

Original article

Intranasal budesonide in children affected by persistent allergic rhinitis and its effect on nasal patency and Nasal Obstruction Symptom Evaluation (NOSE) score

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Abstract**Background:**

Intranasal steroids are recognized as an effective treatment for allergic rhinitis (AR) although their effect on nasal patency has never been evaluated with an objective instrument such as anterior rhinomanometry in children. Moreover this effect has been widely assessed with total Nasal Symptom Scores (NSS) including all symptoms of allergic rhinitis and not with scores specifically focused on nasal obstruction such as the Nasal Obstruction Symptom Evaluation score (NOSE).

Materials and methods:

Sixty children (42 males and 18 female) aged 6–10 years, affected by persistent AR, were randomized and divided in two groups of 30 children to be included in an unblinded trial: one group treated with intranasal budesonide and isotonic nasal saline for 2 weeks and the other group treated only with isotonic nasal saline for 2 weeks. Each child underwent rhinomanometry and completed the NSS and the NOSE scores before and after treatment.

Results:

At the baseline nasal patency and NSS total score, NOSE total scores were correlated ($r = -0.29$, $p < 0.001$; $r = -60$, $p < 0.001$). After 2 weeks of treatment improvements in nasal patency, NSS and NOSE were seen (Δ NSS 4.13 ± 1.38 vs 1.33 ± 1.93 , $p < 0.001$; Δ NOSE 34 ± 17.97 vs 9 ± 18.21 , $p < 0.001$; Δ nasal patency -26.13 ± 25.25 vs -11.83 ± 11.31 , $p < 0.001$). Correlations were found between rhinitis duration and Δ nasal patency and Δ NOSE ($r = -0.84$, $p < 0.001$; $r = 0.43$, $p < 0.01$).

Conclusion:

Intranasal budesonide is effective in increasing nasal patency in children. Moreover the NOSE score was strongly correlated with nasal flow and, hence, this score should be regarded as a valid and reliable instrument in children.

Introduction

Allergic rhinitis (AR) is a common chronic inflammation of the nasal mucosa with a prevalence of 40% in countries with a Western lifestyle¹ and its impact on children's cognitive performance, school performance, sleep disorders and quality of life is well known. Although AR is characterized by local symptoms, a growing body of evidence is indicating that AR may lead to a systemic increase of inflammatory mediators². In these light, its treatment should be regarded not

only as an option to control nasal symptoms but also as an opportunity to prevent its consequences.

Intranasal corticosteroids (INS) are recognized as the most effective treatment for AR and are considered first-line therapy for moderate to severe persistent AR³ since their efficacy is based on their capacity to inhibit both the early- and late-phase inflammatory responses⁴. Moreover, although AR is characterized by symptoms such as nasal discharge, itching and sneezing, nasal blockage or congestion has been reported as a 'key symptom'⁵. Nasal obstruction can be assessed subjectively with visual analogue scales or symptom rating scores, even though most questionnaires such as the Nasal Symptom Score (NSS) include all the symptoms of AR and, hence, are not focused on nasal obstruction. The recently validated in adults^{6,7} NOSE Scale is a disease-specific instrument designed to assess nasal obstruction and it is responsive to change in clinical status. Nevertheless, especially in children, the subjective sensation of nasal obstruction can be difficult to assess accurately^{8,9} and objective methods, such as active anterior rhinomanometry, have been developed to assess nasal patency quantitatively¹⁰.

Although many authors have reported the effects of intranasal budesonide (IB) on clinical symptoms, studies focusing specifically on nasal obstruction and evaluating its effect with a specific symptom score and with inspiratory flow measurements in children are lacking.

In this perspective, our primary purpose is to investigate the effect of IB on nasal patency in children with persistent allergic rhinitis (PAR) and as a secondary outcome to evaluate the reliability of the NOSE score assessing its concordance with rhinomanometric results.

Materials and methods

This study was performed at the Allergology and Immunology service of the Pediatric Department, 'Sapienza' University of Rome. Sixty children (42 males and 18 female) aged between 6 and 10 years (mean age 8 years) affected by PAR³, defined as symptoms that occur for more than 4 days/week and for more than four consecutive weeks and sensitized to house dust mites were enrolled between January and May 2014.

