Changes of immune response and side effects before and after nutritional intervention in cervical cancer patients with concurrent chemoradiotherapy

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ARTICLE INFO

Article history:
Received 12 Jun 2018
Received in revised form 19 Jun 2018
Accepted 28 Jun 2018
Available online 14 Jul 2018

Keywords:
Cervical cancer
Nutritional intervention
Immune response
Side effects

ABSTRACT

Objective: To investigate the changes of immune response and side effects before and after nutritional intervention in cervical cancer patients with concurrent chemoradiotherapy.

Methods: A total of 160 patients with primary cervical cancer who received concurrent chemoradiotherapy in this hospital between May 2016 and September 2017 were selected as the research subjects. Their nutritional intervention plans were reviewed and used to divide the patients into the control group (n=83) who accepted conventional nutritional support and the nutritional intervention group (n=77) who accepted targeted nutritional intervention. The differences in the contents of Th1/Th2 immunity indexes and humoral immunity indexes as well as the levels of bone marrow suppression-related indexes were compared between the two groups before and after intervention. Results: Before intervention, the differences in the contents of Th1/Th2 immunity indexes and humoral immunity indexes as well as the levels of bone marrow suppression-related indexes were not statistically significant between the two groups. After intervention, serum IL-2, IFN-γ, IL-4 and IL-6 contents of nutritional intervention group were lower than those of control group; serum IgA, IgM, IgG, C3 and C4 contents were higher than those of control group; peripheral blood WBC, RBC, Hb and PLT levels were higher than those of control group. Conclusion: Nutritional intervention can effectively optimize the immune status and reduce the bone marrow suppression reaction in cervical cancer patients with concurrent chemoradiotherapy.

1. Introduction

Cervical cancer is the most common malignant tumor disease in female reproductive system. Concurrent chemoradiotherapy is one of the reliable ways to treat the disease, it can effectively weaken the tumor cell activity and even directly kill it, helping optimize the patients’ final treatment outcome[1,2]. But chemoradiotherapy damage is cell selectivity-free, in other words, the normal tissue cells will also be significantly damaged at the same time of significant damage to tumor cells. Serious cases can even cause important viscera function failure, and this deficiency is also the current bottleneck in the realization of chemoradiotherapy effect[3,4]. Poor nutritional status in patients can intensify the side effects of chemoradiotherapy, so some scholars put forward that such patients should receive both treatment and targeted nutrition intervention[5], but there is few related research at present. In this study, the differences in immune state and side effects before and after chemoradiotherapy were compared between patients with cervical cancer who received different nutritional interventions in order to clarify the necessity and effectiveness of nutritional interventions, which is elaborated as follows.

2. Information and methods

2.1 Case information

A total of 160 patients with primary cervical cancer who received concurrent chemoradiotherapy in this hospital between May 2016 and September 2017 were chosen as the research subjects. The nutritional intervention solutions were reviewed and used to divide them into the control group (n=83) who accepted conventional nutritional support and the nutritional intervention group (n=77)
who accepted targeted nutritional intervention. Control group were 41-75 years old; nutrition intervention group were 39-76 years old. There was no significant difference in age distribution between the two groups, and the study plan was reviewed and approved by the ethics committee of the hospital.

Inclusion criteria of the study is as follows: (1) in accordance with the diagnostic criteria for primary cervical cancer; (2) receiving concurrent chemoradiotherapy; (3) who or whose family members signed the informed consent. Exclusion criteria is as follows: (1) with severe malnutrition or autoimmune disease prior to chemoradiotherapy; (2) combined with systemic infectious diseases; (3) pregnant or breast-feeding women.

2.2 Nutritional intervention

Control group only received clinical conventional nutritional support for chemoradiotherapy, including increasing the intake of high-quality protein, reducing the intake of high-oil and high-fat foods, etc.

Nutrition intervention group received targeted nutrition intervention, which was as follows: PG-SGA was used to assess the current nutritional status of cervical cancer patients with concurrent chemoradiotherapy, which was divided into three types: good nutrition (A), severe /suspicous malnutrition (B) and severe malnutrition (C). For patients with type B and C, the heat supply range was 84-126 kJ/(kg·d), the percentage of protein in the daily nutrition was 15%-20% (high-quality protein accounted for more than 50%), the fat 25%-30%, and the carbohydrate 50%-60%. The patients with type A continued their current eating habits and could receive no special intervention, but those who had obvious bad eating habits should be advised and corrected in time. The above nutritional interventions started at the same time when concurrent chemoradiotherapy was implemented and lasted until one week after the end of chemoradiotherapy.

2.3 Observation indexes

Before and after the intervention, 6.0 mL of fasting peripheral blood samples were collected from the two groups respectively. 3.0 mL was centrifuged and the upper serum was obtained and cryopreserved for test, and the other 3.0 mL was directly cryopreserved for test. Enzyme-linked immunosorbent assay was used to detect the serum contents of humoral immunity indexes, including immunoglobulin A (IgA), immunoglobulin M (IgM), immunoglobulin G (IgG) as well as complement C3 and C4. Blood routine detector was used to determine the levels of bone marrow suppression-related indexes in peripheral blood, including white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb) and platelet (PLT).

