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Original Article

Effect of momethasone furoate combined with loratadine and montelukast sodium on inflammatory factors and pulmonary function in children with allergic rhinitis

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Abstract: Objective: To compare the effects of mometasone furoate in combination with loratadine and montelukast sodium on inflammatory factors and pulmonary function in children with allergic rhinitis (AR). Methods: In this retrospective study, a total of 89 children with AR admitted to our hospital from March 2020 to October 2021 were enrolled. Among them, 47 children who received mometasone furoate combined with loratadine were designated group A, while the other 42 with mometasone furoate combined with montelukast sodium were group B. The clinical efficacy of both groups was compared, and the levels of inflammatory factors IL-6 and TNF-α as well as the changes of pulmonary function levels were tested during the treatment. Adverse reactions during treatment were recorded. Finally, children were followed up for 3 months to record rhinitis recurrence after discontinuation of the treatment. Results: There was no statistical difference in clinical treatment efficacy between both groups (P>0.05), while the levels of IL-6, TNF-α, and IgE were lower in children in group A than in group B at 2 weeks of treatment. Group A's lung function indexes, including forced expiratory volume in one second (FEV1%), forced expiratory volume in one second/forced vital capacity (FEV1/FVC) and peak expiratory flow (PEF), were higher than in group B (all P<0.05). The total incidence of adverse reactions was dramatically lower in group A than group B (P<0.05). Follow-up demonstrated no difference in the recurrence rate of rhinitis between both groups of children (P>0.05). Higher TNF-α after treatment, history of allergy, family history of rhinitis, combined asthma, and parental history of smoking were independent risk factors for relapse after discontinuation of the drug in children. Conclusion: Both mometasone furoate combined with either loratadine or montelukast sodium had good effects in AR, while the first option had a faster inhibitory effect on inflammatory factors and a better protection of lung function in children.

Keywords: Mometasone furoate, loratadine, montelukast sodium, allergic rhinitis, inflammatory factors, pulmonary function

Introduction

Allergic rhinitis (AR) is an upper respiratory disease with a high rate of outpatient visits in departments of otorhinolaryngology. It is a non-infectious chronic inflammatory disease of nasal mucosa mediated by IgE, with nasal itching, sneezing, clear mucus, and nasal congestion as the main manifestations, and may be accompanied by itching and conjunctival congestion [1-3]. Children are not yet fully developed; their nasal cavities and nasal passages are relatively narrow and their immunity is relatively poor; thus, they are easily irritated by cold air, dust, mites, and pollen, making them the most prevalent group with AR [4, 5]. Children with AR are also prone to complications such as asthma, secretory otitis media, upper airway cough syndrome, and chronic sinusitis. In long-term development, these children are prone to fatigue, decreased concentration, and reduced energy, subsequently affecting the quality of

life and learning, and even compromising their cardiopulmonary function and brain development [6-8].

Clinical treatment of AR in children is based on pharmacotherapy and immunotherapy. Pharmacotherapy mainly includes antihistamines, nasal glucocorticoids, anti-leukotrienes, and other drugs. One of the first-line drugs is glucocorticoids, which are essential for the treatment of allergic diseases in children as essential drugs to reduce metabolic inflammation [9]. Mometasone furoate is a potent nasal glucocorticoid with good local anti-inflammatory and marked local anti-sensitizing effects, mainly by increasing the stability of lysosomal membranes and endothelial cells, thereby controlling the immune response, reducing antibody synthesis, and inhibiting the release of inflammatory mediators [10]. Leukotrienes play a key role in AR development, promoting the aggregation of inflammatory cells, causing an increase in vascular permeability and contraction of airway smooth muscle, and triggering airway remodeling and airway hyperresponsiveness [11]. Montelukast sodium is a cysteinyl leukotriene receptor antagonist with strong affinity and selectivity that can compensate for some of the inflammatory mechanisms not covered by inhaled glucocorticoids. Montelukast can selectively and competitively occupy leukotriene receptors and exert anti-inflammatory effects by blocking leukotriene receptors [12, 13]. Loratadine is an antihistamine that clinically antagonizes type I metaplasia mainly by reducing vascular permeability and inhibiting the release of histamine as well as inflammatory mediators and is effective against IgE and IgA [14]. However, comparative studies of mometasone furoate in combination with loratadine or montelukast sodium are rare.

