



Treatment Regimen for Acute Viral Rhinitis in Patients with a History of Rhinitis Medicamentosa

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

Aims: The aim of this research is to study the efficacy of intranasal administration of 0.9% saline solution in patients with acute viral rhinitis and a history of Rhinitis medicamentosa.

Materials and Methods: The study included 96 patients with a confirmed diagnosis of acute viral rhinitis and a history of Rhinitis medicamentosa. All patients were equally randomized to two groups. In both groups, patients were treated according to the European Position Paper on Rhinosinusitis and Nasal Polyps with nasal decongestants (oxymetazoline), but in Group 2, the treatment regimen was supplemented with topical use of 0.9% saline solution. Local TNF- α and IL-1 β levels were determined in all patients on Days 1, 5, and 10. In addition, on the next day after oxymetazoline withdrawal, a Nasal airway resistance was measured in all patients using active posterior rhinomanometry.

Results: The duration of rhinorrhea and nasal congestion and, respectively, the duration of oxymetazoline administration significantly differed between the groups ($p < 0.001$) and was 7.9 ± 1.1 days for Group 1 and 4.7 ± 0.9 days for Group 2. In general, the dynamics of changes in local TNF- α and IL-1 β levels in both groups was similar. Throughout the study, there was a progressive

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decrease in both inflammatory mediators, with faster changes occurring in Group 2. A strong positive correlation ($rs=0.89$; $p<0.001$) between $TNF-\alpha$ and $IL-1\beta$ levels was established. According to the results of active posterior rhinomanometry on the day following oxymetazoline withdrawal, Nasal airway resistance was significantly higher in Group 1 ($p<0.001$), which indicates the presence of difficulty breathing in patients of this group. In addition, patient examination showed that manifestations of Rhinitis medicamentosa occurred in 3 (6.25%) patients of Group 1 and in 17 (35.42%) patients of Group 2. Differences between the groups were significant ($p<0.01$).
Conclusion: The use of topical nasal decongestants, in particular oxymetazoline, in patients with acute viral rhinitis and a history of Rhinitis medicamentosa for more than 7 days has a potential risk of development of a recurrence of Rhinitis medicamentosa. Supplementing the treatment regimen for acute viral rhinitis with the topical use of 0.9% saline solution reduces the duration of treatment and the use of topical decongestants, and therefore prevents the recurrence of Rhinitis medicamentosa.

Keywords: Acute viral rhinitis; Rhinitis medicamentosa; oxymetazoline; 0.9% saline solution; $TNF-\alpha$; $IL-1\beta$.

1. INTRODUCTION

“Acute viral rhinitis is one of the most common conditions in the world. It is rhinoviruses that cause about half of all cases of upper respiratory tract infections” [1,2]. “Entering the respiratory tract, viruses infect the epithelium of the nasal mucosa, gradually transferring the process to the distal parts of the tracheobronchial tree” [3].

“The cold itself is considered to last for 5-10 days, after which the symptoms either persist or increase with the development of post-viral acute rhinosinusitis” [4]. “Further overlay of bacterial microflora leads to the development of purulent complications, such as rhinosinusitis, bronchitis, pneumonia” [4].

The treatment of acute viral rhinitis according to the European Position Paper on Rhinosinusitis and Nasal Polyps [4] includes nasal decongestants that cause Rhinitis medicamentosa [5,6].

Rhinitis medicamentosa, also called "rebound syndrome" or "chemical" rhinitis, is defined as a type of drug-induced, chronic, non-allergic rhinitis that is a chronic dysfunction of the nasal mucosa due to prolonged use of topical vasoconstrictors [5,6]. Rhinitis medicamentosa is usually characterized by nasal congestion without rhinorrhea, postnasal congestion, or sneezing that begins after administration of nasal decongestants for more than 5 days [5,7,8].

Although, at first glance, acute viral rhinitis seems to be a simple and well-studied condition, however, its occurrence in patients with a history of Rhinitis medicamentosa encourages the

search for new more effective treatment regimens.

One approach to reducing the duration of the use of nasal decongestants in patients with acute viral rhinitis and a history of Rhinitis medicamentosa may be to introduce 0.9% saline solution for nasal lavage into the treatment regimen.

The aim of this research is to study the efficacy of intranasal administration of 0.9% saline solution in patients with acute viral rhinitis and a history of Rhinitis medicamentosa.

