Effect of glutamine enteral nutrition + low molecular weight heparin on systemic inflammatory response in patients with severe pneumonia

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Objective: To investigate the effect of glutamine enteral nutrition + low molecular weight heparin on systemic inflammatory response in patients with severe pneumonia.

Methods: A total of 52 patients with severe pneumonia who were hospitalized in this hospital between January 2017 and October 2017 were divided into glutamine group (n=26) and control group (n=26) by random number table method. Control group received conventional enteral nutrition + low molecular weight heparin treatment, glutamine group were treated with glutamine nutrient solution on the basis of the therapy for control group, and both therapies lasted for 7 d. The differences in serum levels of inflammatory factors, oxidative stress indexes and myocardial injury indexes were compared between the two groups before and after treatment.

Results: Before treatment, serum levels of inflammatory factors, oxidative stress indexes and myocardial injury indexes were not significantly different between the two groups. After 7 d of treatment, serum inflammatory factors IL-10 and IL-18 levels of glutamine group were higher than those of control group whereas IL-17, sTREM-1 and PCT levels were lower than those of control group; serum oxidative stress indexes MDA and LHP levels were lower than those of control group whereas GSH-Px and CAT levels were higher than those of control group; serum myocardial injury indexes α-HBDH, cTn I, NT-ProBNP and LDH levels were lower than those of control group.

Conclusion: glutamine enteral nutrition + low molecular weight heparin can effectively relieve systemic inflammatory response and oxidative stress response, and reduce the myocardial injury in patients with severe pneumonia.

1. Introduction

Severe pneumonia is the serious stage after pneumonia progresses, systemic inflammatory response syndrome is the core mechanism of its occurrence and development, and along with the disease progression, it can damage multiple viscera function and even lead to multiple organ dysfunction syndrome (MODS) and death[1-2]. Patients with severe pneumonia suffer from malnutrition due to various factors such as nutrient consumption and gastrointestinal function injury. Severe cases can directly inhibit the immune function and accelerate the disease progress. Enteral nutrition can significantly reduce intestinal permeability and stabilize intestinal mucosal structure, so it is recommended by many scholars to be early used in patients with severe pneumonia. Glutamine is one of the non-essential amino acids in the body, the body’s demand for glutamine increases under disease or malnutrition state, but the autosynthesis can't meet the needs completely, so adding exogenous glutamine is very necessary[3,4]. In this study, glutamine enteral nutrition + low molecular weight heparin intervention was used in patients with severe pneumonia, and the effect of this intervention method on the degree of systemic inflammatory response was discussed.

2. General information and research methods

2.1 Inclusion criteria

(1) Clinically diagnosed with severe pneumonia; (2) without history of severe pneumonia within 1 year before admission; (3) diagnosed for the first time, and receiving no other independent treatment out of hospital; (4) 18-80 years old; (5) whose families signed the informed consent.
2.2 Exclusion criteria

(1) Combined with chronic obstructive pulmonary disease, asthma and other basic respiratory diseases; (2) combined with basic severe cardiac, hepatic and renal insufficiency; (3) combined with basic severe malnutrition or gastrointestinal dysfunction; (4) with long-term use of low molecular heparin.

2.3 Case information

A total of 52 patients with severe pneumonia who were hospitalized in this hospital between January 2017 and October 2017 were selected as the research subjects and divided into glutamine group (n=26) and control group (n=26) by random number table method. There were 15 males and 11 females in the glutamine group, and they were 45-78 years old; there were 14 males and 12 females in the control group, and they were 47-77 years old. The differences in the above gender and age distribution were not significant between the two groups, and the study plan was also discussed and approved by the hospital ethics committee.

2.4 Therapy

Both groups received clinical routine therapies for severe pneumonia, including anti-infection, correcting water electrolyte disturbance and acid-base imbalance, mechanical auxiliary ventilation when necessary, etc. Control patients were also given regular enteral nutrition + low molecular heparin therapy, which was as follows: 1d after admission, nasointestinal tube was indwelled in 30 cm below Treits ligament via endoscopy under X-ray perspective, enteral nutrition was Nutrison Fibre, enteral nutrition pump was used to first provide 250 mL of isotonic glucose solution and 400 mL/d of Nutrison Fibre, infusion dose was 20 mL/h, and the dose was gradually increased according to the patients’ condition. They also received subcutaneous injection of low molecular weight heparin injection 4 KU/kg, 1 time/d for continuous 7 d of treatment.