In this study, pediatric patients with AR were selected to analyze the efficacy of mometasone furoate combined with loratadine or montelukast sodium in AR in children.

Materials and methods

Children's data

A total of 89 children with AR admitted to our hospital from March 2020 to October 2021 were enrolled for a retrospective analysis. Forty-seven of them were treated with mometasone furoate combined with loratadine and were considered as group A. There were 26 males and 21 females with a mean age of (7.53±1.70) years and a disease duration of (24.79±5.49) months. The other 42 cases received mometasone furoate combined with montelukast sodium and were regarded as group B. There were 20 males and 22 females with a mean age of (7.43±2.31) years old and a disease duration of (23.24±6.67) months. The research was approved by our medical ethics committee, and an informed consent form was obtained from all family members (IRB20200117).

Inclusion and exclusion criteria

Inclusion criteria: AR children [15] with clinical presentations of nasal congestion, runny nose, nasal itching, positive skin prick or IgE test, watery nasal secretions, and congested nasal mucosa; Children with typical symptoms when exposed to suspected allergens, and positive prick test; Children of age <18 years old; Children with complete clinical data.

Exclusion criteria: Children who have other nasal lesions; Children with presence of lesions in the lungs; Children complicated by other serious inflammatory or infectious diseases; Children who had taken glucocorticoids or receptor antagonist-type drugs within 3 months prior to admission; Children with intolerance or allergy to the medication.

Treatment options

Group A was treated with mometasone furoate nasal spray (Zhejiang Xianju Pharmaceutical Co., Ltd., Lot number: 170214, 180712) combined with loratadine (Bayer Healthcare, Qidong Branch, Lot number: 170321, 181005). The nasal spray was applied once a day in the morning for each of the two nostrils. Loratadine was administered according to the body mass of children, 10 mg/(time·d) for children with body mass ≥30 kg, and 5 mg/(time·d) for children with body mass <30 kg. Group B was treated with mometasone furoate plus montelukast sodium (Merck Sharp & Dohme Ltd., Lot number: K004567). Montelukast sodium (5 mg) was orally administered at bedtime each night. Patients in both groups were treated for 3 months.

Outcome measures

(1) The treatment efficacy was compared between the two groups. Cured: After treatment, the clinical symptoms of sneezing, runny nose and nasal congestion disappeared completely, and the edema of nasal mucosa disappeared completely as indicated by rhinoscopic examination. Effective: After treatment, children's clinical symptoms disappeared or improved dramatically, the edema of the nasal mucosa disappeared or was relieved as indicated by rhinoscopy, and the number of episodes decreased; Ineffective: Children's clinical symptoms and rhinoscopy did not improve or worsened after treatment. Total effective rate of treatment = (number of cured cases + number of effective cases)/total number of cases ×100%.

(2) The adverse reactions during 3 months of treatment were counted and compared between both groups.

(3) Before and after treatment, 5 mL of venous blood was collected from children and centrifuged at 3,000×g for 10 min at 4°C to separate the serum, and the serum levels of inflammatory factors TNF-α, IL-6, and IgE were measured by ELISA assays. All ELISA kits were purchased from Abcam, UK (ab181421, ab178013, ab195216), and the operations were strictly in accordance with the instructions.

(4) The forced expiratory volume in one second (FEV1%) and peak expiratory flow (PEF) of children were measured before and after treatment using a Dutch Sensor Medics V max spectra 229 spirometer, and the forced expiratory volume in one second/forced vital capacity (FEV1/FVC) was calculated.

(5) The AR recurrence 3 months after discontinuation of treatment in children was counted and compared between both groups.

(6) We performed a multifactorial analysis to detect independent risk factors for recurrence in children.

Statistical methods

SPSS 22.0 statistical analysis software was used for data analysis. The measured data all conformed to a normal distribution and were expressed as mean ± standard deviation (Means ± SD). Independent samples t-test was used for inter-group comparison, and paired samples t-test was for intra-group comparison. The counted data were expressed as % and assessed using the χ^2 test. Independent risk factors for relapse after drug discontinuation were analyzed by logistic regression. $P<0.05$ was considered significant.

