

Analysis of effect on tanreqing injection combined with ribavirin on children with hand-foot-mouth disease complicated with pneumonia and its influence on serum inflammatory factors.

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Abstract

Objective: To investigate the efficacy of tanreqing injection combined with Ribavirin for hand-foot-mouth disease complicated with pneumonia and its influence on serum inflammatory factors.

Methods: 72 children with hand-foot-mouth disease complicated with bronchopneumonia were recruited from January 2016 to June 2017 in our hospital, and randomly divided into observation group (n=36) and control group (n=36). The control group was treated with ribavirin injection, and the observation group was treated with tanreqing injection on the basis of the control group. The time of symptoms and signs improvement, and the changes of Interleukin-2 (IL-2), Interleukin-6 (IL-6), Interleukin-10 (IL-10), C-Reactive Protein (CRP) and Tumor Necrosis Factor- α (TNF- α) were compared between the two groups.

Results: The time of pyretolysis, rash subsided, oral mucosal congestion, disappearance of cough and rales in the observation group were significantly less than those in the control group (t=9.667, 4.577, 7.526, 3.651, 5.677, all P<0.05); after treatment, the levels of IL-2, IL-6 and IL-10 in the two groups were significantly decreased (t=6.773, 6.164, 7.581, 2.781, 2.434, 3.023, all P>0.05), and the above indexes in the observation group were significantly lower than those in the control group (t=5.415, 4.616, 4.365, all P<0.05); after treatment, the levels of CRP and TNF- α in the two groups were significantly decreased (t=13.486, 40.914, 14.136, 32.922, all P<0.05), and the above indexes in the observation group were significantly lower than those in the control group (t=16.619, 23.077, all P<0.05).

Conclusion: Tanreqing injection combined with ribavirin can effectively promote the rehabilitation of hand-foot-mouth disease complicated with pneumonia, and reduce the levels of inflammatory factors in serum.

Keywords: Tanreqing injection, Ribavirin, Hand-foot-mouth disease, Pneumonia, Inflammatory factors.

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Introduction

Hand-foot-mouth disease is an acute infectious disease commonly in clinical, which mainly caused by Coxsackievirus A group 16 strain (CVA16), human enterovirus 71 (EV71), with the characteristics of fast infectious speed and complex infectious pathways, especially the highest morbidity for the preschool children under the age of five [1,2]. Virus is the major etiological agent to hand-foot-mouth disease in patients with outbreaks, epidemics, and the clinical symptoms of children with hand-foot-mouth disease mainly include fever, strongly infectious rash or herpes in the hand, feet, mouth or buttock, if they are treated well in time the kids will have the favorable prognosis. If the treatment time was delayed, the

other organs or systems of kids will be affected seriously, and it leads to the occurrence of complications such as pneumonia [3,4]. In addition, the pathogenesis of hand-foot-mouth disease patients is considered to connect with organismal inflammatory cytokines [5].

Generally, the child patients with hand-foot-mouth disease combined with pneumonia accompanying fever, cough and expectoration etc., meanwhile which accompanied with pathological alteration like bronchitis; so, these clinical symptoms aggravate the diseases and have obvious influence on mental and physiology of child patients [6-8].

The results of previous studies showed, the antiviral drugs like ribavirin that is able to inhibit the enzymic activity of a variety

of cells and prevent the replication of RNA virus were major treatment for child patients with hand-foot-mouth disease, because the efficacy of single ribavirin was not effective enough [9,10], and the child patients with hand-foot-mouth disease complicated with pneumonia existed the obvious pulmonary inflammation, how to treat it need to be further research.

Tanreqing injection is a kind of Chinese medicine made by plentiful precious medicinal materials, can inhibit the adverse bacteria and inflammatory, and tanreqing injection is widely becoming the main treatment in different diseases of respiratory system [11]. There are fewer researches to report the influence of Tanreqing combined with ribavirin on inflammatory cytokines. Based on this, our study used the Tanreqing injection combined with ribavirin to treat the child patients with hand-foot-mouth disease complicated with pneumonia to research its efficacy and analyse the effects on serum inflammatory factors, which received the satisfying efficacy.

Methods

General data

From January 2016 to June 2017, a number of 72 cases of child patients with hand-foot-mouth disease complicated with pneumonia were recruited in our hospital. Inclusion criteria: patients conformed to the relevant diagnosis criterion of "Experts consensus on rescue and treatment of serve cases with EV71 infection" [12]; patients combined with the cough, expectoration anhelation and bronchial or pulmonary inflammation, the wet and dry rales could be heard in the lung; patients were inspected to see the pulmonary marking thickening and patchy shadow by X-ray examination; the family of children were informed and signed the informed consent; this study has been approved by the Ethical Committee in our hospital Exclusion criteria: patients received the treatment of other drugs; patients are allergic to the drug composition in this study. The 72 child patients were randomly divided into the observation group and control group, each group of 36 cases, the observation group accepted the combination of Tanreqing and ribavirin, while the control group were given with ribavirin. The general materials such as gender, average age, temperature, course of disease were compared, the differences were not statistically significantly ($P>0.05$). The general data were shown in Table 1.

