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The comparison of nasal irrigation outcome between 3% NaCl and 0.9% NaCl in adults majority with intermittent allergic rhinitis: A randomized double-blind study

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Abstract

Background: Management of allergic rhinitis with oral antihistamine and steroid nasal spray are the standard treatment which is recommended by Allergic Rhinitis and its Impact on Asthma guidelines. In addition, nasal irrigation as an adjuvant therapy also provides a satisfactory result.

Objective: To compare the treatment outcome in adults majority with intermittent allergic rhinitis who receive different concentrations of nasal irrigation.

Methods: The prospective randomized double-blind study was performed in 80 patients. All patients were prescribed oral antihistamine and nasal irrigated solution between 3% NaCl and 0.9% NaCl. Nasal congestion and rhinorrhea were evaluated at baseline, first and second weeks after treatment. Assessments were measured by nasal congestion visual analog scale rhinorrhea visual analog scale, inferior turbinate size, and peak nasal expiratory flow rate (PNEFR). A p value of < 0.05 was considered statistically significant.

Results: There were 40 patients in each group of the study. Patients reported satisfactory experience after using saline irrigation at first and second weeks in both solutions (p value < 0.001). However, when compared between groups, no significant differences for all parameters were reported. PNEFR showed good results after the first week of 3% NaCl irrigation (p value $= 0.001$), while 0.9% NaCl had good results after the second week (p value < 0.001).

Conclusion: Both add-on treatments have a significant improvement of all 4 parameters assessed in the study: nasal congestion, rhinorrhea, inferior turbinate size and PNEFR. Of note, 3% NaCl but not 0.9 NaCl had improved the PNEFR earlier from 1 week of the treatment.

Key words: nasal irrigation, 3% NaCl, 0.9% NaCl, hypertonic saline, allergic rhinitis

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Introduction

Allergic rhinitis is a chronic disease which affects 25-35% of the worldwide population.[1] Thailand has a disease incidence of approximately 10-45%.[2,3] The common presenting symptoms which usually negatively impact patient's quality of life include nasal obstruction, rhinorrhea, nasal itching, and sneezing.[4] According to Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines,[5] allergen avoidance, oral antihistamines, and topical nasal steroid spray are the standard treatment modalities for allergic patients. However, some patients do not achieve a good outcome even they follow the guidelines. Additionally, allergen avoidance is unrealistic in some environments. Therefore, further medications, such as pseudoephedrine or phenylephrine, are prescribed to relieve the allergic symptoms. However, those drugs have side effects and may interact with other medications the patient is taking.[6-8]

Nasal irrigation is an adjuvant therapy that minimizes the problems of allergen avoidance and additional drug usage.[9-15] The mechanisms of the nasal procedure are to wash out

discharge, inflammatory substances, and allergens in the nasal cavity.[16,17] In addition, some studies mentioned in the advantage of hypertonicity solution by decreases nasal edema and improve of nasal mucociliary clearance through the fluid secretion that may associated with upregulation of chloride channel.[16,17] However, there is no definite recommendation for specific concentration in saline solution.

The aim of this study was to compare symptoms of nasal congestion and rhinorrhea in adults majority with intermittent allergic rhinitis patients who receive add-on treatment with hypertonic and isotonic nasal saline solution and to provide evidence for health-care practitioners in the selection of an appropriate saline irrigated solution.

Methods

The prospective randomized controlled trial double-blind, paralleled, study was conducted at the otolaryngology unit and was reported in the line with the CONSORT guidelines. The protocol of the investigation was approved by the Institutional Review Board. The clinical trial registration number was TCTR 20200430003. The study was conducted between July 2018 and June 2019. The study focused on adult allergic rhinitis patients who were diagnosed according to ARIA classification. Inclusion criteria were: 1) age ≥ 15 years old; 2) presence of active symptoms of allergic rhinitis more than 1 week; 3) no history of nasal irrigation or steroid nasal spray used at least 1 month before entry the study; and 4) no symptoms/signs of active upper respiratory tract infection by bacteria or virus. Fever (BT > 37.5°C), discoloring of nasal discharge, cough, facial pain, otalgia, sore throat, and cervical lymphadenopathy were defined as an active infection. Patients who presented with nasal anatomical variation, such as deviated nasal septum, sinonasal polyp and/or neoplasm, prior history of nose and sinus surgery, chronic lung disease, smoking, seeking further medical treatment and used concomitant drugs out of the trial during the study were excluded.

