved, and the other organs are affected in certain individuals. Inflammation of the mucous membranes is characterized by a complex interaction of inflammatory mediators but ultimately is triggered by an immunoglobulin E (IgE)-mediated response to an extrinsic protein^[7].

The tendency to develop allergic, or IgE-mediated, reactions to extrinsic allergens (proteins capable of causing an allergic reaction) has a genetic component. In susceptible individuals, exposure to certain foreign proteins leads to allergic sensitization, which is characterized by the production of specific IgE directed against these proteins. This specific IgE coats the surface of mast cells, which are present in the nasal mucosa. When the specific protein (eg, a specific pollen grain) is inhaled into the nose, it can bind to the IgE on the mast cells, leading to immediate and delayed release of a number of mediators^[8, 9].

The mediators that are immediately released include histamine, tryptase, chymase, kinins, and heparin. The mast cells quickly synthesize other mediators, including leukotrienes and prostaglandin D₂^[10]. These mediators, via various interactions, ultimately lead to the symptoms of rhinorrhea (ie, nasal congestion, sneezing, itching, redness,

tearing, swelling, ear pressure, postnasal drip). Mucous glands are stimulated, leading to increased secretions. Vascular permeability is increased, leading to plasma exudation. Vasodilation occurs, leading to congestion and pressure. Sensory nerves are stimulated, leading to sneezing and itching. All of these events can occur in minutes; hence, this reaction is called the early, or immediate, phase of the reaction.

Over 4-8 hours, these mediators, through a complex interplay of events, lead to the recruitment of other inflammatory cells to the mucosa, such as neutrophils, eosinophils, lymphocytes, and macrophages. This results in continued inflammation, termed the late-phase response. The symptoms of the late-phase response are similar to those of the early phase, but less sneezing and itching and more congestion and mucus production tend to occur ^[11]. The late phase may persist for hours or days.

Systemic effects, including fatigue, sleepiness, and malaise, can occur from the inflammatory response. These symptoms often contribute to impaired quality of life.

The prevalence of allergic rhinitis in the United States ranges from 3% to 19%, and 30 to 60 million people are affected each year. The development of allergic rhinitis before 20 years of age occurs in 80% of cases ^[12]. In 2012, 9% of children younger than 18 years and 7.5% of adults reported allergic rhinitis in the past 12 months ^[13].

Throughout the world, the prevalence of allergic rhinitis has slightly escalated. Currently, approximately 10 to 30% of adults and 40% of children are affected. The European Community Respiratory Health survey recorded a prevalence of 10 to 41% in adults with allergic rhinitis. Scandinavian studies have demonstrated a cumulative prevalence rate of 15% in men and 14% in women. The prevalence of allergic rhinitis may vary within and among countries. Highest prevalence of severe allergic rhinitis symptoms in children were observed in Africa and Latin America ^[14]. This may be due to geographic differences in the types and potency of different allergens and the overall aeroallergen burden.

While allergic rhinitis itself is not life-threatening (unless accompanied by severe asthma or anaphylaxis), morbidity from the condition can be significant. Allergic rhinitis often coexists with other disorders, such as asthma, and may be associated with asthma exacerbations.

Allergic rhinitis is also associated with otitis media, eustachian tube dysfunction, sinusitis, nasal polyps, allergic conjunctivitis, and atopic dermatitis. It may also contribute to learning difficulties, sleep disorders, and fatigue.

Numerous complications that can lead to increased morbidity or even mortality can occur secondary to allergic rhinitis. Possible complications include otitis media, eustachian tube dysfunction, acute sinusitis, and chronic sinusitis.

Allergic rhinitis can be associated with a number of comorbid conditions, including asthma, atopic dermatitis, and nasal polyps. Evidence now suggests that uncontrolled allergic rhinitis can actually worsen the inflammation associated with asthma or atopic dermatitis ^[15]. This could lead to further morbidity and even mortality.