Table 1. General materials of two groups (n , ($\bar{x} \pm SD$)).

Groups	Number of cases	Male/female	Average age (Y)	Temperature (°C)	Course of disease (D)
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Table 2. Comparisons of the time of symptoms and signs improvement ($\bar{x} \pm SD$, d).

Groups	Number of cases	Time of pyretolysis	Time of erythra regression	Time of oral mucosa eruption	Time of disappearance of cough	Time of disappearance of rales
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Observation group	36	21/15	3.01 ± 0.82	38.50 ± 2.77	4.32 ± 1.11	±
Control group	36	19/17	3.26 ± 0.72	38.60 ± 2.47	4.21 ± 1.15	±
t/χ^2		0.225	1.375	0.162	0.413	
P		0.635	0.174	0.872	0.681	

Treatment methods

The child patients of control group accepted ribavirin injection (produced by Jiangsu Fangqiang Pharmaceutical Factory, approval No.: H20169313), with 10 mg/kg•d by intravenous drip for 7 d. Based on the control group, the observation group applied the Tanreqing injection (produced by Shanghai Kaibao Pharmaceutical CO., LTD, approval No.: Z20160054), with 0.5 ml/kg•d plus 100 ml of 5% gluconates solution by intravenous drip for 7 d.

Observational indicators

The time of symptoms and signs improvement including fever, rash, oral mucosa eruption, cough, disappearance rates of rales in two groups were observed and compared.

The fasting blood samples were collected in the child patients of two groups before treatment and at 7 d after treatment respectively, and centrifuged to isolate the serum, Interleukin-2 (IL-2), Interleukin-6 (IL-6), Interleukin-10 (IL-10), C-Reactive Protein (CRP) and Tumor Necrosis Factor- α (TNF- α) were detected by using the Enzyme-Linked Immunosorbent Assay (ELISA). ELISA kits were purchased by Shanghai Zeye Biological Technology CO., LTD.

Statistical analysis

The SPSS 19.0 software was used to analyse all the data. The measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm SD$), analysed by t-test. $P<0.05$ was considered that the difference was statistically significant.

Results

Comparison of the time of symptoms and signs improvement in two groups

The time of fever subsided, erythra regression, disappearance rates of cough, rales were less in the observation group than those in the control group, the differences were statistically significantly ($P<0.05$). The specific results were shown in Table 2.

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Observation group	36	1.46 ± 0.42	3.26 ± 1.12	3.56 ± 0.84	4.46 ± 2.12	3.54 ± 1.34
Control group	36	2.64 ± 0.60	4.75 ± 1.60	5.16 ± 0.96	6.18 ± 1.87	5.36 ± 1.38
t		9.667	4.577	7.526	3.651	5.677
P		0.000	0.003	0.000	0.001	0.000

Comparisons of different interleukin levels in two groups

Before treatment, the IL-2, IL-6, IL-10 levels in two groups showed no significantly differences (P>0.05); after treatment,

the IL-2, IL-6, IL-10 levels in two groups were decreased significantly, and the observation group was lower than the control group, the differences were statistically significant (P<0.05). The specific results were shown in Table 3.

Table 3. Comparisons of different interleukin levels in two groups ($\bar{x} \pm SD$, $\mu\text{g/L}$).

Groups	Number of cases	Time	IL-2	IL-6	IL-10
Observation group	36	Before treatment	5.34 ± 1.80	5.99 ± 2.10	7.74 ± 2.22
		After treatment	3.01 ± 1.01 ^a	3.54 ± 1.13 ^a	4.23 ± 1.67 ^a
t			6.773	6.164	7.581
P			0.000	0.000	0.000
Control group	36	Before treatment	5.59 ± 1.92	5.88 ± 1.87	7.66 ± 2.32
		After treatment	4.51 ± 1.32	4.93 ± 1.41	6.12 ± 1.99
t			2.781	2.434	3.023
P			0.027	0.017	0.003

Note: ^aCompared with the control group at same period, P<0.05.

Comparisons of other inflammatory in two groups

Before treatment, the CRP, TNF- α levels in two groups showed no statistically significant differences (P>0.05); after treatment, the CRP, TNF- α levels in two group were decreased, the observation group were lower than control group, the differences were statistically significantly (P<0.05). The specific results were shown in Table 4.