Results

Baseline data

No statistical difference emerged between both groups in terms of age, gender, course of disease, allergy history, family history of rhinitis, house pets, combined asthma, parental smoking history, or place of residence (all $P>0.05$), as shown in **Table 1**.

Comparison of treatment efficacy between both groups

There was no statistical difference ($P>0.05$) in the total effective rate of treatment between both groups of patients, as shown in **Table 2**.

Comparison of adverse reactions between both groups

The adverse reactions of children in both groups were counted, which included cough, nasal bleeding, dry mouth, nausea and vomiting during treatment. The overall incidence of adverse reactions in group A was dramatically lower than in group B ($P<0.05$) (**Table 3**).

Comparison of changes in inflammatory factors between groups

The changes in inflammatory factors TNF-α, IL-6, and IgE before and after treatment were observed in both groups. There was no difference in TNF-α, IL-6, or IgE between groups before treatment (all $P>0.05$). The levels of inflammatory factors TNF-α, IL-6, and IgE in both groups were lower after treatment than before it (all $P<0.05$). The levels in group A after treatment were dramatically lower than in group B ($P<0.001$) (**Figure 1**).

Comparison of improvement of pulmonary function between both groups

We investigated the effects of the two treatment regimens on pulmonary function of children by observing the changes in FEV1%, FEV1/FVC, and PEF. We found that FEV1%, FEV1/FVC,

Table 1. Baseline data sheet

	Group A (n=47)	Group B (n=42)	t/X^2	P
Age (year)	7.53±1.70	7.43±2.31	0.234	0.815
Gender			0.527	0.468
Male	26 (55.32)	20 (47.62)		
Female	21 (44.68)	22 (52.38)		
Course of disease (month)	24.79±5.49	23.24±6.67	1.202	0.233
Allergy history			0.478	0.489
Yes	19 (40.43)	14 (33.33)		
No	28 (59.57)	28 (66.67)		
Family history of rhinitis			0.535	0.464
Yes	12 (25.53)	8 (19.05)		
No	35 (74.47)	34 (80.95)		
House pet			0.449	0.503
Yes	11 (22.45)	12 (28.57)		
No	38 (77.55)	30 (71.43)		
Combined asthma			0.158	0.691
Yes	16 (34.04)	16 (38.10)		
No	31 (65.96)	26 (61.90)		
Parental smoking history			0.478	0.489
Yes	19 (40.43)	14 (33.33)		
No	28 (59.57)	28 (66.67)		
Place of residence			0.735	0.391
Cities and towns	37 (78.72)	36 (85.71)		
Countryside	10 (21.28)	6 (21.28)		

Table 2. Treatment efficacy

	Group A (n=47)	Group B (n=42)	X^2	P
Markedly effective	20 (42.55)	15 (35.71)	0.435	0.510
Effective	24 (51.06)	22 (52.38)	0.015	0.901
Ineffective	3 (6.38)	5 (11.90)	0.827	0.363
Total efficiency	44 (93.62)	37 (88.10)	0.827	0.363

Table 3. Adverse reactions

	Group A (n=47)	Group B (n=42)	X^2	P
Cough	1 (2.13)	3 (7.14)		
Nasal bleeding	0 (0.00)	1 (2.13)		
Dry mouth	1 (2.13)	3 (7.14)		
Nausea and vomiting	1 (2.13)	2 (4.76)		
Total adverse reactions	3 (6.38)	9 (21.43)	4.304	0.038

and PEF were not statistically different between the two groups before treatment (all P>0.05). After treatment, the levels of FEV1%, FEV1/FVC, and PEF were dramatically higher than those before treatment (all P<0.05), with dramatically higher levels in group A (all P<0.05) (**Figure 2**).

Comparison of relapse after discontinuation of treatment

We compared the AR recurrence rate in children within 3 months after discontinuation of the medication. There were 15 children with recurrence (31.91%) in group A and 15 children in group B (35.71%). Comparison of recurrence between groups revealed no difference (P> 0.05) (**Table 4**).