2. MATERIALS AND METHODS

The study included 96 patients aged 21 to 60 years (40.1 ± 13.2 years) with a confirmed diagnosis of acute viral rhinitis and a history of Rhinitis medicamentosa. There were 55 women (57.3%) and 41 men (42.7%).

The inclusion criteria were:

1. Confirmed diagnosis of acute viral rhinitis.
2. A history of Rhinitis medicamentosa.
3. Time to visit is not more than 24 hours after the onset of symptoms.
4. Age from 21 to 60 years.
5. No urgent conditions at the time of inclusion in the study.
6. No exacerbation of chronic diseases at the time of inclusion.
7. No history of allergic reactions to the prescribed medications.
8. No mechanical damage to the nasal mucosa.
9. No signs of bacterial infection of the respiratory tract.

According to the European Position Paper “on Rhinosinusitis and Nasal Polyps, acute viral rhinitis is diagnosed in the presence of two or more nasal symptoms (nasal congestion/obstruction, rhinorrhea, facial pressure, or loss of smell). If necessary, the diagnosis is confirmed endoscopically (mucosal edema or rhinorrhea)” [4].

All patients were equally randomized to two groups. Fixed simple randomization were used. In both groups, patients were treated according to the European Position Paper on Rhinosinusitis and Nasal Polyps with nasal decongestants (oxymetazoline), but in Group 2, the treatment regimen was supplemented with the topical use of 0.9% saline solution. 0.9% saline solution was used to wash the nasal cavity every two hours with a night break until the symptoms of acute viral rhinitis completely disappeared.

In addition to routine tests, local TNF- α and IL-1 β levels were determined in all patients on Days 1, 5, and 10. TNF- α and IL-1 β levels were determined in nasal mucosal flushes by enzyme-linked immunosorbent assay using the Human TNF- α ELISA kit and Human IL-1 β ELISA Kit (CUSABIO, China).

In addition, on the next day after oxymetazoline withdrawal, a Nasal airway resistance was measured in all patients by means of the active posterior rhinomanometry using an MPR-3100 rhinomanometer (Nihon Kohden Corporation, Tokyo, Japan).

The obtained data was processed using the SPSS Statistics software. The significance of differences in disease duration and TNF- α and IL-1 β levels was determined using an ANOVA test. The significance of differences between the groups in the number of complications was determined using the χ^2 test, χ^2 test with Yates correction for continuity, the accurate two-sided Fisher test. The correlation of indicators was evaluated using the Spearman correlation coefficient.

3. RESULTS AND DISCUSSION

When compared statistically, both groups were homogeneous in terms of gender and age.

All patients in both groups had a good tolerance to the prescribed treatment.

The use of oxymetazoline was accompanied by isolated adverse reactions, which included

mucosal irritation in 1 (1.04%) patient and nasal dryness in 2 (2.08%) patients. Adverse reactions did not significantly affect the general condition of patients and were slightly pronounced. All patients were advised to continue the study.

The duration of rhinorrhea and nasal congestion and, respectively, the duration of oxymetazoline administration significantly differed between the groups ($p < 0.001$) and was 7.9 ± 1.1 days for Group 1 and 4.7 ± 0.9 days for Group 2.

The overlay of bacterial microflora with the development of purulent complications occurred in 5 patients (10.42%) in Group 1 and in 2 patients (4.17%) in Group 2. It should be noted that the statistical significance of differences between the groups has not been proven ($p > 0.05$).

Local TNF- α and IL-1 β levels in patients in our research are shown in Table 1.

In general, the dynamics of changes in local TNF- α and IL-1 β levels in both groups was similar.

At the beginning of the research, TNF- α levels in Groups 1 and 2 showed high values and did not significantly differ ($p > 0.05$). Throughout the research, there was a progressive decrease in the levels of this indicator of inflammation. On Day 5, TNF- α levels were 1.59 times lower than baseline in Group 1 and 2.08 times lower in Group 2 and significantly differed ($p < 0.01$). On Day 10, the levels of the investigated indicator were 6.01 and 7.80 times lower than the initial values, and 3.78 and 3.74 times lower than the values on Day 5 for Groups 1 and 2, respectively. In addition, on Day 10, TNF- α levels in both groups significantly differed ($p < 0.001$).

