Am J Transl Res 2021;13(7):8158-8164
www.ajtr.org /ISSN:1943-8141/AJTR0116574

*Original Article*

# Effect of budesonide combined with salbutamol nebulization on pulmonary function and serum immune factors in children with bronchiolitis

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Received June 18, 2020; Accepted August 4, 2020; Epub July 15, 2021; Published July 30, 2021

**Abstract:** Objective: This study set out to investigate the effect of budesonide combined with salbutamol nebulization on pulmonary function and serum immune factors in children with bronchiolitis. Methods: A total of 127 children with bronchiolitis who were treated in our hospital were collected. Among them, 59 were treated with conventional bronchiolitis and were included in the control group (CG), and 68 were treated by budesonide combined with salbutamol inhalation in addition to the conventional treatment that were included in the research group (RG). The clinical efficacy, disappearance time of cough, pulmonary rales, wheezing and dyspnea, hospitalization time, adverse reactions, lung function and serum immune factors of the two groups were compared. Results: Compared with before treatment, cough, pulmonary rales, wheezing and dyspnea of children in both groups were improved after treatment. Compared with the CG, the disappearance time of cough, pulmonary rales, wheezing and dyspnea in the RG was shortened, the hospitalization time and adverse reactions reduced, and the total effective rate increased. The tidal volume, peak-to-peak time ratio (tPTEF/tE) and peak-to-peak volume ratio (VPTEF/VE) of the RG were dramatically better than those of the CG, and the levels of IgG, IgM and IgA were better than those of the CG. Conclusion: Budesonide combined with salbutamol nebulization is beneficial to improve the pulmonary function and serum immune factors in children with bronchiolitis.

**Keywords:** Infant bronchiolitis, budesonide, salbutamol, pulmonary function, serum immune factors

## Introduction

Infant bronchiolitis is an acute lower respiratory tract infection with a high morbidity among infants under 2 years old [1, 2]. At present, it is generally believed that a respiratory syncytial virus infection is the main cause of infection in children, and those with severe illness often have respiratory failure symptoms and need to the enter intensive care unit for treatment, and children also have sequelae such as stunted growth after recovery [3-6]. Some studies have shown that bronchiolitis in children is not only a disease of the lungs, but that it also affects other extra pulmonary organs. If the disease is not controlled, it may lead to complications such as viral hepatitis, hypoxic hepatitis, liver congestion or right sided heart failure [7, 8]. Therefore, it is crucial to judge and control the disease in a timely and effective manner.

Budesonide is a glucocorticoid with anti-inflammatory and anti-allergic effects; it can significantly improve the airway inflammatory response and respiratory ventilation effects. It mainly enhances the inhibitory effect of calcitriol on airway remodeling by up-regulating the expression of vitamin D receptors in human bronchial fibroblasts [9-11]. Nebulization takes effect faster than oral therapy and it reduces drug degradation [12]. Budesonide can better control respiratory tract inflammation through atomization inhalation [13, 14]. Salbutamol is a β2-adrenoceptor agonist, which inhibits the release of allergic response factors by exciting β2-adrenoceptors, thus relieving congestion and edema of bronchi and respiratory tract, via dilating bronchi [15, 16].

In this study, infant bronchiolitis was treated by budesonide combined with salbutamol nebuli-

**Table 1.** Baseline data table

| | Control group (CG) (n=59) | Observation group (OG) (n=68) | $t/X^2$ | P |
|---|---|---|---|---|
| Age (month) | 15.98±2.62 | 16.25±4.32 | 0.418 | 0.677 |
| Gender | | | 0.659 | 0.417 |
| Male | 38 (64.41) | 39 (57.35) | | |
| Female | 21 (35.59) | 29 (42.65) | | |
| Passive smoking | 15 (25.42) | 13 (19.12) | 0.731 | 0.393 |
| Premature birth | 6 (10.17) | 9 (13.24) | 0.285 | 0.593 |
| Family asthma history | 12 (20.34) | 8 (11.76) | 1.750 | 0.186 |
| Family allergy history | 8 (13.56) | 15 (22.06) | 1.539 | 0.215 |
| Type of infection | | | 1.021 | 0.600 |
| RSV | 43 (72.88) | 47 (69.12) | | |
| CBV | 6 (10.17) | 5 (7.35) | | |
| Other types | 10 (16.95) | 16 (23.53) | | |
| Fever | 46 (77.97) | 57 (83.82) | 0.707 | 0.400 |
| White blood cell count ($\times 10^9$/L) | 7.34±1.67 | 7.95±1.96 | 1.872 | 0.064 |