Participants and Blinding

All participants were provided detailed information about the study by the researcher and completed the written informed consent. Patient demographic data included age, sex, body mass index (BMI), duration of symptoms, and ARIA classification. Each patient was prescribed only oral antihistamine (loratadine (10 mg)) one tablet before bed-time and saline nasal irrigation twice daily. Although the patients were classified as moderate to severe intermittent or mild persistent allergic rhinitis who indicated for intranasal steroid spray, however, they felt uncomfortable with the spray due to its smell and dripping sensation from posterior part of the nose after previous using, so only oral antihistamine was prescribed to them. The blinding process to assign the 2 different types of saline solution between hypertonic and isotonic saline was conducted as follows: 1) the patients, with their study number, drew a sealed card from the box which had 40 hypertonic saline cards and 40 isotonic saline cards; 2) their study numbers were recorded on their own card; 3) patient brought the card to the assistant; 4) the assistant opened the card and gave non-label saline to the patient; 5) the card was returned to the sealed box by the assistant until analysis when all assessment parameters were completed by the researcher.

Intervention

Both saline nasal solutions were self-prepared by our pharmacy unit. Five hundred-milliliter glass bottles were chosen as the containers without any labels; however, the assistant was notified of the type of solution by preparation unit. Hypertonic solution was defined as composition of NaCl equal to 3%, and isotonic solution consisted of NaCl equal to 0.9%. Irrigation equipment consisted of 20-ml syringes with nose adaptors for rinsing nasal cavity. Saline was irrigated into both sides of the nose twice daily for a total volume 160 ml/day. The assistant demonstrated the steps of the irrigation procedure. All patients asked to stopped nasal irrigation when they noticed symptoms of poor tolerance, such as pain, nose bleeding, or other nasal discomfort.

Outcome assessment

The primary outcome in this study was nasal congestion, which was evaluated by subjective and objective assessment, while the secondary outcome of rhinorrhea was assessed only by subjective method. Measurement was performed at 3 points of time: baseline, at the end of the first week, and at the second week of nasal irrigation. Last nasal irrigation before testing was performed in the evening of the day before each visit. Visual analog scale (VAS) which offers ease of response, has a precise scaling of 0 to 10 and more specific to each nasal symptom was selected to be a subjective measurement. Nasal congestion visual analog scale (NCVAS) and rhinorrhea visual analog scale (RVAS) were used for obstruction and rhinorrhea assessment. Objective assessment can provide more accurate results than the subjective method. This study had 1 objective module which was peak nasal expiratory flow rate (PNEFR). PNEFR was the volume of expiratory flow, which was reported as liters per minute (L/min) in exact value. PNEFR was measured using a peak flow meter with anesthetic mask. Patients were asked to sit in the testing room for 30 minutes before testing to familiarize them with the atmosphere. The fitted anesthetic mask was applied to the nose. Then, the patient was asked to take a deep inspiration into the mouth, close the mouth, and breathe out forcefully through the nose. The test was repeated 3 times, and the best value was selected as the PNEFR result. The size of inferior turbinate which referred to total nasal space was modified from the study of Camacho et al.[18] Turbinate was grading from I-IV by anterior rhinoscopy assessment,[18] grade I was 0-25% of total airway space, grade II was 26-50% of total airway space, grade III was 51-75% of total airway space, and grade IV was 76-100% of total airway space. This study modified grading to scoring as 1 to 4 points, respectively: grade I for 1 point, grade II for 2 points, grade II for 3 points, and grade IV for 4 points. In addition, inferior turbinate size (ITS) was measured via flexible nasal endoscopy, and it was regarded as a subjective measurement.