Atopic status was assessed by a Skin Prick Test (SPT)¹¹ (Lofarma, Milan, Italy). A positive SPT was defined by the presence of a wheal 3 mm greater than the wheal size of control (saline solution)¹². Only patients with a positive SPT to house dust mites were included in the study.

Exclusion criteria were the following: history of atopic dermatitis, asthma, nasal abnormalities, concurrent nasal infection, chronic inflammatory disorders, use of systemic or topical corticosteroids or histamine H1-antagonist within the past 4 weeks, or a history of any infection within the past 2 weeks.

Patients were then randomized and divided into two groups of 30 children: one group treated with IB (Aircort nasal spray 100 mcg/nostril twice daily; Italcimici, Pomezia, Rome, Italy) and isotonic nasal saline (irrigation of 5 ml with a bulb syringe twice daily) for 2 weeks and the other group treated only with isotonic nasal saline for 2 weeks.

The study was approved by the Institutional Review Board/Ethic Committee of 'Sapienza' University of Rome and performed with the written informed consent of the parents of all children.

Symptom scores

A Nasal Symptom Score (NSS, maximum 24) and Nasal Obstruction Symptom Evaluation score (NOSE, maximum 20) were obtained for each child. The questionnaire was completed by one investigator who interviewed the patients. When necessary parents were asked to help the child without guiding or interfering with his or her responses. NSS evaluated severity and duration of the following nasal symptoms: stuffy nose, runny nose, sneezing and nasal itching.

A 4 point scale for both severity and duration of those symptoms was calculated as follows: 0 = absent/never; 1 = mild, lightly annoying/once in a while; 2 = moderate, somewhat annoying/often; 3 = severe, very annoying, always or almost of the times. NOSE score included the evaluation of the following symptoms: Nasal congestion or stuffiness, Nasal blockage or obstruction, Trouble breathing through my nose, Trouble sleeping, Unable to get enough air through my nose during exercise or exertion. A 4 point scale was used to identify the severity of each symptom.

Anterior active rhinomanometry

All patients underwent Anterior Active Rhinomanometry (Sibelmed Rinospir PRO 164) in accordance with the International Committee on Standardization of Rhinomanometry¹³. A retest was performed in all patients. The rhinomanometry results were considered relative to nasal flows of 150 Pascals (Pa) and compared with height-dependent pediatric reference values reported in the literature¹⁴. According to Zapletal and Chalupová¹⁴ rhinomanometry classification was considered to be negative (no nasal obstruction) when the fraction of predicted values (p.v.) was ranged between 71% and 100% while it was considered positive when the fraction of p.v. was <70%.

Statistical analyses

Statistical analyses were performed using SPSS (Statistical Package of Social Sciences, Chicago, IL, USA) software

version 19. Descriptive statistics were performed expressing continuous data as means with SDs and categorical data were expressed by frequency and percentage. Differences between scores and nasal patency before and after 2 weeks of treatment with intranasal budesonide were indicated as Δ . Comparisons were evaluated using a *t*-test and a chi-square test while correlations between NSS, NOSE and nasal patency were calculated with Pearson's correlation test. Correlations were considered weak when *r* was between 0.3 and 0.1, moderate between 0.4 and 0.6 and strong between 0.7 and 0.9. The General Linear Model (GLM) for repeated measures was used in order to assess the variations of symptom scores in cases and controls over time. A *p*-value less than 0.05 was considered statistically significant.

Results

At the baseline nasal patency and NSS total score, NOSE total scores, NSS obstruction, NOSE nasal congestion, and NOSE nasal obstruction were correlated ($r = -0.29$, $p < 0.001$; $r = -0.60$, $p < 0.001$; $r = -0.43$, $p < 0.001$; $r = -0.54$, $p < 0.001$; $r = -0.7$, $p < 0.001$) (Figure 1). Specific symptom scores before and after treatment are reported together with the results of the GLM in Table 1. NSS, NOSE and nasal patency were comparable before treatment ($p > 0.05$, data not shown) between cases and controls, while the change in these parameters after 2 weeks of treatment was different with a wider improvement in children treated with IB as shown in Figure 2 and Table 2 (Δ NSS 4.13 ± 1.38 vs 1.33 ± 1.93 , $p < 0.001$; Δ NOSE 34 ± 17.97 vs 9 ± 18.21 , $p < 0.001$;

Δ nasal patency -26.13 ± 25.25 vs -11.83 ± 11.31 , $p < 0.001$). In particular when considering specifically all the items included in the NSS and the NOSE scores there was a statistically significant improvement in all symptoms with the exception of nasal itching (Table 2). Moreover there was a significant correlation between rhinitis duration and Δ nasal patency and Δ NOSE ($r = -0.84$, $p < 0.001$; $r = 0.43$, $p < 0.01$).

