

## Original Article

# Tulobuterol path transdermal drug delivery reduces serum level of ICAM 1, VCAM 1, IL-2, IL-6, IL-8, and IL-10 in children with bronchial asthma

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**Abstract:** Bronchial asthma is a serious threat to the health of children. This study was to explore the effect of tulobuterol path transdermal drug delivery treatment on serum ECP, IL, ECP, ICAM 1, VCAM 1 level in children with bronchial asthma and its molecular mechanism. A total of 180 children with bronchial asthma were divided into two groups: children with bronchial asthma group and the treatment group. The treatment group was given by tulobuterol path transdermal drug delivery treatment. A total of 90 healthy children were selected as the control group. Serum ECP, ICAM 1, VCAM 1 and IL-2, IL-6, IL-8, and IL-10 were detected by the enzyme-linked immunosorbent assay (ELISA). The study analyzed the correlation between the level of serum factors and development of children with bronchial asthma. Compared with the control group, the serum ICAM 1, VCAM 1, IL-2, IL-6, IL-8, IL-10 level was significantly higher in children with bronchial asthma. Tulobuterol path transdermal drug delivery treatment significantly decreased the level of serum of ICAM 1, VCAM 1, IL-2, IL-6, IL-8, and IL-10. ICAM 1, VCAM 1, IL-2, IL-6, IL-8, and IL-10 might thus act as biomarkers for evaluating the treatment effect of drug delivery on children with bronchial asthma.

**Keywords:** Tulobuterol path transdermal drug delivery, serum factors, bronchial asthma

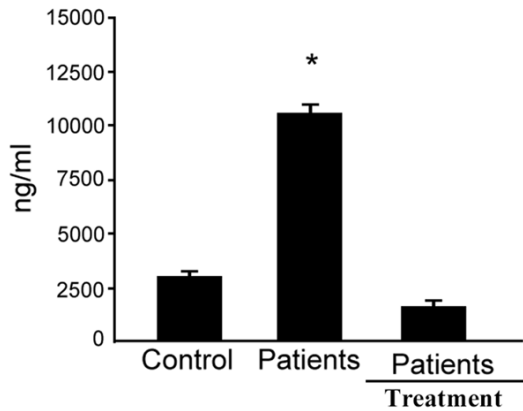
## Introduction

Bronchial asthma in children is an obstructive respiratory disease with symptoms such as cough, dyspnea, and wheezing [1]. Bronchial asthma is a common pediatric respiratory disease [2]. The incidence of bronchial asthma in children has shown an upward trend [3, 4]. Therefore, it has become important to explore detection and treatment of bronchial asthma in children. There are seven main aspects on the test of bronchial asthma in children [5, 6]: (1) detection of eosinophilic cells, (2) the routine blood test, (3) the chest X ray detection, (4) the skin sensitivity test, (5) detection of lung function, (6) blood gas detection, (7) laboratory testing. Blood routine examination is one of the important methods of children's bronchial asthma [7]. When all kinds of blood cells such as the number of white blood cells, the red blood cells and neutrophils are increased, the incidence of bronchial asthma also increases [8, 9]. However, the above methods are relatively

cumbersome, and the sensitivity is limited. It has been necessary to explore molecular markers and more effective clinical testing for childhood bronchial asthma [10, 11]. The study aimed to collect the blood of children with bronchial asthma and use the enzyme-linked immunosorbent assay to detect the levels of various kinds of inflammatory factors and cytokines in plasma.

Currently, molecular mechanisms of children bronchial asthma remains to be further discussed [12]. The result shows that children with bronchial asthma are often accompanied by the increased eosinophilic cells and the emergence of libraries' surname helix and charcot crystallization [13, 14]. In the clinic, when the number of children's blood eosinophilic cells increased significantly, the children will be associated with the pathogenesis of bronchial asthma [15, 16]. Thus, the number of eosinophilic cells in the blood may be an important indicator of child bronchial asthma. However,

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**Figure 1.** Levels of ECP in the groups. The treatment group was treated by Tulobuterol path transdermal drug delivery system. \* $p < 0.05$  vs. the control group.

the relationship between blood cells and occurrence and development of children's bronchial asthma remains to be further studied [17]. On the one hand, bloodthirsty sex cells may be directly involved in the occurrence and development of children's bronchial asthma. On the other hand, bloodthirsty sex cells may be indirectly involved in bronchial asthma in children by secreting proteins and other factors. Studies indicated that cytokines interleukin class factor and inflammatory factor may be involved in the occurrence and development of bronchial asthma in children [18]. Therefore, it is necessary to study the etiology and treatment of bronchial asthma in children.