Recurrence-related univariate analysis

The children were grouped into recurrence and no-recurrence groups according to whether there was a relapse of AR after discontinuation of treatment. The univariate analysis revealed significant differences between groups in terms of allergy history, family history of rhinitis, family pet ownership, combined asthma, parental

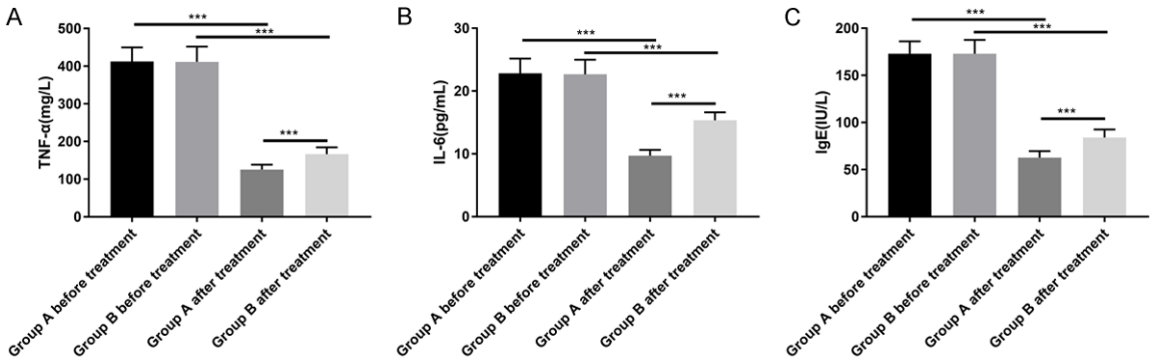

Figure 1. Changes in inflammatory factors in children of both groups. A. After treatment, TNF-α was dramatically lower in both groups than before treatment, and the level in group A was lower than that in group B after treatment (P<0.001). B. After treatment, IL-6 was dramatically lower in both groups than before treatment, and the level was lower in group A than in group B after treatment (P<0.001). C. After treatment, IgE was dramatically lower in both groups than before treatment, and the level was lower in group A than in group B after treatment (P<0.001). ***P<0.001.

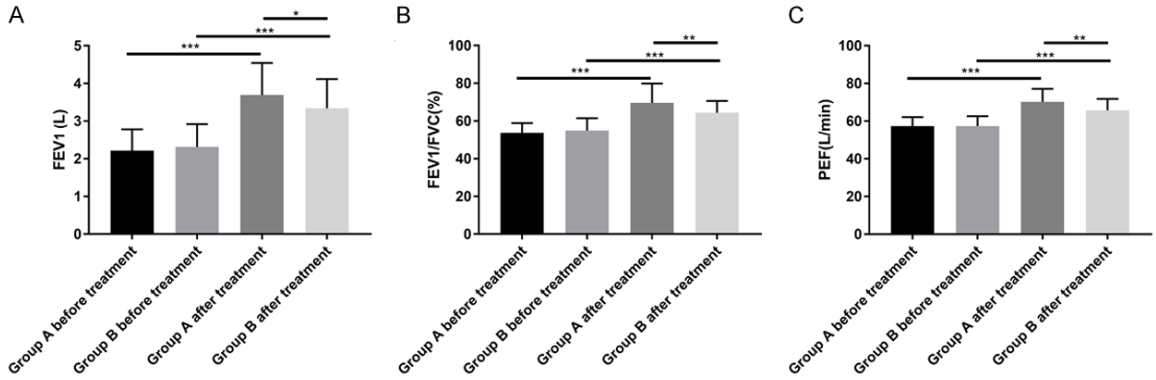

Figure 2. Improvement of pulmonary function in both groups of children. A. The FEV1% of children in both groups was dramatically higher after treatment than before treatment, and the levels in group A were higher than those in group B after treatment (P<0.05). B. The FEV1/FVC of children in both groups was dramatically higher after treatment than before treatment, and the levels in group A were higher than those in group B after treatment (P<0.01). C. The PEF of children in both groups was dramatically higher after treatment than before treatment, and the levels in group A were significantly higher than those in group B after treatment (P<0.01). *P<0.05, **P<0.01, ***P<0.001. forced expiratory volume in one second (FEV1%), forced expiratory volume in one second/forced vital capacity (FEV1/FVC), and peak expiratory flow (PEF).

