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## Intranasal Treatment of Acute Rhinosinusitis - Recommendations, Efficacy and Safety

Maria Sadlik<sup>1\*</sup>, Leila Abod<sup>2</sup>, Natalia Ilnicka<sup>3</sup>, Daria Matyja<sup>4</sup>, Patrycja Zuziak<sup>5</sup>

<sup>1</sup>Jan Mikulicz-Radecki University Teaching Hospital, Borowska 213, 50-556 Wrocław; [sadlik.maria@gmail.com](mailto:sadlik.maria@gmail.com); ORCID iD: 0000-0001-8255-9200

<sup>2</sup>Jan Mikulicz-Radecki University Teaching Hospital, Borowska 213, 50-556 Wrocław; [leila.abood@gmail.com](mailto:leila.abood@gmail.com); ORCID iD: 0000-0002-5895-0944

<sup>3</sup>Regional Specialist Hospital in Wrocław, Research and Development Centre, H. Kaminski Street 73a, 51-124 Wrocław, Poland; [natalia.ilnicka@outlook.com](mailto:natalia.ilnicka@outlook.com); ORCID iD: 0000-0002-7149-8534

<sup>4</sup>J. Gromkowski Regional Specialist Hospital, Koszarowa 5, 51 - 149 Wrocław; [daria.matyja@gmail.com](mailto:daria.matyja@gmail.com); ORCID iD: 0000-0002-9046-7821

<sup>5</sup>T. Marciniak Lower Silesian Specialist Hospital - Emergency Medicine Centre, Fieldorfa 2, 54-049 Wrocław; [pat.zuziak@gmail.com](mailto:pat.zuziak@gmail.com); ORCID iD: 0000-0003-3612-0349

\*Corresponding Author

### Abstract

**Introduction and purpose:** Acute rhinosinusitis is a common condition worldwide, usually caused by respiratory viruses. Nasal epithelium is their primary point of entry and an active responder to the infection. Therefore, it seems reasonable for the treatment approach to include locally applied drugs. Our purpose is to bring forward up-to-date recommendations of intranasal treatment options for acute rhinosinusitis, and assess their efficacy and safety.

**Description of the state of knowledge:** Rhinosinusitis is an inflammation of the mucosa present in the nose and the paranasal sinuses. It affects many patients yearly, bearing significant adverse effects on quality of life, productivity and healthcare expenditure. Acute rhinosinusitis lasts less than 12 weeks and is divided into viral, post-viral and acute bacterial rhinosinusitis. It is one of the prevailing reasons for unfounded antibiotics prescription, although it is usually self-limiting. Its treatment depends on the clinical stage of the infection, however, each of them encloses medications administered intranasally. Based on EPOS2020 and scientific publications it seems that nasal decongestants may be prescribed in viral rhinosinusitis, nasal corticosteroids in post-viral rhinosinusitis and nasal saline can prove beneficial in all clinical stages of rhinosinusitis. While used appropriately all aforementioned medications prove to be safe.

**Conclusions:** In the light of the findings presented in this paper, it can be concluded that acute rhinosinusitis should be treated not only with oral, but also with intranasal drugs. Nasal decongestants are to be considered in viral rhinosinusitis mainly. Nasal corticosteroids show some positive effect in post-viral rhinosinusitis. Nasal saline can be administered in all clinical stages of acute rhinosinusitis. It is crucial to caution the patients against misuse of the medications, in order to prevent their adverse effects.

**Key words:** rhinosinusitis, acute rhinosinusitis, common cold, nasal decongestants, nasal corticosteroids, nasal saline

