

Does atopy influence the effectiveness of treatment of adenoid hypertrophy with mometasone furoate?

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ABSTRACT

Background: The effect of topical mometasone for adenoid hypertrophy treatment is well established. Nevertheless, the influence of atopy on this treatment remains ill defined.

Objective: This study aims to compare the effects of topical mometasone furoate treatment on the adenoid tissue between atopic and nonatopic children.

Methods: Fifty-one children with obstructive respiratory complaints underwent a semistructured clinical questionnaire on nasal symptoms, prick test, and nasoendoscopy. Nasoendoscopic images were digitalized, and both adenoid and nasopharyngeal areas were measured in pixels; the relative adenoid/nasopharyngeal area was calculated. Patients were initially treated for 40 days with nasal saline solution. In a subsequent 40-day period, topical mometasone furoate (total dose, 100 µg/day) was used.

Results: Topical mometasone significantly improved nasal obstruction, snoring, and apnea and also significantly reduced the adenoid tissue area related to the nasopharynx ($p < 0.0001$). Treatment with this glucocorticoid was not influenced by atopy, neither for symptoms nor for adenoid area.

Conclusion: Topical mometasone furoate significantly reduced the adenoid tissue area and led to a supplementary improvement of nasal symptoms. This improvement was similar for atopic and nonatopic patients.

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Chronic respiratory obstruction leads to substantial changes in the neurocognitive response and in facial morphology. Therefore, diagnosis and treatment of respiratory obstruction should be anticipated to avoid major complications. Adenoid hypertrophy and chronic rhinitis are the leading factors causing respiratory obstruction, and these two entities are frequently observed in the same patient.¹ Because allergic inflammation may be related to adenoid edema, it is generally believed that patients with allergic rhinitis may be predisposed to larger adenoid tissue and more prominent symptoms than patients without allergy.

Treatment of adenoid hypertrophy with topical corticosteroids has been largely reported in the literature, and most studies show that this treatment approach may be very useful for improving symptoms^{2–8} and decreasing adenoid tissue size.^{3,6,7} Among the available corticosteroids, mometasone furoate has been demonstrated to be very safe in children older than two years.^{9,10} Nevertheless, little has been explored regarding the influence of atopy on this treatment outcome. Thus, the present study aims to evaluate the effect of nasal mometasone furoate treatment in children with adenoid hypertrophy, comparing the group with associated allergic rhinitis to those without allergy.

MATERIALS AND METHODS

Children aged four to eight years were studied at the Mouth Breathing Center, Ribeirão Preto Medical School, University of São Paulo, Brazil. Inclusion criteria included symptoms of nasal obstruction and/or snoring, and a previous endoscopy or lateral x-ray suggestive of adenoid hypertrophy. Exclusion criteria comprised the use

of topical or systemic corticosteroids, antihistamines, or antibiotics for at least two months before the first consultation, viral or bacterial upper airway infection in the previous month, immunodeficiency, or facial malformation. Because the study center is located in a tropical area where temperature does not vary much throughout the year, we avoided only the three drier months of the year (June, July, and August), when respiratory infections become more frequent.

Children whose parents gave written informed consent were included. The study was approved by local Institutional Review Board, Ethics in Research Committee, Clinical Hospital, Medical School of Ribeirão Preto, University of São Paulo (protocol number 2983/2009).

Patients and parents/caregivers completed a questionnaire regarding respiratory symptoms: nasal obstruction, snoring, rhinorrhea, sneezing, and itching. Symptoms were scored as 0 (absent), 1 (mild), 2 (moderate), or 3 (severe). A prick test for respiratory allergens and a nasal endoscopy were also performed at that initial evaluation. Nasal endoscopies were all performed by the same individual with a flexible endoscope of 3.2 millimeter in diameter (Olympus). All images were digitally recorded for future analysis.

All patients were instructed to use saline solution during 40 days (treatment one, placebo treatment) and topical mometasone furoate (dose of 50 µg/nosril per day, treatment two) for the subsequent 40 days. After each period of treatment, the clinical questionnaire and nasoendoscopy were repeated and the empty flasks were retrieved, to ascertain the correct use of the medication.

The patients who discontinued the medication by any reason, or those who used other medications or developed upper airway infection during the evaluation period, were excluded from the study.

A different examiner calculated the ratio of the adenoid/nasopharyngeal area in all exams. For this purpose, the images of the adenoid tissue and nasopharyngeal areas were quantitated in pixels using ImageJ software. The final adenoid area was considered as the ratio of the adenoid tissue to the nasopharyngeal area. The examiner who performed this evaluation had no information on patient clinical status or period of study.