Discussion

Antihistamines are widely used for AR treatment and are effective in relieving sneezing, rhinorrhea, and itching although they have little effect on nasal congestion and are most effective when ocular symptoms are prominent^{15,16}. They control symptoms of the early-phase inflammatory response through the action on histamine₁ receptors while they have no effect on the late-phase inflammatory response and on the underlying inflammatory process¹⁶. INs have been shown to be the most useful treatment for AR and they are effective against the entire spectrum of AR symptoms since they inhibit both the early- and late-phase inflammatory responses^{15,16}.

In 1984 Henriksen and Wenzel¹⁷ performed the first study on 18 children with nasal obstruction and reported after 4 weeks of treatment with 400 mcg daily a reduction of nasal airway resistance shown by posterior rhinomanometry. The efficacy of nasal budesonide was clinically confirmed at the lower dose of 200 mcg by Day *et al.* in 1990¹⁸ and at 128 mcg by Fokkens *et al.* in 2002¹⁹. These studies highlighted that the effect of this treatment is significant on the symptom of blocked nose through the use of clinical

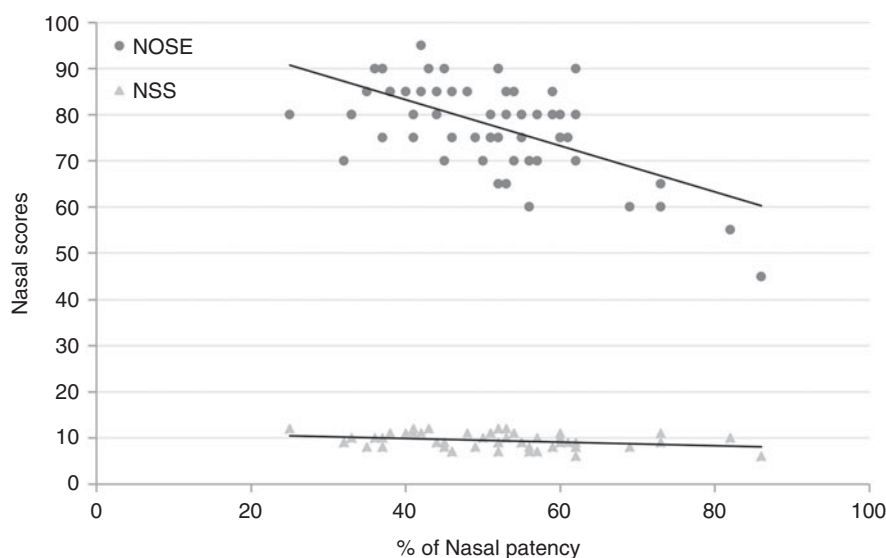


Figure 1. Correlations between nasal patency NOSE and NSS total scores.

Table 1. Nasal scores and percentage of nasal patency before and after treatment.