Allergic rhinitis can frequently lead to significant impairment of quality of life. Symptoms such as fatigue, drowsiness (due to the disease or to medications), and malaise can lead to impaired work and school performance, missed school or work days, and traffic accidents. Cost of

allergic rhinitis have increased substantially in the United States. In 1996, the overall cost (direct and indirect) of allergic rhinitis was estimated to be \$5.3 billion per year ^[5]. In 2002, total costs including indirect costs were estimated at \$11.58 billion.

Allergic rhinitis occurs in persons of all races. Prevalence of allergic rhinitis seems to vary among different populations and cultures, which may be due to genetic differences, geographic factors or environmental differences, or other population-based factors.

In childhood, allergic rhinitis is more common in boys than in girls, but in adulthood, the prevalence is approximately equal between men and women.

Onset of allergic rhinitis is common in childhood, adolescence, and early adult years, with a mean age of onset 8-11 years, but allergic rhinitis may occur in persons of any age. In 80% of cases, allergic rhinitis develops by age 20 years. The prevalence of allergic rhinitis has been reported to be as high as 40% in children, subsequently decreasing with age. In the geriatric population, rhinitis is less commonly allergic in nature.

Allergy testing may reveal the specific allergens to which an individual is sensitive. Skin testing is the most common method of allergy testing ^[16]. This may include a patch test to determine if a particular substance is causing the rhinitis, or an intradermal, scratch, or other test. Less commonly, the suspected allergen is dissolved and dropped onto the lower eyelid as a means of testing for allergies. This test should be done only by a physician, since it can be harmful if done improperly. In some individuals not able to undergo skin testing (as determined by the doctor), the RAST blood test may be helpful in determining specific allergen sensitivity. Peripheral eosinophilia can be seen in differential leukocyte count.

Allergy testing is not definitive. At times, these tests can reveal positive results for certain allergens that are not actually causing symptoms, and can also not pick up allergens that do cause an individual's symptoms. The intradermal allergy test is more sensitive than the skin prick test, but is also more often positive in people that do not have symptoms to that allergen.

Even if a person has negative skin-prick, intradermal and blood tests for allergies, he/she may still have allergic rhinitis, from a local allergy in the nose. This is called local allergic rhinitis. Specialized testing is necessary to diagnose local allergic rhinitis.

Symptoms of allergic rhinitis may include nasal obstruction (blockage or congestion), rhinorrhoea (which can be anterior leading to nasal discharge, or posterior leading to post-nasal drip), nasal itching and sneezing ^[17]. In addition to nasal symptoms, some people with allergic rhinitis also report eye symptoms (watering, redness, itching) and ear symptoms such as pain, pressure or feeling of fullness; however, aural (ear) symptoms have also been reported as an adverse effect of nasal saline irrigation ^[18]. There is evidence that people with allergic rhinitis may experience decreased quality of life due to issues such as loss of sleep, secondary daytime fatigue, impaired school and work performance, decreased cognitive functioning and decreased long-term productivity ^[19].

Hence based on above findings the present study was planned for Treatment of Allergic Rhinitis by Comparative Administration of 3% Hypertonic Saline, Normal Saline and 0.5% Diluted Betadine Saline.

Methodology

The present study was planned in Darbhanga Medical College & Hospital, Darbhanga, Bihar, India. The study was conducted from March 2019 to Oct 2019. Total 30 patients of age 20 – 50 years age of both sexes were enrolled in the present study. The patients were divided in three study groups based on administration. The 10 patients in Group I were administered with the 0.9% Normal Saline. The 10 patients in Group II were administered with the 3% hypertonic saline. The remaining 10 patients in Group III were administered with the 0.5% diluted betadine saline. All cases were administered with the respective irrigation solution for three times as day in nostrils for 4 weeks period. AEC (Absolute Eosinophil Count) Done in all patients with allergic rhinitis pre-treatment and post-treatment. 50 to 450 cells/microliter of blood are considered normal.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: Patients who had been treated with antibiotics, β2 agonists, antihistaminics, topical steroids and systemic steroids were included in the study, but the treatment was stopped one month prior to the beginning of the study.

