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Original article

Obtaining concomitant control of allergic rhinitis and asthma with a nasally inhaled corticosteroid

Allergic rhinitis (AR) and asthma coexist frequently and a dual treatment is recommended by prescribing topical nasal plus oral inhaled corticosteroids. The purpose of this study was to assess the efficacy of a nasally inhaled corticosteroid aiming at concomitant control of AR and asthma. A controlled trial was conducted among 60 patients with AR and asthma, aged 6–18 years, who were randomized into two groups. During 8 weeks, the experimental group (30 patients) received exclusively fluticasone propionate hydrofluoroalkane (FP-HFA) inhaled through the nose (mouth closed) using a large volume spacer attached to a face mask. The comparison group (30 patients) received a nasal spray of isotonic saline plus oral inhalation of FP-HFA through a mouthpiece attached to the same spacer. Clinical scores for AR and asthma, nasal inspiratory peak flow (NIPF), and spirometry were assessed by blinded observers. There was a significant improvement in AR scores and NIPF in the experimental group ($P \leq 0.01$) up to week 8, when a worsening was observed after the intervention was interrupted. Asthma symptoms score, forced expiratory volume $(FEV)_1$, and $FEF_{25-75\%}$ were not statistically different between groups at the baseline visit or along follow-up visits ($P \geq 0.20$). Prebronchodilator FEV_1 (% predicted value) improved by 10% in both groups, comparing values at inclusion with those obtained at the end of follow up. Our results suggest that nasally inhaled FP-HFA through a spacer may control AR and asthma in children and adolescents. This approach is likely to result in higher compliance, lower costs, and fewer side effects.

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Allergic rhinitis (AR) and asthma should not be considered distinct ailments but the expression of a single inflammatory process involving the whole of the respiratory tract, thus representing a *continuum* of disease. Overall, epidemiologic studies have demonstrated that AR coexists with asthma in up to 80% of subjects suffering from asthma (1, 2). Estimates suggest that 80% of asthma sufferers live in low-income countries (3) but the affordability of inhaled and intranasal corticosteroids, the most cost-effective options to control persistent AR and asthma, is very limited in these regions, hindering severely the possibilities of secondary prevention of such comorbidity. Furthermore, the coexistence of AR increases by 46% the cost of asthma treatment (4). Both *Global Initiative for Asthma* (5) and *Allergic Rhinitis and its Impact on Asthma* (2) guidelines recommend a dual management of AR and asthma, i.e. the use of oral inhaled and intranasal corticosteroids.

Previous studies aimed at assessing the efficacy of two different strategies on the concomitant treatment of AR and asthma in children and adolescents with inhaled corticosteroids. The first used a nozzle attached to a spacer and symptoms scores for AR were reduced by 64% after daily inhalation of budesonide-CFC for 3 weeks (6). The second study recruited nonsteroid naive patients with AR and stable asthma. In this latter study, beclomethasone-CFC was delivered through a face mask attached to a large volume spacer and obtained a similar reduction (60%) in AR symptoms, without signs of worsening of asthma (7). However, no clinical trial in the searched literature was found in which an hydrofluoroalkane (HFA) inhaled steroid combination delivered by a face mask attached to a spacer was used as first-line therapy in steroid naive individuals for the treatment of AR and asthma.

Contrarily to oral inhalation, in which the amount of inhaled steroids deposited by inertial impaction in the oropharynx brings no benefit and contributes to adverse events, nasal inhalation would lead aerosol deposition to the nose resulting in control of AR symptoms, while the same drug deposited in the lungs by gravitational sedimentation should result in a therapeutical effect.

Based on these assumptions we hypothesized that a nasally inhaled corticosteroid using HFA as a propellant

could be effective for concomitant control of AR and asthma in real life public health settings in developing countries.

Material and methods

We carried out a randomized-controlled trial with two parallel groups in a pediatric pulmonology outpatient clinic that assists exclusively patients from low-income families.

