Effect of Zinc gluconate adjuvant therapy on myocardial damage, immunologic function and serum inflammatory factors in children with rotaviral enteritis

Jun Zhu*

No.2 Pediatric Department, People’s Hospital of Kaixian County, Chongqing City, 405400, China

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Rotavirus viral enteritis
Zinc gluconate
Immune function

ABSTRACT

Objective: To analyze the effects of Zinc gluconate adjuvant therapy on Rotavirus myocardial injury, immune function and serum inflammatory factors of children with viral enteritis. Methods: A total of 138 Rotavirus viral enteritis children were enrolled as research objects. According to stochastic indicator method, they were divided into control group (n=69 cases) which received clinical routine treatment, and observation group (n=69 cases) which received Zinc gluconate adjuvant therapy, myocardial enzyme spectrum; serum inflammatory cytokines and immune function of the two groups were compared. Results: (1) LDH, CK, CK-MB, cTnI myocardial enzyme indexes of the observation group were significantly lower than that of the control group (P<0.05). (2) serum zinc gluconate auxiliary CD19+CD5+CD1dhi B cells expression level of the observation group were higher than that of the control group, CD11b and CD40-CD40L stimulus molecule expression levels of the observation group were significantly lower than that of the control group (P<0.05). (3) Serum zinc gluconate auxiliary TRF1, TRF2 expression levels of the observation group were significantly higher than that of the control group but IL-12 level was lower than control group (P<0.05). Conclusion: Zinc gluconate adjuvant therapy could help to avoid the heart of the children with rotavirus virus enteritis loss, enhance immune function, reduce level of systemic inflammation.

1. Introduction

Rotaviral enteritis is the common digestive disease in infants and children, with symptoms of typical diarrhea, accompanying with electrolyte imbalance, acid-base disturbance, dehydration, and would cause death in severe case. Children with severe diarrhea present the lack of zinc, the critical element in maintaining the integrity of epithelial cells and tissues, whose lack can further result in dropping in absorption capacity of chorion cells on the intestinal epithelium, and delaying the diarrhea to be cured[1]. For children with rotaviral enteritis, timely supplement of zinc gluconate adjuvant therapy is the clinically rational method to supply zinc, by increasing the zinc intake to compensate the loss of zinc in intestine so that the damage to immunologic function and other functions in children can be reduced[2]. The present research aims to analyze the effect of zinc gluconate adjuvant therapy on myocardial damage, immunologic function and serum inflammatory factors in children with rotaviral enteritis.

2. Materials and methods

2.1. General data

A total of 138 cases of children with rotaviral enteritis in hospital for treatment from September 2012 to September 2014 were taken as experimental objects, in accordance with the diagnosis criteria of rotaviral enteritis and the exclusive criteria of severe dehydration, severe electrolyte imbalance, severe underlying disease. Based on the random number table, the children were grouped into observation group and control group, with 69 cases in each. The conventional therapy for rotaviral enteritis was conducted for
control group, including 39 male cases and 30 female cases, aged 6-32 months, with average age of (1.17 ± 0.32) yr, disease course of 0.5-4 d, and average disease course of (2.11 ± 0.43) d. Zinc gluconate adjuvant therapy was conducted to observation group, including 37 male cases and 32 female cases, aged 6-31 months, with average age of (1.15 ± 0.31) yr, disease course of 0.5-3 d and average disease course of (2.07 ± 0.45) d. The differences in gender, age, course of disease and other general data were not statistically significant (P>0.05), and therefore, were comparable.

2.2. Therapeutic methods

The conventional therapy for children with rotaviral enteritis in control group included antivirus, water compensation, maintaining electrolyte balance, nutrition support, and so forth. In observation group, on the basis of conventional therapy, the zinc gluconate adjuvant therapy was performed with oral administration of zinc gluconate tablets (Guangzhou Baiyunshan Pharmaceutical Holdings Co. LTD., State medical permission No. H10880028), 10 mg·kg⁻¹·d⁻¹, 2 times/d, and 10 d made one course of treatment.