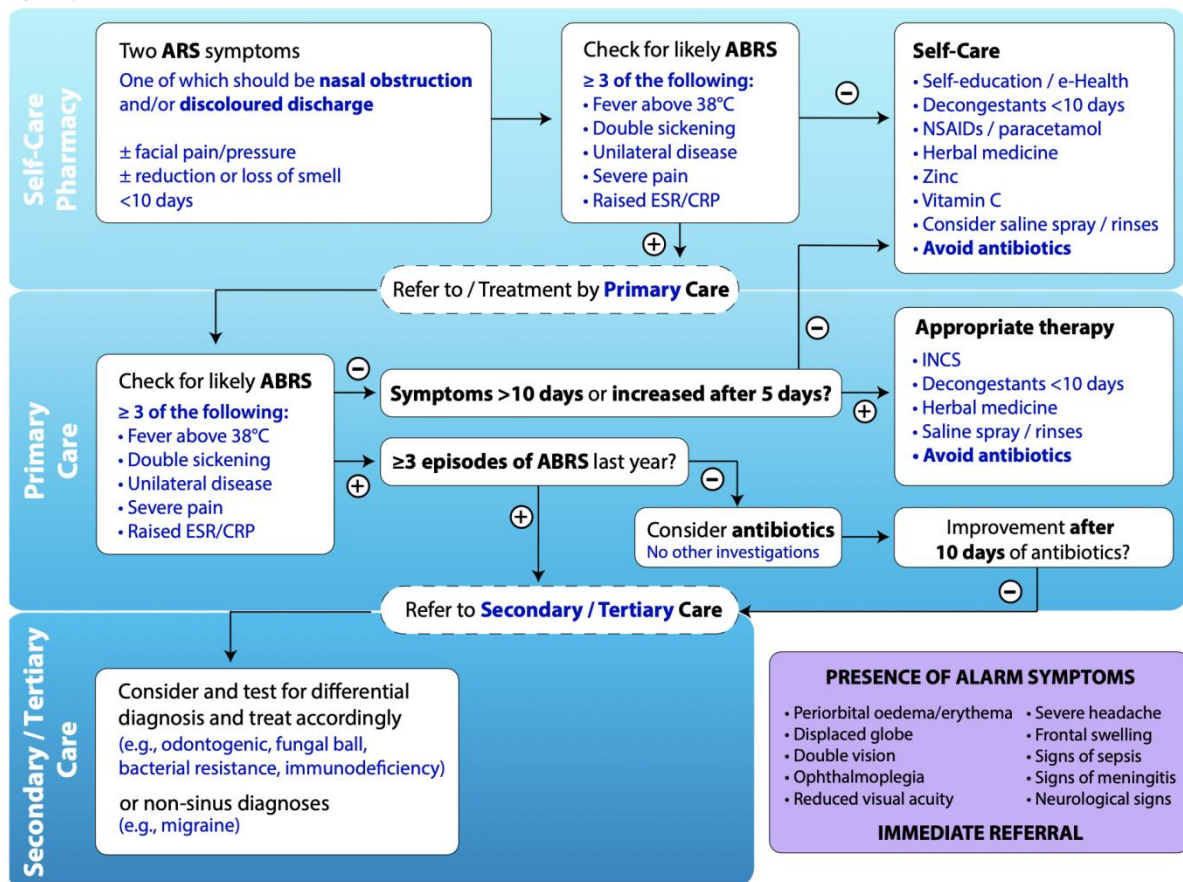
## **Introduction and Purpose**

Acute rhinosinusitis (ARS) is a worldwide common condition and one of the prevailing reasons for unfounded antibiotics prescription, which is a considerable issue in light of the current global resistance crisis [1-4]. It is usually self-limiting and ordinarily caused by respiratory viruses, mainly rhinoviruses and coronaviruses. With nasal epithelium being, both, primary point of their entry and an active responder to the infection, it seems reasonable for the treatment to be applied not only systemically, but also locally. [5-9] Our purpose is to bring forward up-to-date recommendations for intranasal treatment options for ARS, namely nasal decongestants (ND), nasal corticosteroids (NCS) and nasal saline (NS), and assess their validity and safety. Our work consisted of searching through PubMed® using as entries: ‘rhinosinusitis’, ‘common cold’, ‘nasal decongestants’, ‘nasal decongestants safety’, ‘nasal steroids’, ‘nasal steroids safety’, ‘nasal saline’ and analysing scientific publications related to these three groups. A sample of 30 articles met the criteria of relevance and was considered for this publication.

