Askoura *et al.*
The Egyptian Journal of Otolaryngology (2023) 39:51
https://doi.org/10.1186/s43163-023-00414-2

The Egyptian Journal of Otolaryngology

ORIGINAL ARTICLE Open Access

Effect of topical anticholinergic medication on clinical manifestations control among patients with vasomotor rhinitis versus allergic rhinitis: as comparative clinical trials

Anas Mohamed Askoura[1], Sabry Magdy Sabry[1], Samia Ahmed Fawaz[1], Manal Ibrahim Salman[2], Moustafa Ahmed Mahmoud Anter El sordy[1*] and Ossama Mustafa Mady[1]

Abstract

Background The use of a topical anticholinergic medication, ipratropium bromide, and its ability to inhibit methacholine and rhinitis-induced hypersecretion is emphasized. Ipratropium bromide appears to be both safe and effective in reducing this troublesome symptom. This study is designed to show the therapeutic effect of anticholinergic local treatment on nasal mucosa in patients with vasomotor rhinitis.

Objective To assess the therapeutic effect of local anticholinergic treatment on nasal mucosa in patients with vasomotor rhinitis compared to non-vasomotor (allergic) patients and normal individuals, and if there any down regulation of the muscarinic receptors or not.

Patients and methods This prospective intervention study was conducted in Otorhinolaryngology Department, Faculty of Medicine, Ain Shams University. This study was conducted on 60 cases. All patients were divided into 3 groups: study group (1) includes 20 patients diagnosed clinically non-allergic rhinitis suggestive to be vasomotor rhinitis. Study group (2) includes 20 patients diagnosed as allergic rhinitis. Study group (3) includes 20 patients performing surgery for non-vasomotor rhinitis non-allergic causes (as septoplasty or rhinoplasty).

Results Comparison between the pre- and post-SNOT questionnaire of symptoms among vasomotor group showed that there was a significant difference between the pre- and post-treatment SNOT questionnaire symptoms; nasal obstruction, runny nose, post-nasal drip, thick nasal discharge and Lack of good night sleep. Among allergic cases group, there was a significant difference between the pre- and post-treatment IHC (immunohistochemistry) findings considering Epithelium, Glands, arteries and veins. 20% of cases had grade 3 epithelium before treatment while after treatment, this was dropped to 0%. Comparison between the pre- and post-SNOT questionnaire of symptoms among allergic group showed that there was a significant difference between the pre- and post-treatment SNOT questionnaire symptoms; runny nose, post-nasal drip, and thick nasal discharge. Among non-vasomotor rhinitis non-allergic causes (as septoplasty or rhinoplasty) group, there was a significant difference between the pre- and post-treatment IHC findings considering epithelium, glands, and arteries; however, no significant difference between the pre- and

*Correspondence:
Moustafa Ahmed Mahmoud Anter El sordy
Moustafasordy1@gmail.com
Full list of author information is available at the end of the article

post-IHC veins grade. Also, there was no significant difference between the pre- and post-treatment SNOT questionnaire symptoms.

Conclusion Topical anticholinergics such as ipratropium bromide nasal spray are effective in treating rhinorrhea symptoms in allergic and non-allergic rhinitis. Further controlled studies with larger sample size and longer follow-up are needed to confirm our results and to identify risk factors of adverse events.

Keywords Allergic rhinitis, Vasomotor rhinitis, SNOT 10, Topical anticholinergic, Ipratropium bromide

Background

Vasomotor rhinitis is a non-infectious non-allergic disease, which is characterized by nasal hyper reactivity resulting in symptoms of nasal obstruction, rhinorrhea, and sneezing, which are often indistinguishable from nasal symptoms of allergic rhinitis. Diagnosis of Vasomotor rhinitis is established on the basis of persistent symptoms all over the year after exclusion of infection, any medical or anatomical disorder of the nose, and negative skin prick test for IgE-mediated hypersensitivity to relevant aeroallergens [1].

Acetylcholine from post-ganglionic nerve-endings has an important role in pathophysiology. There are five subtypes of muscarinic receptor, labeled M1 to M5. M1, M2, and M3 receptors are found on glands, epithelium, veins, and arteries. M4 receptors are found on arteries, and M5 receptors are found on arteries and glands. M3 subtype is the most common one [2]. M1, M3, and M5 subtypes couple to the inositol polyphosphate, while M2 and M4 subtypes inhibit the production of cAMP [3].

Anticholinergic drugs are consequently useful in treating rhinorrhea in patients with rhinitis. The effectiveness and tolerability profiles were demonstrated in clinical trials, both in long-term treatment [4] and within the prevention of excessive rhinorrhea induced by methacholine [5]. Additionally, the intranasal ipratropium bromide provides good relief of rhinorrhea in the common cold [6]. Recently, a new preparation nasal spray of ipratropium bromide, a solution delivered by a metered pump, has been developed without the usage of potentially ozone-depleting propellants. The aim of that study was to assess whether pretreatment with intranasal ipratropium bromide aqueous spray could prevent the rhinorrhea of vasomotor rhinitis.