Variables	Patients		Mean	SD	Sig (GLM)
NSS	Cases	Before treatment	9.36	1.69	<0.001
		After treatment	5.23	1.10	
	Controls	Before treatment	9.63	1.54	
		After treatment	8.30	2.03	
NOSE	Cases	Before treatment	78.33	10.69	<0.001
		After treatment	44.33	17.21	
	Controls	Before treatment	77.33	9.25	
		After treatment	68.33	16.31	
NOSE congestion	Cases	Before treatment	16.16	2.84	<0.001
		After treatment	8.83	3.39	
	Controls	Before treatment	17.5	3.41	
		After treatment	15	4.54	
NOSE obstruction	Cases	Before treatment	17	2.81	<0.001
		After treatment	8.5	2.67	
	Controls	Before treatment	17.16	2.84	
		After treatment	15.5	4.01	
NOSE breathing	Cases	Before treatment	16.6	3.03	0.012
		After treatment	9.5	4.22	
	Controls	Before treatment	16	3.57	
		After treatment	14.5	4.42	
NOSE sleeping	Cases	Before treatment	15.66	3.14	NS
		After treatment	9	5.15	
	Controls	Before treatment	12.83	2.84	
		After treatment	11.83	3.82	
NOSE exercise	Cases	Before treatment	12.83	5.52	NS
		After treatment	8.5	5.27	
	Controls	Before treatment	13.83	6.11	
		After treatment	11.5	5.59	
NSS obstruction	Cases	Before treatment	2.83	0.379	<0.001
		After treatment	1.23	0.43	
	Controls	Before treatment	2.87	0.346	
		After treatment	2.6	0.49	
NSS rhinorrhea	Cases	Before treatment	2.33	0.47	<0.001
		After treatment	1.23	0.43	
	Controls	Before treatment	2.43	0.5	
		After treatment	2.26	0.58	
NSS sneezing	Cases	Before treatment	2.13	0.73	NS
		After treatment	1.16	0.53	
	Controls	Before treatment	2.07	0.86	
		After treatment	1.7	0.65	
NSS nasal itching	Cases	Before treatment	2.07	0.78	0.04
		After treatment	1.56	0.56	
	Controls	Before treatment	2.27	0.64	
		After treatment	2.03	0.76	
Nasal patency	Cases	Before treatment	50.27	11.44	0.03
		After treatment	76.40	21.08	
	Controls	Before treatment	51.27	12.55	
		After treatment	63.10	11.31	

scores without performing an objective assessment of nasal patency. According to our knowledge the present study is the first focusing specifically on nasal obstruction and showing, with an objective instrument such as rhinomanometry, that intranasal budesonide administered at 200 mcg daily for 2 weeks is effective in increasing nasal patency in children with PAR.

One of the major limitations of the study is represented by the unblindedness of the protocol even though the two groups of patients were comparable for NSS, NOSE and nasal patency before the beginning of the treatment. Another limitation is the small number of children

included in the study which does not allow us to draw any definitive conclusion.

Moreover the present study is the first using the NOSE score in children. Notably, the results of this specific score were assessed in the light of rhinomanometric results and, hence, of objective nasal patency: NOSE score was strongly correlated with the fraction of predicted values of nasal flow. In this perspective, although these preliminary finding should be confirmed by a blinded placebo-controlled study, this score might be regarded as a valid and reliable instrument that can be used for outcomes research in children.