At the beginning of the research, IL-1 β levels in Groups 1 and 2 also showed high values and did not significantly differ ($p > 0.05$). Throughout the entire period of research, there was a progressive decrease in the levels of this indicator of inflammation. On Day 5, IL-1 β levels were 1.28 times lower than baseline in Group 1 and 2.19 times lower in Group 2 and significantly differed ($p < 0.001$). On Day 10, the levels of the investigated indicator were 2.26 and 3.11 times lower than the initial values, and 1.76 and 1.42 times lower than the values on Day 5 for Groups 1 and 2, respectively. In addition, on Day 10, IL-1 β levels in both groups significantly differed ($p < 0.001$) and exceeded the control values by 1.8 times in Group 1 and 1.5 times in Group 2.

A strong positive correlation ($rs=0.89$; $p<0.001$) between TNF- α and IL-1 β levels was evident.

Values of active posterior rhinomanometry in the study groups on the day after oxymetazoline withdrawal are shown in Fig. 1.

Table 1. Local TNF- α and IL-1 β levels in the study patients

Research period	TNF- α , pg/ml	IL-1 β , pg/ml
Group 1 (G1)		
Day 1 (G1.1)	379.15 \pm 93.81 * G1.5, G1.10	22.05 \pm 7.25 * G1.5, G1.10
Day 5 (G1.5)	238.62 \pm 73.51 * G1.1, G1.10 Δ G2.5	17.21 \pm 4.27 * G1.1, G1.10 * G2.5
Day 10 (G1.10)	63.09 \pm 11.76 * G1.1, G1.5 Δ G2.10	9.76 \pm 4.01 * G1.1, G1.5 * G2.10
Group 2 (G2)		
Day 1 (G2.1)	367.91 \pm 88.12 * G2.5, G2.10	22.45 \pm 7.18 * G2.5, G2.10
Day 5 (G2.5)	176.51 \pm 49.86 * G2.1, G2.10 Δ G1.5	10.23 \pm 3.53 * G2.1, G2.10 * G1.5
Day 10 (G2.10)	47.14 \pm 11.95 * G2.1, G2.5 Δ G1.10	7.21 \pm 1.47 * G2.1, G2.5 * G1.10

Note. Statistically significant difference in relation to the specified groups with the corresponding number: Δ – $p<0.01$; * – $p<0.001$