Aim of the work

This study is designed to assess the therapeutic effect of local anticholinergic treatment on nasal mucosa in patients with vasomotor rhinitis compared to non-vasomotor (allergic) patients and normal individuals, and if there any upregulation of the muscarinic receptors or not.

Patients and methods

Type of study

Prospective intervention study

Study setting

Otorhinolaryngology Department, Faculty of Medicine, Ain Shams University.

Study population

Inclusion criteria

All adult patients with vasomotor rhinitis and allergic rhinitis and control group from 18 to 50 years old.

Exclusion criteria

Acute sinusitis. Invasive acute or chronic fungal sinusitis. Chronic granulomatous inflammations. Use of oral or nasal steroids for at least 2 months. Hypertensive patients. Ischemic heart diseases. Local decongestant agents' abuser.

Sampling method

The current study consists of study group (1), which includes 20 patients diagnosed clinically non-allergic rhinitis suggestive to be vasomotor rhinitis. Study group (2) includes 20 patients diagnosed as allergic rhinitis. Study group (3) includes 20 patients performing surgery for non-vasomotor rhinitis non-allergic causes.

Ethical considerations

All patients will be subjected to the following protocol after taking their written consent. approved by an ethical committee before the start of the recruitment (FMASU M D 406/2019).

Study procedures

All patients will be subjected to the following protocol. Full history taking (allergy history, asthma, aspirin sensitivity, and tobacco use) with emphasis on vasomotor rhinitis symptoms. Total IgE levels to suggest symptoms. Otorhinolaryngological examination and endoscopic examination of the nasal cavity to exclude

comorbidities. Biopsy will be obtained from mucosa of inferior turbinate of these patient before any medical treatment under local anesthesia at outpatient clinic. Another biopsy will be obtained from the same patient under general anesthesia after 3 months of local anticholinergic treatment as atrovent (ipratropium bromide) Nasal spray 0.06% 42 mcg/spray with dose of two sprays (84 mcg) per nostril three times daily. Nasal symptomatology will be assessed using the standardized SNOT 22 evaluation score. Nasal tissues collected then embedded in paraffin will be cut into sections. Hematoxylin-eosin (HE) staining is routinely performed for histological examination, and then IHC staining will be performed using muscarinic acetylcholine receptor antibody from Abbexa Ltd., as an objective assessment pre- and post-medical ttt and divided into semi quantitative scores for staining of muscarinic receptor in human inferior turbinate mucosa into grade 0 negative, grade 1 recognizably positive, grade 2 clearly positive, and grade 3 excessively positive.

Data management and analysis

The collected data was reviewed, coded, arranged, and introduced to a PC using Statistical package for the Social Science (IBM Corp., Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). The data was presented and appropriate analysis was done along with the type of data gained for each parameter.

Descriptive statistics

Shapiro-Wilk's test was used to evaluate normal distribution of continuous data. Mean, standard deviation (±SD), and range was used for parametric numerical data. Frequency and percentage of non-numerical data.

Analytical statistics

ANOVA test was used to assess the statistical significance of the difference between more than two study group means. Chi-square test that was used to examine the association between two qualitative variables. Fisher's exact test was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells. Wilcoxon signed rank test used to assess statistical significance of the alteration of an ordinal variable (score) measured two times for the same study group. McNemar test was used to assess the significance of the alteration between the qualitative variable that measured two times in the same study group. P value was used to determine the level of significance: $P > 0.05$: non-significant (NS), $P < 0.05$: significant (S), and $P < 0.01$: highly significant (HS).

Results

This study enrolled three groups:

Group 1 (vasomotor group)
Group 2 (allergic group)
Group 3 (control group)

Discussion

Chronic rhinitis is persistent inflammation of the mucosa of the nasal cavity and is clinically classified to non-allergic, allergic, or mixed (both allergic and non-allergic triggers) etiologies [7]. Trademark symptoms of rhinitis include nasal blockage or congestion, nasal discharge (anterior and/or posterior), facial pain or facial pressure, and dysosmia [8].

Allergic rhinitis (AR), is the most common and recognizable phenotype, which linked to an immunoglobulin E-mediated inflammatory response resulting in swelling and hyperreactivity of the mucosa [9]. Non-allergic rhinitis (NAR) is a mixed collection of distinct pathophysiological subtypes causing rhinologic symptoms, in the absence of allergic inductions [10].

Muscarinic or acetylcholine receptors play a significant role in glandular secretion and vasomotor dilation to blood vessels in the human nasal mucosa [11]. Anticholinergics serve to inhibit the binding of acetylcholine, thus preventing downstream cholinergic activation of the parasympathetic mucosal secretion and inflammation. Intranasal anticholinergic sprays lately became more and more investigated therapy for potential mucin-reducing effects on the mucosa in chronic rhinitis patients. Blockage of these muscarinic pathways play a key role in the reduction of the clinical symptoms such as rhinorrhea [12]. Current treatment strategies for chronic rhinitis include a significant role for topical anticholinergics that is symptom-specific and adjunctive [13, 14].