For comparison between groups, the clinical outcome was defined as:

clinical symptoms: symptom score after treatment, symptom score before treatment;

adenoid ratio: ratio after treatment/ratio before treatment,

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Table 1. Comparison in symptoms between before treatment versus after saline treatment (placebo)

Symptom	Before Treatment	Saline Treatment	95%CI	p-value
Nasal obstruction	2.68 ± 1.16	2.21 ± 1.25	0.29;0.65	<0.0001
Snoring	2.89 ± 1.29	2.60 ± 1.13	0.12;0.45	<0.0001
Rhinorrhea	2.68 ± 1.16	1.71 ± 1.41	0.01;0.30	<0.0001
Sneezing	2.26 ± 1.55	2.16 ± 1.50	0.002;0.20	<0.05
Nasal itching	2.45 ± 1.57	1.92 ± 1.40	0.35;0.69	<0.0001

Statistical analysis was performed with a nonparametric Wilcoxon test and is presented here as the mean ± standard deviation.

Table 2. Comparison between atopic versus nonatopic patients regarding improvement scores after nasal saline solution

	Atopic	Nonatopic	p-value
Nasal obstruction	-0.50 ± 0.51	-0.45 ± 0.60	0.78
Snoring	-0.27 ± 0.46	-0.30 ± 0.57	0.89
Rhinorrhea	-0.16 ± 0.51	-0.15 ± 0.36	0.91
Sneezing	-0.55 ± 0.51	-0.50 ± 0.51	0.74
Itching	-0.11 ± 0.32	-0.10 ± 0.30	0.91

Statistical analysis was performed with a nonparametric Mann-Whitney U-test and is presented here as the mean ± standard deviation.

The intraindividual comparison was statistically analyzed with a paired Student's *t*-test for the adenoid area measurement. Because clinical questionnaire scores failed on normality test, the Wilcoxon test was performed for this variable. The comparison between allergic and nonallergic patients was performed using Student's *t*-test for the adenoid ratio and the Mann-Whitney *U*-test for the clinical questionnaire. Statistics were considered to be significant if $p < 0.05$.

RESULTS

Sixty children were initially included, but only 51 completed the study. The final group was composed of 34 (66.6%) males and 17 (33.3%) females, with a mean age (±standard deviation) of 6.43 ± 1.47. Twenty-four patients (47%) had a positive prick test to at least one respiratory allergen (perennial at 100% of cases), and 27 (53%) were considered to be nonatopic. The mean age was 6.25 ± 1.26 for the atopic patients and 6.53 ± 1.26 for the nonatopic individuals.

Most of the patients showed a significant reduction in symptoms after nasal saline solution, particularly in nasal obstruction ($p < 0.0001$), snoring ($p < 0.0001$), rhinorrhea ($p < 0.0001$), sneezing ($p < 0.05$), and nasal itching ($p < 0.0001$) (Table 1). Atopy did not influence the outcome for any symptom after this treatment (Table 2).

The mean adenoid area in relation to the nasopharynx decreased from 0.71 ± 0.13 to 0.68 ± 0.13 (95% confidence interval [CI]: -0.04; 0.01, $p = 0.56$), but this reduction was modest and not significantly different from before treatment, and it was not influenced by atopy (percentage reduction of 1.01 ± 0.08 in atopic patients and 1.02 ± 0.17 in nonatopic patients, $p = 0.74$).

Mometasone furoate treatment significantly improved nasal obstruction ($p < 0.0001$), snoring ($p < 0.0001$), rhinorrhea ($p < 0.05$), sneezing ($p < 0.01$), and nasal itching ($p < 0.0001$) (Table 3). Also, atopy did not influence the symptom improvement (Table 4).

The adenoid/nasopharyngeal area decreased to 0.61 ± 0.13, which was significantly lower than that observed at the other two moments of evaluation: at initial diagnosis and following saline solution (95%CI: 0.03;0.10, $p < 0.0001$). Patients with atopy had a similar reduction in adenoid tissue compared with nonatopic patients (0.95 ± 0.27 for atopic versus 0.90 ± 0.22 for nonatopic patients, $p = 0.48$) after furoate mometasone treatment.

DISCUSSION

Clinical treatment for adenoid hypertrophy has gained importance in the last few years because of its low prevalence of complications and general good results. Several articles have been published examining this treatment approach for adenoid hypertrophy Cengel and Akyol,³ Berlucchi *et al.*,^{2,11} Bitar *et al.*,¹² and our group⁷ have demonstrated that mometasone furoate decreases adenoid tissue and improves symptoms related to adenoid hypertrophy. Additionally, Jung *et al.*⁶ have observed an improvement in the quality of life of children with adenoid hypertrophy after treatment with mometasone furoate, and Kheirandish-Gozal and Gozal⁵ have demonstrated that intranasal budesonide effectively reduced the apnea-hypopnea index (by polysomnography) and adenoid dimensions. In a systematic review, Chadha *et al.*⁴ concluded that nasal corticosteroids are an effective treatment for adenoid hypertrophy, reducing nasal symptoms and adenoid size. Furthermore, the authors have also considered nasal corticosteroids to be safe and are well tolerated by children.