Table 4. Patients' relapse within 3 months after stopping medication

	Group A (n=47)	Group B (n=42)	X^2	P
Recurrence	15 (31.91)	15 (35.71)	0.143	0.705
No recurrence	32 (68.09)	27 (64.29)		

smoking history, post-treatment TNF-α level, and post-treatment levels of IL-6, IgE, and FEV1/FVC (P<0.05), as shown in **Table 5**.

Recurrence-related multivariate analysis

Logistic regression analysis of the indicators with significant differences in the univariate analysis found that higher TNF-α after treatment, history of allergy, family history of rhinitis, combined asthma, and parental history of smoking were independent risk factors for the relapse after discontinuation of medication, as shown in **Table 6**.

Discussion

After the onset of pediatric allergic rhinitis (AR), the immune response of the body is strengthened. When the child encounters the allergen again, the release of mediator cellular reactive substances is accelerated, the frequency of nasal mucosal vasoconstriction is increased, capillary permeability is also elevated, and

Table 5. Univariate analysis of risk factors

	Recurrence (n=30)	No recurrence (n=59)	t/X^2	P
Age (year)	7.30±1.84	7.58±2.09	0.621	0.536
Gender			1.253	0.263
Male	18 (60.00)	28 (47.46)		
Female	12 (40.00)	31 (52.54)		
Course of disease (month)	25.07±6.37	23.54±5.93	1.122	0.265
Allergy history			5.125	0.024
Yes	16 (53.33)	16 (28.81)		
No	14 (46.67)	42 (71.19)		
Family history of rhinitis			5.234	0.022
Yes	11 (36.67)	9 (15.25)		
No	19 (63.33)	50 (84.75)		
Family pet ownership			4.733	0.030
Yes	12 (40.00)	11 (18.64)		
No	18 (60.00)	48 (81.36)		
Combined asthma			5.935	0.015
Yes	16 (53.33)	16 (27.12)		
No	14 (46.67)	43 (72.88)		
Parental smoking history			7.442	0.006
Yes	17 (56.67)	16 (27.12)		
No	13 (43.33)	43 (72.88)		
Place of residence			0.880	0.348
Cities and towns	23 (76.67)	50 (84.75)		
Countryside	7 (23.33)	9 (15.25)		
TNF-α after treatment (mg/L)	153.36±21.32	140.57±26.85	2.269	0.026
IL-6 after treatment (pg/mL)	13.27±3.21	11.90±2.84	2.058	0.043
IgE after treatment (U/L)	77.42±13.82	70.56±12.19	2.398	0.019
FEV1% after treatment	3.50±0.72	3.54±0.89	0.213	0.832
FEV1/FVC after treatment (%)	64.26±8.91	68.59±8.75	2.193	0.031
PEF after treatment (L/min)	67.76±8.19	68.26±6.17	0.323	0.748

forced expiratory volume in one second (FEV1%), forced expiratory volume in one second/forced vital capacity (FEV1/FVC) and peak expiratory flow (PEF).

Table 6. Multivariate analysis of risk factors

	B	S.E.	Wals	Sig.	Exp (B)	95% of EXP (B) C.I.	
						Lower limit	Upper limit
TNF-α	0.040	0.020	3.921	0.048	1.041	1.000	1.083
Allergy history	1.580	0.629	6.316	0.012	4.854	1.416	16.639
Family history of rhinitis	1.754	0.728	5.807	0.016	5.775	1.387	24.041
Combined asthma	1.691	0.679	6.197	0.013	5.426	1.433	20.548
Parental smoking history	1.972	0.667	8.754	0.003	7.187	1.946	26.543