Regarding the demographic data of the studied groups, we found that there were no statistically significant differences between the vasomotor, allergic and control groups as regards age and sex.

Comparison between the three study groups as regards IHC data before treatment, showed that there was a significant difference between the three study groups as regards pretreatment IHC findings considering epithelium, glands, and vein; however no significant difference was found regarding arteries. Sixty percent of vasomotor group had grade 3 Epithelium compared to 20% and 0% of allergic and control groups respectively. Similarly,

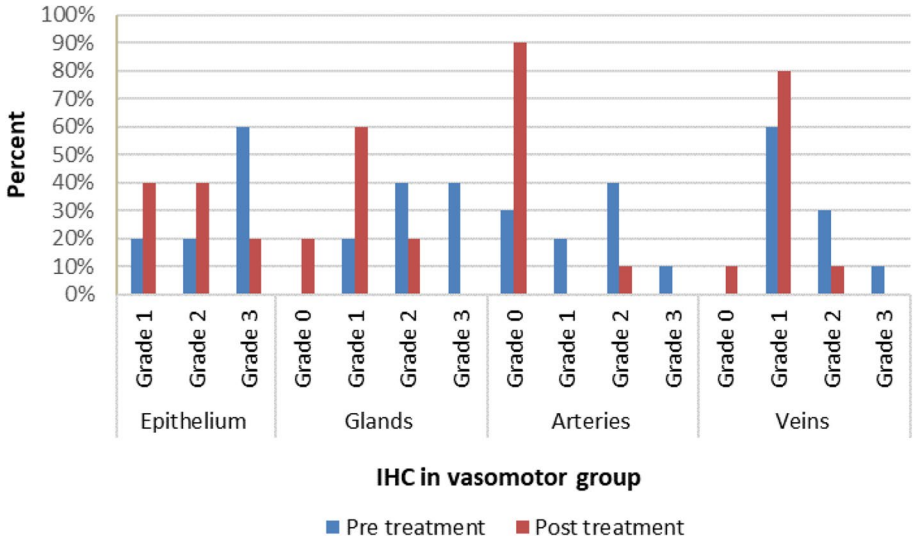

Fig. 1 Comparison between the pre- and post-IHC data among vasomotor cases study groups

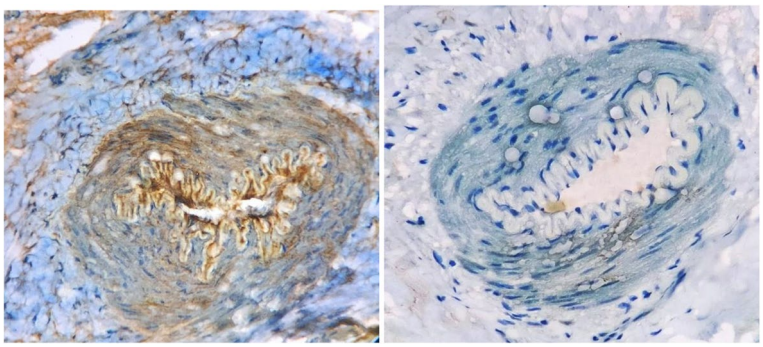

Fig. 2 A case of vasomotor rhinitis pre- and post-treatment with immunohistochemical staining show staining of arteries grade 3 to grade 0

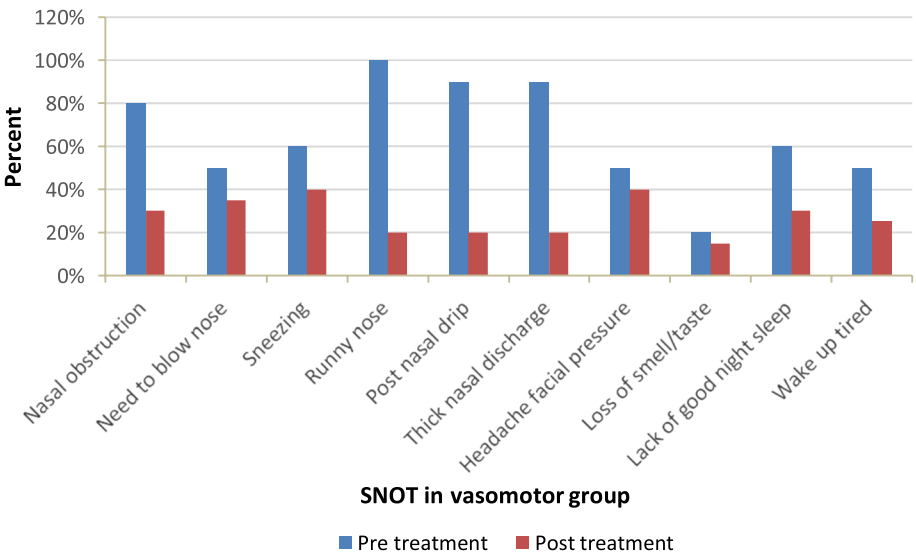

Fig. 3 Comparison between the pre- and post-SNOT questionnaire of symptoms among vasomotor group