**Table 2.** Comparison of clinical efficacy of patients between the two groups

| | Control group (CG) (n=59) | Observation group (OG) (n=68) | $X^2$ | P |
|---|---|---|---|---|
| Significantly effective | 18 (30.51) | 27 (39.71) | 1.168 | 0.280 |
| Effective | 25 (42.37) | 33 (48.53) | 0.483 | 0.487 |
| Ineffective | 16 (27.12) | 8 (11.76) | 4.859 | 0.028 |
| Total effective rate | 43 (72.88) | 60 (88.24) | | |

zation, and its efficacy and application effect were observed.

## Methods

### *Patient data*

A total of 127 children with bronchiolitis who were treated in our hospital from February 2018 to June 2019 were collected and divided into an observation group (OG) and a control group (CG) based on different treatment methods. Fifty-nine cases were treated with conventional bronchiolitis treatment that were included in the CG, including 38 males and 21 females, aged 7-26 months, with an average age of (15.98±2.62) months. Sixty-eightcases were treated by budesonide combined with salbutamol nebulization in addition to the conventional treatment who were enrolled in the RG, including 39 males and 29 females, aged 8-27 months, with an average age of (16.25±4.32) months. This study was approved by the Medical Ethics Committee. All children and their families were informed and they signed informed consent forms.

### *Inclusion and exclusion criteria*

Inclusion criteria: All children were younger than 14 years old, and they were diagnosed with bronchiolitis by imaging techniques. All children had cough, lung rales, wheezing, dyspnea and other clinical symptoms. Their clinical data were complete, and the family members were willing to cooperate with the follow-up.

Exclusion criteria: children with bronchial foreign bodies, or congenital dysplasia of bronchus were excluded; those who were allergic to therapeutic drugs, complicated with liver and kidney insufficiency, or other lung diseases such asphthisis, accompanied by autoimmune diseases, and those who had immunosuppressants or glucocorticoids within the past two months were excluded.

### *Therapeutic regimens*

Patients in both groups received conventional treatment, including antiviral care, sputum aspiration and other methods to alleviate disease progression. Additionally, the CG was given budesonide combined with salbutamol nebulization therapy. Budesonide was given twice daily at a dose of 200 μg/15 min/inhalation, and salbutamol was given twice daily at 200 μg/15 min/inhalation therapy for 2 weeks.

### *Detection methods of IgG, IgM and IgA*

Altogether 5 mL of fasting venous blood was collected from both groups into pro-coagulation tubes, and centrifuged (3000×g at 4°C for 10

**Table 3.** Time for symptoms to disappear

| | Control group (CG) (n=59) | Observation group (OG) (n=68) | t | P |
|---|---|---|---|---|
| Cough (d) | 4.53±1.53 | 3.65±1.37 | 3.419 | <0.001 |
| Pulmonary rales (d) | 3.81±1.26 | 2.71±0.93 | 5.643 | <0.001 |
| Wheezing (d) | 4.11±1.15 | 3.26±1.26 | 3.948 | <0.001 |
| Dyspnea (d) | 3.25±1.04 | 2.01±0.81 | 7.544 | <0.001 |

**Table 4.** Incidence of adverse reactions

| | Control group (CG) (n=59) | Observation group (OG) (n=68) | $X^2$ | P |
|---|---|---|---|---|
| Cough | 2 (3.39) | 1 (1.47) | 0.505 | 0.478 |
| Nausea | 4 (6.78) | 2 (2.94) | 1.034 | 0.309 |
| Headache | 3 (5.08) | 1 (1.47) | 1.353 | 0.245 |
| Vomiting | 3 (5.08) | 1 (1.47) | 1.353 | 0.245 |
| Total adverse reactions | 12 (20.34) | 5 (7.35) | 4.595 | 0.032 |

min) to collect serum. The serum IgG, IgM and IgA were detected by Toshiba TBA-200FR automatic biochemical analyzer and Roche's kit.

