Postoperative nasal irrigation with hypertonic saline versus adding mucolytic agents: cohort prospective study

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Received 06 December 2020
Revised 09 December 2020
Accepted 07 January 2021
Published 09 August 2021

Pan Arab Journal of Rhinology
2021, 11:47–53

Objective

This cohort prospective intervention study was initiated to investigate the effectiveness of mucolytic nasal wash on postoperative healing after endoscopic nasal surgery (ENS).

Patients and methods

A total of 60 patients of both sexes, above 21 years, underwent ENS, who were randomly distributed into two groups according to inclusion and exclusion criteria, with 30 patients each. Postoperative hypertonic saline nasal irrigation was used for group A, and in addition of N-acetylcysteine (NAC) in group B. Measurement of outcome was done using modified Symptom based Modified Sino-Nasal-Outcome Test score-22 and Lund–Kennedy endoscopic score.

Results

We noticed that nasal irrigation with combined hypertonic saline with NAC is effective in reducing postoperative symptoms scores and endoscopic scores for patients following ENS or functional endoscopic sinus surgery.

Conclusion

NAC combined hypertonic saline irrigation had significant better results than standard hypertonic saline nasal irrigation only following endoscopic sinus surgery, significantly improving patient's quality of life.

Keywords:

endoscopic sinus surgery, functional endoscopic sinus surgery, hypertonic saline, N-acetylcysteine

Pan Arab J Rhinol 11:47–53
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Background

For many years, ENT surgeons all over the world used postoperative nasal irrigation after nasal surgeries, and it became one of the standard postoperative procedures. After introducing endoscopic nasal surgery (ENS), the need for effective irrigation that removes debris, crusts, liquefies mucus, and washes organisms as well as causes changes in their growth environment became more mandatory for effective healing and improving quality of life (QOL) of patients [1].

Isotonic saline nasal irrigation has been considered as one of the oldest methods after nasal surgeries as it is an easy used and cheap preparation. Its use was restricted, as it inhibits mucociliary beating and was less effective in reducing tissue edema and crust removal [2].

Hypertonic nasal washes were found to produce an obvious statistically significant beneficial effect resulting in the relief of discomfort caused by crusting and accumulation of abnormal nasal discharge after functional endoscopic sinus surgery. It was recommended for nasal douching after corrective nasal septal surgery (septoplasty), functional endoscopic sinus surgery, and surgical removal of nasal polyps (polypectomy). The use of hypertonic wash facilitates maintenance of normal patency of the nasal cavities, reduces tissue edema, improves mucociliary mechanisms, reduce biofilm formation, and speeds up healing of iatrogenic injuries of the mucous membrane of the nose [3].

The only disadvantage of hypertonic solutions is mild nasal irritation and burning sensation at the start of use; usually most of the patients rapidly accommodates with this [4].

Although there is a wealth of literature available, the establishment of treatment protocol can be difficult because of the great variability in recommended composition (normal and hypertonic saline, sea water, with or without additives), and the technique of irrigation, its pressure, frequency, and volume.

Adding mucolytics seems to be an elegant idea which logically goes with all the purposes needed for complete effective postoperative nasal care and rapid healing after ENS.

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Hypertonic saline (2.3%) was the most recommended following ENS, with very few papers using mucolytics in addition. N-acetylcysteine (NAC) could be considered a mucolytic drug of choice owing to its availability, multiple forms, low price, easy use, and high safety profile [5,6].

This cohort prospective comparative intervention study was initiated to investigate the effectiveness and added value of mucolytics combined hypertonic saline nasal wash versus hypertonic saline alone following ENS.

Patients and methods

This study was conducted in ENT Department, Dallah Hospital, KSA, and was designed to include 60 adult patients undergoing ENS during the period between March 2017 and March 2019. It included all patients who agreed to join the study and signed a clear informed consent, after providing them with complete information about protocol, benefits, and risks. The study was approved by the hospital medical ethical committee.

Patients fulfilling inclusion and exclusion criteria (Table 1) were divided randomly in a parallel assignment into two groups, with 30 patients each, using a computer software program, and the box containing the bottles was the same, regardless which one was used.