## **Definition**

Rhinosinusitis is a bothersome condition which affects many patients yearly. It bears significant adverse effects on quality of life, productivity and healthcare expenditure. Both in adults and children, it is defined as inflammation of the mucosa present in the nose and the paranasal sinuses. Nasal epithelial cells initiate the cascade of inflammation, which causes oedema, engorgement, fluid extravasation, mucus production and subsequent sinus obstruction. It is diagnosed in presence of at least two symptoms, one of which ought to be either nasal discharge (anterior or posterior nasal drip), or nasal congestion, obstruction or blockage. The other symptom being either facial pain or pressure, or reduction or loss of smell in adults, or cough in children. Acute rhinosinusitis lasts less than 12 weeks. It is usually self-limiting, however, its complications may be severe. Furthermore, ARS is divided into viral ARS (common cold) which lasts up to 10 days, post-viral ARS which lasts longer than 10 days or worsens after 5 days, and acute bacterial rhinosinusitis (ABRS) which is suspected in presence of at least three out of the following symptoms: fever, severe local pain, elevated ESR or CRP, discoloured discharge and double sickening. Treatment depends on the clinical stage of the infection and the care pathways can be seen on the diagram from the European Position Paper on Rhinosinusitis and Nasal Polyps 2020 (EPOS2020) shown in Figure 1. [5,10,11]

## EPOS 2020: Care pathways for acute rhinosinusitis (ARS)



ABRS, acute bacterial rhinosinusitis; INCS, intranasal corticosteroids.

Figure 1. Integrated care pathway of acute rhinosinusitis from EPOS2020 [5]

### Nasal Decongestants

ND are  $\alpha$ -adrenergic agonists which, by stimulating  $\alpha$  receptors present in the nasal mucosa, cause vasoconstriction with following reduction of oedema and rhinorrhea [12,13].

According to EPOS2020, multiple doses of ND seem to have a small positive effect on alleviation of nasal obstruction in viral ARS without increasing the risk of adverse effects in adults when used short term. In acute phase of post-viral ARS they may improve mucociliary clearance, however, in the absence of clinically relevant data, they are not advised to be prescribed. There is no recommendation regarding the usage of ND in ABR in the consulted literature. [5,10,14]

Examples of available ND are oxymetazoline, xylometazoline and phenylephrine [12]. They are advised to be applied for no longer than 10 days [5]. However, there is no consensus regarding what duration of therapy elicits adverse effects. As stated by Morris et al. [15] drug-induced rhinitis may be observed 3 days after the initiation of oxymetazoline administration. Contrarily, Watanabe et al. [16] witnessed neither significant nasal blockage, nor impaired response to oxymetazoline following 4 weeks of treatment. As mentioned above, ND are claimed to provoke rebound congestion, also known as rhinitis medicamentosa, in prolonged use. There are various hypotheses regarding the pathophysiology of this effect, namely chronic vasoconstriction leading to ischemia of the nasal mucosa, which predisposes to interstitial oedema; alteration in vasomotor tone resulting in increased vascular permeability and oedema;  $\beta$ -adrenoreceptor activity outlasting the  $\alpha$  effects leading to rebound vasodilatation; and fatigue of the constrictor mechanisms resulting in reactive hyperemia and congestion, where the adrenoreceptors become refractory to nasal decongestants. The exact mechanism of its development remains, nonetheless, unknown. [17] In mild cases, cessation of ND administration should suffice to stop and reverse the condition. However, severe cases exemplary of rebound congestion may be found in literature, with complications as serious as locally increased intra-operative bleeding and nasal septal perforation. [18,19] Other

possible adverse effects of ND misuse are nasal dryness and irritation, tachycardia, restlessness, palpitations, arrhythmias and angina [13].

### **Nasal Corticosteroids**

Corticosteroids are lipid-soluble molecules of anti-inflammatory profile which bind to intracellular glucocorticoid receptors. Their mechanism of action is complex and not fully understood. They are said to suppress gene expression of factors responsible for inflammatory processes and up-regulate the anti-inflammatory genes. When administered intranasally, they decrease mucus production by goblet cells and inhibit recruitment of inflammatory cells to the nasal mucosa. [20]

According to EPOS2020, NCS are not recommended in viral ARS and prove to have a small effect in post-viral ARS, therefore should be prescribed only when reduction of the symptoms is considered necessary. There is no recommendation regarding the usage of NCS in ABRS in EPOS2020. [5,10] Zalmanovici Trestioreanu et al. [21], however, claim that evidence supports NCS use in ARS as a monotherapy, as well as, as an adjuvant to antibiotics therapy.

