

# Efficacy of topical corticosteroids and oral antibiotic combination therapy vs Oral antibiotic alone in acute rhinosinusitis

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**Background:** Intranasal corticosteroids are known to improve the symptoms of rhinosinusitis. However, in acute rhinosinusitis, the efficacy of intranasal corticosteroid used with oral antibiotics still needs further evidence.

**Aim of Work:** The aim of this study was to clinically compare the efficacy of topical corticosteroid and oral antibiotic combination therapy versus the use of oral antibiotic alone when treating acute rhinosinusitis regarding main symptoms (nasal obstruction, purulent nasal discharge, anosmia and facial pain), and also evaluating congestion and edema of middle meatus by using nasal endoscopy.

**Materials and Methods:** One hundred patients diagnosed with acute rhinosinusitis were divided into two groups. Group A received a combination of oral antibiotic (amoxicillin clavulanic acid) 50mg/kg/day for 10 days and local steroid spray (mometasone furoate) 2 sprays (50 mcg of mometasone furoate in each spray) in each nostril once daily for 10 days, while group B, the control group, received the oral antibiotic alone. Follow-up was after 10 days with Sino-Nasal Outcome test questionnaire and nasal endoscopy. A comparison between both groups regarding major nasal symptoms and endoscopic findings was done.

**Results:** Group A showed superior results than group B, which received antibiotics alone, regarding the obstructive symptoms. There were statistical significant differences between both groups regarding nasal obstruction, hyposmia, facial pain, nasal congestion and edema at the middle meatus with p values 0.012, 0.013, < 0.001, and 0.006 respectively. There was no significant difference between the two groups as regards the purulent nasal discharge.

**Conclusion:** Intranasal corticosteroid spray in ABR is very useful when used beside oral antibiotics despite the minimal side effects reported. This showed a great effect in relieving obstructive symptoms and signs including nasal obstruction, hyposmia, facial pain, nasal congestion and edema at the middle turbinate.

**Keywords:** Acute rhinosinusitis, amoxicillin clavulanic acid, intranasal corticosteroid, mometasone furoate.

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## Introduction

Rhinosinusitis is one of the most common conditions for which patients seek medical care. It can be defined according to the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) as inflammation of the nose and the paranasal sinuses characterised by two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip), and maybe facial pain/pressure, or reduction/ loss of smell. Definition also entails endoscopic signs of nasal polyps, and/or mucopurulent discharge primarily from middle meatus, and/or oedema/mucosal obstruction primarily in the middle meatus and/or CT findings of mucosal changes with the ostiomeatal complex (OMC) and/or sinuses. [1]

Acute rhinosinusitis (ARS) is defined as rhinosinusitis lasting up to four weeks. Viruses cause most ARS but discriminating between viral and bacterial rhinosinusitis is challenging and impossible in daily practice. [2] Factors suggesting acute bacterial rhinosinusitis (ABRS) entails worsening of the symptoms after five days, or the persistence of symptoms for more than 10 days, or the presence of symptoms out of proportion to those typically associated with upper viral respiratory tract infections. [3]

For assessment of the severity of rhinosinusitis, the EPOS

has formulated the question "How troublesome are your symptoms of rhinosinusitis?" and the patient is given a visual analogue scale (VAS) from 1 to 10, and according to his/her answer the severity of rhinosinusitis can be assessed, where 0-3 score is considered mild, >3-7 is considered moderate, and >7-10 score is severe. It was found that VAS score >5 affects the patient quality of life. [2]

The initial treatment for ARS is always medical. The majority of patients seen in primary care for acute sinusitis are prescribed antibiotics, despite evidence that they provide limited benefit. The effectiveness of other treatments such as decongestants and antihistamines is largely unknown. [4] Antibiotics are effective in patients with ARS only in cases involving bacterial origin. Expert consensus guidelines recommend antibiotics only for patients with severe symptoms persisting for 10 days or more or for worsening of symptoms after initial improvement. [5] One group of authors concluded that ARS resolves without antibiotic treatment, [6] while another group found that the overall efficacy of antibiotics is moderate. [7]

The recommended length of antibiotic therapy is 10 days, however, a shorter treatment course of three to five days may be just as effective and is associated with fewer adverse effects. [8] The incidence of b-lactamase production

of *H. influenzae*, and *M. catarrhalis* is around 40 and 90%, respectively. Thus, antibiotics that cover  $\beta$ -lactamase producing bacteria are reasonable choices if initial antibiotics, such as amoxicillin, trimethoprim-sulfamethoxazole or doxycycline fail to improve symptoms. [9]