*Outcome measures*

Main outcome measures: We compared the efficacy of the two groups after treatment. Markedly effective: The symptoms of the children disappeared, their conditions returned to normal. Effective: The symptoms of the children improved, their condition returned. Ineffective: The symptoms did not improve or even worsened. Total effective = markedly effective + effective. We also compared the tidal volume (VT), peak-to-peak time ratio (tPTEF/tE) and peak-to-peak volume ratio (VPTEF/VE) of lung function indexes before and after treatment between both groups.

Secondary outcome measures: We compared the disappearance of cough, pulmonary rales, wheezing, dyspnea and other symptoms, as well as incidence of adverse reactions between the two groups.

*Statistical methods*

The usage rate (%) of counting data was assessed by chi-square test and expressed by $X^2$. The measurement data were expressed by mean ± standard deviation (Mean ± SD), and they all conformed to a normal distribution. The comparison between the two groups was analyzed via independent-samples t test and expressed by *t*. P<0.05 was considered to be statistically significant. The collected data were analyzed via SPSS 20.0 (Chicago SPSS Co., Ltd.), and the figures were illustrated via GraphPad Prism 7 (San Diego graphpad Software Co., Ltd.).

## Results

*Baseline data*

By comparing the clinical baseline data of patients in both groups, we found that there was no marked difference in age, gender, passive smoking, premature delivery, family asthma history, family allergy history, infection type, fever and white blood cell count between both groups, as shown in **Table 1**.

*Clinical efficacy of the OG is better than that of the CG*

By comparing the efficacy of patients in the two groups after treatment, we found that there was no obvious difference between the OG and the CG in the significant rate of efficacy and effective rate of treatment, but the total effective rate of the OG was dramatically higher than that of the CG (P<0.05), as shown in **Table 2**.

*Disappearance time of symptoms in both groups*

By comparing the time taken for cough, pulmonary rales, wheezing and dyspnea to disappear between the two groups, we found that the disappearance time in the OG was significantly shorter than that in the CG (P<0.05), as shown in **Table 3**.

*Incidence of adverse reactions in the OG is lower than that in the CG*

By comparing the occurrence of adverse reactions between the two groups, we found that there was no marked difference in cough, nausea, headache and vomiting between both groups. The total incidence of adverse reactions in the OG was dramatically lower than that in the CG, as shown in **Table 4**.