Diagnosis of persistent AR was based on the presence of one or more of the following six signs or symptoms for 4 or more days per week and more than 4 weeks before their recruitment: pharyngeal pruritus, sneezing, watery rhinorrhea, itchy nose, and eyes and nasal obstruction (2). The clinical score described by Wilson et al. (8) was modified for the assessment of AR severity upon admission and at each follow-up visit. Each of the aforementioned symptoms received a number of points ranging from 0 (best) to 3 (worst). Thus, 0 point reflected the absence of a given symptom; 1 point indicated the sign/symptom as mild, well tolerated, not interfering with sleep or daily activities; 2 points indicated the sign/symptom as well-defined, discomforting, interfering only with activities that demanded a higher degree of concentration, and finally, 3 points accounted as a symptom of high intensity, very bothersome, barely-tolerated, hindering the patient's sleep and daily activities. The total score ranged from 0 to 18 points, allowing the assessment of AR severity as mild, moderate, and severe if rated 1–6, 7–12, and 13–18 points, respectively.

Additionally, for asthma, severity assessment was graded according to the clinical score developed by Rosier et al. (9). Such score take into consideration (five-items), as follows, use of β_2-agonists, severity of exacerbations, night symptoms, and limitations of habitual activities and of sports, and/or entertainment. For the use of β_2-agonists – 3 points reflected daily use of β_2-agonists, 2 points indicated weekly, and 1 point never; for severity of exacerbations – 4 points more than once a month hospital admissions, 3 points once a month, and 0 if no hospital admissions or emergency visits; for night symptoms – 4 points for most nights, 3 points indicated 1–3 nights/week, and 1 point was attributed to no night symptoms; for limitations on usual activities – 4 points indicated daily, 3 points indicated moderate activity, and 0 no limitation; for limitation of sports/entertainment – 4 points indicated total limitation, 3 points occasional limitation, and 0 indicate normal activity. The total score ranged from 2 (best) to 19 points (worst), allowing the assessment of asthma severity as mild/light, moderate and severe if rated 2–8, 9–14, and 15–19 points, respectively.

Patients

We included patients aged 6–18 years who suffered from steroid naive asthma, without treatment for at least 3 months, with moderate or severe persistent AR and asthma. They all had positive skin prick tests to at least one aeroallergen and presented an improvement ≥12% in forced expiratory volume $(FEV)_1$ after using 400 μg of albuterol.

Subjects who presented asthma exacerbations within the four preceding weeks and a prebronchodilator FEV_1 of $<40\%$ of the predicted value, those using any medicines for AR and asthma and, also, subjects with other physician-diagnosed concurrent illnesses were excluded.

Procedures

Clinical scoring for AR and asthma, nasal inspiratory peak flow (NIPF), and spirometry were carried out by an independent observer who was blinded to the therapeutical regimens. The complete assessment was performed at admission and every 2 weeks during the 10-week follow-up period.

Functional evaluation of AR and asthma was carried out by in-office NIPF (In-check-inspiratory flow meter®, Clement Clarke, Harlow, UK) and forced expiratory spirometry (SBG spirometer®, SDI Diagnostics, Easton, MA, USA). The highest of three FEV_1 readings was recorded. Pulmonary function testing followed the American Thoracic Society recommendations (10) and Polgar's equations were taken as reference values (11).

Skin prick tests (International Pharmaceutical Immunology, Spain) to evaluate sensitivity to usual aeroallergens were performed according to the European Academy of Allergy and Clinical Immunology recommendations (12). Tests were conducted and interpreted prior to group assignment.

Patients were randomly assigned into two treatment groups. The experimental [fluticasone propionate (FP) face mask; FFM] group received FP through a pressurized-HFA metered dose inhaler (pMDI; Flixotide®, GlaxoSmithKline, Rio de Janeiro, Brazil). A large volume (650 ml) pear-shaped valved plastic spacer (Flumax®, Flumax Medical Equipments, Belo Horizonte, Brazil), attached to a close-fitting face mask was employed. Patients repeatedly inhaled deeply and slowly through their nose for 30 s (mouth closed). The comparison (FP mouth piece -FMP-) group received: (i) for AR, 0.9% sodium chloride intranasal spray in each nostril twice a day, and (ii) for asthma, FP-HFA-pMDI through oral inhalation (Flixotide®, GlaxoSmithKline), using the same spacer attached to a mouthpiece. Fluticasone propionate dosages to treat asthma varied according to age group: subjects up to 11 years old received 100 μg and those older than 11 years used 150 μg of FP-HFA administered in the morning and at night. Such doses are in accordance with GINA Guidelines for moderate persistent asthma, i.e. up to 500 μg/day of FP or equivalent.

