Effect of postoperative early enteral nutrition support on anti-tumor immune response and inflammatory response process in the elderly patients with esophageal cancer

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ABSTRACT

Objective: To explore the effect of postoperative early enteral nutrition support on anti-tumor immune response and inflammatory response process in the elderly patients with esophageal cancer. Methods: A total of 110 cases of elderly patients with esophageal cancer who underwent radical operation in this hospital between January 2015 and December 2017 were divided into the parenteral nutrition group (n=57) who received parenteral nutrition support and the enteral nutrition group (n=53) who received enteral nutrition support according to the postoperative nutrition intervention methods. The differences in anti-tumor immune response and inflammatory response degree were compared between the two groups of patients immediately after the patients returned to the ward (T0), 48h after nutritional support (T1) and 72h after nutritional support (T2). Results: At T0, there was no statistically significant difference in the contents of Th1/Th2 immune response and Th17/Treg immune response indexes as well as inflammatory mediators in serum between the two groups of patients. At T1 and T2, serum Th1 cytokines IFN-γ and IL-12 contents of enteral nutrition group were higher than those of parenteral nutrition group whereas Th2 cytokines IL-4 and IL-13 contents were lower than those of parenteral nutrition group; serum contents of Th17 cytokines IL-6 and IL-17 as well as Treg cytokines TGF-β and IL-10 were lower than those of parenteral nutrition group; serum inflammatory mediators hs-CRP, PGE and HMGB1 contents were lower than those of parenteral nutrition group. Conclusion: Postoperative early enteral nutrition support can effectively regulate the Th1/Th2 and Th17/Treg immune response balance and inhibit the systemic inflammatory response in elderly patients with esophageal cancer.

1. Introduction

Esophageal cancer is a tumor disease with high clinical malignancy, radical resection is the most reliable therapy for patients with early-to-mid disease, patients are unable to eat through the mouth, and the early selection of nutrition method to guarantee patients’ postoperative nutritional needs is the current clinical research focus[1,2]. Both enteral nutrition and parenteral nutrition are the common clinical ways of nutritional support, and enteral nutrition includes nasogastric tube, nasal duodenal tube, nasal jejunal tube, etc., which can make the nutrients be directly absorbed via the intestinal tract and help maintain the integrity of the intestinal mucosal structure and barrier function[3,4]; parenteral nutrition is a way of intravenous nutrition, which includes peripheral intravenous nutrition and central intravenous nutrition, and is suitable for those with gastrointestinal dysfunction or failure[5,6]. In this study, the above two nutritional support methods were used respectively for the elderly patients after esophageal cancer surgery so as to clarify the better way of postoperative nutrition support for these patients.

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2. Information and methods

2.1 Case information

A total of 110 cases of elderly patients with esophageal cancer underwent radical operation in this hospital between January 2015 and December 2017 and were divided into the parenteral nutrition group (n=57) who received parenteral nutrition support and the enteral nutrition group (n=53) who received enteral nutrition support according to the postoperative nutrition intervention methods. There were 29 males and 28 females in the parenteral nutrition group, and they were 65-79 years old; there were 27 males and 26 females in the enteral nutrition group, and they were 63-78 years old. There was no significant difference in the above gender and age distribution between the groups (P>0.05), and the hospital ethics committee reviewed and approved the study plan.

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) diagnosed with primary esophageal cancer; (2) undergoing radical operation for the first time; (3) the patients themselves or their families signed the informed consent.

Exclusion criteria: (1) combined with preoperative pneumonia or other systemic infectious diseases; (2) combined with severe autoimmune diseases; (3) combined with other primary malignant tumor diseases.

2.3 Nutrition intervention

Parenteral nutrition group of patients received early postoperative parenteral nutrition support, specifically as follows: jugular vein catheterization was done to infuse nutrient solution, it contained glucose, fat, amino acids, vitamins, trace elements and so on, heat nitrogen ratio was 100-150:1, glucose lipid ratio was 6:4, and daily heat was ensured at 15 kcal/(kg·d).

Enteral nutrition group received early postoperative enteral nutrition support, specifically as follows: nasogastric tube was placed after surgery for gastrointestinal decompression, the nasointestinal tube inserted during surgery was used to infuse Nutrison Fibre at 20 mL/h at first for continuous 24 h, and mosapride was provided via nasointestinal tube at 5 mg/time and 3 times/d to promote gastrointestinal motility. According to the patient’s tolerance, the infusion speed was increased gradually to full dose of 30 kcal/(kg·d).

2.4 Observation indexes

Immediately after the patients returned to the ward (T0), 48 h after nutritional support (T1) and 72 h after nutritional support (T2), fasting peripheral blood samples were obtained from the two groups to separate serum, enzyme-linked immunosorbent assay was used to detect the expression of antitumor immune response indexes, they included the Th1/Th2 immune response and Th17/Treg immune response, Th1 cytokines included interferon γ (IFN-γ) and interleukin-12 (IL-12), Th2 cytokines included interleukin-4 (IL-4) and interleukin-13 (IL-13), Th17 cytokines included interleukin-6 (IL-6) and interleukin-17 (IL-17), and Treg cytokines included transformation growth factor β (TGF-β) and interleukin-10 (IL-10). Peripheral blood serum specimens were collected again at the above time points, and enzyme-linked immunosorbent assay was used to determine the contents of inflammatory mediators hypersensitive C-reactive protein (hs-CRP), prostaglandin E (PGE) and high mobility group B1 (HMGB1).