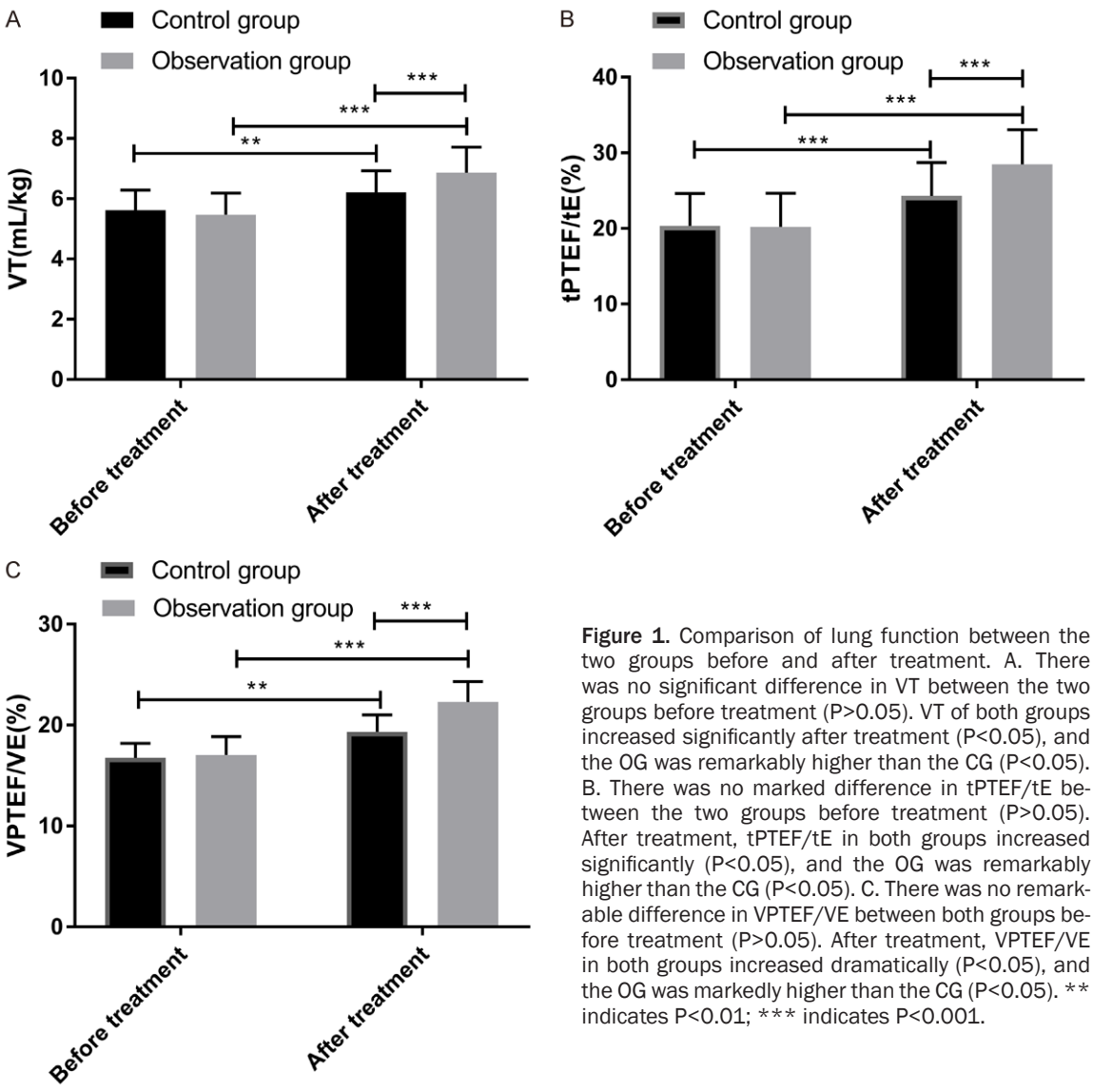


**Figure 1**. Comparison of lung function between the two groups before and after treatment. A. There was no significant difference in VT between the two groups before treatment (P>0.05). VT of both groups increased significantly after treatment (P<0.05), and the OG was remarkably higher than the CG (P<0.05). B. There was no marked difference in tPTEF/tE between the two groups before treatment (P>0.05). After treatment, tPTEF/tE in both groups increased significantly (P<0.05), and the OG was remarkably higher than the CG (P<0.05). C. There was no remarkable difference in VPTEF/VE between both groups before treatment (P>0.05). After treatment, VPTEF/VE in both groups increased dramatically (P<0.05), and the OG was markedly higher than the CG (P<0.05). ** indicates P<0.01; *** indicates P<0.001.

*Lung function in the OG improves better than that in the CG*

By comparing the pulmonary function indexes (VT, tPTEF/tE, VPTEF/VE) of children in the two groups before and after treatment, we found that there was no remarkable difference before treatment. After treatment, the three were significantly higher than those before treatment, and the OG had significantly higher scores than the CG (**Figure 1**).

