Effect of pidotimod combined with ribavirin treatment on serum indexes of children with hand-foot-mouth disease

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Objective: To study the effect of pidotimod combined with ribavirin treatment on serum indexes of children with hand-foot-mouth disease. Methods: A total of 78 children with hand-foot-mouth disease who received pidotimod combined with ribavirin treatment in our hospital from May 2013 to December 2015 were selected as the experimental group of the research, 84 children with hand-foot-mouth disease who received ribavirin monotherapy in our hospital from January 2012 to April 2013 were selected as the control group of the research. Serum inflammatory response indexes and biochemical indexes and immune function indexes of two groups were compared. Results: During the treatment, the maculopapule and herpes progression of experimental group were significantly better than those of control group; 7 day after treatment, CD3+CD4+CD8+ T cell, CD3+CD4+CD8+ T cell, CD19+B cell, CD14highCD16+ monocyte and CD14lowCD16+ monocyte content in peripheral blood of experimental group were significantly higher than those of control group, serum CRP, IL-6 and IL-10 levels were significantly lower than those of control group, and blood insulin, blood glucose, lactic acid, D-dimer and procalcitonin levels were significantly lower than those of control group. Conclusions: Pidotimod combined with ribavirin treatment can improve maculopapule and herpes, enhance immune function and reduce inflammatory reaction, and it is an ideal treatment for the treatment of children with hand-foot-mouth disease.

1. Introduction

Hand-foot-mouth disease is a common infectious disease of preschool children, and the main pathogen is Coxsackie virus A16 model[1], which can cause maculopapule and herpes in hand, foot, mouth and other parts after spreading through the digestive tract and respiratory tract, and severe cases can cause meningitis, pulmonary edema, circulatory disturbance and other life-threatening complications[2,3]. Children with hand-foot-mouth disease need to receive antiviral treatment, and ribavirin is common clinical antiviral drug that can competitively inhibit RNA polymerase and inosine monophosphate dehydrogenase so as to impede the viral RNA replication and protein synthesis, thereby suppressing the virus amplification[4]. However, the effect of ribavirin antiviral therapy alone is not very ideal and combined use of drugs with different mechanism of action can improve curative effect. Pidotimod is a kind of biological response regulator that can promote and improve the body's immune function[5]. Pidotimod combined with ribavirin was used in our hospital to treat children with hand-foot-mouth disease from May 2013 to December 2015, they were compared with children with hand-foot-mouth disease who received ribavirin monotherapy from January 2012 to April 2013 so as to reflect the effect of combination therapy, and detailed report was as follows.

2. Materials and methods

2.1. Subjects

A total of 78 children with hand-foot-mouth disease who received pidotimod combined with ribavirin treatment in our hospital from May 2013 to December 2015 were selected as the experimental group of the research, 84 children with hand-foot-mouth disease who received ribavirin monotherapy in our hospital from January 2012 to April 2013 were selected as the control group of the research. All children were with complete case information, were followed up 1 week after treatment and received blood sample collection. Experimental group included 48 male cases and 30 female cases who were (4.1±0.8) years old; control group included 52 male cases and 32 female cases who were (4.3±0.9) years old.
Comparison of general information between two groups showed no significant differences.

2.2. Treatment methods

Control group received ribavirin monotherapy, and the method was as follows: ribavirin injection 10 mg/kg in normal saline 100 mL, intravenous drip, 1 time/day, treatment for 7 days in a row. Experimental group received many pidotimod combined with ribavirin treatment, pidotimod granules 0.4 g, administration after dissolved with warm water, 1-2 times/day; ribavirin injection 10 mg/kg in normal saline 100 mL, intravenous drip, 1 time/day, treatment 7 days in a row for both.

2.3. Clinical index collection methods

During treatment, the maculopapule and herpes in children’s hand, foot, mouth and other parts were observed and photographically record every day; 7 day after treatment, peripheral blood 4-6 mL was collected from two groups and divided into two. One blood sample was used to incubate fluorescent antibody, and then flow cytometer was used to determine CD3+CD4+CD8-T cell, CD3⁺CD4⁺CD8⁺CD16⁺ cell, CD19⁺B cell, CD4⁺CD16⁺CD16¹ monocyte and CD14⁺CD16⁺ monocyte proportion; another blood sample was centrifuged to collect serum, enzyme-linked immunosorbent kit was used to determine procalcitonin (PCT), C-reactive protein (CRP), interleukin-6 (IL-6) and interleukin-10 (IL-10) content, chemiluminescence was used to determine glucose and insulin levels, enzymatic colorimetry kit was used to determine lactic acid content, and immunoturbidimetry was used to determine D-dimer content.

2.4. Statistical methods

SPSS20.0 software was used to input and analyze data, measurement data of two groups was analyzed by t test and P<0.05 indicated statistical significant differences.