Corticosteroids have a profound effect on the inflammatory response and suppress many elements of the allergic inflammatory cascade. They reduce eosinophil infiltration and suppress cytokines, dramatically reducing the infiltration of inflammatory cells into the nasal mucosa. Corticosteroids also reduce the release of histamine and leukotrienes, though this may be due to a reduction in the overall number of inflammatory cells in the epithelium. [10] In patients with recurring acute rhinosinusitis, The Steroid nasal sprays (SNSs) have been shown to improve the global symptoms of acute episodes, especially those related to "obstruction" such as headache, congestion, and facial pain. [11]

The steroid nasal sprays (SNSs) without antibiotic showed a greater improvement in total and major symptoms than the antibiotic alone, raising the question of the relative importance of antimicrobial as compared to anti-inflammatory treatment. Intranasal corticosteroids used with antibiotics showed improvement in ARS symptoms compared with antibiotic therapy alone. [12]

Although the efficacy and safety of intranasal corticosteroids (INCs) are well established for the management of allergic rhinitis, rhinosinusitis, and nasal polyps, concerns remain that these agents may reach the systemic circulation in sufficient concentration to produce adverse effects. [13] There are two aspects of absorption regarding the Intranasal spray (INS). One is topical absorption at the target site that determines therapeutic efficacy and the other is systemic absorption. Systemic absorption either occurs from the fraction of INS swallowed and subsequently absorbed through the gastrointestinal tract or from the fraction absorbed into the blood at the nasal mucosa. [14]

The reported side effects of intranasal corticosteroids are epistaxis, nasal burning and irritation, and a dry nose. These are usually well tolerated, and the benefit of treatment clearly outweighs the associated risks. [15]

The aim of this study was to clinically compare the efficacy of topical corticosteroid and oral antibiotic combination therapy versus the use of oral antibiotic alone when treating acute rhinosinusitis regarding main symptoms of acute rhino sinusitis (nasal obstruction, purulent nasal discharge, anosmia and facial pain), and also evaluating congestion and edema of middle meatus by using nasal endoscopy.

## Materials and Methods

One hundred patients were selected from ENT clinic during the period from January 2016 till December 2016 at Kasr Alainy hospital, Cairo, Egypt. Their ages ranged between (18-55) years old and were diagnosed as acute rhinosinusitis by the presence of two or more major signs or one major and two minor signs of acute rhinosinusitis. Major signs included facial pain/pressure/fullness, nasal obstruction/blockage, nasal/postnasal discharge/Purulence (either by history or by examination), hyposmia/anosmia, and/or fever. While minor signs included headache, fatigue, dental pain, cough, and/or ear pain/pressure/fullness.

Patients were divided into two groups. Group A received a combination of oral antibiotic (amoxicillin clavulanic acid) 50mg/kg/day for 10 days and local steroid spray (mometasone furoate) 2 sprays (50 mcg of mometasone furoate in each spray) in each nostril once daily for 10 days, while group B,

the control group, received oral antibiotic alone (amoxicillin clavulanic acid) 50mg/kg/day for 10 days. Nasal endoscopy was used to assess different signs at day 0 and at end of day 10. Exclusion criteria included patients with complicated ARS, patients who had chronic or allergic rhinosinusitis, patients who were hypersensitive to amoxicillin clavulanic acid and/or patients who had ARS on top of neoplastic lesions in the nose and paranasal sinuses. Patients were then examined by 0-degree nasal endoscope before and after treatment to assess degree of congestion, edema, and purulent nasal discharge at middle meatus.

All patients were asked to complete a questionnaire assessing their nasal symptoms at day 0 and at the end of day 10 using Sino-Nasal Outcome test (SNOT-22).

Data were coded and entered using the statistical package SPSS version 23. Data was summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between quantitative variables in the 2 groups were done using unpaired t test. For comparing categorical data, Chi square ( $\chi^2$ ) test was performed. Exact test was used instead when the expected frequency is less than 5. P-values less than 0.05 were considered as statistically significant.

## Results

The age in this study ranged from 18 till 55 years in the two groups with mean value  $34.78 \pm 9.77$  in group A, and mean value  $32.94 \pm 9.79$  in group B, with insignificant difference between the two groups (p value 0.349). This study included 57 males representing 57 % of the total cases and 43 females representing 43 %, with 28 males (56%) and 22 females (44%) in group A and 29 males (58%) and 21 females (42%) in group B.

Results of comparison between both groups were summarized in **Table 1**. Regarding Nasal obstruction, there was a statistically significant difference between patients in the two groups at the end of day 10 with (p value 0.012).

Patients with no nasal obstruction post treatment in group A were 28 (56%) while in group B were 14 (28%). There was only one patient (2%) with severe nasal obstruction post treatment in group A, while there were 6 patients in group B (12%). were 0 (0%) while in group B were 0 (0%).