Glutamine group were given glutamine nutrient solution on the basis of the therapy for control group, which was as follows: glutamine nutrient solution was injected via nasointestinal tube, and 10 g was added into the 100 mL of warm water each time, which was evenly injected, 3 times/d for 7 d in a row.

2.5 Observation indexes

Immediately after admission and after 7 d of treatment, cubital venous blood samples were obtained from two groups of patients respectively, and the serum was isolated and cryopreserved for test. Elisa kit was used to determine the contents of inflammatory factors and oxidative stress indexes in serum specimens, inflammatory factors included interleukin-10 (IL-10), interleukin-17 (IL-17), interleukin-18 (IL-18), human soluble triggering receptor expressed on myeloid cells-1 (sTREM-1) and procalcitonin (PCT); oxidative stress indexes included malondialdehyde (MDA), lipid hydroperoxide (LHP), glutathione peroxidase (GSH-Px) and catalase (CAT). Ria kit was adopted to determine the serum contents of myocardial injury indexes, including -hydroxybutyrate dehydrogenase (α-HBDH), troponin I (cTn I), N-terminal pro-B-type natriuretic peptide (NT-ProBNP) and lactic dehydrogenase (LDH).

2.6 Statistical methods

Inflammatory factors, oxidative stress indexes and myocardial injury indexes were all expressed as mean ± standard deviation and input in software SPSS 23.0 to calculate the statistic P. P<0.05 was set as the standard of statistical significance in the differences in the study.

3. Results

3.1 Inflammatory factors

Comparison of serum inflammatory factors IL-10 (pg/mL), IL-17 (pg/mL), IL-18 (pg/mL), sTREM-1 (pg/mL) and PCT (ng/mL) levels between the two groups was as follows: before treatment, serum IL-10, IL-17, IL-18, sTREM-1 and PCT levels were not significantly different between the two groups (P>0.05); after 7 d of treatment, serum IL-10 and IL-18 levels of both groups were higher than those before treatment whereas IL-17, sTREM-1 and PCT levels were lower than those before treatment (P<0.05). After 7 d of treatment, serum IL-10 and IL-18 levels of glutamine group were higher than those of control group whereas IL-17, sTREM-1 and PCT levels were lower than those of control group (P<0.05), shown in Table 1.

Table 1.
Comparison of serum inflammatory factor levels before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>IL-10</th>
<th>IL-17</th>
<th>IL-18</th>
<th>sTREM-1</th>
<th>PCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>26</td>
<td>Before treatment</td>
<td>11.04±1.76</td>
<td>30.49±3.71</td>
<td>14.28±1.69</td>
<td>69.37±8.12</td>
<td>8.29±0.91</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After 7 d of treatment</td>
<td>15.23±1.77*</td>
<td>18.64±2.09*</td>
<td>17.94±2.11*</td>
<td>45.28±5.95*</td>
<td>5.11±0.55*</td>
</tr>
<tr>
<td>Glutamine group</td>
<td>26</td>
<td>Before treatment</td>
<td>11.08±1.69</td>
<td>30.56±3.48</td>
<td>14.23±1.62</td>
<td>69.23±7.96</td>
<td>8.34±0.89</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After 7 d of treatment</td>
<td>21.06±2.58*</td>
<td>11.37±1.65*</td>
<td>22.18±2.69*</td>
<td>27.64±3.18*</td>
<td>2.76±0.31*</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, *P<0.05; compared with control group after 7d of treatment, #P<0.05.
Table 3.
Comparison of serum myocardial injury indexes before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>α-HBDH (IU/L)</th>
<th>cTnⅠ (μg/L)</th>
<th>NT-ProBNP (pg/mL)</th>
<th>LDH (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>26</td>
<td>Before treatment</td>
<td>30.28±3.71</td>
<td>19.41±2.07</td>
<td>45.82±5.19</td>
<td>11.6±1.83</td>
</tr>
<tr>
<td>Glutamine group</td>
<td>26</td>
<td>Before treatment</td>
<td>30.46±3.68</td>
<td>19.53±2.11</td>
<td>45.76±5.03</td>
<td>11.7±1.77</td>
</tr>
<tr>
<td>Glutamine group</td>
<td>26</td>
<td>After 7 d of treatment</td>
<td>13.28±1.19</td>
<td>6.59±0.72</td>
<td>21.08±2.54</td>
<td>4.18±0.43</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, *P<0.05; compared with control group after 7d of treatment, #P<0.05.