glandular choline activity is enhanced. This causes recurrent clinical symptoms such as nasal itching, nasal congestion, runny nose, and sneezing [16]. If not treated in a timely manner, patients are highly susceptible to complications of other diseases such as sinusitis and bronchial asthma, which can have serious effects on subsequent growth and learning [17]. Mometasone furoate is a commonly used corticosteroid drug in clinical practice for the treatment of nasal diseases, and has a good effect on local inflammation and improves clini-

cal symptoms such as nasal congestion, runny nose, and sneezing [18]. Montelukast sodium is a selective leukotriene receptor antagonist that specifically inhibits cysteinyl leukotriene receptors to suppress inflammation while promoting eosinophil apoptosis [19]. Loratadine is a long-acting tricyclic antihistamine that suppresses allergic symptoms by inhibiting histamine receptors, and it is effective in improving AR symptoms [20].

In the present study, we first compared the efficacy of mometasone furoate combined with loratadine or montelukast sodium in AR children, and found that there was no statistical difference in the total efficacy in both groups after 2 months of treatment. This suggests that both of our treatment regimens provide good therapeutic efficacy for AR children. At the same time, we also observed the incidence of adverse reactions in both groups, including cough, nosebleed, dry mouth, nausea, and vomiting. The incidence of total adverse reactions in group A was 6.38%, which was lower than group B (21.43%). This suggests that although the efficacy of the two treatments was close, mometasone furoate combined with loratadine had a lower incidence of adverse reactions and a higher safety profile. Jia et al. [21] compared the improvement of symptoms in patients with severe AR treated with mometasone furoate alone and with mometasone furoate combined with loratadine or montelukast sodium, respectively. The treatment regimen of mometasone furoate combined with montelukast sodium was more effective for nasal congestion. In terms of improving nasal itching and sneezing, the combination of mometasone furoate and loratadine was more effective, while the effect of the two combinations was similar for the symptoms of runny nose. Overall, both combination regimens were effective in controlling patients' symptoms, and superior to that of mometasone furoate alone.

Inflammatory factors can repeatedly irritate the mucosa, leading to inflammatory damage and can cause increased mucosal permeability, leaving the symptoms of rhinitis unimproved [22, 23]. We found that the inflammatory factors TNF-α and IL-6 were dramatically lower in group A than in group B after treatment, suggesting that mometasone furoate combined with loratadine had a better anti-inflammatory effect. AR is accompanied by changes in ventilatory function, mainly small airway dysfunction, especially in children with a long duration and moderately severe symptoms who may already have reduced pulmonary function and a hyperreactive airway [24]. We discovered that the lung function indexes FEV1%, FEV1/FVC, and PEF increased after treatment, which suggested that the lung ventilation improved in both groups, and the FEV1%, FEV1/FVC, and PEF indexes in group A were higher than those in group B after the treatment, indicating that the treatment of mometasone furoate combined with loratadine could better improve the lung function of children. The recurrence rate was 31.91% in group A and 35.71% in group B, and there was no difference in the recurrence rate between groups. Wei et al. [25] investigated the effect of montelukast sodium combined with loratadine and montelukast sodium combined with budesonide on pediatric asthma, and the results showed inflammation and lung function were improved in both groups, but the difference was not statistically significant. We then conducted multivariate analysis and found that higher TNF-α after treatment, history of allergy, family history of rhinitis, combined asthma, and parental history of smoking were independent risk factors for the relapse after discontinuation of medication in children. Sella et al. [26] claimed that asthma was also a risk factor for recurrence after surgery in patients with rhinitis, and such children were more susceptible to recurrence due to irritation by allergens in the environment. Orb et al. [27] also clarified that there was a significant familial risk for rhinitis and that families with a history of rhinitis had a higher risk of recurrence.

There are some limitationsto the study. It did not differentiate children according to the severity of their symptoms, so it is difficult to understand the effectiveness of the treatment protocol for children with different severity levels. Second, a large age range of patients was included in this study. Hence, the age range will be narrowed for further analysis in future studies. Finally, the current study did not conduct quality-of-life related assessment in the children.

Overall, mometasone furoate combined with either loratadine or montelukast sodium have good effects in AR treatment. However, mome-

tasone furoate combined with loratadine had a faster inhibitory effect on inflammatory factors and a better protection for lung function in children.

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Disclosure of conflict of interest

None.

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