2.3. Observation indicators

2.3.1. Myocardial enzyme spectrum

Before and after treatment, 2 mL of peripheral venous blood was taken from two groups. The lactate dehydrogenase (LDH), creatine kinase (CK) and creatine kinase MB isoenzyme (CK-MB) were determined by Hitachi 7170A Biochemistry Analyzer while the cardiac troponin I (cTn I) was determined by chemiluminescence immunoassay.

2.3.2. Immunologic function

Before and after treatment, 2 mL of peripheral venous blood was taken from two groups. The expression of CD19⁺CD5⁺CD1dhi B cell, CD11b and CD40-CD40L was determined by flow cytometry.

2.3.3. Inflammatory cytokines

Before and after treatment, 2 mL of peripheral venous blood was taken from two groups. The expression of interleukin (IL)-1, -17 and -12 and other inflammatory cytokines was determined by ELISA.

2.4. Statistical processing

All of the data were analyzed and processed by SPSS 18.0 software. The t test was carried out on measurement data while the chi-square test was on enumeration data. If P<0.05, the differences were considered to be statistically significant.

3. Results

3.1. Myocardial enzyme spectrum

The differences in levels of myocardial enzyme spectrum before treatment in two groups were not statistically significant (P>0.05). After the zinc gluconate adjuvant therapy, the levels of LDH, CK, CK-MB, cTnI and other indicators of myocardial enzyme spectrum in observation group were significantly lower than those in control group, with statistically significant differences (P<0.05). Detailed information was in Table 1.

3.2. Immunologic function

The differences in levels of immunologic function before treatment in two groups were not statistically significant (P>0.05). After the zinc gluconate adjuvant therapy, the expression level of CD19⁺CD5⁺CD1dhi B cell in serum in observation group was significantly higher than that in control group, while the expression levels of CD11b and CD40-CD40L costimulatory molecules were significantly lower than in control group, with statistically significant differences (P<0.05). Detailed information was in Table 2.

Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>LDH (U/L)</th>
<th>CK (U/L)</th>
<th>CK-MB (U/L)</th>
<th>cTn I (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>Before treatment</td>
<td>228.17 ± 58.24</td>
<td>153.29 ± 12.38</td>
<td>79.72 ± 7.29</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>105.27 ± 8.24</td>
<td>103.28 ± 8.93</td>
<td>35.29 ± 4.28</td>
</tr>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>231.09 ± 56.33</td>
<td>157.17 ± 16.02</td>
<td>78.82 ± 7.05</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>159.26 ± 13.28</td>
<td>127.63 ± 11.73</td>
<td>57.25 ± 6.05</td>
</tr>
</tbody>
</table>

Table 2.

<table>
<thead>
<tr>
<th>Groups</th>
<th>CD19⁺CD5⁺CD1dhi B</th>
<th>CD11b</th>
<th>CD40-CD40L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>Before treatment</td>
<td>5.38 ± 0.76</td>
<td>80.24 ± 7.82</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>9.28 ± 1.16</td>
<td>63.28 ± 5.92</td>
</tr>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>5.29 ± 0.83</td>
<td>81.27 ± 8.13</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>6.47 ± 0.87</td>
<td>73.17 ± 7.62</td>
</tr>
</tbody>
</table>
3.3. Inflammatory cytokines

The differences in levels of serum inflammatory cytokines before treatment in two groups were not statistically significant ($P>0.05$). After the zinc gluconate adjuvant therapy, the expression levels of serum telomeric repeat binding factors (TRF) 1 and 2 in observation group were significantly higher than those in control group, while the IL-12 expression level was significantly lower than in control group, with statistically significant differences ($P<0.05$). Detailed information was in Table 3.

4. Discussion

Rotaviral infection is the most common explanation for diarrhea in infants and children, and about 50% of children would sequentially suffer from lactose intolerance, with more susceptibility to morbidity in children at younger age[3]. The symptom of lactose intolerance mostly is diarrhea after dairy food intake. There are clinical researches on the diarrhea of this kind showing that poor therapeutic effect is found in conventional therapy only consisting of antivirus, fluid infusion, nutrition maintenance and so forth, and meanwhile the conventional therapy would delay the condition and eventually affect the growth and development of children. World Health Organization considers it very necessary to provide timely supplement of zinc when obstacles of digestion as well as absorption, and reducing absorption of zinc in vivo occur in children with acute diarrhea; zinc, the key component of many enzymes, is involved in the synthesis of DNA, RNA and proteins, so when the concentration of zinc in blood drops, the immunity of organism is sequentially declined and the ability of anti-infection becomes worse[4,5]. It is efficient to prevent the excessive loss of zinc by providing supplement of zinc gluconate to children with rotaviral enteritis, acknowledged by many experts to be a method to enhance the effect of conventional therapy like antivirus and others.