There is still some controversy about the association between allergy and adenoid hypertrophy. These two diagnoses are the most common causes for respiratory obstruction in children, and they may be frequently observed in the same patient. Although some articles reported higher prevalence of atopy in children with adenotonsillar hypertrophy (as described by Sadeghi-Shabestari *et al.*,¹³ who measured atopy by symptoms and positive prick test for respiratory allergens), others failed to confirm this association. Using different methods to diagnose atopy, our group¹⁴ (using clinical history and prick test) and Zhang *et al.*¹⁵ (applying clinical history and ImmunoCap to measure specific serum IgE) observed similar prevalence of atopy between patients with and without adenotonsillar hypertrophy.

This subject seems to be even more controversial when we consider the diagnostic methods for atopy. Recently, the concept of local rhinitis, in which patients may show clear allergic inflammatory findings in nasal tissue, although demonstrating low levels of IgE expression, has gained force. Zhang *et al.*¹⁵ have investigated this concept in children with adenotonsillar hypertrophy, and they reported positive local specific IgE in adenoid and tonsillar tissue in approximately 40% of patients with negative prick test.

In the present study, we performed a clinical trial in which the patients were submitted to a placebo treatment (saline solution), followed by the mometasone furoate treatment. This schedule allowed us to design two observational endpoints for the same study group: the initial saline group treatment, examining at which extent nasal saline flushing alone would reduce nasal symptoms and following the treatment with the glucocorticoid medication (mometasone furoate). Also, we applied an objective method (endoscopy with digitalized images measurements) to observe the adenoid tissue and airway passage areas. This is a reliable and objective evaluation, which also allowed us to perform a double-blinded assessment and that was previously described and validated in literature by our group.⁷ However, one important question remained from this previous study: does atopy play some influence in the treatment outcome for these patients with adenoid hypertrophy?

Table 3. Comparison in symptoms between before treatment versus after saline treatment (placebo)

Symptom	Saline Treatment	Mometasone Treatment	95%CI	p-value
Nasal obstruction	2.21 ± 1.25	1.50 ± 1.35	0.84;1.52	<0.0001
Snoring	2.60 ± 1.13	2.10 ± 1.29	0.30;0.69	<0.0001
Rhinorrhea	1.71 ± 1.41	1.45 ± 1.48	0.09;0.42	<0.05
Sneezing	2.16 ± 1.50	1.87 ± 1.45	0.12;0.66	<0.01
Nasal itching	1.92 ± 1.40	1.29 ± 1.31	0.80;1.51	<0.0001

Statistical analysis was performed with a nonparametric Wilcoxon test and is presented here as the mean ± standard deviation. CI = confidence interval.

Table 4. Comparison between atopic versus nonatopic patients regarding improvement scores after furoate mometasone treatment

	Atopic	Nonatopic	p-value
Nasal obstruction	-1.22 ± 1.06	-1.15 ± 1.04	0.83
Snoring	-0.72 ± 1.01	-0.65 ± 0.98	0.82
Rhinorrhea	-0.33 ± 0.68	-0.50 ± 0.76	0.43
Sneezing	-1.11 ± 0.96	-1.20 ± 1.19	0.81
Itching	-0.33 ± 0.84	-0.45 ± 0.82	0.42

Statistical analysis was performed with a nonparametric Mann-Whitney U-test and is presented here as the mean ± standard deviation.

We have observed that mometasone improved nasal symptoms and diminished adenoid tissue when compared with placebo-controlled nasal douching. Because the evaluation of the adenoid tissue was performed by a blinded observer who had no information regarding treatment condition and clinical data, we were able to get more robust results.

There are a few studies evaluating the influence of atopy on mometasone treatment in children with adenoid hypertrophy, and these studies did not specifically compare atopic with nonatopic children. Nevertheless, both studies from Jung *et al.*⁶ and Bitar *et al.*¹² stated that they could not observe any specific difference in response to mometasone treatment between the groups.^{6,12} Accordingly, we decided to compare two groups: patients with adenoid hypertrophy alone and those with adenoid hypertrophy associated with atopy. Our initial hypothesis was that the atopic patients would have a better outcome on corticosteroid treatment because they would initially present with more prominent allergic edema and inflammatory influx. Nevertheless, this superior outcome was not observed in our study; atopic patients had the same clinical response to treatment as nonatopic patients, and there was also a similar pattern in the adenoid to nasopharyngeal area between both groups.

Our results suggest that the antiinflammatory action of topical glucocorticoids in the adenoid tissue is not limited to allergic conditions and that patients without atopy can also benefit from this medical treatment. This outcome seems to occur because glucocorticoids have a broad antiinflammatory action: glucocorticoid receptor is present in every human cell and, when attached to glucocorticoid, acts as a nuclear factor, inducing the transcription of several antiinflammatory genes, as well as inhibiting several proinflammatory ones. In addition, glucocorticoid receptor inhibits the interaction between other proinflammatory transcription factors, such as activator protein-1 and nuclear factor κ B. Moreover, a nontranscriptional action of glucocorticoids has been recognized to allow an immediate antiinflammatory action (within seconds), generally mediated through kinases.^{16,17}

We can conclude that mometasone significantly reduces the adenoid dimension and improves nasal symptoms in children. Furthermore, this response to topical treatment was similar in atopic and nonatopic patients.

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