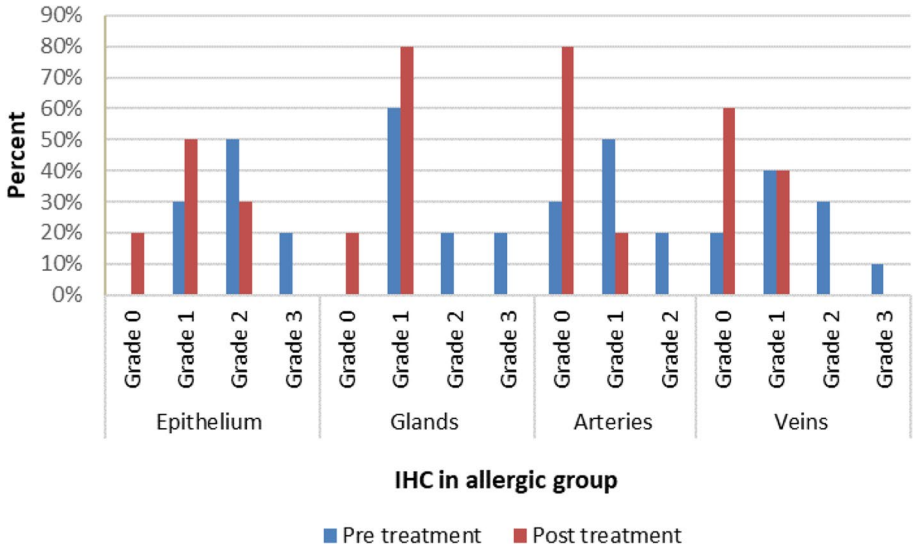

Fig. 4 Comparison between the pre- and post-IHC data among allergic cases study groups

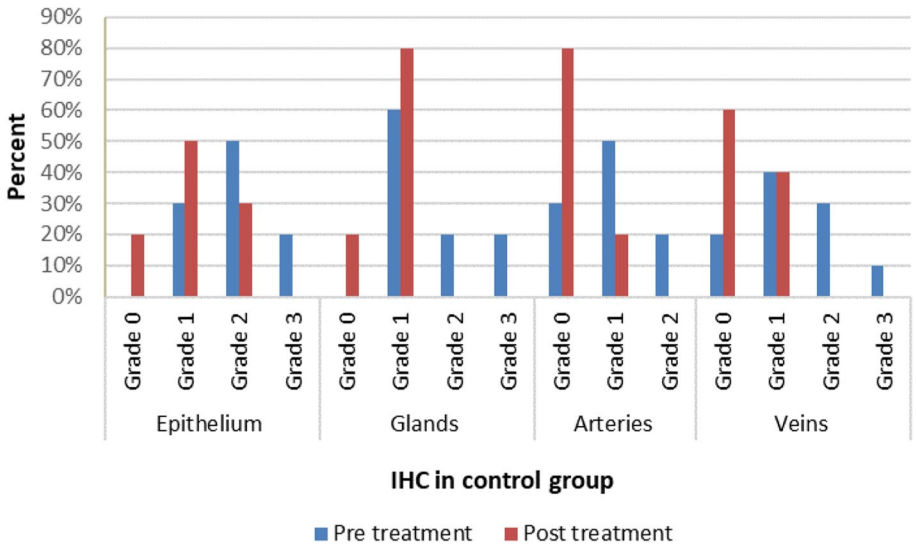

Fig. 5 Comparison between the pre- and post-IHC data among control group

40% of vasomotor group had grade 3 glands compared to 20% and 0% of allergic and control groups respectively. As regards veins, 10% of each of vasomotor and allergic groups had grade 3 veins compared to 0% of control group. Also, Comparison between the 3 study groups as regards IHC data after treatment showed that there was a significant difference between the 3 study groups as regards post-treatment IHC findings considering epithelium, glands, and vein; however, no significant difference was found regarding arteries.

The current study showed that the best improvements in epithelium and veins were found in allergic group followed by vasomotor group while the best improvement in glands was found in vasomotor group followed by allergic group. Improvement in arteries was similar in vasomotor and allergic groups. Minimal or no improvement was found in control group.

Comparison between the three study groups as regards SNOT questionnaire before treatment showed that there was a significant difference between the three study groups as regards pretreatment SNOT questionnaire.