2.4 Statistical methods

The contents of Th1/Th2 immunity indexes and humoral immunity indexes as well as the levels of bone marrow suppression-related indexes all belonged to measurement data and were input in statistical software SPSS24.0 to calculate the statistic P. P<0.05 indicated that the difference was statistically significant in the study.

3. Results

3.1 Th1/Th2 immunity indexes

Comparison of serum Th1/Th2 immunity indexes IL-2, IFN-γ, IL-4 and IL-6 contents between the two groups was as follows: before intervention, serum IL-2, IFN-γ, IL-4 and IL-6 contents were not significantly different between the two groups (P>0.05); after intervention, serum IL-2, IFN-γ, IL-4 and IL-6 contents of both groups were lower than those before intervention (P<0.05). After intervention, serum IL-2, IFN-γ, IL-4 and IL-6 contents of nutritional intervention group were lower than those of control group (P<0.05), as shown in Table 1.

3.2 Humoral immunity indexes

Comparison of serum humoral immunity indexes IgA, IgM, IgG, C3 and C4 contents between the two groups was as follows: before intervention, serum IgA, IgM, IgG, C3 and C4 contents were not significantly different between the two groups (P>0.05); after intervention, serum IgA, IgM, IgG, C3 and C4 contents of both groups were lower than those before intervention (P<0.05). After intervention, serum IgA, IgM, IgG, C3 and C4 contents of nutritional intervention group were higher than those of control group (P<0.05), as shown in Table 2.

Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>IL-2</th>
<th>IFN-γ</th>
<th>IL-4</th>
<th>IL-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>83</td>
<td>Before intervention</td>
<td>35.29±4.12</td>
<td>50.88±6.12</td>
<td>24.84±2.71</td>
<td>31.28±3.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>28.64±3.09</td>
<td>39.74±4.91</td>
<td>18.74±2.34</td>
<td>22.64±2.81</td>
</tr>
<tr>
<td>Nutritional intervention group</td>
<td>77</td>
<td>Before intervention</td>
<td>35.23±4.07</td>
<td>51.17±5.39</td>
<td>24.59±2.63</td>
<td>31.09±3.32</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>21.04±2.85</td>
<td>30.51±3.64</td>
<td>13.27±1.95</td>
<td>15.46±1.78</td>
</tr>
</tbody>
</table>

Compared with same group before intervention, 0.05; compared with control group after intervention, 0.05.

Table 2

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>IgA</th>
<th>IgM</th>
<th>IgG</th>
<th>C3</th>
<th>C4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>83</td>
<td>Before intervention</td>
<td>0.84±0.01</td>
<td>1.26±0.15</td>
<td>0.91±0.11</td>
<td>1.04±0.13</td>
<td>0.78±0.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>0.51±0.06</td>
<td>0.93±0.11</td>
<td>0.63±0.07</td>
<td>0.68±0.08</td>
<td>0.47±0.05</td>
</tr>
<tr>
<td>Nutritional intervention group</td>
<td>77</td>
<td>Before intervention</td>
<td>0.83±0.01</td>
<td>1.23±0.17</td>
<td>0.90±0.13</td>
<td>1.06±0.12</td>
<td>0.79±0.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>0.71±0.08</td>
<td>1.14±0.18</td>
<td>0.79±0.08</td>
<td>0.91±0.11</td>
<td>0.68±0.07</td>
</tr>
</tbody>
</table>

Compared with same group before intervention, 0.05; compared with control group after intervention, 0.05.

2.5 Nutritional indexes

Nutritional indexes of patients with type A were close to normal, with no significant difference between the two groups; patients with type B and C were in poor nutrition status, with nutritional indexes significantly different between the two groups.
Table 3.
Comparison of peripheral blood bone marrow suppression-related index levels.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>WBC (×10^9/L)</th>
<th>RBC (×10^12/L)</th>
<th>Hb (g/L)</th>
<th>PLT (×10^9/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>83</td>
<td>Before intervention</td>
<td>5.83±0.61</td>
<td>4.53±0.61</td>
<td>129.47±14.38</td>
<td>198.47±22.85</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>2.77±0.31</td>
<td>3.19±0.34</td>
<td>98.34±10.38</td>
<td>109.34±13.27</td>
</tr>
<tr>
<td>Nutritional intervention group</td>
<td>77</td>
<td>Before intervention</td>
<td>5.85±0.64</td>
<td>4.57±0.59</td>
<td>129.35±14.22</td>
<td>198.25±21.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After intervention</td>
<td>3.85±0.41</td>
<td>3.86±0.39</td>
<td>112.31±13.84</td>
<td>127.45±14.06</td>
</tr>
</tbody>
</table>

Compared with same group before intervention, *P<0.05;* compared with control group after intervention, *P<0.05.