There was no statistically significant difference in purulent nasal discharge between patients in the two groups at the end of day 10 with (p value 0.901). Patients with no purulent discharge post treatment in group A were 32 (64%) while there were 31 (62%) in group B. There were no patients with purulent nasal discharge post treatment in both groups. As for hyposmia, there was a statistically significant difference between patients in the two groups at the end of day 10 with (p value 0.013). Patients with no hyposmia post treatment in group A were 38 (78%) while in group B were 31 (62%). In group A, there was only one patient (2%) showed moderate hyposmia while there were no patients with severe hyposmia. While in group B, patients with moderate and severe hyposmia post treatment were 11 (10 moderate and 1 severe). There was a statistically significant difference in the facial pain between patients in the two groups at the end of day 10 with (p value < 0.001). Patients with no facial pain post treatment were 24 (48%) in group A, while in group B were 9 (18%). Only one patient complaint of severe facial pain post treatment in group A (2%), while in group B thirteen had this symptom post treatment (26%).

Regarding congestion and edema at the middle meatus,

there was a statically significant difference between patients in the two groups at the end of day 10 with (p value 0.006). Patients showed no obstruction post treatment in group A

were 39 (78%) and 20 (40%) in group B. patients. There were 5 patients (10%) with complete obstruction in group B, while there was none in group A.

**Table 1 Comparison between group A and group B regarding nasal obstruction, hyposmia, facial pain, purulent nasal discharge, and congestion/edema at middle turbinate**

		Post treatment				P value
		Group A		Group B		
		Count	%	Count	%	
<b>Nasal obstruction</b>	<b>No</b>	28	56.0%	14	28.0%	0.012
	<b>Mild</b>	11	22.0%	20	40.0%	
	<b>Moderate</b>	10	20.0%	10	20.0%	
	<b>Severe</b>	1	2.0%	6	12.0%	
<b>Hyposmia</b>	<b>No</b>	38	76.0%	31	62.0%	0.013
	<b>Mild</b>	11	22.0%	8	16.0%	
	<b>Moderate</b>	1	2.0%	10	20.0%	
	<b>Severe</b>	0	0.0%	1	2.0%	
<b>Facial pain</b>	<b>No</b>	24	48.00%	9	18.00%	< 0.001
	<b>Mild</b>	15	30.00%	5	10.00%	
	<b>Moderate</b>	4	8.00%	14	28.00%	
	<b>Severe</b>	1	2.00%	13	26.00%	
<b>Purulent nasal discharge</b>	<b>No</b>	32	64.0%	31	62.0%	0.901
	<b>Mild</b>	14	28.0%	16	32.0%	
	<b>Moderate</b>	4	8.0%	3	6.0%	
	<b>Severe</b>	0	.0%	0	.0%	
<b>Congestion and edema at middle meatus</b>	<b>No obstruction</b>	39	78.0%	20	40.0%	0.006
	<b>Partial obstruction and edema</b>	11	22.0%	24	48.0%	
	<b>Complete obstruction and edema</b>	0	.0%	5	10.0%	

**Discussion**

Sinusitis or rhinosinusitis is inflammation of the paranasal sinuses. It can be due to infection, allergy, or autoimmune issues. It is a common condition in medical practice, which affects many people worldwide and its prevalence is rising. [16]

In this study, we compared patients who were diagnosed with ABR and treated with topical corticosteroid and oral antibiotics (group A) with those treated with oral antibiotics alone (group B).

Patients in group A who received topical nasal corticosteroid spray with oral antibiotics showed greater improvement regarding most of the major symptoms of acute rhinosinusitis (nasal obstruction, hyposmia, and facial pain) than patients in group B who received oral antibiotics alone, although there was no statistically significant difference as regarding purulent nasal discharge.

The majority of patients seen in primary care for acute sinusitis are prescribed antibiotics, despite evidence that they provide limited benefit. [4] Although most cases of rhinosinusitis are of viral origin, still the use of antibiotics is preferred. Prevention of complications of bacterial rhinosinusitis, such as meningitis, orbital or intracranial complications, is sometimes mentioned as a reason for antibiotic treatment. [17]

In our study, patients in both group received oral antibiotic in the form of amoxicillin clavulanic acid as the first line antibiotic for acute bacterial rhinosinusitis related to its safety, efficacy, low cost, and narrow microbiologic spectrum. Patients known to have allergy from penicillin were excluded from the study. Karageorgopoulos et al (2008) , showed that newer fluoroquinolones conferred no benefit over beta-lactam antibiotics and are not recommended as first-line agents. [18]