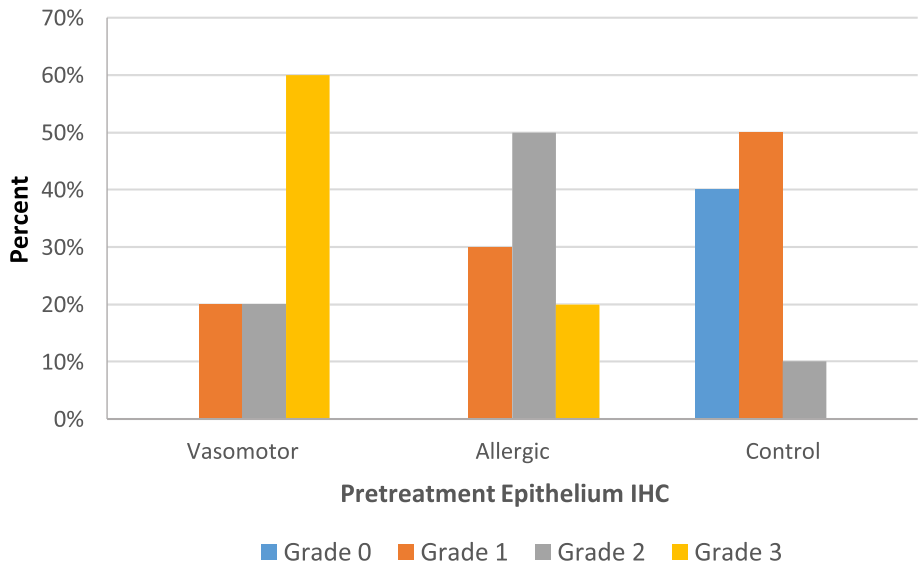

Fig. 6 Comparison between the 3 study groups as regards IHC data before treatment

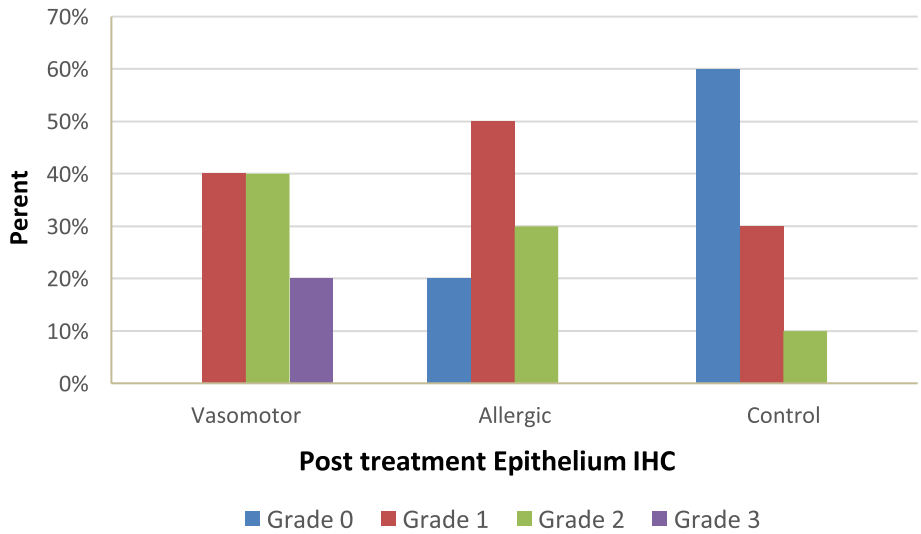

Fig. 7 Comparison between the 3 study groups as regards IHC data after treatment

Also, there was a significant difference between the three study groups as regards post-treatment SNOT questionnaire except for runny nose, post-nasal drip, and thick nasal discharge.

Comparison between the 3 study groups as regards improvement in SNOT questionnaire after treatment showed that there was a significant difference between the three study groups as regards improvement in SNOT questionnaire in 5 symptoms; nasal obstruction, running nose, post-nasal drip, thick nasal discharge, and night sleep.

The present study showed that there were comparable improvement in SNOT questionnaire was found in vasomotor and allergic groups. However, almost no improvement was found in control group.

To the best of our knowledge, there were no studies in literature have compared the efficacy of topical anticholinergic on vasomotor, allergic, and control groups.