The FFM and FMP groups were treated continuously for 8 weeks, after which nasal inhalation of FP-HFA or intranasal saline was interrupted in the two groups. For these last two weeks – a washout period for AR treatment – both groups received the same usual asthma treatment with the above-mentioned dosages of orally inhaled FP. The quality of oral and nasal inhalation was monitored by two independent nurses at admission and in every follow-up visit. To reduce electrostatic charge, spacers were coated with household detergent every 15 days.

No specific recommendation regarding allergen avoidance and immunotherapy was given to any of the patients during this study.

Statistical aspects

Sample size. Previous clinical observations of our group obtained an average reduction from 10 to 4 points (a difference of 6 points) in the same nasal score for the subjects receiving FP exclusively via nasal inhalation, and by 3 points for subjects using saline spray. A pooled variance of 10.1 was obtained from analysis of these preliminary observations. Assuming: (i) that the difference between groups would be of 3 points, and (ii) a α- and β-error equal to 5% and 10% respectively (power = 0.90), the required sample size was 50 patients, 25 subjects in each group. Taking a rate of 20% for dropout and/or therapeutical failure, the total sample was increased to 60 patients, 30 in each group.

Primary and secondary outcomes and analysis. The main predefined outcome measures were the changes from baseline in the clinical score for AR and NIPF at the end of week 8 of the scheduled follow up. Predefined secondary outcome measures were the changes from baseline in asthma clinical scoring and measurements of FEV_1 and

$FEF_{25-75\%}$ over the same follow-up period. Our analysis was by intention-to-treat.

Frequency distribution, chi-square test, Student's *t*-test, and Fisher's exact test were used to compare AR and asthma symptom score and functional parameters.

Also, the difference between baseline values and the subsequent weeks in the AR score, NIPF, asthma score, FEV_1, and $FEF_{25-75\%}$ was calculated separately for each one of the study groups (intra-group analysis), through a paired *t*-test. For these comparisons, statistical significance of any differences was evaluated after applying Bonferroni's correction, which provides a *P*-value of 0.001 for the observed differences, taking into account 50 distinct pairs of comparisons.

Ethics

The study protocol and the written informed consent were approved by the Committee for Ethics in Human Research of the Federal University of Minas Gerais.

Results

According to inclusion criteria patients should have an improvement equal or higher than 12% in FEV_1 after bronchodilator and only 60 of 238 subjects screened (25.2%) fulfilled this criterion. Of the 60 admitted participants, two were assigned to the FMP group and lost to follow up, but they were taken for intention-to-treat analysis with all information available.

Table 1 displays the descriptive characteristics of the 60 subjects who fulfilled the inclusion criteria.

As shown, the randomization process ensured a good comparability between FFM and FMP groups. No statistically significant difference was observed for any demographic, clinical, and functional variables.

Mean age of participants was 12.54 years (SD: ±3.15) and 12.79 years (SD: ±3.55), and mean height was 149.25 cm (SD: ±16.71) and 149.96 cm (SD: ±15.95) for FFM and FMP groups, respectively.

Taking into account only the predicted values for prebronchodilator FEV_1, the majority of the patients of the two groups suffered from moderate persistent asthma. Moderate persistent AR also predominates among the studied patients.

Mean prebronchodilator FEV_1 and postbronchodilator FEV_1 (% predicted) of participants were 68.83% (±6.89) and 71.42% (±6.43, $P = 0.14$) and 84.78% (±6.15) and 86.62% (±6.98, $P = 0.28$) for FFM and FMP groups, respectively.

Outcomes

Table 2 shows that statistically significant improvements were observed from admission to week 8 for both primary outcomes. Symptoms scores for AR, were reduced by 75% in FFM group and only by 20% in FMP group, while NIPF increased by 50% and 16% in FFM and FMP groups, respectively.