In the current study, intranasal corticosteroid spray was used by patients in group A. Intranasal corticosteroid spray was used to facilitate drainage and reduce mucosal swelling of inflamed tissues. [19]

Similar to this study, Meltzer et al. (2000) showed a high degree of agreement with our results. In their study, antibiotics were prescribed in addition to mometasone furoate nasal corticosteroids spray or placebo and it showed that adjunctive treatment with corticosteroid spray caused a significantly greater decrease in total symptom score and in individual scores of inflammatory symptoms associated with the obstruction process (headache, congestion, and facial pain) compared with placebo. Symptoms associated with the secretory processes were improved to a lesser degree. [11]

The absence of a significant difference between patients in the two groups regarding purulent nasal discharge can be explained as patients in both group have received the same type of antibiotic for the same period of time leading to same improvement in both groups.

As our results, Nayak et al., 2002 in their study showed the relative safety and efficacy of INCSs in providing modest symptom relief in patients with ABRs, patients treated with amoxicillin clavulanate were randomized to receive mometasone furoate nasal spray (MFNS) 400 mg twice daily or placebo. Data indicated that the inflammatory symptoms of headache, nasal congestion, and facial pain were significantly reduced with MFNS adjunctive therapy versus placebo. The rationale for intranasal corticosteroids in acute rhinosinusitis resides in their anti-inflammatory properties, as inflammation and edema of the mucous membrane of the nasal turbinates and sinus ostia block the drainage routes and impair mucociliary clearance mechanisms, so reducing inflammation by using intranasal corticosteroids leads to faster drainage, increased aeration and better access for antibiotics. [20]

This can give a good explanation for the improvement of nasal obstruction in patients of group A more than patients in group B as nasal obstruction in acute rhinosinusitis is known to be because of the stagnation of the secretions due to the impaired function of the mucociliary clearance mechanism thus leading to nasal obstruction and also creating a media for bacterial growth. Anosmia/Hyposmia improvement in group A more than in group B can also be explained as nasal obstruction, edema and congestion of nasal mucosa are known to be one of the most important cause of temporarily loss of smell.

Fokkens et al., 2007 recommended the use of intranasal corticosteroids (INCS)—but not antibiotics—as a first step in treatment. In mild to moderate severity illness, antibiotics are reserved for patients who fail to respond to INCS after 3 days and whose symptoms continue for more than 7 days. For patients presenting with severe illness, INCS and antibiotics are recommended in combination as a first step in treatment. [1]

In contrast to our study, Williamson et al., 2007 found that antibiotics and intranasal corticosteroids, alone or in combination, were ineffective. This study suggested that intranasal corticosteroids may be effective in patients with less severe symptoms at baseline. [21] In a meta-analysis which included 6 studies having a total of 2,495 patients, 5 studies of which antibiotics were prescribed in addition to corticosteroids or placebo. This meta-analysis concluded that Intranasal corticosteroids offer a small therapeutic benefit in acute sinusitis, which may be greater with high doses and

with courses of 21 days' duration. [22]

On the other hand, the use of intranasal corticosteroid spray is safe which is confirmed by (Giger et al., 2003) study. In a randomized, double-blind, parallel-group trial involving 112 patients with non-allergic chronic rhinosinusitis, they did not detect any signs of adrenal suppression or significant changes in morning serum cortisol values with once- or twice-daily intranasal beclomethasone dipropionate (400 µg/day) administered for 12 weeks. [23]

In our study, the most frequently reported adverse effects from the treatment in both group A and group B were diarrhea and nausea/vomiting, for which the given antibiotic was blamed more than a side effect of the INCS which was given only to group A and only a small number of patients withdrew from the study by stopping taking the medication.

In this study, patients with recurrent acute rhinosinusitis, which is defined by symptoms and physical findings consistent with acute rhinosinusitis, with these symptoms and findings worsening after five days or when persisting more than 10 days there, were found to be 10 patients in both group (10%) with 4 patients in group A (40%) and 6 patients in group B (60%). While patients who fail to respond to treatment in both groups and presented with persistent severe symptoms were 7 patients regarding nasal obstruction (7%), 1 patient regarding anosmia (1%), 14 patients regarding facial pain (14%) and 5 patients regarding congestion at middle meatus (5%).

### Conclusion

It was concluded that the use of intranasal corticosteroid spray in ABR is very useful when used beside oral antibiotics despite the minimal side effects reported. This showed a great effect in relieving symptoms especially those related to nasal obstruction, hyposmia, and facial pain. It also showed a great effect on congestion and edema at the middle meatus which helps in quick improvement of patients' symptoms. However, regarding the purulent nasal discharge, there was no great difference in patients treated with oral antibiotics alone and patients treated with combination of oral antibiotics and intranasal corticosteroids.

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