Statistical analysis

Statistical methods were calculated using IBM SPSS Statistics for Windows, version 20 (IBM Crop). All continuous data were presented as mean; independent t-test and paired t-test were used to compare between group and same group means, respectively. However, for nonparametric variable, the statistical analysis was calculated by using Mann Whitney U test to compare difference between two groups median and Wilcoxson signed rank test to compare two related samples median. All categorical data were reported in percentage. Clinical data and disease variables were analyzed and compared between groups by calculating the odds ratio (OR) and 95% confidence interval (CI) univariate regression analyses to assess the significant difference. The chi-squared test and Fisher's exact test were used for the comparison. P-values less than 0.05 were considered significant.

Results

Eighty patients were eligible for this study. Patients were randomized in-to 2 groups equally. Intervention with 3% and 0.9% NaCl saline irrigation was assigned for each group. Subjective and objective outcome assessments were measured to identify the nasal congestion and rhinorrhea symptoms which were the outcome of this study. Baseline 1 and 2 weeks after starting the nasal irrigation measurement were performed in all patients with no drop out of participants. CONSORT flow chart is shown in **Figure 1**. Female sex was predominant, making up 63 cases (78.7%). Average age was 44.9 years old. The majority of patients present with normal range of BMI (68.7%). According to ARIA classification, 67.5% of participants were classified as mild intermittent, followed by 30% who were classified as moderate to severe intermittent, and only 2.5% were classified as having mild persistent symptoms. The average duration of symptoms was 5.4 years.

Baseline demographic data and clinical characteristic of each group are described in **Table 1**, which showed no statistical significance. The subjective scale before irrigation started was quite similar in both groups, with 8 of NCVAS, 8 of RVAS, and 3 of ITS. The objective assessed was also similar, with PNEFR reported as 60 L/min. At first week after using saline irrigation, patients reported satisfactory outcomes in both concentrations. (**Table 2**) Rhinorrhea evaluated by RVAS was personally minimized (p value < 0.001), while nasal congestion also improved by subjective (NCVAS) (p value < 0.001) and (ITS) measurement (p value < 0.001). Furthermore, PNEFR showed good results only in 3% NaCl irrigation (p value = 0.001). Second week evaluation demonstrated improvement of all assessment parameters in both hypertonic and isotonic solutions. (**Table 3**) However, when compared between groups for each parameter in the same period of times, no significant difference for all parameters were reported. (**Table 4**)

Two cases (5%) in the hypertonic saline noticed nasal discomfort (light pain sensation) after irrigation at first time but their spontaneous recovery. All patients tolerated nasal saline irrigation well. No adverse effects that interrupted the study was reported.