Table 1. Baseline characteristics of participants

	FFM group		FMP group		
	n	%	n	%	*P*-value
Gender					
Male	20	66.7	17	56.7	0.59
Female	10	33.3	13	43.3	
Ethnic group					
White	22	77.3	25	83.3	0.53
Others	8	26.7	5	16.7	
Age group (years)					
Up to 11	19	63.3	18	60.0	0.62
>11	11	36.7	12	40.0	
Positive skin test					
To more than 1 allergen	29	96.7	29	96.7	0.36
To one allergen	1	3.3	1	3.3	
Familial history of atopy					
Yes	26	86.7	25	83.3	0.83
No	4	13.3	5	16.7	
Passive exposure to tobacco smoking					
No	24	80.0	25	83.3	0.14
Yes	6	20.0	5	16.7	
Prebronchodilator FEV_1 (% predicted value)					
60–80	26	86.7	21	70.0	0.23
40–59	4	13.3	9	30.0	
Postbronchodilator FEV_1 (% predicted value)					
>80	25	83.3	26	86.7	0.19
60–80	5	17.3	4	13.3	
AR severity					
Moderate persistent	18	60.0	21	70.0	0.22
Severe persistent	12	40.0	9	30.0	

FFM, fluticasone face mask; FMP, fluticasone mouth piece; AR, allergic rhinitis FEV, forced expiratory volume.

After the treatment was interrupted there was a worsening in symptoms score in FFM group that increased from 3 points in week 8 to 10 points in week 10. However, the interruption of nasal inhalation of FP-HFA had a less pronounced effect on NIPF, which was reduced to an intermediate value (86.00 l/min) between the observed in baseline (67.33 l/min) and the observed in week 8 (102.00 l/min). Figure 1 shows that the differences between baseline values found upon admission and the subsequent observations during nasal inhalation is greater for FFM than FMP group.

With regard to asthma outcomes, the unconventional inhalation strategy used in the FFM group has determined an early and sustained control of symptoms (from week 2), as well as a progressive improvement of FEV_1 and $FEF_{25-75\%}$ with no statistical difference from the conventional oral inhalation up to week 8, when both groups continue the treatment by oral inhalation and maintained their FEV_1 and $FEF_{25-75\%}$ stable until the end of follow up at week 10. From baseline to week 8 of treatment predicted values for FEV_1 increased 17.5% and 12.3% as well as $FEF_{25-75\%}$ from 30.6% to 13.7% for FFM and FMP groups, respectively.

In Table 3 one may observe that after Bonferroni's correction, the values of AR score and NIPF presented a

Table 2. Clinical and functional assessments for allergic rhinitis and asthma at admission and during the follow up

