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Montelukast and budesonide combination for children with chronic cough-variant asthma

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Abstract

This study investigated the effectiveness and safety of montelukast combined budesonide (MCB) treatment for children with chronic cough-variant asthma (CCVA).

In total, 82 cases of children with CCVA, aged 4 to 11 years were included in this study. All cases received either MCB or budesonide alone between May 2015 and April 2017. The primary outcome was lung function, measured by the peak expiratory flow rates (PEFRs) and forced expiratory volume in 1 second (FEV_1). The secondary outcome was measured by the clinical assessment score. Furthermore, adverse events (AEs) were also recorded in this study. All outcomes were measured after 8-week treatment.

After 8-week treatment, MCB showed greater effectiveness than did budesonide alone in improving the lung function, measured by PEFR V_1 ($P = .02$), and FEV_1 ($P < .01$). Similarly, the clinical assessment score also demonstrated significant difference between the 2 groups ($P < .05$). In addition, no serious AEs occurred in both groups.

The results of this study demonstrate that the effectiveness of MCB is superior to budesonide alone in the treatment of children with CCVA.

Abbreviations: CCVA = chronic cough-variant asthma, cysteinyl leukotriene; AE = adverse events, FEV_1 = forced expiratory volume in 1 second, LTRA = leukotriene receptor antagonist, MCB = montelukast combined budesonide, PEFR = peak expiratory flow rate.

Keywords: budesonide, cough-variant asthma, effectiveness, montelukast

1. Introduction

Chronic cough-variant asthma (CCVA) is a very common subtype of bronchial asthma among children population.[1–3] This condition often manifests with acute cough, chronic cough, and intractable cough, especially at night.[4,5] It has been reported that CCVA contributed 24.0% to 33.3% of chronic cough cases, and children alone accounted for the incidence of 0.18% among the total CCVA population.[6]

Pharmacotherapy is predominantly used for the treatment of patients with CVA.[7–11] Such intervention includes glucocorticoids, antihistamine drugs, β2-agonists, and leukotriene receptor antagonists (LTRAs).[7,12–17] Of those medications, LTRAs have been used as the first-line treatment for such condition, and montelukast comprises the most commonly used type 1 cysteinyl leukotriene antagonist.

Previous studies have reported that montelukast can improve both the symptoms and lung function in patients with CCVA.[18–23] However, limit data are still available about montelukast and budesonide for the treatment of CCVA. In this retrospective study, we investigated the effectiveness and safety of montelukast and budesonide for the treatment of children with CCVA aged 4 to 11 years.

2. Methods

2.1. Design

This study was designed as a retrospective study. It included 82 eligible cases of Chinese children, aged 4 to 11 years with CCVA. Of those patients, 41 received montelukast combined budesonide (MCB) and were assigned to an intervention group, whereas the other 41 subjects underwent budesonide alone and were assigned to a control group. All the cases were collected at The People's Hospital of Yan'an between May 2015 and April 2017.

This study was approved by the Medical Ethical Committee of Yan'an People's Hospital. Legal guardians of all included children provided the informed written consent in this study.

2.2. Inclusion and exclusion criteria

The cases of both male and female Chinese children with CCVA aged from 4 to 11 years were included in this study. The cases were excluded if the children had prophylactic medications, budesonide, and montelukast 1-month before this study. In addition, the cases were excluded if the children had taken theophylline, inhaled corticosteroids, nasal steroid, and cromolyn during the period of this study. Furthermore, the cases were also excluded if they had insufficient information, and characteristic values, as well as the outcome data.

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The authors have no conflicts of interest to disclose.

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2.3. Intervention

All participants with CCVA in both groups received budesonide (1 mg, 3 times daily) for a total of 8 weeks. In addition, patients in the intervention group also underwent montelukast (4 mg daily) chewable tablet in the evening at bedtime for a total of 8 weeks.

2.4. Effectiveness evaluation

The primary outcome measurement of lung function was measured by the peak expiratory flow rates (PEFR)[24] and forced expiratory volume in one second (FEV_1).[25] The secondary outcome was measured by the clinical assessment score. PEFR was measured by a bedside spirometry using PiKo-1 (ATS and EU electronic peak flow monitor, Ferraris Respiratory Europe Ltd, Westford, UK) software. It was performed between 08:30 AM and 10:30 AM each morning by the experienced physicians at Yan'an People's Hospital, who were trained strictly before this study by 3 times. Moreover, adverse events (AEs) were recorded in this study. All outcomes were measured before and 8 weeks after the treatment.

2.5. Statistical analysis

All the data of this study were analyzed by using IBM SPSS Statistics 19.0 (IBM Corp, Armonk, NY). The categorical data were performed by using Chi-squared test. The continuous data were applied by *t* test or Mann-Whitney *U* test to analyze the differences between 2 groups. The statistical significance was set as $P < .05$.

3. Results

The patient characteristics are summarized in Table 1. The 2 groups did not differ significantly in all characteristics and clinical variables in this study.

After 8-week treatment, patients received MCB exerted better outcome in lung function, measured by the PEFR ($P = .02$, Table 2) and FEV_1 ($P < .01$, Table 3); and clinical assessment score (wheeze, $P < .01$; activity, $P = .04$; cough, $P = .03$; sleep, $P < .01$, Table 4) compared with patients who underwent budesonide alone.