Group A included 30 who had irrigation with hypertonic saline 2.3%, with 20 ml for each nostril three times daily (hypertonic saline poured and delivered using commercially manufactured bottles) (Fig 1).

Group B included 30 patients who had irrigation with hypertonic saline and mucolytics (NAC powder 200 mg dissolved in 200 ml hypertonic saline used in other group), with 20 ml for each nostril three times daily (hypertonic saline poured and delivered using commercially manufactured bottles).

All medication was used for 6 weeks postoperatively, and patients were instructed regarding the correct irrigation technique before discharge from the hospital and remained in each clinic follow-up.

Outcome assessment was subjectively done using Symptom based Modified Sino-Nasal-Outcome Test scores (SNOT-7). We selected seven main symptoms, as they were most reliable, creditable, clear, and consistent with the subject of this research (Table 2). For objective outcome, we found sign-based endoscopic scoring system by Lund–Kennedy the most simple and informative without a lot of gray zones (Table 3).

Statistical analysis of the collected data was done by using SPSS, version 17 (Chicago, IL, USA). Quantitative data were presented as mean and SD and were analyzed by using one-way analysis of variance test. Qualitative data were presented as numbers and percentages and were analyzed by using χ^2 test and Fisher extract test. *P* value less than 0.05 was considered significant, whereas *P* value less than 0.01 was considered highly significant.

Table 1 Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Age over 21and below 60 years	Allergy to N-acetylcysteine
	Inflammatory nasal pathology (Wegener, sarcoidosis, etc.)
Patients undergoing ENS for chronic sinusitis, nasal polyposis, septoplasty, and turbinectomy (either separately or combined)	Systemic nasal affection (cystic fibrosis, Kartagener, etc.)
	Nasal tumor surgery or proved postoperatively
	Previous radiotherapy to the head and neck
	Revision surgery

ENS, endoscopic nasal surgery.

Table 2 Symptom based Modified Sino-Nasal-Outcome Test-7) Questionnaire [7]

	No problem	Very mild problem	Mild or slight problem	Moderate problem	Sever problem	Problem as bad as it can be	Important notes
Need to blow nose	0	1	2	3	4	5	
Nasal obstruction	0	1	2	3	4	5	
Loss of smell or taste	0	1	2	3	4	5	
Postnasal discharge	0	1	2	3	4	5	
Thick nasal discharge	0	1	2	3	4	5	
Facial pain	0	1	2	3	4	5	
Sleep-related difficulties	0	1	2	3	4	5	
Total score							

Results

Although during this study we did parallel randomization, the results regarding age and sex showed no significant statistical difference between groups A and B (Tables 4 and 5).

The first main arm of postoperative assessment in this study was the subjective symptomatic improvement or complications based on our modification of SNOT-test. Seven main symptoms that were most relevant to this study were as much as possible effectively and accurately obtained and subjected to relevant statistical analysis.

We found significant statistical difference favoring group B (added mucolytic) in postoperative subjective improvement. Group B showed more significant improvement with less need to blow the nose, less postnasal discharge both in amount and thickness, more open nose, less facial pain, more good smelling ability, and more improvement regarding the total score (in the main three follow-up timings at 15, 30, and 45 days postoperatively).

Regarding the snoring, both groups showed no significant difference (Table 6).

The second arm was the objective postoperative endoscopic assessment using Lund–Kennedy scoring, where group B (added mucolytics) showed more significant improvement including less nasal mucosal edema with more patent nose, less accumulated discharge, and less crusting, with more better total score.

In both groups until the end of follow-up period for at least 6 months, no patient was found to have permanent adhesions or nasal polyp recurrence (Table 7 and Figs. 2–5).

Figure 1

Commercially used bottles for nasal irrigation.

Discussion

Postoperative follow-up for endoscopic sinus surgery was a very important issue and also considered as important as surgery. This was done mainly by suction and debridement during endoscopic examination, combined with irrigation of the nose and paranasal sinuses [9].

Suction and irrigation remove any blood clot, crust, and fibrin, thereby preventing adhesion postoperatively. Hypertonic saline now provides more efficacy and safety in postoperative nasal irrigation than normal saline, with less defaults like nasal irritation and burning sensation [10–13].