Table 3.
Comparison of serum myocardial injury indexes before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>α-HBDH (IU/L)</th>
<th>cTnⅠ (μg/L)</th>
<th>NT-ProBNP (pg/mL)</th>
<th>LDH (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>26</td>
<td>Before treatment</td>
<td>10.29±1.75</td>
<td>7.39±0.81</td>
<td>24.37±2.66</td>
<td>16.1±1.75</td>
</tr>
<tr>
<td>Glutamine group</td>
<td>26</td>
<td>Before treatment</td>
<td>10.34±1.68</td>
<td>7.41±0.75</td>
<td>24.28±2.94</td>
<td>16.23±1.78</td>
</tr>
<tr>
<td>Glutamine group</td>
<td>26</td>
<td>After 7 d of treatment</td>
<td>4.18±0.49</td>
<td>2.14±0.23</td>
<td>40.88±4.75</td>
<td>30.93±3.45</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, *P<0.05; compared with control group after 7 d of treatment, #P<0.05.

3.2 Oxidative stress indexes

Comparison of serum oxidative stress indexes MDA (nmol/L), LHP (umol/L), GSH-Px (g/L) and CAT (U/mL) levels between the two groups was as follows: before treatment, serum MDA, LHP, GSH-Px and CAT levels were not significantly different between the two groups (P>0.05); after 7 d of treatment, serum MDA and LHP levels of both groups were lower than those before treatment whereas GSH-Px and CAT levels were higher than those before treatment (P<0.05). After 7 d of treatment, serum MDA and LHP levels of glutamine group were lower than those of control group whereas GSH-Px and CAT levels were higher than those of control group (P<0.05), shown in Table 2.

3.3 Myocardial injury indexes

Comparison of serum myocardial injury indexes α-HBDH (IU/L), cTnⅠ (μg/L), NT-ProBNP (pg/mL) and LDH (IU/L) levels between the two groups was as follows: before treatment, serum α-HBDH, cTnⅠ, NT-ProBNP and LDH levels were not significantly different between the two groups (P>0.05); after 7 d of treatment, serum α-HBDH, cTnⅠ, NT-ProBNP and LDH levels of both groups were lower than those before treatment (P<0.05). After 7 d of treatment, serum α-HBDH, cTnⅠ, NT-ProBNP and LDH levels of glutamine group were lower than those of control group (P<0.05), shown in Table 3.

4. Discussion

Severe pneumonia is serious and progresses rapidly, and the mass nutrition consumption further suppresses immune function, causes aggravation of inflammation and even endangers life. Enteral nutrition is a highly recommended way of nutrition intervention for severe patients, which can help to restore gastrointestinal function and inhibit the reproduction of intestinal pathogens. Glutamine is the energy supply substance of intestinal mucosal epithelial cells and immune cells, its consumption is greatly increased after the body is stressed, and the deficiency of glutamine can cause immune compromise[5,6]. In this research, enteral nutrition pathway was adopted to exogenously supplement the glutamine necessary for human, and the effect of the intervention way on patients' condition was explored to provide clinical practical reference for the clinical application of glutamine.