Research of Al-Shibli et al. showed that the CK-MB level was extremely elevated in serum of over 50% children infected with rotavirus and that several children even suddenly died of paroxysmal myocarditis, from which it can be seen that the rotaviral enteritis may do damage to myocardium of children[6]. At present, it is still unclear about the mechanism of myocardial damage caused by rotavirus infection which may be relevant to viremia, hemoconcentration as well as circulatory disturbance at the acute phase of disease, and other factors[7]. LDH is a kind of glycolytic enzyme in the cytoplasm of all the tissue cells of organism, among which heart and kidney have the higher contents, and can catalyze lactate dehydrogenase to produce pyruvic acid. The LDH level in serum would be significantly elevated when acute myocardial infarction occurs, thus, the LDH can be used for the early diagnosis of myocardial damage. CK is of significance in clinical diagnosis. When amyotrophy and myocardial infarction occur, the CK level in serum is significantly elevated. At present, the CK level determination is considered more reliable than electrocardiogram. CK level can be elevated in the 6 h and reach the peak at 24 h when myocardial infarction occurs. CK-MB, a kind of myocardial specific enzyme, almost exists only in endochylema of myocardial cells and carries more value in diagnosis of myocardial damage in myocardial enzyme spectrum compared with other indicators[8]. CTn I is myocardial specific antigen, whose level in serum is extremely low. It can be released into blood at the early stage of myocardial damage and the folds it increase generally exceed CK and CK-MB; CTn I is the serum maker with high sensitivity. With unique amino acid sequence, CTn I will not exceed the threshold level when lesion or damage occurs in tissue except for myocardium, thus, it possess high specificity[9]. The above research showed that in observation group after the zinc gluconate adjuvant therapy, the levels of indicators in myocardial enzyme spectrum, like LDH, CK, CK-MB, CTn I and others, were significantly lower than those in control group, implying that the zinc gluconate adjuvant therapy can reduce the myocardial damage in children with rotaviral enteritis so that the myocardium can be protected.

Regulatory B cell is the cell with negative immunologic function characterized by secreting IL-10, gets involved in kinds of autoimmune disease and promotes the tumor metastasis. At the present, in the case of rheumatoid arthritis, it is known that the elimination of B cell in rat model would worsen the condition and reduce the tendency of self-healing[10]. Generally, the B cell is expressed by CD19+CD5+CD1dhi. Turner, et al. found in rat model with enteritis that the proportion of CD19+CD5+CD1dhi increased at the acute phase of inflammation, and decreased in the case of inflammation resolution, implying that it and inflammatory immune cells may mutually restrain each other[11]. CD11b mainly existing in macrophages, monocytes and natural killer cells, is a member of adhesion molecule B2 integrin, whose increasing expression is considered the symbol of activation of neutrophile granulocyte. CD40, belonging to transmembrane glycoprotein, is a member of tumor necrosis factor receptor, and plays an important role in cell survival and death.

Table 3.
Comparison of expression levels of inflammatory cytokines before and after treatment ($\mu$g/L, Mean±SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>TRF1</th>
<th>TRF2</th>
<th>IL-12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>Before treatment</td>
<td>2.28 ± 0.46</td>
<td>2.74 ± 0.52</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>4.95 ± 0.78</td>
<td>3.57 ± 0.45</td>
</tr>
<tr>
<td>Control group</td>
<td>Before treatment</td>
<td>2.16 ± 0.41</td>
<td>2.15 ± 0.76</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>2.77 ± 0.53</td>
<td>2.63 ± 0.41</td>
</tr>
</tbody>
</table>
role in proliferation and differentiation of B cell[12]. CD40 and its
alexin CG40L are a stimulus signaling pathway, whose interaction
can promote the best activation and proliferation of T cell and
monocytes. Once the signal is blocked, the activation effect of
antigen presenting cell on T cell would be decreased, and the
secretion of cytokines like IL-1, IFN-γ, etc. would be decreased.
The results of above research showed that the expression level of
CD19+CD5+CD16hi B cell in serum of children in observation
group after zinc gluconate adjuvant therapy was higher than that in
control group, while expression level of CD11b and CD40-CD-40
L costimulatory molecules was significantly lower than in control
group, implying that zinc gluconate adjuvant therapy is of help
in promoting the immunologic function of children with rotaviral
enteritis.