	FFM group		FMP group				
	Mean	SD	Mean	SD	*P*-value	Difference	95% CI
AR (points)							
Admission	11.20	1.99	10.63	1.88	0.262	0.56	−0.43 to 1.56
Week 2	3.40	3.26	8.92	2.85	<0.001	−5.52	−7.14 to −3.91
Week 4	3.07	2.33	8.96	3.14	<0.001	−5.89	−7.34 to −4.44
Week 6	3.43	2.82	8.35	3.20	<0.001	−4.92	−6.50 to −3.33
Week 8	3.00	2.43	8.46	3.26	<0.001	−5.46	−6.97 to −3.95
Week 10	10.00	2.66	9.39	2.68	0.391	0.60	−0.80 to 2.01
NIPF (l/min)							
Admission	67.33	17.60	66.33	25.11	0.859	1.00	−10.21 to 12.21
Week 2	88.00	32.94	71.78	25.68	0.042	16.21	0.59–31.83
Week 4	101.00	33.87	72.85	26.64	0.001	28.14	12.03–44.25
Week 6	93.33	34.63	75.00	33.05	0.008	24.33	6.49–42.16
Week 8	102.00	35.66	76.42	34.98	0.008	52.57	6.97–44.17
Week 10	86.00	29.31	75.35	31.67	0.189	10.65	−5.45 to 26.88
Asthma score (points)							
Admission	8.20	3.35	7.40	2.86	0.325	0.80	−0.81 to 2.41
Week 2	3.10	2.07	3.00	2.63	0.873	0.10	−1.14 to 1.34
Week 4	3.10	2.04	2.79	2.48	0.600	0.31	−0.87 to 1.50
Week 6	2.70	1.82	2.29	1.27	0.323	0.41	−0.41 to 1.24
Week 8	2.53	1.40	2.14	1.04	0.238	0.39	−0.26 to 1.04
Week 10	2.60	1.77	2.14	1.04	0.241	0.46	−0.31 to 1.23
FEV_1 (% predicted)							
Admission	68.83	6.89	71.42	6.43	0.279	−1.59	−6.03 to 0.86
Week 2	74.59	9.33	77.96	8.14	0.150	−3.36	−7.98 to 1.25
Week 4	76.20	8.08	78.57	7.10	0.242	−2.36	−6.38 to 1.64
Week 6	78.69	9.02	78.85	7.32	0.943	−0.15	−4.49 to 4.18
Week 8	80.88	6.69	80.23	7.32	0.729	0.64	−3.04 to 4.32
Week 10	81.13	7.68	81.67	6.14	0.769	−0.54	−4.21 to 3.13
$FEF_{25-75\%}$ (% predicted)							
Admission	51.30	21.27	58.02	18.57	0.205	−6.72	−17.25 to 3.81
Week 2	61.70	19.75	59.46	18.06	0.655	2.24	−7.74 to 12.21
Week 4	63.20	17.29	63.07	19.16	0.979	0.13	−9.46 to 9.72
Week 6	64.30	17.86	64.79	19.33	0.921	−0.49	−10.27 to 9.30
Week 8	67.04	19.19	66.01	19.41	0.785	1.39	−8.77 to 11.54
Week 10	69.94	18.37	67.37	19.08	0.603	2.57	−7.28 to 12.42

FFM, fluticasone face mask; FMP, fluticasone mouth piece; AR, allergic rhinitis; FEV, forced expiratory volume; NIPF, nasal inspiratory peak flow; CI, confidence interval.

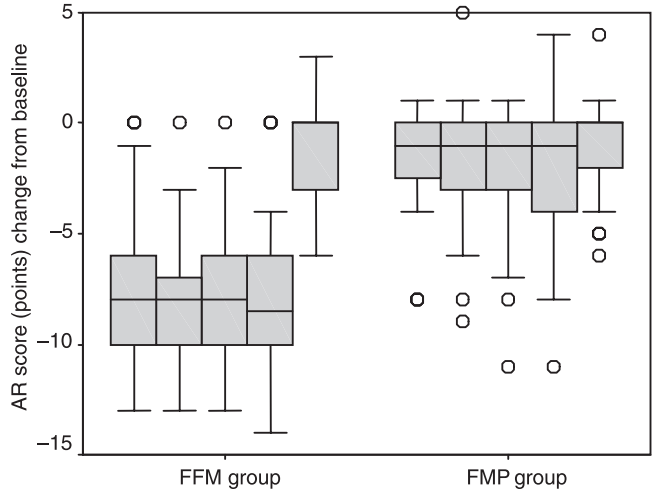

Figure 1. Comparison between baseline and subsequent values of allergic rhinitis score.

significant reduction when compared with baseline from weeks 2 to 8 in FFM group, as opposed to subjects allocated to the oral inhalation (FMP group). Moreover, there was a significant reduction in asthma scores and FEV_1 values in both groups. Also, $FEF_{25-75\%}$ was significantly increased within FFM group in all re-evaluations, whereas a significant increase was seen in weeks 8 and 10 within FMP group.

During the follow-up period, only one exacerbation was recorded and treated with inhaled albuterol plus oral prednisone in a patient from FMP group.

Discussion

In the present study, we assessed the efficacy of the administration of FP-HFA in children with concomitant persistent AR and asthma, and demonstrated that nasal inhalation may simultaneously control this comorbidity.