Pathogen infection in lungs causes mononuclear macrophages to massively secrete inflammatory factors into the blood via pulmonary vessels, there will be systemic inflammatory response syndrome in the body if pathogen virulence is strong and infection persists, and more inflammatory mediators are produced and damage the important tissue organs[7,8]. IL-17 is the most typical inflammatory factor, which has powerful pro-inflammatory effect, and can promote the aggregation of neutrophils and increase the expression of IL1-β and TNF-α [9,10]. IL-10 is an anti-inflammatory factor that can inhibit the secretion of pro-inflammatory mediators and reduce systemic inflammation[11]. IL-18 is a class of cytokine with immunosuppressive activity discovered in recent years, which can inhibit macrophage and mononuclear cell function, thereby inhibit Th1/Th2 cell generation and limit the spread of inflammatory response[12,13]. sTREM-1 is also a sensitive inflammatory factor that reflects the severity of patients with pneumonia, and the plasma sTREM-1 significantly increases in patients with pneumonia. PCT is a sensitive indicator for the identification of viral and bacterial infection as well as mild infection and severe infection. The study resultsconfirmed that the serum PCT content of patients with severe pneumonia was significantly higher than that of non-death group[14,15]. The study results show that serum IL-10 and IL-18 levels of glutamine group were higher whereas IL-17, sTREM-1 and PCT levels were lower after treatment, which shows that enteral nutrition glutamine can effectively suppress the inflammatory response.

Systemic inflammatory response can lead to the increase of ROS synthesis and the occurrence of oxidative stress response, and the mass synthesis of oxidative metabolites and the weakening of antioxidant capacity are important internal causes of MODS. MDA is a metabolite of peroxidation reaction, and its content can indirectly reflect the ROS content in the body[16,17]. LHP is a substance with strong oxidizing effect, which can massively consume antioxidant substances and aggravate the oxidation/anti-oxidation imbalance[18]. Both GSH-Px and CAT are antioxidants in the body, and their consumption further suppresses immune function, thereby inhibit macrophage and mononuclear cell function, thereby inhibit Th1/Th2 cell generation and limit the spread of inflammatory response[12,13]. sTREM-1 is also a sensitive inflammatory factor that reflects the severity of patients with pneumonia, and the plasma sTREM-1 significantly increases in patients with pneumonia. PCT is a sensitive indicator for the identification of viral and bacterial infection as well as mild infection and severe infection. The study results confirmed that the serum PCT content of patients with severe pneumonia was significantly higher than that of non-death group[14,15]. The study results show that serum IL-10 and IL-18 levels of glutamine group were higher whereas IL-17, sTREM-1 and PCT levels were lower after treatment, which shows that enteral nutrition glutamine can effectively suppress the inflammatory response.

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contents are negatively correlated with the overall oxidative stress response[19]. The study results showed that serum MDA and LHP levels of glutamine group were lower whereas GSH-Px and CAT levels were higher after treatment, it shows that glutamine enteral nutrition can effectively reduce the oxidative stress response in the body, and this is also the convincing proof of it to hinder systemic inflammation progression and exert active therapeutic action.

Severe pneumonia is most likely to involve the myocardium and cause cardiac dysfunction, and may even lead to death. Myocardial cells contain a variety of enzymes, their contents in the circulating blood are little under physical condition, and they massively enter into the peripheral blood and are detected after the cell membrane damage, so the unusually highly expressed myocardial enzymes in serum are the specific markers of myocardial injury in the body. α-HBDH is an early indicator of myocardial injury, which can reflect LDH activity; cTnⅠ is the recognized gold standard to reflect the degree of myocardial injury, and its serum level has risen sharply in patients with cardiac function deterioration and heart failure[20]; NT-ProBNP can reflect BNP content, BNP is secreted and secreted by ventricular myocytes, and its secretion increases when myocardium is ischemic and ventricular load increases[21,22]. The study results showed that serum α-HBDH, cTnⅠ, NT-ProBNP and LDH levels of glutamine group after treatment were lower than those of control group, it confirms that glutamine enteral nutrition can effectively reduce the degree of myocardial injury in patients with severe pneumonia and exert positive cardioprotective effect, and this is also the inevitable result after it inhibits systemic inflammatory response process.

To sum up, it is concluded that glutamine enteral nutrition + low molecular heparin therapy can effectively suppress the systemic inflammatory response process and help to optimize the condition of patients with severe pneumonia, and it is worthy of popularization and application in clinical practice in the future.

References

[15] Bakos Z, Chatterjee NC, Reitan C, Singh JP, Borgquist R. Prediction of control group, it confirms that glutamine enteral nutrition can