The mucolytic effect of NAC is explained by its thiol (sulfhydryl) groups ‘hydrolyze disulfide bonds of mucins and other proteins.’ Acetylcysteine is also an antioxidant and reduces oxidative stress, had rapid healing neuropsychotropic effects, and lastly, acetylcysteine also possesses some anti-inflammatory effects possibly via inhibiting NF-KB through redox activation of the nuclear factor kappa kinases, thereby modulating cytokine synthesis in addition to inhibition of biofilm formation, which contributes to chronicity of infection [14,15].

Our results were independent of demographic variables. We used strict inclusion and exclusion criteria, and all operations were performed by the same technique to prevent the introduction of confounding factors and to ensure standardization, which decrease bias.

During preparation for this study, we excluded patients with granulomas, tumors, systemic nasal affection,

Table 3 Sign-based scoring (Lund-Kennedy endoscopic score): it was applied to each side of the nose using endoscopic examination [8]

	Grade 0	Grade 1	Grade 2
Edema	None	Mild	Severe
Discharge	None	Clear/thin	Thick/purulent
Crusts	None	Middle meatus (MM) only	Beyond MM
Adhesion	None	MM only	Beyond MM
Polyps	None	MM only	Beyond MM

Table 4 Comparison between the study groups regarding age

Group	Mean±SD	*t*	*P*	Significance
A	35.5±1.75	−1.52	0.133	Non
B	36.2±1.81			

Table 5 Comparison between the study groups regarding sex

	Sex		χ^2 test	*P*	Significance
	Female	Male			
Group					Non
A	19	11		0.300	0.584
B	21	9			

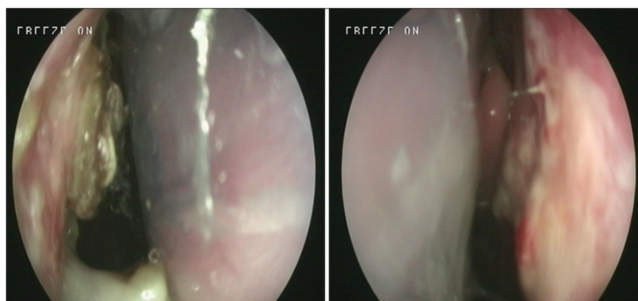
Table 6 Collective comparative postoperative subjective scoring results using modified Symptom based Modified Sino-Nasal-Outcome Test score-7 test with its statistical analysis and *P* significance value in the main three postoperative assessment visits

	After 15 days				30 up to 45 days				After 45 days			
	Group A	Group B	*t*	*P*	Group A	Group B	*t*	*P*	Group A	Group B	*t*	*P*
Need to blow the nose	4.73±1.7	3.67±1.1	2.79	0.008<0.01	3.68±1.5	2.81±1.8	2.03	0.047<0.05	1.4±1.3	0.47±1.7	2.38	0.021<0.05
Nose block	4.07±0.2	2.2±0.6	22.9	0.001<0.01	2.4±0.5	1.07±0.6	9.33	0.001<0.01	0.97±0.7	0.10±0.9	4.18	0.001<0.01
Postnasal discharge	3.07±0.22	1.07±0.25	31.25	0.001<0.01	2.03±0.43	0.30±0.48	17.48	0.001<0.01	0.97±0.32	0.67±0.23	4.17	0.001<0.01
Thick discharge	4.87±0.90	2.9±0.70	9.46	0.001<0.01	2.9±0.34	0.53±0.22	32.05	0.001<0.01	0.73±0.67	0.10±0.54	4.01	0.001<0.01
Facial pain	3.73±0.47	3.00±0.52	5.70	0.001<0.01	2.03±0.51	0.70±0.63	8.99	0.001<0.01	0.30±0.41	0.033±0.38	2.62	0.011<0.05
Smell	3.37±0.42	2.57±0.33	8.2	0.001<0.01	1.13±0.31	0.63±0.43	6.15	0.001<0.01	0.23±0.20	0.10±0.25	2.22	0.030<0.05
Sleep diff.	2.57±0.22	2.35±0.3	1.411	0.157>0.05	0.57±0.25	0.49±0.23	1.15	0.108>0.05	0.13±0.15	0.12±0.59	0.87	0.286>0.05
Total score	3.79±0.59	2.48±0.54	8.97	0.001<0.01	2.11±0.55	0.92±0.45	9.17	0.001<0.01	0.68±0.15	0.22±0.13	12.69	0.001<0.05