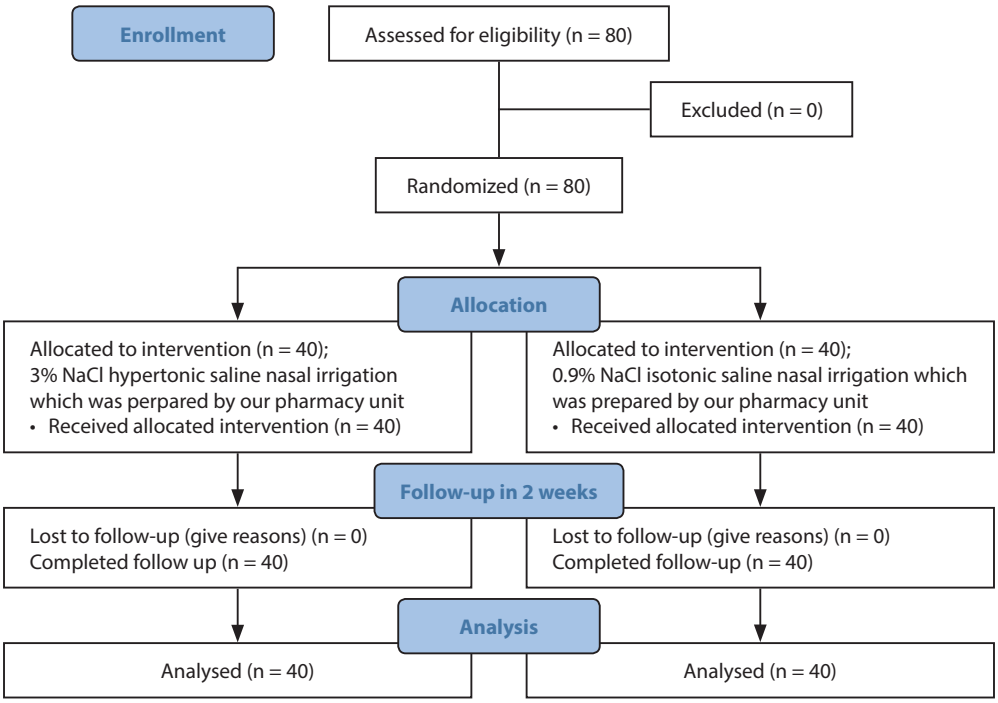

Figure 1. CONSORT flow diagram.

Table 1. Patient demographic data

Variable	3% NaCl	0.9% NaCl	*p* value	OR, 95%CI
Sex				
Male	9 (22.5)	8 (20)	0.900	0.969, (0.397-3.395)
Female	31 (77.5)	32 (80)		
Age (y) median (IQR)	43 (25.75)	43 (25.50)	0.634*	-
BMI				
Abnormal	15 (37.5)	10 (25)	0.230	0.556, (0.213-1.451)
Normal	25 (62.5)	30 (75)		
Duration of symptoms (y) median (IQR)	3 (7.25)	2.50 (6.75)	0.833*	-
ARIA classification				
Mild intermittent	27 (67.5) **	27 (67.5) **	0.734	0.846, (0.323-2.219)
Moderate-severe intermittent	11 (27.5) **	13 (32.5) **		
Mild persistent	2 (5) **	-		
Moderate-severe persistent	-	-		

IQR = interquartile range, BMI = body mass index, ARIA = Allergic Rhinitis and its Impact on Asthma
(*) Mann Whitney U test
(**) The patients received only oral antihistamine (without intranasal steroid spray)

Table 2. The comparison of outcome assessment at baseline and first week after saline nasal irrigation

Outcome assessment	Saline solution	Baseline	First week	*p* value
NCVAS; median (IQR)	3% NaCl	8 (2.50)	6 (3.00)	< 0.001**
	0.9% NaCl	8 (2.75)	5.50 (3.00)	< 0.001**
RVAS; median (IQR)	3% NaCl	8 (2.75)	6 (2.75)	< 0.001**
	0.9% NaCl	8 (1.00)	5.50 (3.00)	< 0.001**
ITS; median (IQR)	3% NaCl	3 (0.00)	2 (1.00)	< 0.001**
	0.9% NaCl	3 (1.00)	2 (1.00)	< 0.001**
PNEFR (L/min); median (IQR)	3% NaCl	60 (27.50)	70 (28.75)	0.001**
	0.9% NaCl	60 (20.00)	65 (25.00)	0.083**

NCVAS = nasal congestion visual analog scale, IQR = interquartile range, RVAS = rhinorrhea visual analog scale, ITS = inferior turbinate size, PNEFR = peak nasal expiratory flow rate
(**) Wilcoxson signed rank test

Table 3. The comparison of outcome assessment at baseline and second week after saline nasal irrigation

Outcome assessment	Saline solution	Baseline	Second week	*p* value
NCVAS; median (IQR)	3% NaCl	8 (2.50)	4 (2.00)	< 0.001**
	0.9% NaCl	8 (2.75)	4 (2.75)	< 0.001**
RVAS; median (IQR)	3% NaCl	8 (2.75)	4 (2.00)	< 0.001**
	0.9% NaCl	8 (1.00)	4 (3.00)	< 0.001**
ITS; median (IQR)	3% NaCl	3 (0.00)	1 (1.00)	< 0.001**
	0.9% NaCl	3 (1.00)	1 (1.00)	< 0.001**
PNEFR (L/min); median (IQR)	3% NaCl	60 (27.50)	75 (25.00)	< 0.001**
	0.9% NaCl	60 (20.00)	75 (30.00)	< 0.001**

