Effect of early warning and evidence-based intervention combined with drug therapy on the infection process in children with mycoplasma pneumonia

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Objective: To study the effect of early warning and evidence-based intervention combined with drug therapy on the infection process in children with mycoplasma pneumonia. Methods: Children who were treated and clearly diagnosed with mycoplasma pneumonia in Zigong Third People’s Hospital between May 2014 and October 2017 were chosen and randomly divided into two groups, experimental group accepted early warning and evidence-based intervention combined with drug therapy, and control group accepted routine drug therapy. The levels of inflammatory cytokines and oxidative stress response indicators in serum as well as the expression of inflammation and oxidative stress signal molecules in peripheral blood were measured before treatment and 3 d after treatment. Results: Compared with those of same group before treatment, serum TNF-α, CysLTs, sTREM1, sP-selectin, sICAM1, MDA, SF and COR levels as well as peripheral blood TLR4, NF-κB, COX2, NOX4, MPO and iNOS expression intensity of both groups of patients significantly decreased whereas SOD and IgA levels significantly increased after treatment. Moreover, serum TNF-α, CysLTs, sTREM1, sP-selectin, sICAM1, MDA, SF and COR levels as well as peripheral blood TLR4, NF-κB, COX2, NOX4, MPO and iNOS expression intensity of experimental group were lower than those of control group whereas SOD and IgA levels were higher than those of control group. Conclusion: Early warning and evidence-based intervention combined with drug therapy can reduce the inflammatory response and oxidative stress response in the infection process of children with mycoplasma pneumonia.

1. Introduction

Mycoplasma pneumonia is a common clinical community-acquired pneumonia in children. Mycoplasma pneumoniae is the pathogen of the disease and mainly causes the excessive activation of inflammatory response in the pulmonary interstitium and capillaries. Severe cases can cause the activation of systemic inflammatory response and be accompanied by mass generation of oxygen free radicals and oxidative stress damage of various organs, which will increase the risk of severe pneumonia and multiple organ dysfunction[1,2]. Early warning intervention and evidence-based intervention are the medical intervention means developed in recent years, the former is to avoid the error in the process of treatment through the early warning mechanism, and the latter is to adjust the treatment plan through related research reports. Studies have reported that early warning combined with evidence-based intervention during the treatment of children with mycoplasma pneumonia can shorten the duration of the course of disease[3], but its effect on inflammation and oxidative stress in the course of the disease has not yet been reported. In the following study, in order to define the application value of early warning and evidence-based intervention for mycoplasma pneumonia, we analyzed the effect of early warning and evidence-based intervention combined with drug therapy on the inflammation and oxidative stress during infection process in children with mycoplasma pneumonia.
2. Case information and research methods

2.1 General case information

Children who were treated and clearly diagnosed with mycoplasma pneumonia in Zigong Third People’s Hospital between May 2014 and October 2017 were selected as the research subjects. All children were diagnosed with pneumonia by clinical symptoms and signs as well as imageological examination, and they were detected positive in serum mycoplasma nucleic acids test. Besides, they were in acute phase on admission and with the disease course of less than 3 d. Children with septic shock, bronchial asthma or allergic rhinitis and those who were unable to complete early warning and evidence-based intervention were excluded. A total of 96 cases were included and divided into two groups by random number table method, each with 48 cases. There were 28 males and 20 females in the experimental group, who were 3-9 years old, and the disease course was (39.6±6.2) h; there were 27 males and 21 females in the control group, who were 3-10 years old, and the disease course was (39.1±6.4) h. There was no significant difference in the general data between the two groups (P>0.05).

2.2 Intervention and treatment

Both groups of children were given azithromycin for anti-infection and aerosol inhalation of ambroxol hydrochloride + budesonide suspension for phlegm reduction and anti-inflammation. Experimental group received early warning combined with evidence-based intervention on the basis of routine therapy, which was as follows: the nursing plan was formulated correspondingly according to the patient’s specific situation and the possible problems predicted from theoretical knowledge and clinical experience during treatment; during the treatment, according to the nursing plan, the changes of the disease were closely monitored, and the symptoms such as fever, stridor, increased heart rate and lower blood pressure should be reported to the doctors and treated in time; the ward was sterilized strictly, and the children were quarantined to avoid cross infection.