Exclusion Criteria: Patients who were immunocompromised i.e. suffering from diseases like Diabetes and HIV. Patients with polyps and mucocele that obstructs the sinuses.

Results & Discussion

Nasal irrigations may be used for a variety of conditions [20]. Their use is included in the management of acute and chronic rhinosinusitis [21], allergic and nonallergic rhinitis, nonspecific nasal symptoms (including postnasal drip), septal perforations, and the postoperative care of surgical patients. Prescription medication use can be decreased as a result of nasal irrigations in some circumstances [22]. Nasal irrigations are often thought of as adjunctive measures. Frequently, they are mentioned only in passing in publications addressing sinonasal symptomatology. Indeed, a joint publication between the American Academy of Otolaryngology–Head and Neck Surgery and the American Academy of Allergy, Asthma, and Immunology made only a brief mention of nasal irrigations [23]. Nasal irrigations are often much more than adjunctive. They are an important component in the management of sinonasal complaints. Unfortunately, studies of nasal irrigations are often small and poorly controlled, and unsupported conclusions are sometimes drawn. No standard uniform recommendations exist for the use of nasal irrigations. In addition, different theories exist as to how they work. Indeed, various nasal irrigation solutions are available: Different “home recipes” exist, manufactured powders or solutions can be bought, the tonicity can be varied (isotonic vs hypertonic saline), additives can be included, the pH can be changed, and numerous devices, including the cupped hand, can be used to administer nasal irrigations.

Allergic rhinitis is inflammation (swelling and/or irritation) of the inside of the nose caused by allergies. It is common in both children and adults. Allergic rhinitis can be intermittent (fewer than four days per week, or four weeks per year) or persistent (more than four days per week, or four weeks per

year). The allergy can be caused by many different things but common allergens (things causing allergy) are: grass or tree pollen, mould, dust mites or animal dander (tiny flakes of skin). People with allergic rhinitis experience symptoms (nasal obstruction, runny nose, nasal itching and sneezing) that may affect their quality of life.

Nasal saline irrigation (also known as nasal douche, wash or lavage) is a procedure that rinses the nasal cavity with saline (salt water) solutions. How saline works is not fully understood but it is probably through making the mucus (snot) thinner, making it easier to remove and also removing some of the allergens from the nose that cause irritation. Nasal saline irrigation can be performed with sprays, pumps or squirt bottles. Saline solutions can be isotonic (the same concentration of salt that is found in the body - 0.9% NaCl) or hypertonic (more salty than found in the body - more than 0.9% NaCl). Although saline irrigation is thought to be safe there have been reports of epistaxis (nosebleeds) and irritation or discomfort in the nose and ears. This therapy is available without prescription and can be used alone or as an add-on to other pharmacological treatment for allergic rhinitis, such as intranasal (in the nose) steroids and oral antihistamines).

Table 1: Demographic Details

Groups	Group I	Group II	Group III
Administration of	0.9% Normal Saline	3% Hypertonic saline	0.5% Diluted betadine saline
Parameters	No. of Cases	No. of Cases	No. of Cases
Age			
20 – 30 years	3	2	4
31 – 40 years	4	5	3
41 – 50 years	3	3	3
Sex			
Males	6	3	5
Females	4	7	5
Total Cases	10	10	10

Table 2: Symptoms

Groups	Group I	Group II	Group III
Administration of	0.9% Normal Saline	3% Hypertonic saline	0.5% Diluted betadine saline
Recurrent sneezing	5	3	4
Nasal obstruction	3	2	2
Nasal discharge	2	4	1
Headache	2	2	2

Table 3: Absolute Eosinophil Count

Groups	Group I	Group II	Group III
Administration of	0.9% Normal Saline	3% Hypertonic saline	0.5% Diluted betadine saline
Pre-Operative	685.2 ± 163.5	678.8 ± 112.4	715.8 ± 148.3
Post-Operative	547.4 ± 146.3	477.6 ± 118.6	519.2 ± 157.1