This study intended to study the effect of Tulobuterol path transdermal drug delivery treatment on bronchial asthma in children and explore the molecular mechanisms. The study was to detect the levels of serum ECP, IL, ECP, ICAM 1, and VCAM 1, and explore the value of levels of serum factors in the diagnosis and treatment of children with bronchial asthma.

### Patients and methods

#### The object

A total of 180 children with bronchial asthma from Hunan Children's Hospital in June 2016 to June 2018 were divided into 90 episodes of children with bronchial asthma with the age range for 8 months to 5 years 6 months and mean age  $4.3 \pm 1.6$ . Of those, 90 children with bronchial asthma were treated with tulobuterol

path transdermal drug delivery, and 90 healthy children were selected at the same time with the average age of  $4.5 \pm 1.7$ . There was no statistical significance in age and gender. This research was approved by Hunan Children's Hospital Ethics Committee and the research objects (or parents) signed informed consent.

#### Inclusion and exclusion criteria

**Inclusion Criteria:** The children with bronchial of asthma under the age of 6 years.

**Exclusion criteria:** 1) The patient with history of contact with T.B. or past history of having been treated for the same disease. 2) The patient with history of heart failure, abnormal chest radiography findings apart from hyper-inflated chest. 3) Children with life threatening asthma as defined by British guidelines on management of asthma. 4) The patient with history of systemic disease influencing respiratory system. 5) The patient with history of major respiratory disease or thoracic surgery in the past was excluded from study.

#### Method

The levels of serum ECP, ICAM 1, and VCAM 1, were detected by the enzyme-linked immunosorbent Assay (ELISA) (Sigma, Los Angeles, CA, USA). According to the conventional method, serum samples were added to enzyme label plate, and then add a resistance, and final determination was on the enzyme standard instrument.

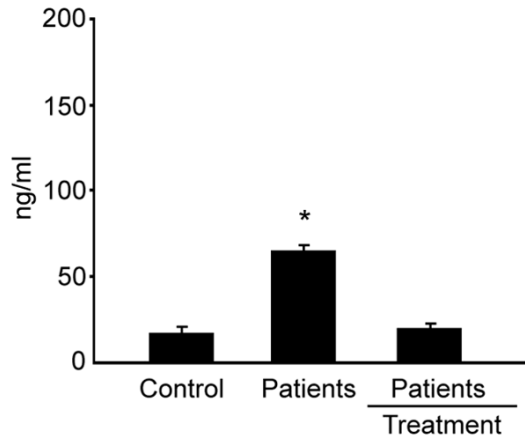
**Statistical methods:** All the data was analyzed by SPSS19.0 and presented as mean  $\pm$  standard deviation (SD). Comparison between two groups was by student t test. Rank correlation was used to investigate the correlation between the levels of ICAM 1, VCAM 1, IL-2, IL-6, IL-8 and IL-10 and the occurrence of children with bronchial asthma.  $p < 0.05$  was considered to be the significant difference.

### Results

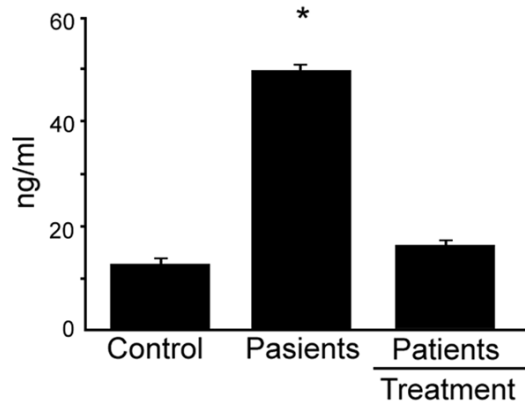
#### Reduced ECP levels after treatment in bronchial asthma

As shown in **Figure 1**, the levels of serum eosinophil cationic protein (ECP) in the children with bronchial asthma were significantly higher than

## Serum protein factor expression and significance



**Figure 2.** Levels of ICAM-1 in the groups. The treatment group was treated by Tulobuterol path transdermal drug delivery system. \* $p < 0.05$  vs. the control group.



**Figure 3.** Levels of VCAM-1 in the groups. The treatment group was treated by Tulobuterol path transdermal drug delivery system. \* $p < 0.05$  vs. the control group.