TRF1 and TRF2 belong to telomerase binding protein and are
the new method to regulate telomerase found in recent years.
TRF1 and TRF2 are negative regulatory factors of telomerase.
The overexpression of TRF1 can mediate cells with short telomere into
mitosis and induce apoptosis; TRF2 is involved in maintenance of
integrated morphology and structure of telomere and protecting
normal function of telomere. It belongs to the negative regulator
of telomere length and is not dependent on activity of telomere.
Researches showed that in the patients with inflammatory enteritis,
the expression levels of TRF1 and TRF2 in peripheral blood had
an average reduction from which the regulatory effect of them on
morbidity of enteritis can be seen[13]. Interleukin is a set of immune
activation factor produced by monocytes. IL-12 is proinflammatory
factor, with functions of promoting immunoreactions, reducing the
further production of cytokines, activating the cascade reaction,
combining the adherence factors of vascular endothelial cells in
rotavirus infected children, making the inflammatory cells aggregate
and infiltrate, and producing the inflammatory response[14,15]. The
above research showed that TRF1 and TRF2 expression levels in
serum in observation group after zinc gluconate adjuvant therapy
were higher than in control group, while IL-12 expression level
was on average lower than that in control group, implying that zinc
gluconate adjuvant therapy can inhibit the intestinal and systemic
inflammatory response.

In conclusion, zinc gluconate adjuvant therapy is of help in
avoiding the heart damage in children with rotaviral enteritis,
elevating the immunologic function and reducing the systemic
inflammation, and thus, is worth popularization and application in
the future clinical practice.

Reference

[1] Wu ZC, Li JA, Yan NR, Song LA. Value of cardiac troponin I in diagnosis
of myocardial damage in children with rotaviral enteritis. Chongqing Med

C, et al. Alterations in oxidant/antioxidant balance, high-mobility group
box 1 protein and acute phase response in cross-bred suckling piglets
suffering from rotaviral enteritis. Trop Anim Health Prod 2014; 46(7):
1127-33.

with rotavirus A enteritis. Maternal Child Health Care China 2011;
26(33): 5188-90.

[4] Gu YD, Chen ZH, Huang Y, Zhao YM. Effect of lactose-free diet and
oral administration of zinc gluconate on infants with rotaviral enteritis.

hospital-based surveillance of rotavirus gastroenteritis in children < 5


between febrile and afebrile seizures associated with mild rotavirus

detection of serum and CSF interleukin in children with rotavirus enteritis

combination use in treating children non-infectious diarrhea and its
influence on serum IL-6, IL-17 expression. Changming Med 2013; 42(15):
1703-5.

Surveillance of rotavirus gastro-enteritis in children in Blantyre, Malawi.

KK, et al. Reduction in rotavirus-associated acute gastroenteritis
following introduction of rotavirus vaccine into Australia’s National
Childhood vaccine schedule. Pediatr Infect Dis J 2011; 30(1 Suppl):
S25-9.

[13] Su HP, Qian SH, Zhang L. Effects of lactose-free milk in adjunctive
treatment of infants with rotaviral enteritis and lactose intolerance: an

C, et al. Alterations in oxidant/antioxidant balance, high-mobility group
box 1 protein and acute phase response in cross-bred suckling piglets
suffering from rotaviral enteritis. Trop Anim Health Prod 2014; 46(7):
1127-33.

[15] Bu YQ, Dong SY. Changes and significance of IL-1β, IL-6, IL-12, and
859-61.