

Clinical Efficacy of Early Administration of Human Immunoglobulin on Children with Severe Hand-foot-mouth Disease

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ABSTRACT

The objective of this study was to investigate the clinical effect of early administration of human immunoglobulin in children with severe hand, foot and mouth disease (HFMD) and its influence on serum c-reactive protein (CRP), creatine kinase (CK), and creatine kinase isoenzyme (CK-MB). One hundred and forty children with severe HFMD were randomly divided into Group A (n=70) and Group B (n=70) according to the random number table method. Group A was treated with routine treatment. Group B was treated with routine treatment, and an early intravenous injection of human immunoglobulin. Serum CRP, CK, and CK-MB in Group B were lower than those in Group A after treatment (all $p < 0.001$). The total clinical effective rate of Group B was 92.9%, which was higher than that of Group A (80.0%, $p = 0.026$). Early administration of human immunoglobulin may reduce the levels of serum markers CRP, CK, and CK-MB in children with severe HFMD.

Key Words: Human immunoglobulin, Children, HFMD (Hand, foot and mouth disease).

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Hand, foot and mouth disease (HFMD) often occurs in infants and young children. HFMD is an infectious disease, and treatment should be taken early. There is no specific medicine for the treatment of severe HFMD. Antipyretic, anti-inflammatory, antiviral, nutritional support, anti-infection, and other routine treatment are used to control the development of HFMD and further improve the clinical symptoms of children, but the actual clinical effect is not ideal.

The main component of human immunoglobulin is human immunoglobulin IgG globulin, and it plays a role in immunomodulatory, anti-infection and antiviral. It has been found that early intravenous injection of human immunoglobulin can effectively control fever, oral ulcer and rash in children with HFMD.^{1,2}

Creatine phosphokinase (CK) mainly exists in skeletal muscle, cardiac muscle, placenta and brain tissue, that plays an important role in cell energy metabolism. Myokinase isoenzyme (CK-MB) is a myocardial CK isoenzyme, which mainly exists in cardiomyocytes and can be used to judge myocardial damage.

Some studies suggest that CK-MB can be used to estimate myocardial damage in children with HFMD.³ C-reactive protein (CRP) is a marker of acute inflammation.⁴ The significant increase of CRP suggests infection or tissue injury.⁵ The objective of the study was to investigate the clinical effect of early administration of human immunoglobulin in children with severe HFMD and its influence on serum markers, including CRP, CK, and CK-MB.

This study was conducted in Beijing Luhe Hospital affiliated to Capital University of Medical Sciences, China, from January 2020 to October 2021. The sample size was calculated by G*Power software. One hundred and forty severe HFMD children were enrolled in this randomised controlled trial. Inclusion criteria were children clinically diagnosed with severe HFMD type, namely mental fatigue, indifference, somnolence, vomiting, persistent high fever, extremity adynamia, increase of respiration and heart rate, poor peripheral circulation, significant increase of peripheral white blood cell count, hypertension and hyperglycemia; children who did not receive other treatment before admission; absence other cardiac, hepatic or renal complications; and age between 2-5 years. The family members of children agreed and voluntarily signed the informed consent. Exclusion criteria were paediatric patients who suffered from other serious cardiac, hepatic or renal complications, or complicated with other malignant tumours; patients complicated with septic shock, meningitis, myocarditis, and pneumonia; severe abnormal liver and kidney function; severe bacterial infection; mild HFMD children (only fever, rash, etc., without any nervous system manifestations); critical HFMD children (breathing difficulties, recurrent convulsion or coma, frothy bloody sputum, etc.); and allergy to human immunoglobulin.

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Table I: Comparison of serum markers.