Nasal irrigation is a simple, safe, effective therapeutic procedure that has been used in the treatment of nasal diseases for many years. Together with corticosteroid/pharmacological treatment, nasal irrigation is also recommended as first-line treatment in acute and chronic rhinosinusitis and after sinonasal surgery as well as adjunctive treatment for allergic rhinitis, acute upper respiratory tract infections, rhinitis in pregnancy, etc [24]. Nasal irrigation may be effective in reducing nasal

congestion and mucopurulent secretion, stimulating cleansing of the nasal and paranasal cavities, and in preventing crusting and moisturizing the mucosa after endonasal surgery. Nasal irrigation also appears to improve the mucociliary transport function of the nasal mucosa [25].

Different kinds of nasal irrigation solutions, such as normal saline as well as various concentrations of hypertonic saline, Ringer-Lactate solution, isotonic and hypertonic seawater solution have been used in clinical practice. Saline solutions have been widely used in nasal irrigation for many years and are recommended for the treatment of various nasal diseases by several international expert groups [26]. While the majority of studies on the effects of saline solution of different osmolarities on mucociliary clearance have reported hypertonic saline to be more effective than normal saline in improving mucociliary clearance [27], few studies have found no difference between hypertonic and normal saline [28]. Interestingly, a study by Ural and colleagues [29] has reported that irrigation with hypertonic saline restored impaired mucociliary clearance in chronic sinusitis patients, while isotonic saline improved mucociliary clearance in allergic rhinitis and acute sinusitis patients, suggesting that nasal irrigation with isotonic or hypertonic saline may improve mucociliary clearance time in various nasal pathologies [30]. Studies on the effects of saline solutions of different osmolarities on CBF in vitro have indicated that while 0.9% normal saline did not affect or had a moderately negative effect on CBF of human nasal epithelium, an increase in saline tonicity was associated with increased inhibition of CBF, reversible ciliostasis or irreversible ciliostatic effect, depending on saline hypertonicity [31]. Considering the findings from both in vivo and in vitro studies, isotonic or hypertonic saline solutions at concentrations of 2%–3% may be most appropriate for nasal irrigation.

In a recent study, Rabago *et al.* [32] performed a randomized, controlled trial looking at patients with two episodes of acute sinusitis or one episode of chronic sinusitis per year for 2 consecutive years. Fifty-two patients received hypertonic saline, whereas 24 patients did not receive any irrigations. When using hypertonic nasal irrigations, improvements in quality-of-life and overall symptom severity scores were statistically significant. Steroid nasal spray use was also decreased. Toomoka *et al.* [33] used pulsatile hypertonic saline nasal irrigations for a range of sinonasal conditions, extending from atrophic rhinitis to the symptom of postnasal drainage. They reported that patients who used nasal irrigations for the treatment of sinonasal complaints experienced statistically significant improvements in 23 of 30 nasal symptoms. Nasal irrigations can also be effective in rhinitis [34], including allergic and nonallergic rhinitis. Atrophic rhinitis, a difficult condition to treat, is often only effectively managed when combined with regular, diligent nasal irrigations.

In recent years, isotonic or hypertonic seawater solution has commonly been used for nasal irrigation because of high levels of minerals and trace elements, such as calcium, potassium, magnesium and zinc ions, which can assist in epithelial wound repair and ciliary beat regulation. Indeed, Süslü and colleagues [35] have reported that in patients who underwent septoplasty, 20 days' nasal irrigation with hypertonic seawater significantly improved mucociliary clearance to a greater extent than isotonic saline irrigation, as indicated using the saccharine test [35]. Similarly,

Foanant and colleagues [36] have shown that dexpanthenol in seawater spray resulted in better mucociliary clearance than saline irrigation in sinusitis patients following ESS.68 More recently, Bonnomet and colleagues [37] conducted a randomized, controlled, blinded, in vitro study to assess the effect of normal saline and diluted or non-diluted seawater on CBF and epithelial wound repair speed (WRS) in airway epithelial cells from 13 nasal polyps explants. They demonstrated that non-diluted seawater enhanced the CBF and WRS of nasal epithelial cells when compared to normal saline and diluted seawater.