Table 3. Comparisons between clinical and functional assessments obtained at baseline with values observed in each of the subsequent weeks (analysis by paired *t*-test with Bonferroni's correction)

	FFM group				FMP group			
	Mean	SD	95% CI	*P*-value	Mean	SD	95% CI	*P*-value
AR score (week)								
2	−7.80	3.66	−9.17 to −6.43	<0.001	−1.61	2.36	−2.52 to −0.69	0.001
4	−8.13	2.85	−9.20 to −7.07	<0.001	−1.57	2.83	−2.67 to −0.47	0.007
6	−7.77	3.35	−9.02 to −6.52	<0.001	−2.18	2.92	−3.31 to −1.05	0.001
8	−8.20	3.46	−9.49 to −6.91	<0.001	−2.07	3.14	−3.29 to −0.85	0.002
10	−1.20	3.06	−2.34 to −0.05	0.040	−1.14	2.14	−1.97 to −0.31	0.009
NIPF (week)								
2	20.67	25.99	10.96–30.37	<0.001	4.64	12.32	−0.13 to 9.42	0.056
4	33.67	32.43	21.56–45.78	<0.001	5.71	18.94	−1.63 to 13.06	0.122
6	32.00	36.05	18.54–45.46	<0.001	7.86	27.54	−2.82 to 18.53	0.143
8	34.67	33.40	22.20–47.14	<0.001	9.29	28.54	−1.78 to 20.35	0.097
10	18.67	27.00	8.58–28.75	0.001	8.21	23.74	−0.99 to 17.42	0.078
Asthma score (week)								
2	−5.10	2.98	−3.99 to −0.54	<0.001	−4.21	3.17	−5.44 to −2.99	<0.001
4	−5.10	3.00	−3.98 to −0.55	<0.001	−4.43	3.10	−5.63 to −3.23	<0.001
6	−5.50	2.91	−4.41 to −0.53	<0.001	−4.93	2.73	−5.99 to −3.87	<0.001
8	−5.67	2.90	−4.58 to −0.53	<0.001	−5.07	2.68	−6.11 to −4.03	<0.001
10	−5.60	3.22	−4.40 to −0.59	<0.001	−5.07	2.68	−6.11 to −4.03	<0.001
FEV_1 (% predicted; week)								
2	5.17	10.98	1.07–9.27	0.015	6.43	6.31	3.98–8.87	<0.001
4	6.78	10.32	2.93–10.64	0.001	7.04	6.39	5.13–9.52	<0.001
6	9.28	10.92	5.19–13.36	<0.001	7.32	5.65	5.13–9.51	<0.001
8	11.46	9.14	8.05–14.88	<0.001	8.71	6.95	6.01–11.40	<0.001
10	11.71	9.09	8.31–15.11	<0.001	10.14	6.43	7.65–12.64	<0.001
$FEF_{25-75\%}$ (% predicted; week)								
2	10.39	14.28	15.73–5.06	<0.001	1.44	8.71	4.81–1.94	0.390
4	11.89	13.70	17.01–6.77	<0.001	5.05	9.90	8.88–1.20	0.012
6	12.99	13.27	17.95–8.03	<0.001	6.76	10.53	10.85–2.67	0.002
8	16.09	17.36	22.58–9.61	<0.001	7.98	10.93	12.22–3.75	0.001
10	18.63	17.25	25.08–12.19	<0.001	9.34	10.05	13.24–5.44	<0.001

FFM, fluticasone face mask; FMP, fluticasone mouth piece; AR, allergic rhinitis; FEV, forced expiratory volume; NIPF, nasal inspiratory peak flow; CI, confidence interval.

A statistically significant and sustainable improvement from week 2 was demonstrated in the primary outcomes (symptoms scores for AR and measurements of NIPF), in the nasal inhalation group, suggesting that nasal deposition is able to open a blocked nose. Interestingly, even in the presence of previous nasal obstruction, AR score were reduced from 11.20 to 3.40 points already in week 2 in the FFM group. These favorable results are likely to reflect the therapeutical effect of the nasal deposition of FP-HFA on AR, and this is reinforced by the observation that after the interruption of nasal inhalation AR symptoms scores returned to baseline levels in the FFM group. The deterioration of NIPF after nasal inhalation interruption was lower, probably due to the residual anti-inflammatory effect of deposited FP-HFA in nasal cavities previous to the washout period.