NCVAS = nasal congestion visual analog scale, IQR = interquartile range, RVAS = rhinorrhea visual analog scale, ITS = inferior turbinate size, PNEFR = peak nasal expiratory flow rate
(**) Wilcoxson signed rank test

Table 4. Outcome assessment between 3% NaCl and 0.9% NaCl nasal irrigation at baseline, 1 week, and 2 weeks after starting the irrigation in the same period of time

Outcome assessment	3% NaCl	0.9% NaCl	*p* value
NCVAS; median (IQR)			
baseline	8 (2.50)	8 (2.75)	0.854*
1 week	6 (3.00)	5.50 (3.00)	0.440*
2 weeks	4 (2.00)	4 (2.75)	0.918*
RVAS; median (IQR)			
baseline	8 (2.75)	8 (1.00)	0.557*
1 week	6 (2.75)	5.50 (3.00)	0.542*
2 weeks	4 (2.00)	4 (3.00)	0.304*
ITS; median (IQR)			
baseline	3 (0.00)	3 (1.00)	0.175*
1 week	2 (1.00)	2 (1.00)	0.071*
2 weeks	1 (1.00)	1 (1.00)	0.759*
PNEFR (L/min); median (IQR)			
baseline	60 (27.50)	60 (20.00)	0.934*
1 week	70 (28.75)	65 (25.00)	0.656*
2 weeks	75 (25.00)	75 (30)	0.572*

NCVAS = nasal congestion visual analog scale, IQR = interquartile range, RVAS = rhinorrhea visual analog scale, ITS = inferior turbinate size, PNEFR = peak nasal expiratory flow rate
(*) Mann Whitney U test

Discussion

Saline solution is commonly used for nasal irrigation in allergic rhinitis patients to decrease nasal symptoms and minimize over-usage of medication. The authors also encouraged that nasal saline irrigation is actually an add-on intervention according to there is not present in the ARIA standard treatment guideline. As presented in several medical studies,[9-11,13] researchers have discovered an appropriate saline concentration for allergic patients; however, no definite recommendation was reported. Either isotonic saline solution, which has a composition of NaCl equal to 0.9%, or hypertonic saline solution, which consists of NaCl more than 0.9%, are widely accepted for irrigation. The hypertonic solution is prepared in several concentration of NaCl from 1.25 to 3%.[9-11,13] Prior studies identified the satisfactory results in different hypertonic solutions compared to isotonic saline, including 1.25% NaCl buffered with baking soda,[11] 1.8% NaCl,[13] 2.7% NaCl,[10] and 3% NaCl.[9] However, higher concentrations than 3% of NaCl were not recommended.[15] The study of 5.4% NaCl showed that hypertonic saline leads to substance P release and glandular secretion, stimulates nociceptive nerves and induces pain, rhinorrhea and nasal obstruction.[19] On the other hand, some studies didn't show different outcomes when the nose was irrigated by hypertonic or isotonic saline.[20-23] In 2003, prospective, randomized, investigator-blinded study showed both hypertonic and isotonic solution decreased rhinorrhea, however, only hypertonic solution improved nasal congestion.[23] This study also showed similar results between hypertonic and isotonic solution as an evidenced by decreased rhinorrhea in both groups without any significant difference. In contrast, either hypertonic or isotonic solution can minimized nasal congestion in this study. In addition, further reason that made this study's result didn't show any different of add-on treatment with hypertonic and isotonic nasal irrigation might be from; an approximated 70% of the patients were presented with intermittent allergic rhinitis and they were prescribed oral antihistamine which was acknowledged as an effective treatment for intermittent symptoms. Nevertheless, first week results also ensured that hypertonic saline had slight benefits to relieve nasal obstruction earlier than isotonic solution when measured by objective assessment method resulting in PNEFR.