*Serum immune factors in the OG improved better that those in the CG*

By comparing the serum immune factors (IgG, IgM, IgA) of children in the two groups before and after treatment, we found that there was no remarkable difference before treatment. After treatment, the three were significantly higher than before treatment, and the OG had significantly higher immune factors than the CG (**Figure 2**).

## Discussion

In this study, we first compared the clinical efficacy of treatment in the two groups, and found that the total effective rate of the OG was significantly higher than that of the CG, which indicated that budesonide combined with salbutamol nebulization could strengthen the efficacy of basic therapy. Then, we compared the disappearance time of symptoms of all patients and

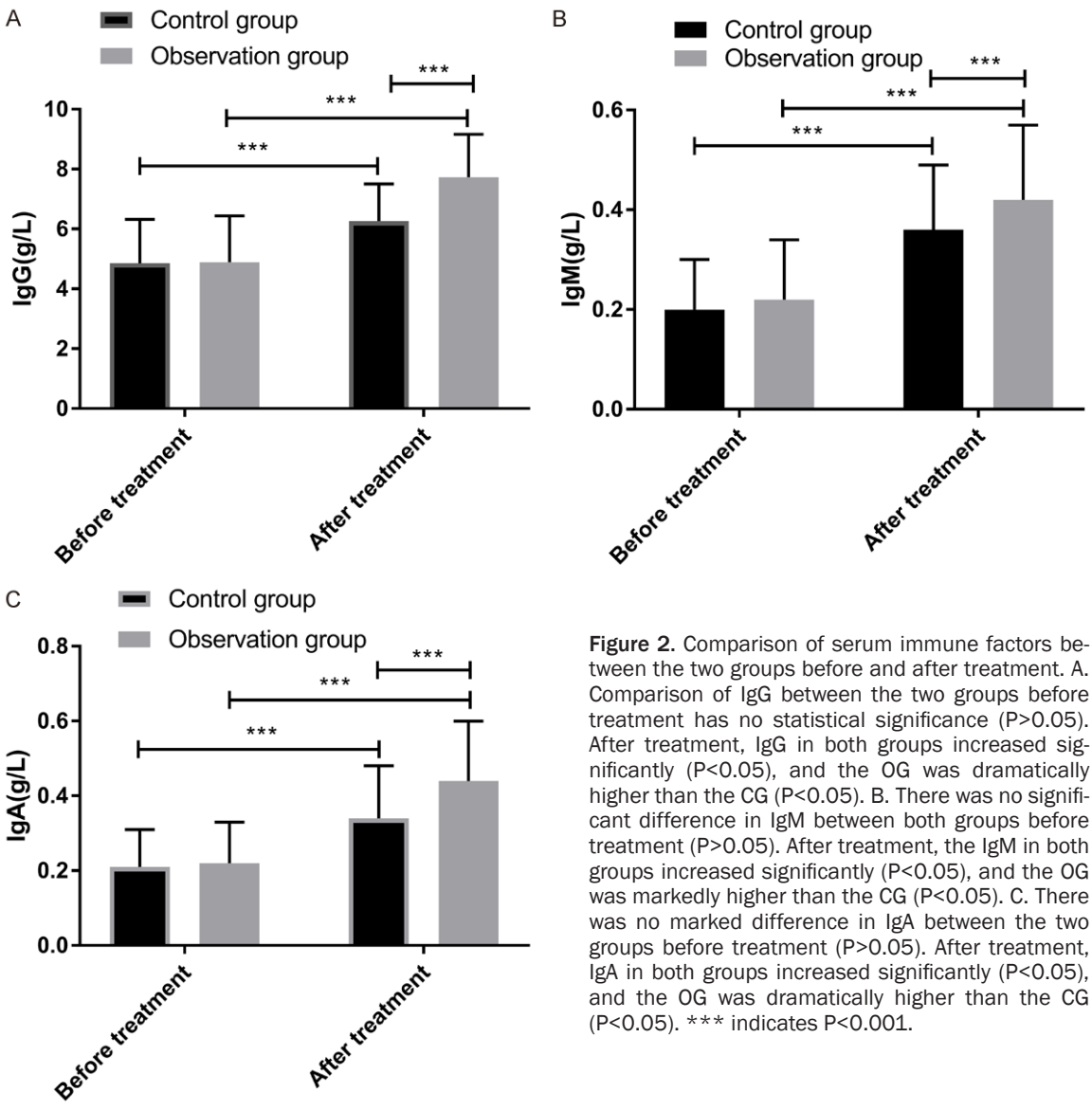


**Figure 2.** Comparison of serum immune factors between the two groups before and after treatment. A. Comparison of IgG between the two groups before treatment has no statistical significance (P>0.05). After treatment, IgG in both groups increased significantly (P<0.05), and the OG was dramatically higher than the CG (P<0.05). B. There was no significant difference in IgM between both groups before treatment (P>0.05). After treatment, the IgM in both groups increased significantly (P<0.05), and the OG was markedly higher than the CG (P<0.05). C. There was no marked difference in IgA between the two groups before treatment (P>0.05). After treatment, IgA in both groups increased significantly (P<0.05), and the OG was dramatically higher than the CG (P<0.05). *** indicates P<0.001.

found that the time of cough, pulmonary rales, wheezing, dyspnea and other symptoms in the OG was dramatically less than that in the CG. During treatment, the CG had 2 cases of cough, 4 cases of nausea, 2 cases of headache and 3 cases of vomiting, while the OG had only 1 case of cough, 2 cases of nausea, 3 cases of headache and 1 case of vomiting. The total incidence of adverse reactions in the OG was dramatically lower than that in the CG.

Then, we compared VT, tPTEF/tE and VPTEF/VE of lung function indexes before and after treatment. In general, children's lung function is often damaged after the occurrence of infant bronchiolitis [17, 18]. These three measures can well reflect lung function [19]. We found that the three indexes in children of both groups increased compared with those before treatment, and those of the OG after treatment were significantly higher than those of the CG. Zhang et al. [20] mentioned that budesonide could reduce the pathological