Conclusion

The data generated from the present study concludes that there was significant outcome following nasal irrigation, in all the three treatments but no significant differences between the treatments. All three modalities of treatment improve the quality of life. The diagnosis should be based on combination of proper history, physical examination, radiological investigation, endoscopic nasal evaluation & laboratory results. The complications of sinusitis must be dealt with urgently. If action is taken in time many irreversible conditions are avoided and patients have potential to recover and function independently as was the case with our patient.

References

1. Druce HM. Allergic and nonallergic rhinitis. Middleton EM Jr, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, Busse WW, eds. Allergy: Principles and Practice. 5th ed. St. Louis, Mo: Mosby Year-Book, 1998, 1005-16.
2. Togias AG. Systemic immunologic and inflammatory aspects of allergic rhinitis. *J Allergy Clin Immunol.* 2000; 106(5 Suppl):S247-50.
3. Blaiss MS. Quality of life in allergic rhinitis. *Ann Allergy Asthma Immunol.* 1999; 83(5):449-54.
4. Thompson AK, Juniper E, Meltzer EO. Quality of life in patients with allergic rhinitis. *Ann Allergy Asthma Immunol.* 2000; 85(5):338-47; quiz 347-8.
5. Ray NF, Baraniuk JN, Thamer M, Rinehart CS, Gergen PJ, Kaliner M, *et al.* Direct expenditures for the treatment of allergic rhinoconjunctivitis in 1996, including the contributions of related airway illnesses. *J Allergy Clin Immunol.* 1999; 103(3 Pt 1):401-7. [Medline].
6. Bhattacharyya N. Incremental healthcare utilization and expenditures for allergic rhinitis in the United States. *Laryngoscope.* 2011; 121(9):1830-3.
7. Skoner DP. Allergic rhinitis: definition, epidemiology, pathophysiology, detection, and diagnosis. *J Allergy Clin Immunol.* 2001; 108(1 Suppl):S2-8. [Medline].
8. Walls AF, He S, Buckley MG, McEuen AR. Roles of the mast cell and basophil in asthma. *Clin Exp Allergy,* 2001, 1:68.
9. Haberal I, Corey JP. The role of leukotrienes in nasal allergy. *Otolaryngol Head Neck Surg.* 2003; 129(3):274-9. [Medline].
10. Iwasaki M, Saito K, Takemura M, Sekikawa K, Fujii H, Yamada Y, *et al.* TNF-alpha contributes to the development of allergic rhinitis in mice. *J Allergy Clin Immunol.* 2003; 112(1):134-40.
11. Hansen I, Klimek L, Mosges R, Hormann K. Mediators of inflammation in the early and the late phase of