All AEs were mild in both groups (Table 5). No serious AEs occurred in either group. No patient withdrew from the study due to the AEs in both groups. In addition, no significant differences were found regarding the AEs between 2 groups (Table 5).

Table 1

Characteristics of participants before the treatment.

Characteristics	Intervention group (n = 41)	Control group (n = 41)	P
Age, yr: mean (±SD)	6.2 (2.5)	6.0 (2.8)	.73
Sex, n (%)			
Male	24 (58.5)	22 (53.7)	.66
Female	17 (41.5)	19 (46.3)	.66
Race, n (%)			
Asian (Chinese)	41(100.0)	41 (100.0)	—
Asthma history, n (%)			
Past history of sudden severe exacerbations	15 (36.6)	17(41.5)	.71
<2 admissions	19 (46.3)	21 (51.2)	.65
Family history of asthma, n (%)	31 (75.6)	28 (68.3)	.46
Cough duration(week), mean (±SD)	13.8 (2.1)	13.1 (2.7)	.19
Clinical assessment score, mean (±SD)			
Wheeze	1.61 (0.49)	1.64 (0.51)	.16
Activity	1.67 (0.58)	1.69 (0.61)	.19
Cough	1.48 (0.62)	1.50 (0.65)	.70
Sleep	1.42 (0.51)	1.44 (0.54)	.50

SD = standard deviation.

Table 2

Comparison of peak expiratory flow rate before and 8-week after treatment between 2 groups.

PEFR	Intervention group (n = 41)	Control group (n = 41)	P
At baseline	118.9 (14.6)	121.3 (15.1)	.46
After treatment	133.4 (16.3)	126.1 (16.5)	
Difference from baseline	14.4 (9.9–17.7)	4.9 (1.5–9.3)	
Difference between groups		9.5 (6.2–12.1)	.02

Data are present as mean ± standard deviation.
PEFR = peak expiratory flow rates.

Table 3

Comparison of forced expiratory volume in one second before and 8 weeks after treatment between 2 groups.

NRS score	Intervention group (n = 41)	Control group (n = 41)	P
At baseline	70.8 (1.6)	71.1 (1.5)	.38
After treatment	83.2 (5.9)	77.4 (3.8)	
Difference from baseline	12.4 (8.1, 16.3)	6.3 (3.5, 9.2)	
Difference between groups		6.1 (4.0, 8.8)	<.01

Data are present as mean ± standard deviation.
FEV_1, forced expiratory volume in 1 second.

Table 4

Comparison of clinical assessment score 8 weeks after treatment between 2 groups.

After treatment	Intervention group (n = 41)	Control group (n = 41)	Difference between groups	P
Wheeze	0.91 (0.57)	1.26 (0.64)	0.35 (0.19, 0.51)	<.01
Activity	1.04 (0.65)	1.34 (0.69)	0.30 (0.11, 0.47)	.04
Cough	0.97 (0.68)	1.30 (0.71)	0.33 (0.14, 0.49)	.03
Sleep	0.93 (0.60)	1.28 (0.62)	0.36 (0.21, 0.54)	<.01

Data are present as mean ± standard deviation.

Table 5

Safety between 2 groups after 8 weeks treatment.

Safety	Intervention group (n = 41)	Control group (n = 41)	P
Anorexia	5 (12.1)	4 (9.8)	.72
Headache	7 (17.1)	5 (12.1)	.53
Depression	5 (12.1)	4 (9.8)	.72
Insomnia	4 (9.8)	3 (7.3)	.69
Anxiety	2 (4.9)	2 (4.9)	1.00
Skin rash	3 (7.3)	4 (9.8)	.69
Nausea	5 (12.1)	3 (7.3)	.46

Data are present as mean ± standard deviation.

4. Discussion

Cys-LTs play a very important role in the pathogenesis of asthma.[26,27] Generally speaking, although the anti-inflammatory

effects of montelukast are regarded to be milder as compared to inhaled corticosteroids in the management of asthma, most studies used it as an add-on therapy to budesonide.[28,29] It has been reported that the combination of MCB may help to better manage the symptom control, lung function improvement, and also against the airway narrow protection compared with inhaled corticosteroids alone.[28–30]

This retrospective study firstly investigated the effectiveness of MCB for treating CCVA in children aged 4 to 11 years in China. The results showed that significant differences were found in the pulmonary function tests by FEV_1 and PEFR, as well as the clinical assessment score after 8-week treatment. In addition, no serious AEs occurred in this study. Our results are partly consistent with data published of related study by Ghosh et al.[31] They included 50 children and found that clinical outcomes showed significant improvement after 4 and 12 weeks of treatment.[31]

To the best of our knowledge, this study specifically focused on the pediatric population in China, and provided significant clinical benefit in children with CCVA. The results of this study demonstrated that MCB can either improve lung function, measured by the PEFR and FEV_1, or enhance the clinical symptoms for children with CCVA.

This study has several following limitations. First, the sample size was quite small in this study, which may affect the results of this study. Second, the cases of this retrospective were selected from a single center, and thus, it may be not generalized to other pediatric population. Third, this study is a retrospective study with its own limitation, which may increase the selection bias.

5. Conclusion

The results of this study found that MCB may be benefit for treating CCVA in children aged 4 to 11 years. However, larger sample size with longer treatment duration would still be required for further evaluation of the role of MCB in the treatment of CCVA.

Author contributions

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