changes caused by bronchitis in rats by activating Nrf2/Keap1, and played a protective role by reducing oxidative stress damage, which indicated the therapeutic principle of budesonide. Therefore, we found that budesonide combined with salbutamol can better improve children's lung function. At the same time, we believe that nebulization has a larger area of action, better absorption of the drug, higher selectivity of smooth muscle,

and more obvious effects. Hence, the dosage of glucocorticoid and tracheal dilator is lower, but the effect of improving symptoms is excellent. Kulalert et al. [21] showed that the effect of continuous nebulization of salbutamol was better than that of intermittent atomization therapy, but this study did not make a comparison.

Finally, we tested the serum immune factors (IgG, IgM, IgA) of children in the two groups. In some studies, children with bronchiolitis are often associated with immunocompetence [22]. Shan et al. [23] have confirmed that IgG, IgM and IgA of children with severe bronchiolitis are significantly lower than those of normal healthy children. Immunoglobulin injection can improve the symptoms of patients and enhance their immunity. We found that the levels of IgG, IgM and IgA in children of both groups were improved after treatment, and the levels of the three in the OG were dramatically higher than those of the CG. In the past, there were references revealing that budesonide and salbutamol could regulate the immune function of patients [24, 25]. Therefore, budesonide combined with salbutamol can also better improve the immunity of children, and the improvement of immunity is conducive to disease rehabilitation.

However, there are still some deficiencies. First, this study does not compare the differences of therapeutic indexes between budesonide and salbutamol nebulization and non-nebulized inhalation. At present, there are also other clinical combination schemes for the treatment of infant bronchiolitis, such as magnesium sulfate combined with salbutamol or ipratropium bromide [26, 27]. So, it is hoped that the later research can be improved by comparing these treatment schemes to find the best treatment scheme. At last, we hope to carry out some basic research in a follow-up study, to explore the mechanism of the influence of budesonide and salbutamol.

To summarize, budesonide combined with salbutamol nebulization is beneficial to improve pulmonary function and serum immune factors in children with bronchiolitis.

## Disclosure of conflict of interest

None.

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