Table 7 Collective comparative postoperative objective scoring results using Lund-Kennedy endoscopic scoring system with its statistical analysis and *P* significance value in the main three postoperative assessment visits

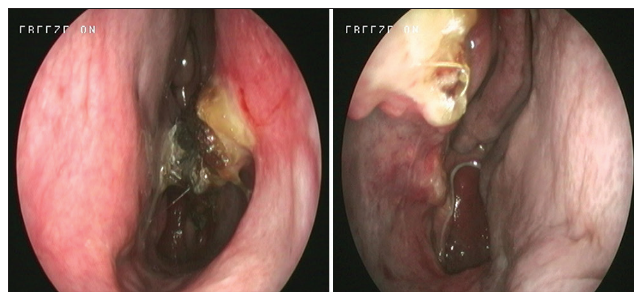
	After 15 days				30 up to 45 days				After 45 days			
	Group A	Group B	*t*	*P*	Group A	Group B	*t*	*P*	Group A	Group B	*t*	*P*
Nasal mucosa edema	1.90±0.39	1.36±0.30	6.01	0.001<0.01	1.3±0.29	0.367±0.22	14.02	0.001<0.01	0.33±0.54	0.067±0.15	6.57	0.001<0.01
Nasal discharge.	1.87±0.35	1.43±0.32	5.08	0.001<0.01	1.067±0.27	0.267±0.21	12.81	0.001<0.01	0.30±0.14	0.067±0.15	6.22	0.001<0.01
Crusts	1.97±0.33	1.43±0.3	6.63	0.001<0.01	1.23±0.24	0.37±0.23	14.17	0.001<0.01	0.40±0.11	0.033±0.12	12.35	0.000<0.01
Adhesion	0	0		NA	0	0		NA	0	0		NA
Polyps	0	0		NA	0	0		NA	0	0		NA
Total score	1.913±0.356	1.109±0.306	9.38	0.001<0.01	1.999±0.266	0.334±0.220	13.37	0.0001<0.01	0.343±0.263	0.055±0.140	5.29	0.001<0.01

Figure 2



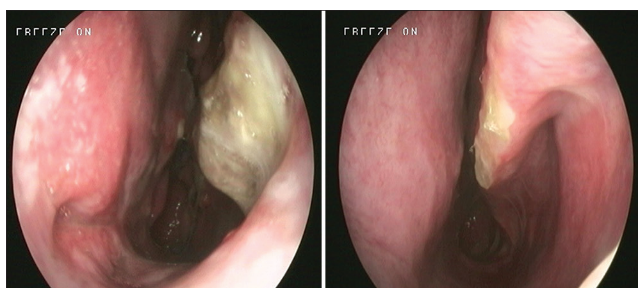
(a and b) Early postoperative endoscopic view with splints in both groups.

Figure 3



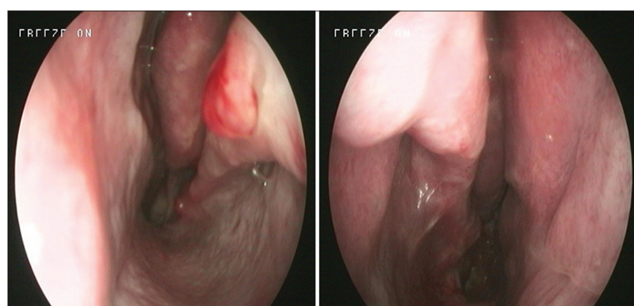
(a and b) 15-day postoperative endoscopic view in both groups.

Figure 4



(a and b) 30-day postoperative endoscopic view in both groups.

Figure 5



(a and b) 45-day postoperative endoscopic view in both groups.

and revision nasal surgery. These disorders need wide surgical field and extensive resection, with subsequent severe crustations, thereby delaying healing, with consequent bias of results.

Most of literature agreed to use hypertonic saline (2.3% NaCl) as a standard irrigation concentration, with 20 ml at least for each nostril. We used the same standard three times daily procedure, which we think was sufficient for effective irrigation and cleaning of nasal mucosa.