2.3 Laboratory detection

Before treatment and 3 d after treatment, 3-5 mL of cubital venous blood was collected for laboratory detection. The Elisa kit manual was referred to detect TNF-α, CysLTs, sTREM1, sP-selectin, sICAM1, COR and IgA contents, and the radioimmunoprecipitation kit instructions were followed to determine the contents of MDA, SF and SOD; part of the venous blood was taken and anti-coagulated by EDTA to incubate the fluorescent antibody of TLR4, NF-κ B, COX2, NOX4, MPO and INOS, and their expression intensity was determined on flow cytometer.

2.4 Statistical analysis

Software SPSS 22.0 was used to input data. The differences in measurement data between two groups were analyzed by t test and P<0.05 meant statistical significance in the differences.

3. Results

3.1 Serum inflammatory cytokine levels

Before treatment and 3 d after treatment, analysis of serum inflammatory cytokines TNF-α (pg/mL), CysLTs (ng/mL), sTREM1 (ng/mL), sP-selectin (ng/mL) and sICAM1 (ng/mL) between the two groups of children was as follows: serum TNF-α, CysLTs, sTREM1, sP-selectin and sICAM1 levels were significantly different between before and after treatment within the two groups of children (P<0.05); they were not significantly different between groups before treatment (P>0.05), while there were significantly differences in these levels between groups after treatment (P<0.05); serum TNF-α, CysLTs, sTREM1, sP-selectin and sICAM1 levels of experimental group were lower than those of control group.

3.2 Serum oxidative stress indicator levels

Before treatment and 3 d after treatment, analysis of serum oxidative stress indicators MDA (nmol/mL), SF (ng/mL), SOD (U/L), COR (ng/mL) and IgA (g/L) between the two groups of children was as follows: serum MDA, SF, SOD, COR and IgA levels were significantly different between before and after treatment within the two groups of children (P<0.05); they were not significantly different between groups before treatment (P>0.05), while there were significantly differences in these levels between groups after treatment (P<0.05); serum MDA, SF, SOD, COR and IgA levels were significantly different between before and after treatment within the

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>TNF-α (pg/mL)</th>
<th>CysLTs (ng/mL)</th>
<th>sTREM1 (ng/mL)</th>
<th>sP-selectin (ng/mL)</th>
<th>sICAM1 (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental</td>
<td>48</td>
<td>Before treatment</td>
<td>98.5±11.6</td>
<td>1.29±0.18</td>
<td>63.7±7.9</td>
<td>93.5±11.3</td>
<td>341.8±42.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>41.6±6.2</td>
<td>0.72±0.09</td>
<td>30.2±4.4</td>
<td>41.3±4.9</td>
<td>184.5±22.3</td>
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<td>Control group</td>
<td>48</td>
<td>Before treatment</td>
<td>99.3±10.8</td>
<td>1.32±0.16</td>
<td>64.3±7.6</td>
<td>94.7±10.8</td>
<td>343.1±48.5</td>
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<td></td>
<td>After treatment</td>
<td>59.6±7.2</td>
<td>1.04±0.16</td>
<td>45.2±6.2</td>
<td>62.3±8.7</td>
<td>255.4±31.3</td>
</tr>
</tbody>
</table>

*: comparison between before and after treatment within group, P<0.05; #: comparison between groups after treatment, P<0.05.
Changes of peripheral blood inflammation and oxidative stress signal molecules before and after treatment.

