



The Libyan International Medical University
Faculty of Basic Medical Science



RELATION BETWEEN BRONCHITIS AND IMMUNOGLOBULIN

Arwa omar 1951

Supervised by:mohamed hamza

Assisted by:suzan mohamed

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Abstract

The goal of the present study is to explore the physiological effects of injected human immunoglobulin on patients with severe bronchiolitis before and after treatment. 86 young children with severe bronchiolitis were randomly divided into the observation group (43 cases) and the treatment group (43 cases). On the basis of conventional therapy, the children in the treatment group were given human immunoglobulin (400 mg/kg, 1–3 times) via intravenous injection. 60 healthy young children, as determined by a physical examination given at the Zhumadian Central Hospital, were enrolled as the control group. The T lymphocytes, cytokines, IgA, IgG, and IgM immunoglobulins in the peripheral blood of all 3 groups were measured. The clinical efficacy of the immunoglobulins to mitigate the effects of bronchiolitis and the amount of time for the reduction of symptoms to occur were observed. The serum Ca, Fe, and Zn levels of children with severe bronchiolitis were significantly lower than those of the healthy control group ($p < 0.05$). As such, the CD8, IgA, IgG, IgM and IFN- γ levels were also significantly lower in the children with severe bronchiolitis than in the children in the healthy control group ($p < 0.05$). Furthermore, the CD4, IgE, IL-4, and IL-4/IFN- γ levels and CD4/CD8 ratio were dramatically higher than in the healthy control group ($p < 0.05$). Serum levels of the aforementioned indicators either increased or decreased after IVIG treatment. The amount of time required for coughing, wheezing, and pulmonary rales to seize, and the duration of illness for the children with the severe bronchiolitis children was significantly shorter for those in the treatment group than for those in the observation group. Human immunoglobulin via intravenous injection showed active therapeutical effects on trace elements, T lymphocytes, and cytokines in patients with severe bronchiolitis.

Introduction

Severe bronchiolitis is a lower respiratory tract infectious disease, a common clinical acute and critical case in pediatrics, and the leading cause of death among children, and it is more common in children less than 2 y old. The main symptoms are recurrent wheezing, difficulty breathing, thus causing hypoxia, endothelial damage, and platelet activation leading to a hypercoagulable state..

Intravenous immunoglobulin (IVIG) contains plenty of antibodies with high potency. It possesses dual therapy effect of immune replacement and immune regulation. It is an immunoglobulin G (IgG) antibody with broad-spectrum anti-virus, bacteria or other pathogenic function. By inhibiting Th2 and activating Th1, IVIG can restore the imbalance of Th1/Th2 where bronchiolitis exists and can prevent the occurrence of airway inflammation. By directly neutralizing immunoglobulin E (IgE) and inhibiting interleukin-4 (IL-4) production of interferon- γ (IFN- γ), IVIG lowers levels of IgE indirectly, prohibiting the type I allergy of severe bronchiolitis and reducing the release of inflammatory mediators. Additionally, IVIG can also neutralize inflammatory mediators and cytokines, causing a decrease in their concentrations as well as mitigating the harm to the body caused by inflammatory mediator cytokines. This leads to a restoration of the tracheal epithelium as soon as possible and shortening of the course of disease.¹ Research also shows that large doses of IVIG have certain effects on preventing severe bronchitis from developing into asthma.² IVIG can reduce the abnormal activation of immunization, reduce levels of cytokines, and improve clinical symptoms.³ The exact pathogenesis of bronchiolitis is uncertain. The vast majority of current research considers the disease to be an immune dysfunction disease stimulated by infection, with a variety of immune

cells and cytokines involved in the pathogenesis. The specific pathogenesis has not been clear. By detecting and analyzing the trace elements and T-cell subset levels in the serum of young children with severe bronchiolitis, this study aims to investigate the internal relations between immunology and the pathogens of severe bronchiolitis. The ultimate goal is to provide an experimental basis for exploring the pathogenesis of bronchiolitis and to develop new therapeutic methods and early intervention protocols.