- allergic rhinitis. *Curr Opin Allergy Clin Immunol*. 2004; 4(3):159-63.
12. World Allergy Organization (WAO). Pawanker R, Canonica GW, Holgate ST, Lockey RF, Blaiss MS. *White Book on Allergy: Update 2013*. Milwaukee, WI: World Allergy Organization, 2013.
 13. Bloom B, Jones LI, Freeman G. Summary health statistics for U.S. children: National Health Interview Survey, 2012. *Vital Health Stat* 10, 2013, 1-81.
 14. Ait-Khaled N, Pearce N, Anderson HR, Ellwood P, Montefort S, Shah J, *et al*. Global map of the prevalence of symptoms of rhinoconjunctivitis in children: The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three. *Allergy*. 2009; 64(1):123-48.
 15. Kiyohara C, Tanaka K, Miyake Y. Genetic susceptibility to atopic dermatitis. *Allergol Int*. 2008; 57(1):39-56.
 16. Meltzer EO, Grant JA. Impact of cetirizine on the burden of allergic rhinitis. *Ann Allergy Asthma Immunol*. 1999 Nov. 83(5):455-63.
 17. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, *et al*. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA (2) LEN and AllerGen). *Allergy*. 2008; 63:8-160.
 18. Chusakul S, Warathanasin S, Suksangpanya N, Phannaso C, Ruxrungtham S, Snidvongs K, *et al*. Comparison of buffered and nonbuffered nasal saline irrigations in treating allergic rhinitis. *Laryngoscope*. 2013; 123:53-6.
 19. Schoenwetter WF, Dupclay L, Appajosyula S, Botteman MF, Pashos CL. Economic impact and quality-of-life burden of allergic rhinitis. *Current Medical Research and Opinion*. 2004; 20(3):305-17.
 20. Papsin B, McTavish A. Saline nasal irrigation: its role as an adjunct treatment. *Can Fam Physician*. 2003; 49:168-273. This is a good review of the indications for using nasal irrigations.
 21. Lanza DC, Kennedy DW. Adult rhinosinusitis defined. *Otolaryngol Head Neck Surg*. 1997; 117:S1-S7.
 22. Heatley DG, McConnell KE, Kille TL, *et al*. Nasal irrigation for the alleviation of sinonasal symptoms. *Otolaryngol Head Neck Surg*. 2001; 125:44-48.
 23. Kaliner MA, Osguthorpe JD, Fireman P, *et al*. Sinusitis: bench to bedside. Current findings, future directions. *Otolaryngol Head Neck Surg*. 1997; 116:S1-S20.
 24. Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, *et al*. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. *Rhinology*. 2012; 50:1-12.
 25. Keojampa BK, Nguyen MH, Ryan MW. Effects of buffered saline solution on nasal mucociliary clearance and nasal airway patency. *Otolaryngol Head Neck Surg*. 2004; 131:679-682.
 26. Roberts G, Xatzipsalti M, Borrego LM, Custovic A, Halcken S, Hellings PW, *et al*. Paediatric rhinitis: position paper of the European Academy of Allergy and Clinical Immunology. *Allergy*. 2013; 68:1102-1116.
 27. 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; 63:309-313.
 28. Michel O, Dreßler AK. Hypertonic (3%) vs. isotonic brine nosespray--a controlled study. *Laryngorhinootologie*. 2011; 90:206-210.
 29. 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; 123:517-521.
 30. Boek WM, Keleş N, Graamans K, Huizing EH. Physiologic and hypertonic saline solutions impair ciliary activity in vitro. *Laryngoscope*. 1999; 109:396-399.
 31. Min YG, Lee KS, Yun JB, Rhee CS, Rhyoo C, Koh YY, *et al*. Hypertonic saline decreases ciliary movement in human nasal epithelium in vitro. *Otolaryngol Head Neck Surg*. 2001; 124:313-316.
 32. Rabago D, Zgierska A, Mundt M, *et al*. Efficacy of daily hypertonic saline nasal irrigation among patients with sinusitis: a randomized controlled trial. *J Fam Pract*. 2002; 51:1049-1055.
 33. Tomooka LT, Murphy C, Davidson TM. Clinical study and literature review of nasal irrigation. *Laryngoscope*. 2000; 110:1189-1193.
 34. Primer on allergic and immunologic diseases. *JAMA*. 1997; 278:1803-2030.
 35. 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; 266:685-689.
 36. Foonant S, Chaiyasate S, Roongrotwattanasiri K. Comparison on the efficacy of dexpanthenol in sea water and saline in postoperative endoscopic sinus surgery. *J Med Assoc Thai*. 2008; 91:1558-1563.
 37. Bonnomet A, Luczka E, Coraux C, de Gabory L. Non-diluted seawater enhances nasal ciliary beat frequency and wound repair speed compared to diluted seawater and normal saline. *Int Forum Allergy Rhinol*. 2016; 6:1062-1068.