Table 3.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>MDA</th>
<th>SF</th>
<th>SOD</th>
<th>COR</th>
<th>IgA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental group</td>
<td>48</td>
<td>Before treatment</td>
<td>13.5±1.7</td>
<td>186.2±22.3</td>
<td>58.4±7.7</td>
<td>231.2±28.7</td>
<td>0.68±0.07</td>
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<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>6.7±0.9*</td>
<td>89.5±11.4*</td>
<td>93.4±11.4*</td>
<td>180.2±22.3*</td>
<td>1.22±0.16*</td>
</tr>
<tr>
<td>Control group</td>
<td>48</td>
<td>Before treatment</td>
<td>14.1±1.5</td>
<td>188.1±20.9</td>
<td>57.8±7.2</td>
<td>233.1±26.8</td>
<td>0.70±0.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>9.8±1.1*</td>
<td>132.5±16.7*</td>
<td>70.3±8.8*</td>
<td>203.6±27.5*</td>
<td>0.93±0.12*</td>
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</tbody>
</table>

*: comparison between before and after treatment within group, \( P<0.05 \); #: comparison between groups after treatment, \( P<0.05 \).

Changes of serum oxidative stress indicators before and after treatment.

Table 2.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>MDA</th>
<th>SF</th>
<th>SOD</th>
<th>COR</th>
<th>IgA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>48</td>
<td>Before</td>
<td>203.6±27.5</td>
<td>13.5±1.7</td>
<td>186.2±22.3</td>
<td>58.4±7.7</td>
<td>231.2±28.7</td>
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<tr>
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<td></td>
<td>treatment</td>
<td>1.03±0.15</td>
<td>1.04±0.17</td>
<td>1.02±0.13</td>
<td>1.04±0.16</td>
<td>0.99±0.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>0.59±0.07*</td>
<td>0.77±0.09*</td>
<td>0.62±0.09*</td>
<td>0.74±0.08*</td>
<td>0.63±0.08*</td>
</tr>
</tbody>
</table>

*: comparison between before and after treatment within group, \( P<0.05 \); #: comparison between groups after treatment, \( P<0.05 \).

Two groups of children (\( P<0.05 \)). These levels were not significantly different between groups before treatment (\( P>0.05 \)), while significantly different after treatment (\( P<0.05 \)). Serum MDA, SF and COR levels of experimental group were lower than those of control group whereas SOD and IgA levels were higher than those of control group.

3.3 Peripheral blood inflammation and oxidative stress signal molecule expression

Before treatment and 3 d after treatment, analysis of peripheral blood inflammation and oxidative stress signal molecules TLR4, NF-κB, COX2, NOX4, MPO and iNOS between the two groups of children was as follows: peripheral blood TLR4, NF-κ B, COX2, NOX4, MPO and iNOS expression intensity were significantly different between before and after treatment within the two groups of children (\( P<0.05 \)); they were not significantly different between groups before treatment (\( P>0.05 \)), while significantly different after treatment (\( P<0.05 \)); peripheral blood TLR4, NF-κ B, COX2, NOX4, MPO and iNOS expression intensity of experimental group were lower than those of control group.

4. Discussion

Warning combined with evidence-based intervention is the clinical intervention means increasingly used in recent years and has been confirmed to be able to shorten the disease course of children with mycoplasma pneumonia[3], but there is no report about its effect on inflammation, oxidative stress and other pathological links in the course of disease. Inflammatory response activation is the most basic pathologic change in mycoplasma pneumonia, and many inflammatory cytokines show excessive secretion. TNF-α is a cytokine secreted by mononuclear macrophages in the early stage of inflammatory response, which can directly cause airway epithelial injury, and also cause inflammation cascade amplification[4]; CysLTs are a group of arachidonic acid metabolites with strong pro-inflammatory activity, including CysLT-C3, CysLT-D4, CysLT-E4 and so on, and can cause mass neutrophil infiltration in the alveoli and activate inflammatory response; sTREM1 is the soluble form of immunoglobulin superfamily TREM1, which triggers and activates inflammatory response[5]; sP-selectin and sICAM1 are two kinds of soluble adhesion molecules that can mediate the adhesion of inflammatory cells with vascular endothelial cells, airway epithelial cells and so on to promote the inflammatory cell infiltration in the pulmonary interstitium and participate in the amplification and activation of the inflammatory response[6]. In the study, analysis of the change of above inflammatory cytokines before and after treatment showed that serum TNF-α, CysLTs, sTREM1, sP-selectin and sICAM1 levels of both groups decreased after treatment, and serum TNF-α, CysLTs, sTREM1, sP-selectin and sICAM1 levels of experimental group were lower than those of control group. This means that the conventional drug treatment can reduce the secretion of a variety of inflammatory cytokines in children with mycoplasma pneumonia and relieve the inflammatory reaction in the course of the disease. Drug treatment combined with early warning and evidence-based intervention can more effectively reduce inflammation reaction.