Materials and Methods

A literature search was performed to discover studies reviewing the correlation between relation between bronchitis and immunoglobulin. Online sites and databases included in this report are PubMed database, and the American Society of Clinical Oncology for relevant Search terms included relation between bronchitis and immunoglobulin. Titles and abstracts were observed for significance. d to develop new therapeutic methods and early intervention protocols.

General information

- 86 severe bronchiolitis infants treated at the Pediatric Intensive Care Unit (PICU) ward of Zhumadian Central Hospital from January 2011 to January 2014 were selected, 47 males and 39 females, ranging in age from 1 to 13 months with an average age of 9.62 (± 1.15) months. There were 43 cases in both the observation group and treatment group. All of them had been diagnosed as having severe bronchiolitis by X-rays and blood oxygen saturation, and infants with congenital asthma were excluded. 60 healthy infants who received physical examination in the hospital at the same period were chosen as the control group, 35 males and 25 females, aged from 1 to 13 months, with an average age of 10.14

(± 1.27) months. Differences in gender, age, and other general information was not statistically significant ($p < 0.05$) between the 2 groups.

The inclusion and exclusion criteria

Inclusion criteria: less than 2 y old, the first onset of the disease, clinical diagnosis of fever, cough, severe wheezing, shortness of breath, and other symptoms, the lungs mainly displaying signs of stridor, the total number and distribution of white blood cells and C-reactive protein were to be within the normal range, varying degrees of obstructive pulmonary emphysemas and spot film shadows on the chest were allowed for inclusion.

Exclusion criteria: mild wheezing, congenital heart disease, bronchopulmonary dysplasia, whooping cough, rickets, moderate and severe anemia, foreign bodies in the bronchus, tuberculosis infection, congenital laryngeal stridor, and other diseases that may manifest.

Detection of trace elements

Trace elements are necessary for human body. The excessive or deficient intake, imbalance or a shortage of them will cause human physiological abnormalities in different degrees or even disease. Calcium, iron, and zinc have strong ties to the body's normal physiological activities. These trace elements have the ability to affect immune function. If the content of these elements is reduced, it will lead to a decline in body's resistance to the incidence of diseases.²⁴ Zinc is one of the necessary trace elements. It plays an extremely important role in the physiological process such as body growth and development, reproduction and genetics, immune and endocrine. Previous data reports that zinc deficiency can significantly

reduce T-cell function, thus weakening the body's defenses. Iron also has a role in promoting immunization; a deficiency in this key element also leads to a decrease in immunity. Calcium is required to maintain and regulate many biochemical processes within the body; it maintains the acid-base balance, maintains the integrity and permeability of the cell membrane, reduces capillary permeability, prevents exudation, and controls inflammation and edema.

40 μ L of peripheral blood of infants was collected and thoroughly dissolved into 1.2 mL of cytolysis fluid. The BH-5100 atomic absorption spectrometer (Beijing Bohui Innovation Technology Co., Ltd., Beijing, China) was used for detection. All operations were in strict accordance with the instructions.

Detection of immunoglobulin and T lymphocyte subsets levels

T lymphocytes are the main immune cells, but they are also an important indicator for the evaluation of cellular immune function. IgM plays a key role in the early phase of anti-infection and it is a vanward antibody against pathogenic microorganisms. IgG is the major antibody against infection, and it has a high level in the blood during infection. IgA is a first line of defense for mucosa resisting pathogenic microorganism and harmful substances. It is the main effector molecule of humoral immunity.

Two mL of fasting venous blood was taken. The Roche P module automatic biochemical analyzer and the matching reagents were utilized to conduct the immunoturbidimetric immunoglobulin assay. Levels of Cluster of Differentiation 4 (CD4) and Cluster of Differentiation 8 (CD8) were detected, as these are surface markers for T-cell subsets. The anti-human T cells monoclonal antibody APAAP bridge-linked enzyme linked

immunosorbent assay (ELISA) was used to detect T lymphocyte subsets (provided by Wuhan Institute of Biological Products Co., Ltd.).