Our colleagues in biochemistry advised NAC concentration not exceeding 200 mg/200 ml hypertonic saline, as this was proved effective in mucolytic function and did not alter the tonicity of the solution.

We started first follow-up assessment after 2 weeks from surgery when all packs and splints were removed to avoid their conflict over the results, and then ended in 6 weeks, where healing was stabilized and crustations stopped, and results from this time onward are dependent on many factors other than irrigation.

For standardization purpose, we used the same commercially available bottle for all patients of both groups, to ensure same irrigation pattern and volume.

In literature, nasal symptoms were best assessed with SNOT-22. It was the most used questionnaire, with good consistency, reliability, and reproducibility in literature. It is important in studying patient's QOL outcomes and subjective perception of improvement. We selected even symptoms, as they were most reliable, creditable, clear, and consistent with the subject of this research.

Moreover, we found that Lund–Kennedy endoscopic sign-based scale was most simple, informative, rapid to do, and none conflicting more details which will not add to outcome.

In this study, effective randomization was done, with no significant differences between the two groups regarding age and sex.

Most of studies about postoperative nasal irrigation such as Talbot *et al.*[16] and Keojampa *et al.*[4] agreed that the use of hypertonic saline for nasal irrigation has better outcome of mucociliary clearance by decrease in edema and inflammation and softening of the secretion owing to its alkaline nature. Moreover, hypertonic saline was found to increase Ca release from the intracellular stores stimulating the ciliary beat by regulating the use of adenosine triphosphate [17]. This also agreed with Kumar *et al.* [18]. Nasal irrigation after endoscopic sinus surgery is effective in symptom resolution and normalization of mucosa appearance. Hypertonic saline irrigation was significantly more effective as compared with isotonic saline.

Moreover, Kurtaran *et al.* [19], reported hypertonic sea water, especially 2.3%, is the best solution for relieving

nasal crusting, dryness, and obstruction following septoplasty and concha radiofrequency.

Robinson *et al*.[20] and Homer *et al*.[21] reported that the use of hypertonic saline has steadily increased because it reduces edema and increases mucociliary clearance.

The use of hypertonic saline with NAC had more significant effect in improving postoperative symptoms like need to blow the nose, nasal blockage, postnasal discharge, thick nasal discharge, decrease sense of smell, and facial pain. All were highly improved with addition of NAC to the hypertonic solution, with a great effect on patient's QOL.

Only the sleep-related symptoms were found not significant between the two groups. This could be related to its multifactorial predisposition.

The total score of modified SNOT-7 was significantly improved in the NAC group. This could be attributed to decrease in edema by its anti-inflammatory effect and decrease the viscosity of secretion and increase the mucociliary clearance.

In this study, nasal mucosal edema, discharge, and crusts all showed more significant improvement with the use of hypertonic saline with mucolytic NAC than hypertonic nasal saline irrigation alone. Adhesion and recurrent polyposis in the first 6 weeks fortunately did not happen in both groups.

NAC decreases inflammation and goblet cell loss. Therefore, NAC has potential beneficial effects on the wound healing of nasal mucosa [22].

Moreover, (Hubert) Low *et al*. [23], reported hypertonic saline solution resulted in the quicker resolution of polypoidal mucosa. This finding is consistent with other studies where nasal irrigation with hypertonic solution with NAC resulted in improved radiological appearances of the sinuses among patients with chronic rhinosinusitis.

The use of hypertonic saline with mucolytics is considered a safe method for postoperative nasal irrigation with no adverse effects. Occasionally patients felt some discomfort, but it is a well-tolerated therapy, comfortable, convenient, available, easy use, low cost, safe, and effective. We did not perceive any risks with this combination.

Conclusion

From this study, the use of combination of hypertonic saline and mucolytics is effective to improve QOL and reducing postoperative symptoms as assessed by modified SNTO-7 score and reducing postoperative signs as assessed by Lund–Kennedy endoscopic score.

Acknowledgements

The authors thank Dr Salah Ramadan, Asst. Prof. at Cairo University, for his help and effort in data analysis and statistics interpretation. He was so helpful and cooperative.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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