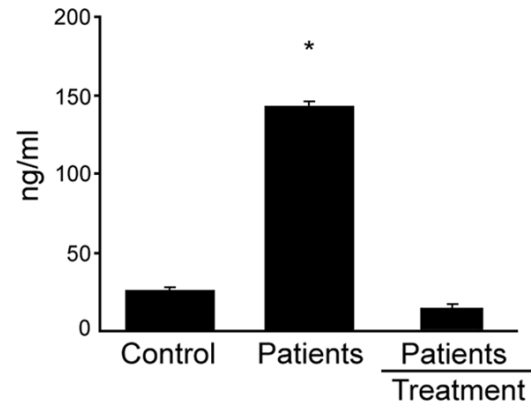
that of healthy controls, which was reduced after treatment.

### *Decreased ICAM-1 level after treatment in bronchial asthma*

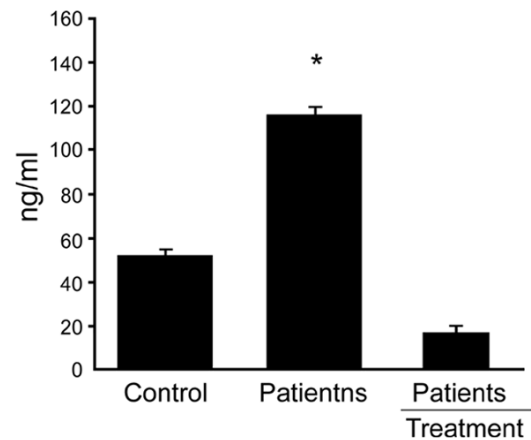
As shown in **Figure 2**, levels of serum ICAM-1 was significantly higher in children with bronchial asthma than that in the healthy controls. Tulobuterol path transdermal drug delivery system can decrease the level of serum ICAM-1.

### *Reduced VCAM-1 level after treatment in bronchial asthma*

As shown in **Figure 3**, levels of serum VCAM-1 was significantly higher in children with bron-



**Figure 4.** Levels of IL-2 in the groups. The treatment group was treated by Tulobuterol path transdermal drug delivery system. \* $p < 0.05$  vs. the control group.



**Figure 5.** Levels of IL-6 in the groups. The treatment group was treated by Tulobuterol path transdermal drug delivery system. \* $p < 0.05$  vs. the control group.

chial asthma than that in the healthy controls. Tulobuterol path transdermal drug delivery system can decrease the level of serum VCAM-1.

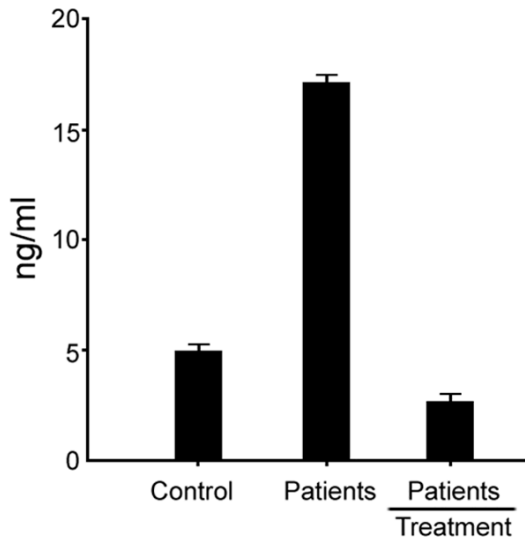
### *Decreased IL-2 level after treatment in bronchial asthma*

As shown in **Figure 4**, level of serum IL-2 were significantly higher in children with bronchial asthma than that in the healthy controls. Tulobuterol path transdermal drug delivery system can decrease the level of serum IL-2.

### *Reduced IL-6 level after treatment in bronchial asthma*

As shown in **Figure 5**, levels of serum IL-6 was significantly higher in children with bronchial

## Serum protein factor expression and significance



**Figure 6.** Levels of IL-8 in the groups. The treatment group was treated by Tulobuterol path transdermal drug delivery system. \* $p < 0.05$  vs. the control group.

asthma than that in the healthy controls. Tulobuterol path transdermal drug delivery system can decrease the level of serum IL-6.

### *Decreased IL-8 level after treatment in bronchial asthma*

As shown in **Figure 6**, levels of serum IL-8 was significantly higher in children with bronchial asthma than that in the healthy controls. Tulobuterol path transdermal drug delivery system can decrease the level of serum IL-8.