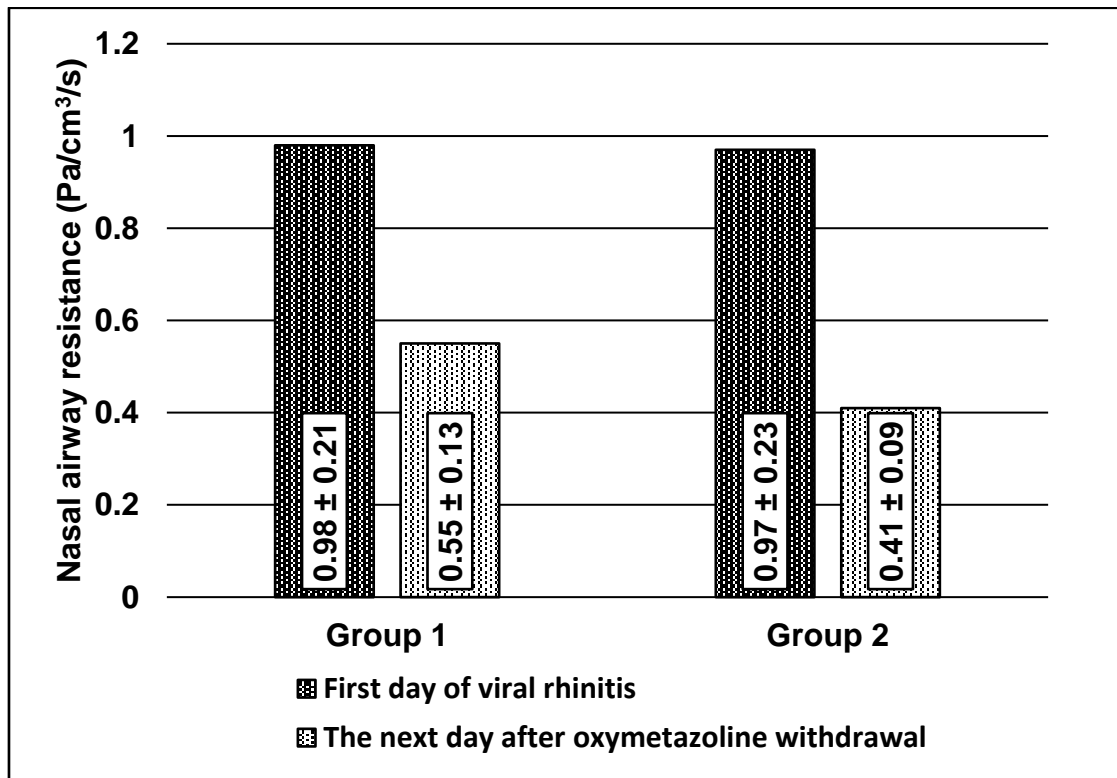


Fig. 1. Nasal airway resistance according to active posterior rhinomanometry in the study groups on the day after oxymetazoline withdrawal

As Fig. 1 shows, according to the results of active posterior rhinomanometry, on the first day of the viral rhinitis there was no any statistical difference between groups. On the day following oxymetazoline withdrawal, Nasal airway resistance was significantly higher in Group 1 ($p < 0.001$), which indicates the presence of difficulty breathing in patients of this group. It should also be noted that the Nasal airway resistance in both groups was significantly ($p < 0.001$) different from the initial values.

In addition, patient examination showed that manifestations of Rhinitis medicamentosa occurred in 3 (6.25%) patients of Group 1 and in 17 (35.42%) patients of Group 2. Differences between the groups were significant ($p < 0.01$).

The results of the analysis of the dynamics of local TNF- α and IL-1 β levels allowed to establish a number of patterns.

Thus, the dynamics of local inflammatory mediator levels is almost similar for TNF- α and IL-1 β [9] and characterizes the inflammatory process in the nasal mucosa [10].

Also, in the course of our research, supplementing the traditional treatment regimen with 0.9% saline solution was found to significantly reduce the duration of treatment in patients of Group 2. In addition, patients in this group were less likely to experience bacterial complications, and there was an evidence of a significantly faster recovery of the investigated indicators compared to Group 1.

Better results of treatment of patients in Group 2 are probably associated with mechanical cleaning of the nasal cavity with 0.9% saline solution. Washing microflora out decreased the concentration of factors that contributed to the inflammatory process.

As for Rhinitis medicamentosa, its development is slow. Thus, neither a 10-day [11], nor a 4-week [12] oxymetazoline study has showed the development of Rhinitis medicamentosa. At the same time, the results of another 4-week oxymetazoline study on healthy volunteers [13] showed the absence of Rhinitis medicamentosa events after 10 days, but the presence of such events in all participants on Day 30 of the study.

Having a history of Rhinitis medicamentosa, even a short-term repeated use of topical nasal decongestants can lead to a relapse of symptoms [14]. That is why an important aspect

of the treatment of patients with a history of Rhinitis medicamentosa is either the complete exclusion of topical nasal decongestants, or their combination with other groups of drugs to achieve a shorter duration of their use.

As demonstrated by this study, the use of 0.9% saline solution reduced the duration of symptoms, and, accordingly, the duration of oxymetazoline use from 7.9 ± 1.1 days to 4.7 ± 0.9 days. Due to this reduction in the duration of oxymetazoline use, Nasal airway resistance according to the results of active posterior rhinomanometry on the day following its withdrawal was significantly lower in the group of 0.9% saline solution. At the same time, Group 1 showed difficulty in nasal breathing, which was probably associated with a relapse of Rhinitis medicamentosa.

The patterns established by us give grounds for their further in-depth study in a larger number of patients and with the involvement of related specialists and additional methods of laboratory and instrumental research.

4. CONCLUSION

1. The use of topical nasal decongestants, in particular oxymetazoline, in patients with acute viral rhinitis and a history of Rhinitis medicamentosa for more than 7 days has a potential risk of development of a recurrence of Rhinitis medicamentosa.
2. Supplementing the treatment regimen for acute viral rhinitis with the topical use of 0.9% saline solution reduces the duration of treatment and the use of topical decongestants, and therefore prevents the recurrence of Rhinitis medicamentosa.

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

COMPETING INTERESTS

Author has declared that no competing interests exist.

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