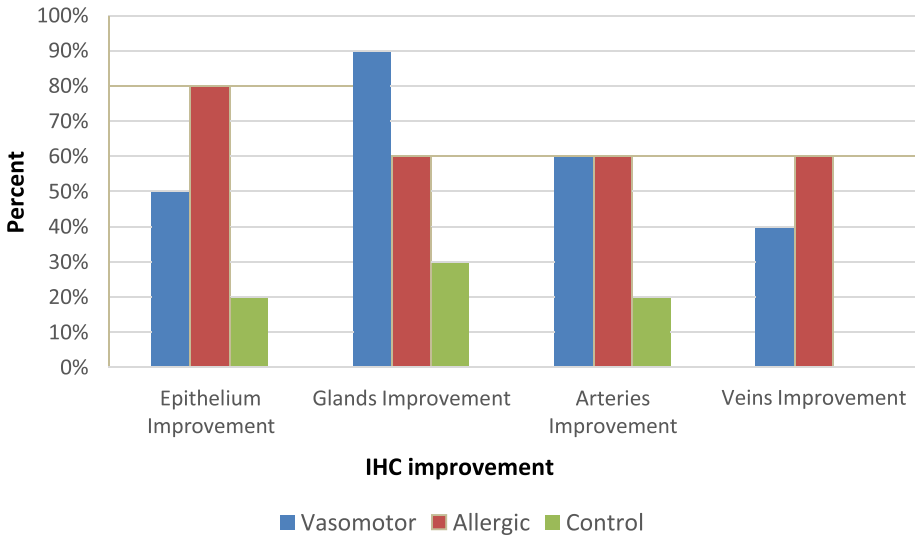

Fig. 8 Comparison between the 3 study groups as regards improvement in IHC data after treatment

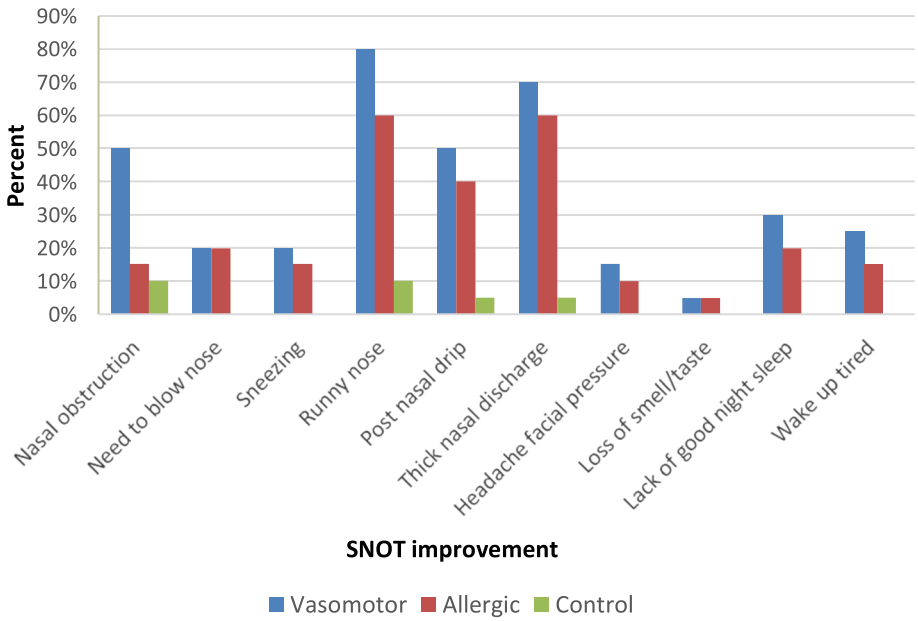

Fig. 9 Comparison between the 3 study groups as regards improvement in SNOT questionnaire after treatment

However, there were several studies have assessed the efficacy of this treatment in each group separately.

Among vasomotor group the current study showed that there was a significant difference between the pre- and post-treatment IHC findings considering epithelium, glands, arteries, and veins. Sixty percent of cases had grade 3 epithelium before treatment while after treatment, this was dropped to 20% only.

Comparison between the pre- and post-SNOT questionnaire of symptoms among vasomotor group showed that there was a significant difference between the pre- and post-treatment SNOT questionnaire symptoms; nasal obstruction, runny nose, post-nasal drip, thick nasal discharge, and lack of good night sleep.

In agreement with our results, [15] studied the long-term safety and success of ipratropium bromide spray 0.03% in the treatment of non-allergic rhinitis, and they enrolled 285 patients. The study revealed that ipratropium bromide was good tolerated without serious side effects in these patients.

Table 1 Comparison between the pre- and post-SNOT questionnaire of symptoms among allergic group

		Pre		Post		*P*	Sig
		N	%	*N*	%		
Nasal obstruction	Negative	2	10.0%	5	25.0%	0.250	NS
	Positive	18	90.0%	15	75.0%		
Need to blow nose	Negative	4	20.0%	8	40.0%	0.125	NS
	Positive	16	80.0%	12	60.0%		
Sneezing	Negative	4	20.0%	7	35.0%	0.250	NS
	Positive	16	80.0%	13	65.0%		
Runny nose	Negative	2	10.0%	14	70.0%	0.0001	HS
	Positive	18	90.0%	6	30.0%		
Post-nasal drip	Negative	4	20.0%	12	60.0%	0.008	HS
	Positive	16	80.0%	8	40.0%		
Thick nasal discharge	Negative	2	10.0%	14	70.0%	0.0001	HS
	Positive	18	90.0%	6	30.0%		
Headache facial pressure	Negative	8	40.0%	10	50.0%	0.50	NS
	Positive	12	60.0%	10	50.0%		
Loss of smell taste	Negative	10	50.0%	11	55.0%	1.0	NS
	Positive	10	50.0%	9	45.0%		
Lack of good night sleep	Negative	6	30.0%	10	50.0%	0.125	NS
	Positive	14	70.0%	10	50.0%		
Wake up tired	Negative	8	40.0%	11	55.0%	0.250	NS
	Positive	12	60.0%	9	45.0%		