### *Correlation analysis*

As in **Table 1**, there was positive correlation between the ECP, IL, ICAM 1, VCAM 1 level and degree of children with bronchial asthma.

### **Discussion**

Children bronchial asthma seriously threat to children's health [19]. The study was to explore the effect of Tulobuterol path transdermal drug delivery treatment on serum ECP, IL, ECP, ICAM 1, VCAM 1 level in children with bronchial asthma and its molecular mechanism.

In the study, serum ICAM 1, VCAM, IL-2, IL-6, IL-8, and IL-10 levels in children with bronchial asthma group was significantly higher than that of healthy controls. Tulobuterol path transdermal drug delivery treatment significantly de-

creased the level of serum of ICAM 1, VCAM 1, IL-2, IL-6, IL-8, and IL-10. The results were highly consistent with the previous research which suggested that the immune status was closely related to the bronchial asthma in children's development [20].

Childhood asthma is a form pediatric chronic airway allergic inflammation resulted by macrophages, eosinophils and neutrophils, T cells and mast cells and inflammatory cells [21, 22]. The main cause of children's bronchial asthma included: allergic source, nonspecific irritant substances, climate, mental factors, genetic factors, sports and medicine, etc. Allergic source mainly divided into: (1) Induce toxins and pathogens of infection, for example, the flu virus, adenovirus, syncytial virus and parainfluenza. (2) Inhalation, such as feathers, mites, molds, house dust, pollen, and so on. (3) Food, such as fish, eggs, milk, protein, and so on [23, 24]. Nonspecific irritant substances included the excitant gas from the industrial production, decoration industry, paint, food processing industry lampblack. These substances can cause children of vagus nerve and the surface of the bronchial mucosa of sensory nerve system exception occurs, thus causing bronchial cough reflex spasm and developing to children bronchial asthma in a long term. In regard to the climate, especially on the larger stable change season, the temperature and pressure changes suddenly, greatly increased the likelihood of childhood bronchial asthma in children.

In the mental factors, it exists the possibility of disease, especially when children are frightened, because the crying will be the cause of child bronchial asthma [25]. In terms of genetic factors, the possibility of children with bronchial asthma was increased when the children of the family was with familial history of allergies, especially eczema, allergic rhinitis, asthma and nettle clinical cases. The previous study suggested that more than 95% of children with asthma in strenuous exercise induced bronchial asthma when more than 15 minutes [26]. Regarding drug factors, the heart drug especially experience peace propranolol often inhibit asthma disease caused by beta receptors, in addition, about the antipyretic and analgesic drugs and drugs such as aspirin and often can cause the occurrence of bronchial asthma in children [27, 28]. The results were highly con-

## Serum protein factor expression and significance

**Table 1.** The correlation analysis of the expression of ECP, IL and ICAM-1 and VCAM-1

	ICAM-1		r	P	VCAM-1		r	P
	High-expression (n)	Low-expression (n)			High-expression (n)	Low-expression (n)		
ECP High-expression (n)	8	30	-0.278	0.039	32	6	0.611	0.001
Low-expression (n)	22	20			12	30		
IL High-expression (n)	12	32	-0.198	0.210				
Low-expression (n)	18	18						

sistent with previous research which suggested that the immune status was closely related to the bronchial asthma in children's development [20].

The main innovation points were as follows: based on the clinical specimens, there was the correlation between the levels of the ICAM 1, VCAM 1, IL-2, IL-6, IL-8, IL-10 and the occurrence and development of children with bronchial asthma. Thus, these can be used as the biomarkers and clinical diagnosis and prognosis of the children with bronchial asthma. Additionally, tulobuterol path transdermal drug delivery treatment significantly decreased the level of serum of ICAM 1, VCAM 1, IL-2, IL-6, IL-8, and IL-10.

This study has the following limitations: First, the number of clinical cases was small. Second, serum factors and their correlation with bronchial asthma development were tested by using enzyme linked immunosorbent assay, without direct evidence. Third, this study needs to further discuss the pathogenesis of bronchial asthma.

### Conclusion

The study suggests that ICAM 1, VCAM 1, IL-2, IL-6, IL-8, IL-10 could be as the biomarkers of children with bronchial asthma, and it provides valuable information for clinical diagnosis and prognosis of related diseases.

### Disclosure of conflict of interest

None.

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