Comparable sustainable improvement from the same second week was obtained for the clinical and functional outcomes related to asthma throughout the follow up in both groups. Actually, patients progressively improved both their prebronchodilator FEV_1 values, which had reached 80% of the predicted values in weeks 8 to 10, and their $FEF_{25-75\%}$, which was improved by 15% in the same period.

Despite nasally inhaled FP would achieve a much lower lung dose than orally inhaled FP at the same nominal dose, FEV_1 and $FEF_{25-75\%}$ improvement obtained in the FFM group suggests that the lung deposition of FP-HFA seems to be enough to control the inflammatory process throughout the respiratory tract, probably due to the fact that the nasal inhalation of an inhaled corticosteroid allows the drug to follow the same pathway of inhaled aeroallergens and irritants.

Our results suggest that nasal inhalation might be considered as a feasible alternative to the dual approach to treatment recommended by international guidelines, i.e. intranasal and orally inhaled corticosteroids. These recommendations are in agreement with recent observations (13). Dahl et al. studied 262 patients with pollen-induced rhinitis and asthma, and demonstrated that topical nasal fluticasone is not sufficient to avoid lower airway symptoms. The combination of topical intranasal FP 200 μg and orally inhaled FP 250 μg was needed to control the seasonal increase in both nasal and asthmatic

symptom (13) Our proposed strategy of nasal inhalation of corticosteroid has used a total dose of FP which is half of that used in Dahl et al.'s study (13). This certainly would reduce the overall cost of treatment and improve therapeutical index by reducing the extra risks of additional administration of a topical nasal corticosteroid.

One might speculate that adherence rate to treatment of AR and asthma would also improve, by reducing the number of devices and medicines to be administered, and also by optimizing and maximizing the clinical effects of standard dosages of the inhaled corticosteroid to treat only asthma at a lower cost. It is possible that the high level of the compliance obtained in the present study would reflect a high level of patient acceptance of this strategy by our patients. Moreover, according to current market prices of FP in Brazil, the addition of intranasal FP to treat the coexisting AR in asthmatics would raise the cost of treatment by 40–50%, similarly to what described by Yawn et al. (4).

To date, only two studies aimed at assessing the efficacy of two alternative strategies on the simultaneous treatment of AR and asthma in children and adolescents with topical corticosteroids. In the first, using a non-commercialized nozzle attached to a large volume spacer, symptom score for AR were reduced by 64%, and statistically significant improvements were observed in NIPF and peak expiratory flow after a mean dose of 1292 μg/day of budesonide-CFC (6). The second study recruited nonsteroid naive patients with stable asthma treated with orally inhaled beclomethasone-CFC that was replaced by nasal inhalation aiming at controlling AR symptoms. With an average dosage of 532.05 μg/day, it was observed a comparable reduction (60%) in AR symptoms, without deterioration of clinical and functional parameters for asthma during the follow up (7).

Despite several methodological differences, e.g. previous use of steroids, sample size, type, and dose of the propellant and the inhaled steroid used, monitoring strategy throughout the study, adherence assessment, AR and asthma severity, it is worthy of note that the results of the three studies suggest consistently that nasal inhalation of corticosteroids may be efficacious to control AR and asthma.

Additionally, in the present study, both groups presented a marked improvement from baseline in symptoms of asthma, as seen in other controlled studies in asthma (14). However, our study was adequately powered to show differences on nasal symptoms scores; however, it is underpowered to demonstrate differences regarding asthma scores and lung function. Although nasal inhalation of topical corticosteroids may not be the ideal option for controlling the systemic features of AR and asthma sufferers (15), at least some systemic activity of the nasally inhaled FP-HFA could be achieved, as nasally inhaled FP-HFA can be absorbed-like intranasal steroids (16). On the other hand, the intranasal distribution of a nasally inhaled aerosol of corticosteroid may be less heterogeneous than that obtained with an aqueous formulation.

Finally, we emphasize that: (i) the need to take the entire respiratory tract into account when treating asthma (17), and (ii) the practical and economical challenges of treating AR and asthma in the developing world should lead to the consideration of nasal inhalation of HFA-corticosteroids for individuals with concomitant AR and asthma. It is likely to improve adherence, reduce costs, and allow for the utilization of a lower dose of corticosteroid.

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