### 3.3 Bone marrow suppression-related indexes

Comparison of peripheral blood bone marrow suppression-related indexes WBC (×10^9/L), RBC (×10^12/L), Hb (g/L) and PLT (×10^9/L) levels between the two groups was as follows: before intervention, peripheral blood WBC, RBC, Hb and PLT levels were not significantly different between the two groups (P>0.05); after intervention, peripheral blood WBC, RBC, Hb and PLT levels of both groups were lower than those before intervention (P<0.05). After intervention, peripheral blood WBC, RBC, Hb and PLT levels of nutritional intervention group were higher than those of control group (P<0.05), as shown in Table 3.

### 4. Discussion

Concurrent chemoradiotherapy is a common clinical therapy for patients with primary cervical cancer, and its role is significant in reducing the tumor cell malignancy and inhibiting the disease progression. But the chemoradiotherapy also kills the normal cells and can cause multiple organ function damage. Therefore, positive nutritional supplementation is expected to optimize the patients’ physique, enhance their tolerance to chemoradiotherapy and reduce the treatment interruption caused by severe malnutrition and adverse reactions during treatment[6,7]. At present, there is not much research about the targeted nutrition intervention measures and their roles for patients with concurrent chemoradiotherapy. The conventional nutritional guidance and targeted nutrition intervention were both used for cervical cancer patients with concurrent chemoradiotherapy in the study, and their value was explored from the body’s immune response, adverse reactions and other aspects.

Th1/Th2 cellular immunity is the main component of the anti-tumor immunity, and the inflammatory factors secreted by it can induce mononuclear macrophage and neutrophil infiltration, which play an important role in increasing cervical epithelial damage, promoting normal cervical epithelial cell canceration, etc[8,9]. Th1 cells mainly secrete cytokines such as IL-2 and IFN-γ, which can enhance antigen presenting cell activity and activate T cell function to cause immune disorders and enhance the invasion ability of cancer cells[10,11]; Th2 cells mainly secrete cytokines such as IL-4 and IL-6, and the increase of their expressions can break the equilibrium state of Th1/Th2 cells and lead to abnormal regulation of cervical epithelial cell cycle[12,13]. Concurrent chemoradiotherapy can damage cervical cancer cells and partially restore the immune balance of Th1/Th2 cells, but malnutrition may weaken this effect and hinder the complete implementation of the therapeutic effect. The results of this study showed that compared with those before intervention, Th1 cytokine and Th2 cytokine levels of both groups were lower after intervention, which indicates that concurrent chemoradiotherapy can effectively balance the Th1/Th2 immune balance in patients with cervical cancer; further compared with those of control group, Th1 cytokine and Th2 cytokine levels of nutrition intervention group were lower after intervention, which indicates that positive nutrition support can effectively enhance the patients’ physique and reduce the immune injury caused by malnutrition so as to further achieve the enhancing effect of concurrent chemoradiotherapy on the antitumor immune response function.

Humoral immune function is closely related to the nutritional status and chemoradiotherapy damage degree in patients with cervical cancer. Chemoradiotherapy can directly damage the humoral immune function and reduce the levels of a variety of immunoglobulins and complements, and good nutrition status is expected to reduce this side effect of chemoradiotherapy and optimize the humoral immune function[14-16]. In this paper, the result showed that compared with those before intervention, serum IgA, IgM, IgG, C3 and C4 contents of both groups were lower after intervention, which indicates that the toxic effects of concurrent chemoradiotherapy directly damage the humoral immune system in patients with cervical cancer; compared with those of control group, serum IgA, IgM, IgG, C3 and C4 contents of nutritional intervention group were higher after intervention, showing that positive nutritional intervention can effectively optimize the overall nutritional status and reduce the damage of humoral immune system function caused by concurrent chemoradiotherapy, and this is also one of the important internal reasons to eventually realize the treatment effect of chemoradiotherapy.

There are numerous side reactions of chemoradiotherapy, the bone marrow suppression is the most common and severe one. Infection, hemorrhage, anemia and other clinical manifestations are all caused by bone marrow suppression, and the hemogram is characterized by the declined levels of a series of indexes such as WBC, RBC, Hb and PLT[17-19]. Positive nutrition intervention can effectively reduce the toxic and side effects of concurrent chemoradiotherapy. But does it also mean that the bone marrow suppression is relieved in those with good nutrition state[20,21]? In this study, the differences in the levels of peripheral blood bone marrow suppression-related indicators were compared between the two groups of patients, and the results...
showed that compared with those before intervention, WBC, RBC, Hb and PLT levels of both groups decreased after intervention, it means that the patients have shown different degrees of bone marrow suppression as a whole, and this is in accordance with the generation mechanism of side effects of concurrent chemoradiotherapy; compared with those of control group, peripheral blood WBC, RBC, Hb and PLT levels of nutritional intervention group were higher after intervention, which shows that targeted nutrition intervention can effectively reduce the bone marrow suppression degree in cervical cancer patients with concurrent chemoradiotherapy.

To sum up, targeted nutrition intervention can effectively optimize the cellular immune and humoral immune function, and reduce the level of bone marrow suppression and other side effects in cervical cancer patients with concurrent chemoradiotherapy, which is of positive clinical significance, and is worth popularization and application in clinical practice in the future.

References