Detection of the serum inflammatory factors' levels

Double-antibody sandwich ELISA was used for quantitative detection of human IL-4, IFN- γ , and IgE. The ELISA kits were all provided by Beijing SinoSec MicroTest Sci. & Tech. Co. Ltd. The Qtat-fax-2100 microplate reader produced by US AWARENESS Company was used.

Results

Comparing the levels of trace elements before and after treatment in the severe bronchiolitis group and control group

As observed in , the serum levels of Ca, Fe, and Zn in the severe bronchiolitis group were significantly lower than those in the healthy control group, reaching a level of significant difference ($p < 0.05$), After IVIG treatment, the Ca, Fe, and Zn levels in the severe bronchiolitis group all increased to some extent, and they also reached a level of significant difference ($p < 0.05$,) compared with levels observed before treatment

Comparing the levels of trace elements before and after treatment in the severe bronchiolitis group and control group (mg/L).

Comparing the levels of T cell subsets before and after treatment in the severe bronchiolitis group and control group

bronchiolitis group declined to a certain degree when compared with those of the control group, but the reduction level was not significant However, the CD4 level was significantly higher in the severe

bronchiolitis group than in the control group ($p < 0.05$). After IVIG treatment, the level of T-cell subsets, compared with that before treatment, increased or decreased in varying degrees without significant difference. The ratio of CD4/CD8 is an important indicator of the body's immune system homeostasis, the imbalance of which will lead to a variety of immune diseases. The CD4/CD8 ratio of the bronchiolitis group was greatly higher than that of the control group before treatment, indicating that changes may exist in T-cell subsets in the bronchiolitis group and that an excessive T-cell differentiation may occur to CD4 in the bronchiolitis group. This would lead to the imbalance of CD4/CD8 ratio and the abnormal immunological mechanisms involved in the pathogenesis of bronchiolitis. The ratio of CD4/CD8 reduced dramatically post-treatment, and the difference from the pre-treatment ratio was significant ($p < 0.05$). As can be seen in CD3 and CD8 levels in serum of the severe

Comparing the levels of T-cell subsets before and after treatment in the severe bronchiolitis group and control group (%).

Comparing the levels of serum immunoglobulin before and after treatment in the severe bronchiolitis group and control group

shows that serum immunoglobulin A (IgA), IgG, and immunoglobulin M (IgM) levels in children with severe bronchiolitis were significantly lower than those in the control group. IgG was significantly different ($p < 0.05$) between groups, and IgA levels showed extremely significant differences ($p < 0.01$) between groups. Compared with the previous controls, the IgE level was significantly higher ($p < 0.01$). IgA, IgG, and IgM levels of patients were higher after IVIG than before treatment, with IgA and IgG being significantly different ($p < 0.05$). IgE levels also

achieved a significant decrease after treatment ($p < 0.05$), illustrating that immunoglobulin levels in children with severe bronchiolitis are abnormally expressed. After IVIG treatment, content of serum immunoglobulins had improved to some extent.

Comparing the levels of serum inflammatory cytokines before and after treatment in the severe bronchiolitis group and control group

demonstrates that serum IFN- γ level of children with severe bronchiolitis showed a highly significant decrease in comparison with controls ($p < 0.01$), and IL-4 levels and the IL-4/IFN- γ ratio were significantly higher than the controls ($p < 0.05$). After IVIG treatment, IL-4, IFN- γ , and IL-4/IFN- γ levels decreased or increased in varying degrees, reaching a significant difference ($p < 0.05$). This suggests a Th1/Th2 imbalance. Th1 function declined in patients prior to treatment, but inflammatory cytokines in the serum had been somewhat recovered and conditions had improved after treatment.

Conclusions

Through a series of reactions of T lymphocytes and cytokines in the body, severe bronchiolitis plays its role. Therefore, for patients with severe bronchiolitis, detecting the related indicators of peripheral blood upon entering the intensive care unit can allow for prediction of disease severity and prognosis at an early stage. This could help doctors provide the right interventions and evaluate the efficacies in order to effectively adjust the appropriate therapeutic measures, providing a theoretical basis for the development of immunological therapy for diseases and the prevention of repeated wheezing of severe bronchiolitis

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