A methodology of allergic rhinitis treatment outcome assessment is also important. Although objective measurement gives more reliability, subjective testing is also extensively used. Total nasal symptom score (TNSS) was utilized in prior studies to assess the treatment outcome.[10,11,13] The main objective of this study was the effect of saline irrigation on nasal congestion and rhinorrhea; therefore, NCVAS and RVAS were chosen to be evaluated parameters. Furthermore, a precise score from 0 to 10 provided an accurate outcome.[24,25] A disadvantage of subjective assessment was reported, especially in pediatric patients, because it depends on assessor experience.[26] Rhinomanometry is the gold standard to objectively assess.[27,28] However, it is expensive and has a complicated technique.[27,28] Further equipment, such as peak nasal inspiratory flow meter[28-30] and peak flow meter with anesthetic mask[30-32] were adjusted for more practical usages. This study preferred peak flow meter with anesthetic mask as an assessment tool because of an availability in primary and secondary care hospital and utilization for evaluating nasal obstruction. This device provided PNEFR results, which were used to compare the nasal expiratory flow rate before and after allergic rhinitis treatment, similar to the prior studies that measured peak expiratory flow rate in allergic rhinitis patients.[30-32] Additionally, this study had one more precise subjective assessment method, ITS scoring performed by flexible nasal endoscope, that reflected the degree of nasal congestion. Camacho et al[18] developed grading of ITS and classified them as total airway space with grade I (0-25% of total airway space), grade II (26-50% of total airway space), grade III (51-75% of total airway space), and grade IV (76-100% of total airway space) by anterior rhinoscopy technique. This study modified their grading to scoring as 1 to 4 points, respectively. Flexible nasal endoscopy was used to assess the total airway space because this procedure provided more detail of the Cottles area,[33] entire nasal cavity, and accuracy of nasal information. In their study, Abou-Elhamd KE et al[34] mentioned an advantage of flexible endoscopy in identified obstruction area at posterior end of inferior turbinated. van Spronsen et al reported in 2008[24] that nasal endoscopy is subjective in nature; however, standardized scoring methods performed by physicians using validated scales are an objective measurement. Krouse et al[35] also agree that nasal endoscopy was an objective assessment method that cannot be achieved by conventional anterior rhinoscopy.

Adverse effects from nasal irrigation using any concentration of saline solution were minimal, as reported previously, and included irritation, nasal discomfort, otalgia, and pooling of saline in sinus cavity.[9-11,13,15] Mild side effects always presented with short duration and spontaneous recovery within a few days[10] to two weeks[11,13] after starting the irrigation. Furthermore, no serious adverse reaction which interrupted nasal irrigation procedure was detected.[9-11,13,15] This study finding also agreed with reports of transient adverse reactions. Only 5% of the hypertonic group reported mild nasal discomfort on the first day of the procedure. On the other hand, adverse effects were more common (10-20% of cases) when very high-volume devices (more than 100 ml/time) were used.[15] Saline volume of 20 ml/time was preferred in this study, and nasal adaptors were also applied to syringes to create more suitable irrigation devices. The majority of patients in this study tolerated irrigation procedures well.

The limitations of this study included 1) small population enrollment, 2) short duration of follow-up and 3) peak flow meter with anesthetic mask is not a gold standard device for assess the nasal patency. However, the study highlights were assessment methods. Subjective assessment by VAS offered ease of response, more precise scaling, and specific to each nasal symptom, while ITS with flexible nasal endoscopy also provided more precise detail than conventional anterior rhinoscopy. And objective evaluation by PNEFR with peak flow meter and anesthetic mask also identified the alteration of nasal symptoms after nasal irrigation.

Conclusion

Both hypertonic saline or normal saline as add-on treatments have a significant improvement of all 4 parameters assessed in the study: nasal congestion, rhinorrhea, inferior turbinate size and PNEFR. Of note, 3% NaCl but not 0.9% NaCl had improved the PNEFR (L/min) earlier from 1 week of the treatment. A 20-ml syringe with nasal adaptor appliance was preferred as an irrigation device with good compliance. Finally, this study of objective assessment equipment is more practical for primary and secondary health-care settings.

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Conflict of interest

The author has no conflict of interest in the past 3 years.

Author contribution

- Kedsaraporn yata: responsible for conception, design of this work, assessment/collect/interpretation the data, data analysis, writing the first draft of manuscript, approve the submitted version and any substantially modified version.
- Chonticha srivanitchapoom: responsible for data analysis, critic and edit the submitted version.

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