Table 4. Comparisons of other inflammatory in two groups ($\bar{x} \pm SD$).

Group	Number cases	Time	CRP (mg/L)	TNF- α (pg/ml)
Observation group	36	Before treatment	20.56 ± 8.20	345.10 ± 41.16
		After treatment	2.12 ± 0.26 ^a	55.86 ± 10.25 ^a
t			13.486	40.914
P			0.000	0.000
Control group	36	Before treatment	19.97 ± 6.19	340.58 ± 40.55
		After treatment	5.17 ± 1.07	111.26 ± 10.12
t			14.136	32.922
P			0.000	0.000

Note: ^aCompared with the control group at same period, P<0.05.

Discussion

Hand-foot-mouth disease is a common acute infectious disease in the department of pediatrics in clinic, the relevant data showed the morbidity and mortality of hand-foot-mouth disease are rising, which has already become the one of important public health issues [13]. Currently, a lot of clinical studies proved that the ribavirin could be used in the treatment of hand-foot-mouth disease, which also could inhibit the inosine 5-monophosphate dehydrogenase, prevent the inosine turning into guanylic acid, and the virus DNA, RNA replication, which have the favorable inactivation and cause less harm to body [9,14]. However, the ribavirin can effectively inhibit the virus, but the child patients with hand-foot-mouth disease have the pulmonary inflammation obviously, the drug resistance is easy to be caused by single ribavirin, therefore, to explore the effective drugs combined with ribavirin treating the child patients with hand-foot-mouth disease complicated with pneumonia has a very important clinical value.

The theory of Chinese medicine said, hand-foot-mouth disease is belong to epidemic disease in wet and warm scope, the corporeity of kids is either positive or negative to easy to be infected with epidemic virus, because the wet and hot virus can attack the body of kids from their mouth or nose, which leads

the lungs are infected due to the accumulation of the wet and hot virus, causes the cough seriously, then child patients show the lung-wei pattern (a concept of traditional Chinese medicine) [15]. Tanreqing injection, a kind of pure Chinese medical injection, is made of an amount of Chinese medical herbs, such as scutellaria, cornugorais, honeysuckles, bear gallbladder powder, fructus forsythiae etc., with the effects of removing the hepatic depression, clearing the phlegm, heat and toxic materials. In this study, the control group accepted the single ribavirin, while the observation group combined with Tanreqing injection on the basis of the control group, the results showed that the time of fever subsided, erythra regression, disappearance rates of cough, rales in the observation group were significantly less than those in the control group, it proved that Tanreqing injection combined with ribavirin can be an effective treatment for hand-foot-mouth disease complicated with pneumonia, and promote the rehabilitation of child patients, which is similar with the conclusion of Xiru et al. [16]. The IL-2, IL-6, IL-10, CRP and TNF- α are the common inflammatory clinically, IL-2 have the function of promoting the inflammatory reaction, IL-6 can play a stimulative role in adjusting the inflammatory, and the secretion of IL-10 is too high to aggravate the infection, CRP is a classical marker during the acute inflammatory reaction, TNF- α can mediate a series of inflammatory [17-19]. When hand-foot-mouth disease is developing or developed with the inflammatory, leading to the constantly increasing secretions of IL-2, IL-6, IL-10, CRP and TNF- α [20], then the child patients with pneumonia occur the changed inflammatory in their lung and capillary bronchus, which can result in rising the levels of IL-2, IL-6, IL-10, CRP and TNF- α [21,22]. The studies of Jian et al. [23] and Weizhong et al. [24] concluded that tanreqing injection have the significant effects on anti-inflammatory, also lower the levels of inflammatory factors in pneumonia patients; Li et al. [7] reported the tanreqing injection can not only inhibit the secretion of inflammatory factors, but it can also further reduce the detect of lung in patients; the report of Weijie et al. [20] indicated that tanreqing injection can lower the detect of lung in patients. This study reported that before treatment, the levels of IL-2, IL-6, IL-10, CRP and TNF- α were relatively close, after treatment the levels of IL-2, IL-6, IL-10, CRP and TNF- α of two group were all decreased, but the above indicators in the observation group were significantly lower than those of control group, which suggested that the anti-inflammatory efficacy of tanreqing injection combined with ribavirin are much better than single ribavirin. The analysis of results showed that the special ingredients like honeysuckles, bear bile powder etc. in tanreqing injection can clear the heat and toxic materials, besides, it can inhibit the bacteria and inflammatory reaction [16].

Conclusion

In conclusion, tanreqing injection combined with ribavirin injection can effectively promote the fast recovery of child patients with hand-foot-mouth disease complicated with pneumonia, in addition, it can reduce the levels of inflammatory factors, which is worthy of reference.

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