* McNemar test

Table 2 Comparison between the pre- and post-SNOT questionnaire of symptoms among control group

		Pre		Post		*P*	Sig
		N	%	*N*	%		
Nasal obstruction	Negative	12	60.0%	14	70.0%	0.5	NS
	Positive	8	40.0%	6	30.0%		
Need to blow nose	Negative	18	90.0%	18	90.0%	1.0	NS
	Positive	2	10.0%	2	10.0%		
Sneezing	Negative	19	95.0%	19	95.0%	1.0	NS
	Positive	1	5.0%	1	5.0%		
Runny nose	Negative	17	85.0%	19	95.0%	0.5	NS
	Positive	3	15.0%	1	5.0%		
Post-nasal drip	Negative	18	90.0%	19	95.0%	1.0	NS
	Positive	2	10.0%	1	5.0%		
Thick nasal discharge	Negative	18	90.0%	19	95.0%	1.0	NS
	Positive	2	10.0%	1	5.0%		
Headache facial pressure	Negative	19	95.0%	19	95.0%	1.0	NS
	Positive	1	5.0%	1	5.0%		
Loss of smell taste	Negative	20	100.0%	20	100.0%	N/A	N/A
	Positive	0	0.0%	0	0.0%		
Lack of good night sleep	Negative	18	90.0%	18	90.0%	1.0	NS
	Positive	2	10.0%	2	10.0%		
Wake up tired	Negative	19	95.0%	19	95.0%	1.0	NS
	Positive	1	5.0%	1	5.0%		

*McNemar test

Also, [16] assessed the new isotonic aqueous ipratropium bromide nasal spray pump, precisely in patients with non-allergic rhinitis. Two hundred thirty-three patients shared in an 8-week double-blind parallel evaluation of ipratropium bromide nasal spray with a saline solution. Treatment with the ipratropium spray resulted in a 30% reduction in rhinorrhea; this reduction was greater than that seen with the saline vehicle. There was a modest reduction in post-nasal drip, sneezing, and congestion with both treatments, which may be attributable to the salutary results of the saline solution.

Also, [17] compared the value and safety of the combined use of ipratropium bromide nasal spray 0.03% (42 microg per nostril tid) and beclomethasone dipropionate nasal spray (84 microg per nostril bid) against that of either active agent alone for the treatment of rhinorrhea. The study enrolled 533 patients with perennial rhinitis (279 allergic and 274 non-allergic). The study decided that the combined use of the ipratropium bromide nasal spray with beclomethasone dipropionate nasal spray is more effective than either active agent for the treatment of rhinorrhea, and does not result in a potentiation of adverse drug reactions. Ipratropium bromide nasal spray 0.03% alone should be considered in patients for whom rhinorrhea is the primary symptom, and its use in combination with a nasal steroid should be considered in patients where rhinorrhea is one of the chief symptoms, or in patients with rhinorrhea not completely responsive to other therapy.

Finally, our results supported by the recent systematic review by [18] aimed to assess the safety and efficiency of anticholinergic nasal sprays in managing of allergic and non-allergic rhinitis regarding symptom severity and duration, The study included 12 studies ($n = 2024$ patients). And anticholinergic treatment was demonstrated to significantly reduce rhinorrhea severity and duration in allergic and non-allergic rhinitis patients (Figs. 1, 2, 3, 4, 5, 6, 7, 8, and 9; Tables 1 and 2).

Conclusion

Topical anticholinergics such as ipratropium bromide nasal spray are effective in treating wet symptoms as rhinorrhea in allergic and non-allergic rhinitis. Further controlled studies with larger sample size and longer follow-up are needed to confirm our results and to identify risk factors of adverse events.

Acknowledgements
Not applicable

Authors' contributions
AMA has drafted the work or substantively revised it and approved the submitted version and has agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work. SMS has made design of the work and approved the submitted version and has agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work. SAF has made substantial contributions to the conception and approved the submitted version and has agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work. MIS has made interpretation of data and approved the submitted version and has agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work. MAME ensured that all listed authors had approved the manuscript before submission, including the names and order of authors, and that all authors received the submission and all substantive correspondence with editors, as well as the full reviews, verified that all data, figures, materials (including reagents), and code, even those developed or provided by other authors, comply with the transparency and reproducibility standards of both the field and journal. OMM has drafted the work or substantively revised it and approved the submitted version and has agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work.

Funding
Not applicable.

Availability of data and materials
All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate
Informed consent from participants obtained to participate in the study at otorhinolaryngology department Faculty of Medicine Ain Shams University. Approved by an ethical committee of Faculty of Medicine Ain Shams University before the start of the recruitment (FMASU M D 406/2019).