Numerous NCS are available on the market, such as fluticasone propionate, fluticasone furoate, triamcinolone acetonide, beclomethasone dipropionate, ciclesonide, budesonide and mometasone furoate [22]. As they remain the main allergic rhinitis treatment, many comparative studies have been performed regarding the side effects, efficacy and relative cost of each of the aforementioned drugs. It has been established that they hold similar profile and vary only with regard to costs and patient's personal preference. [23-25] Corticosteroids administered orally are associated with severe side effects, such as hypothalamic-pituitary-adrenal axis suppression, growth retardation in children, bone mineral density loss, cataract formation and glaucoma. Thereby, the concern of their safety when administered intranasally has given raise to a number of investigations. Studies have shown no significant correlation between NCS and aforementioned adverse effects. [26] However, they should be avoided in patients already suffering from glaucoma and cataract as they may cause exacerbation of these conditions [12]. Altogether, NCS are safe to use at recommended dosages both in adults, in children and, according to Wallace et al. [27], in pregnant women. An important aspect of the therapy is the proper technique of administration — the spray nozzle should be directed away from the nasal septum in order to prevent local adverse effects such as epistaxis, discomfort, dryness and rarely septal perforation. [12,28]

### **Nasal Saline**

NS can be delivered as nasal spray, irrigation, nebuliser, bottle or pump. It moisturises dry nasal passages and cleanses the nose by thinning the mucus, making it easier to dispose of. [12,29]

According to EPOS2020, NS is beneficial in relieving symptoms of acute upper respiratory tract infections in viral ARS, especially in children. Due to very low quality of evidence, NS is not being advised neither in post-viral ARS, nor in ABRS. However, it is expected to have a beneficial rather than harmful effect and can, therefore, be administered without concern for the wellbeing of the patient. [5] According to Chitsuthipakorn et al. [30] NS as an add-on treatment proves helpful with regard to nasal discharge solely.

NS is available in various compositions, such as seawater, isotonic and hypertonic solutions. As treatment with NS is non-pharmacological, it has minimal side effects and can be used conventionally. Among very few adverse effects, one can observe nasal discomfort, epistaxis, headache and ear pain. Since saline irrigation delivery systems are not single-use devices, some concerns regarding sinonasal infections secondary to contamination arouse. It has been concluded that contagion can be avoided by thorough hygiene routine of disinfecting or microwaving the irrigation devices and clean water usage or boiling it for 1 to 5 minutes in case of tap water usage. [12,13,29]

### **Conclusions**

ARS is a condition that affects many people yearly. Apart from the systemic approach, using medications administered intranasally seems to improve the treatment effectiveness. ND are to be considered mainly in viral ARS. Should they be continued in post-viral ARS, their administration is to be limited to 10 days. NCS, on the other hand, show some positive effect in post-viral ARS. NS may be helpful in treating viral ARS, especially in children and can be administered in other clinical stages of ARS as well. While used according to prescription, applied with a proper technique and following hygiene guidelines, all aforementioned treatments prove to be

safe. Additionally, we present the essential data, namely available options, treatment recommendations and adverse effects in a form of table (Table 1).

	Nasal decongestants	Nasal corticosteroids	Nasal saline spray / irrigation
Available options	oxymetazoline, xylometazoline, phenylephrine	fluticasone propionate, fluticasone furoate, triamcinolone acetonide, beclomethasone dipropionate, ciclesonide, budesonide, mometasone furoate	isotonic solution, hypertonic solution, seawater
Viral ARS	multiple doses have a small positive effect on the nasal obstruction alleviation	not recommended	beneficial in relieving symptoms of acute upper respiratory tract infections, especially in children
Post-viral ARS	may improve mucociliary clearance; no clinically relevant data	small positive effect; prescribe when necessary	not advised due to very low quality of evidence; can be administered
Bacterial ARS	-	-	not advised due to very low quality of evidence; can be administered
Adverse effects	nasal dryness and irritation, rhinitis medicamentosa; rarely tachycardia, restlessness, palpitations, arrhythmias, angina	epistaxis, nasal discomfort and dryness; rarely septal perforation	nasal discomfort; rarely epistaxis, headache, ear pain

Table 1. Summary of the collected data regarding NS, NCS and NS

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