3. Results

3.1. Immune function

On the 7th day after treatment, CD3⁺CD4⁺CD8⁻T cell, CD3⁺CD4⁻CD8⁺T cell, CD19⁺B cell, CD14⁺CD16⁺ monocyte and CD14⁺CD16⁺ monocyte content in peripheral blood of experimental group were significantly higher than those of control group, and immune function indexes in peripheral blood of two groups were significantly different (P<0.05) (Table 1).

3.2. Improvement of maculopapule and herpes

Maculopapule and herpes of two groups were not different before treatment; on the third day after treatment, maculopapule and herpes of experimental group were significantly improved while the improvement of maculopapule and herpes of control group were not significant; on the 7th day after treatment, maculopapule and herpes of experimental group were basically recovered, and the maculopapule and herpes of control group were also improved.

3.3. Serum inflammatory response indexes

On the 7th day after treatment, serum CRP content, IL-6 content and IL-10 content of experimental group were significantly lower than those of control group, and serum inflammatory response indexes of two groups were significantly different (P<0.05) (Table 2).

3.4. Blood biochemical indexes

On the 7th day after treatment, blood insulin content, blood glucose content, lactic acid content, D-dimer content and procalcitonin content of experimental group were significantly lower than those of control group, and blood biochemical indexes of two groups were significantly different (P<0.05) (Table 3).

4. Discussion

The main function of pidotimod is to regulate the body's immune function, which strengthens the body's humoral immune and cellular immune function to kill pathogenic bacteria(6-8). T cells mainly mediate cellular immune response, the naive T cells become mature CD3⁺CD4⁺CD8⁻ and CD3⁺CD4⁺CD8⁺T cells after double positive selection in the thymus, the former is the helper T cell that can assist the completion of cellular immune response, and the latter is cytotoxic T cell that can kill infected cells(9,10). B lymphocytes
mainly mediate humoral immunity, and their surface molecule is CD19[11]. In addition to T lymphocytes and B lymphocytes, mononuclear cells in the peripheral blood also play an important role in the regulation of immune function, among which CD14+CD16+ and CD14++CD16+ are also known as sedentary mononuclear cells and have immunoregulation function[12]. In the research, analysis of immune function indexes of the two groups confirmed that CD3+CD4+CD8+T cell, CD3+CD4+CD8+T cell, CD19+B cell, CD14+CD16+ monocyte and CD14++CD16+ monocyte content in peripheral blood of experimental group were significantly higher than those of control group. It confirmed that pidotimod could enhance the immune function of children with hand-foot-mouth disease.

Cellular immunity and humoral immunity are the body's important antiviral mechanisms, and in order to further clarify whether pidotimod could improve the condition of children with hand-foot-mouth disease on the basis of strengthening the body's immune function, the improvement of maculopapule and herpes of the two groups were compared after treatment: within 7 days after treatment, the maculopapule and herpes progression of experimental group were significantly better than those of control group. Hand-foot-mouth disease is mainly caused by Coxsackie virus A6 infection, virus infection will further cause the waterfall inflammatory reaction and anti-inflammatory reaction, and the corresponding inflammatory mediators are massively synthesized[13,14]. C-reactive protein is the index reflecting the degree of body's acute inflammation, and has the good consistency with the degree of inflammatory response[15]; IL-6 is an important pro-inflammatory mediator that is mainly synthesized and secreted by Th1 cells in the process of infection and mediates inflammation cascade amplification; IL-10 is an important anti-inflammatory factor, is mainly synthesized and secreted by Th2 cells and delays the process of inflammation, and is the body's self-protection and compensatory mechanism[16]. In the research, the analysis of serum inflammatory response index confirmed that pidotimod therapy could reduce the content of CRP, IL-6 and IL-10, and reduce the body's inflammatory response.

Acute infection caused by viral infection would put stress on the body and cause insulin resistance, manifested as elevated blood glucose levels and insulin levels; short-term continuous high-glucose state will affect the blood perfusion of the body and coagulation-fibrinolysis balance, lactic acid is a sensitive index reflecting tissue perfusion and hypoperfusion can cause elevated lactic acid levels, D-dimer is the hydrolysis product of cross-linking protein by fibrinolytic enzyme and its content increase is associated with coagulation-fibrinolysis disorder[17]. In addition, acute infection can also cause massive synthesis of procalcitonin by thyroid C cells, and serum procalcitonin level is directly correlated with the degree of acute state. In the research, the above serum biochemical indexes that reflected the body’s acute state were analyzed, and the results showed that blood insulin, blood glucose, lactic acid, D-dimer and procalcitonin levels of experimental group significantly reduced after treatment. It meant that pidotimod combined with ribavirin treatment could more effectively improve the acute state of children with hand-foot-mouth disease.

To sum up, pidotimod combined with ribavirin treatment can improve maculopapule and herpes, enhance immune function and reduce inflammatory reaction, and it is an ideal scheme for the treatment of children with hand-foot-mouth disease.

References