Consent for publication
Not applicable.

Competing interests
Dr Samia Ahmed Fawaz is a co-author of this study and an Editorial Board member of the journal. She was not involved in handling this manuscript during the submission and the review processes. The rest of the authors have no conflict of interest to declare.

Author details
[1]Otorhinolaryngology, Faculty of Medicine, Ain Shams University, Cairo, Egypt. [2]Pathology, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

Received: 24 November 2022 Accepted: 2 January 2023
Published online: 23 March 2023

References

1. Settipane RA, Lieberman P (2001) Update on nonallergic rhinitis. Ann Allergy Asthma Immunol 86:494–507
2. Sarin S, Undem B, Sanico A, Togias A (2006) The role of the nervous system in rhinitis. J Allergy Clin Immunol 118:999–1014
3. Van Crombruggen K, Zhang N, Gevaert P, Tomassen P et al (2011) Pathogenesis of chronic rhinosinusitis: inflammation. J Allergy Clin Immunol 128:728–732
4. Smeraldi A, Crimi E, Milanese M, Rossetti A, Cantini L (2002) Brusasco V (2002): Efficacy of ipratropium bromide aqueous nasal spray in the prevention of nasal secretion induced by inhaled methacholine. Clin Drug Investig 22(4):263–268
5. Marquez F, Sastre J, Hernandez G, Cenjor C, Sanchez-Hernandez JM, Sanchez J, Gutierrez R, Sanabria J (2000) Nasal hyperreactivity to methacholine measured by acoustic rhinometry in asymptomatic allergic and perennial nonallergic rhinitis. Am J Rhinol 14(4):251–256

6. AlBalawi ZH, Othman SS, AlFaleh K (2011) Intranasal ipratropium bromide for the common cold. Cochrane Database Syst Rev 7:008231
7. Greiwe JC, Bernstein JA (2019) Allergic and mixed rhinitis: diagnosis and natural evolution. J Clin Med 8(11):2019
8. Philpott C, Ta NH, Hopkins C, Ray J, Ahmed S, Almeyda R (2021) Socio-economic, comorbidity, lifestyle, and quality of life comparisons between chronic rhinosinusitis phenotypes. Laryngoscope 131(10):2179–2186
9. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, Williams D (2008) Allergic rhinitis and its impact on asthma (ARIA) 2008. Allergy 63:8–160
10. Scarupa MD, Kaliner MA (2009) Nonallergic rhinitis, with a focus on vasomotor rhinitis clinical importance, differential diagnosis, and effective treatment recommendations. World Allergy Organ J 2(3):20–25
11. Matera MG, Cazzola M (2016) Muscarinic receptor antagonists. Pharmacology and Therapeutics of Asthma and COPD. pp 41–62
12. Naclerio R (2009) Anticholinergic drugs in nonallergic rhinitis. World Allergy Organ J 2(8):162–165
13. Tran NP, Vickery J, Blaiss MS (2011) Management of rhinitis: allergic and non-allergic. Allergy Asthma Immunol Res 3(3):148–156
14. Watts AM, Cripps AW, West NP, Cox AJ (2019) Modulation of allergic inflammation in the nasal mucosa of allergic rhinitis sufferers with topical pharmaceutical agents. Front Pharmacol 10:294
15. Grossman J, Banov C, Boggs P, Bronsky EA, Dockhorn RJ, Druce H, Findlay SR, Georgitis JW, Hampel FC, Kaiser H (1995) Use of ipratropium bromide nasal spray in chronic treatment of nonallergic perennial rhinitis, alone and in combination with other perennial rhinitis medications. J Allergy Clin Immunol 95(5 Pt 2):1123–1127
16. Bronsky EA, Druce H, Findlay SR, Hampel FC, Kaiser H, Ratner P, Valentine MD, Wood CC (1995) A clinical trial of ipratropium bromide nasal spray in patients with perennial nonallergic rhinitis. J Allergy Clin Immunol 95(5 Pt 2):1117–1122
17. Dockhorn R, Aaronson D, Bronsky E, Chervinsky P, Cohen R, Ehtessabian R, Finn A, Grossman J, Howland W, Kaiser H, Pearlman D, Sublett J, Ratner P, Settipane G, Sim T, Storms W, Webb R, Drda K, Wood C (1999) Ipratropium bromide nasal spray 0.03% and beclomethasone nasal spray alone and in combination for the treatment of rhinorrhea in perennial rhinitis. Ann Allergy Asthma Immunol. 82(4):349–359
18. Pang JC, Vasudev M, Du AT, Nottoli MM, Dang K, Kuan EC (2022) Intranasal anticholinergics for treatment of chronic rhinitis: systematic review and meta-analysis. Laryngoscope. https://doi.org/10.1002/lary.30306. Advance online publication

Publisher's Note