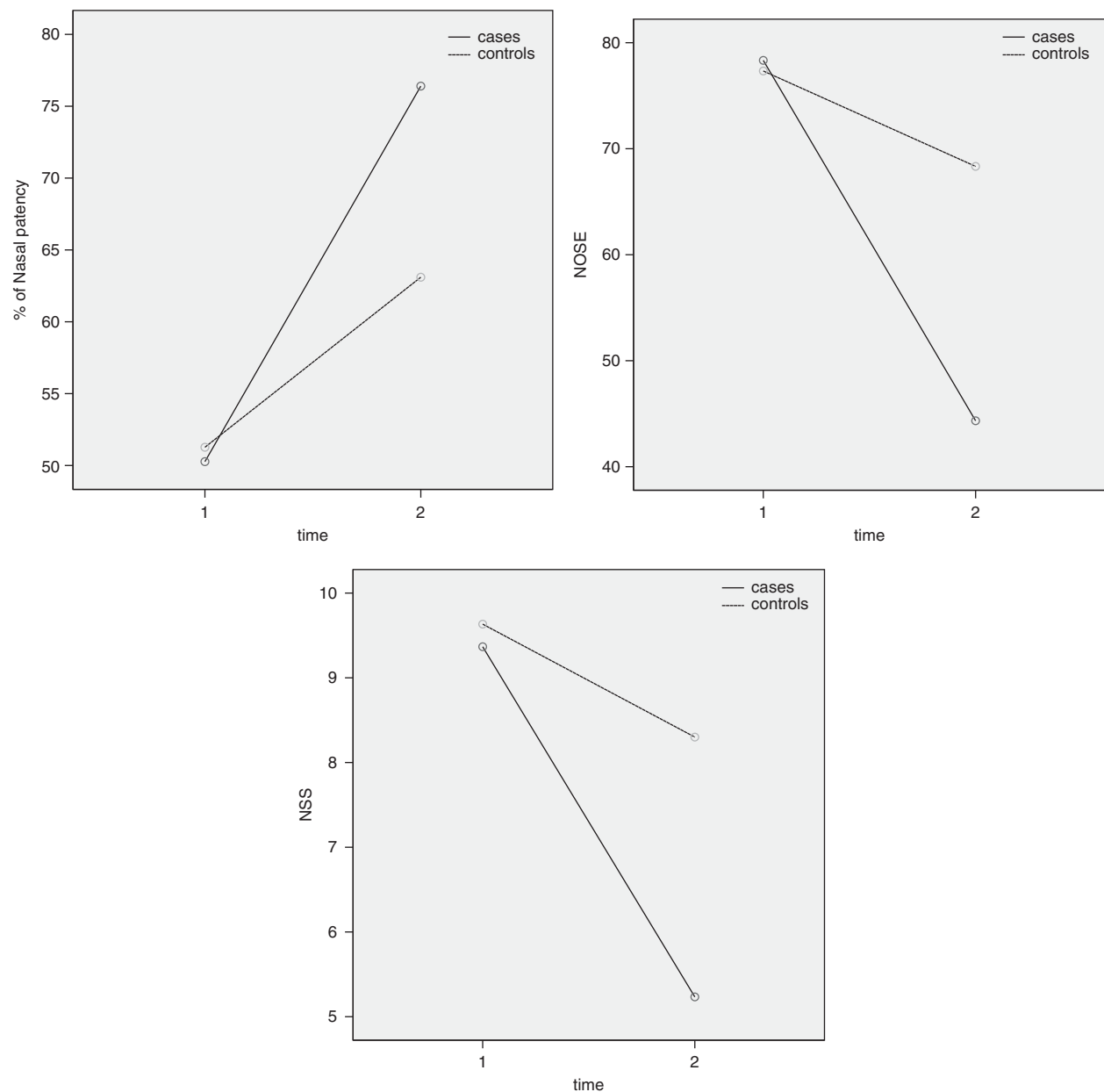


Figure 2. Nasal patency, NOSE and NSS before and after 2 weeks of treatment with intranasal budesonide.

Table 2. Differences (Δ) between scores and nasal patency before and after 2 weeks of treatment with intranasal budesonide.

Variables	Patients	Mean	SD	Sig (<i>p</i>)
Δ NSS	Cases	4.13	1.38	<0.001
	Controls	1.33	1.93	
Δ NOSE	Cases	34	17.97	<0.001
	Controls	9	18.21	
Δ NOSE congestion	Cases	7.33	4.68	<0.001
	Controls	2.5	4.68	
Δ NOSE obstruction	Cases	8.5	3.25	<0.001
	Controls	1.66	3.3	
Δ NOSE breathing	Cases	7.16	4.29	<0.001
	Controls	1.5	3.97	

(continued)

Table 2. Continued.

Variables	Patients	Mean	SD	Sig (p)
△ NOSE sleeping	Cases	6.66	5.14	<0.001
	Controls	1	4.02	
△ NOSE exercise	Cases	4.33	6.26	0.18
	Controls	2.33	5.37	
△ NSS obstruction	Cases	1.60	0.56	<0.001
	Controls	0.26	0.44	
△ NSS rhinorrhea	Cases	1.10	0.60	<0.001
	Controls	0.16	0.53	
△ NSS sneezing	Cases	0.96	0.71	0.005
	Controls	0.36	0.85	
△ NSS nasal itching	Cases	0.50	0.50	0.12
	Controls	0.23	0.77	
△ Nasal patency	Cases	-26.13	25.25	0.007
	Controls	-11.83	11.31	

*Sig is significance (Sig), NSS is Nasal Symptom Score, NOSE is Nasal Obstruction Symptom Evaluation, NR is number.

Transparency

Declaration of funding

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Declaration of financial/other relationships

A.M.Z., F.O., M.G., L.I., G.D.C., G.T. and M.D. have disclosed that they have no significant relationships with or financial interests in any commercial companies related to this study or article.

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