In the course of mycoplasma pneumonia, the excessive activation of the inflammatory response can also further influence mitochondrial oxidation respiratory process in local tissue, damage the electronic transfer in oxidation respiratory chain and cause a lot of electrons to transfer to the oxygen and generate reactive oxygen species. Reactive oxygen species are strongly oxidizing and can cause oxidative stress damage of local tissue, the lipid in cell membrane has oxidation reaction with reactive oxygen species and produces MDA, and a large amount of SF in cells enters blood circulation after the cell membrane damage; SOD is an important antioxidant enzyme in the body and can catalyze reduction reaction and scavenge ROS, but the excessively generated reactive oxygen species will continue to consume SOD, so the SOD content decreases and the antioxidant capacity of local tissue is weakened[7,8]. The oxidative stress reaction activation process can also change the synthesis and secretion of a variety of endocrine hormones, COR is an important endocrine hormone that is secreted by the adrenal cortex and involved in stress process, it can stabilize lysosome membrane and enhance the...
body’s ability to endure traumatic stress, but it will also affect the immune function, generate immunosuppressive activity and reduce the secretion of immunoglobulin IgA\[9,10\]. In the study, we further analyzed the change of above oxidative stress indicators before and after the treatment, and the results showed that serum MDA, SF and COR levels of both groups significantly decreased whereas SOD and IgA levels significantly increased after treatment, and serum MDA, SF and COR levels of experimental group were lower than those of control group whereas SOD and IgA levels were higher than those of control group. It means that routine drug treatment can reduce the generation of oxidative stress products, increase the content of antioxidants in children with mycoplasma pneumonia, and relieve the oxidative stress in the course of the disease. Furthermore, drug therapy combined with early warning and evidence-based intervention can more significantly reduce the oxidative stress than drug therapy alone.

The activation of inflammation and oxidative stress in children with mycoplasmal pneumonia is regulated by various signaling molecules. TLR4 is the pattern recognition receptor that regulates inflammation, and it is able to identify the mycoplasma and other pathogens pattern molecules, and start the downstream signal transduction\[11,12\], which will result in transcription factor NF-κB activation and start the expression of a variety of inflammatory genes in the nucleus\[13\]. COX2 is a catalyzing enzyme that regulates arachidonic acid metabolism, it mediates the prostaglandin generation from arachidonic acid metabolism, prostaglandin expands microcirculation and increases vascular permeability in local tissue, and it can promote the infiltration of inflammatory mediators and activate the inflammatory response\[14\]. NOX4 and MPO are metabolic enzymes that catalyze reactive oxygen species generation, the former mediates the transfer of electrons to oxygen molecules, the latter mediates peroxidation, and they can increase the production of reactive oxygen species after activation\[15\]; iNOS is inducible nitric oxide synthase, it is massively expressed in the process of inflammation and oxidative stress, and then it catalyzes L-arginine to generate gas signal molecule nitric oxide and magnifies inflammation and oxidative stress through the biological activities of nitric oxide\[16\]. In the study, analysis of the inflammation and oxidative stress signal molecules before and after treatment showed that peripheral blood TLR4, NF-κB, COX2, NOX4, MPO and iNOS expression intensity of both groups significantly decreased after treatment, and peripheral blood TLR4, NF-κB, COX2, NOX4, MPO and iNOS expression intensity of experimental group were lower than those of control group. This means that routine drug treatment can inhibit the activation of inflammation and oxidative stress signal molecules in children with mycoplasmal pneumonia, and drug therapy combined early warning and evidence-based intervention can more significantly inhibit the inflammation and oxidative stress signal molecules than drug therapy alone.

It can be concluded that early warning and evidence-based intervention combined with drug therapy for children with mycoplasmal pneumonia can reduce the inflammatory response and oxidative stress response in the course of disease.

References