Index	Group A (n=70)	Group B (n=70)	p-value
Serum CRP before treatment (mg/L)	21.15±1.55	21.40±1.38	0.320*
Serum CRP after treatment (mg/L)	5.71±0.42	4.92±0.36	<0.001*
Serum CK before treatment (U/L)	216.79±15.78	220.06±15.82	0.223*
Serum CK after treatment (U/L)	173.38±12.69	153.93±11.04	<0.001*
Serum CK-MB before treatment (U/L)	34.84±2.56	35.46±2.62	0.158*
Serum CK-MB after treatment (U/L)	20.91±1.53	18.10±1.34	<0.001*

*Independent samples t-test.

According to the random number table method, one hundred and forty severe HFMD children were randomly divided into Group A (n=70) and Group B (n=70). Group A was treated with routine treatment, including antipyretic, anti-inflammatory, antiviral, nutritional support, bedside isolation, oral and skin care, prevention of hospital cross-infection, and monitoring heart rate and blood pressure. Antibiotics were used if secondary infection occurred and cimetidine was used to stop vomiting.

Group B was treated with the above-mentioned routine treatment and early intravenous injection of human immunoglobulin with the following procedures. The children were given *via* intravenous injection with dexamethasone at 0.2 mg/kg, and if they showed mental tension, restlessness and so on, 20% mannitol was then given at 0.5 g/Kg. After the conditions were stable, 2 g human immunoglobulin was injected for 2 days.

Serum markers including CK, CK-MB and CRP were compared before and after treatment. Serum CK and CK-MB were measured by automatic biochemical analyzer. The level of CRP was measured by immunoturbidimetry.

Outcome was considered as markedly effective when the temperature returned to normal and herpes in hands, feet and oral completely disappeared after treatment; effective when the body temperature basically returned to normal and herpes in hands, feet and oral cavity basically disappeared after treatment; and ineffective, when the body temperature still elevated and herpes in hands, feet and mouth did not subside after treatment.⁶ Total clinical effective rate = (number of markedly effective cases + number of effective cases) / total number of cases × 100%. The occurrence of adverse reactions in the two groups was observed and recorded.

SPSS 25 was used for data analysis. Measurement data were expressed as mean ± SD, and independent samples t-test was used. Enumeration data were expressed as n (%) and chi-square test was used. A value of p<0.05 was considered statistically significant.

In Group A, 39 (55.7%) were males, 31 (44.3%) were females, and their mean age was 3.58±0.26 years. In Group B, 38 (54.3%) were males and 32 (45.7%) were females, and their mean age was 3.62±0.27 years.

Before treatment, serum CRP, CK and CK-MB between the two groups has no significant difference (p=0.320, 0.223, and

0.158, respectively Table I), but serum CRP, CK and CK-MB in Group B were lower than those in Group A after treatment (all p<0.001, Table I).

The 30 cases (42.9%) were markedly effective in Group A, and 26 cases (37.1%) were effective, while 14 cases (20.0%) were ineffective, and the total effective rate was 80.0% (56 cases). The 40 cases (57.1%) were markedly effective in Group B, and 25 cases (35.7%) were effective, while 5 cases (7.1%) were ineffective, and the total effective rate was 92.9% (65 cases). The total clinical effective rate of Group B was higher than that of Group A (p=0.026).

There was no obvious adverse reaction among the children in the two groups.

In the present study, early administration of human immunoglobulin may reduce serum markers CRP, CK and CK-MB levels in children with severe HFMD, and it is worth applying in the treatment of children with severe HFMD. This research conclusion was basically consistent with the result reported in previous studies.² However, there is no unified standard for the dose and course of intravenous human immunoglobulin in clinical application, and different doses and courses of intravenous human immunoglobulin are not studied in this study. The disappearance time of clinical symptoms after treatment is not observed. These are the limitation of this study, so further study is required in the future.

ETHICAL APPROVAL:

Ethical approval has been obtained from the Beijing Luhe Hospital Affiliated to the Capital University of Medical Sciences, China (No. 2020012).

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

HW: Conceptualisation and methodology and manuscript preparation.

LL: Review and editing.

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