2.5 Statistical methods

Th1/Th2 immune response indexes, Th17/Treg immune response indexes and inflammatory mediators belonged to measurement data and were input in SPSS 23.0, t test was used to calculate the statistic and P<0.05 was used as the standard of statistical significance in the differences.

3. Results

3.1 Th1/Th2 immune response indexes

Comparison of serum contents of Th1 cytokines IFN-γ and IL-12 as well as Th2 cytokines IL-4 and IL-13 between the two groups of patients was as follows: at T0, there was no statistically significant difference in serum IFN-γ, IL-12, IL-4 and IL-13 contents between the two groups of patients (P>0.05). At T1 and T2, serum IFN-γ and IL-12 contents of both groups were higher than those at T0 whereas IL-4 and IL-13 contents were lower than those at T0; serum IFN-γ and IL-12 contents of enteral nutrition group were higher than those of parenteral nutrition group whereas IL-4 and IL-13 contents were lower than those of parenteral nutrition group (P<0.05), shown in Table 1.

Table 1.

Comparison of Th1/Th2 immune response index contents between the two groups at different time points after surgery (pg/mL).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time points</th>
<th>IFN-γ</th>
<th>IL-12</th>
<th>IL-4</th>
<th>IL-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral nutrition group</td>
<td>57</td>
<td>T0</td>
<td>4.38±0.51</td>
<td>5.17±0.53</td>
<td>11.09±1.76</td>
<td>23.74±2.68</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>4.71±0.48*</td>
<td>5.62±0.57*</td>
<td>10.56±1.72*</td>
<td>21.09±2.64*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>4.98±0.53*</td>
<td>5.91±0.64*</td>
<td>9.17±0.98*</td>
<td>20.36±2.41*</td>
</tr>
<tr>
<td>Enteral nutrition group</td>
<td>53</td>
<td>T0</td>
<td>4.41±0.49</td>
<td>5.22±0.49</td>
<td>11.12±1.83</td>
<td>23.65±2.62</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>5.13±0.54*</td>
<td>6.17±0.65*</td>
<td>9.77±0.92*</td>
<td>19.84±2.11*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>5.78±0.56*</td>
<td>6.86±0.71*</td>
<td>7.68±0.81*</td>
<td>15.47±1.68*</td>
</tr>
</tbody>
</table>

Note: compared with same group at T0, P<0.05.

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Comparison of Th17/Treg immune response indexes

Comparison of serum contents of Th17 cytokines IL-6 and IL-17 as well as Treg cytokines TGF-β and IL-10 between the two groups of patients was as follows: at T0, there was no statistically significant difference in serum IL-6, IL-17, TGF-β and IL-10 contents between the two groups of patients (P>0.05). At T1 and T2, serum IL-6, IL-17, TGF-β and IL-10 contents of both groups were lower than those at T0; serum IL-6, IL-17, TGF-β and IL-10 contents of enteral nutrition group were lower than those of parenteral nutrition group (P<0.05), shown in Table 2.

Comparison of inflammatory mediator contents between the two groups at different time points after surgery.

Table 2.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time points</th>
<th>IL-6</th>
<th>IL-17</th>
<th>TGF-β</th>
<th>IL-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral nutrition</td>
<td>57</td>
<td>T0</td>
<td>20.18±2.49</td>
<td>34.19±4.26</td>
<td>17.23±1.69</td>
<td>20.39±2.76</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>18.45±1.76</td>
<td>31.08±3.74</td>
<td>16.54±1.74</td>
<td>19.45±1.76</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>15.29±1.61</td>
<td>27.22±3.05</td>
<td>15.88±1.76</td>
<td>16.28±1.73</td>
</tr>
<tr>
<td>Enteral nutrition</td>
<td>53</td>
<td>T0</td>
<td>20.24±2.58</td>
<td>34.51±4.23</td>
<td>17.19±1.54</td>
<td>20.43±2.68</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>14.71±1.69</td>
<td>27.40±2.86</td>
<td>11.78±1.63</td>
<td>14.53±1.77</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>11.07±1.34</td>
<td>20.64±2.48</td>
<td>9.07±0.98</td>
<td>10.71±1.82</td>
</tr>
</tbody>
</table>

Note: compared with same group at T0, *P<0.05.

Table 3.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time points</th>
<th>hs-CRP</th>
<th>PGE</th>
<th>HMGB1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral nutrition</td>
<td>57</td>
<td>T0</td>
<td>13.28±1.77</td>
<td>20.95±2.88</td>
<td>45.38±5.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>11.57±1.63</td>
<td>18.72±1.69</td>
<td>42.76±4.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>10.46±1.23</td>
<td>17.63±1.58</td>
<td>40.38±4.24</td>
</tr>
<tr>
<td>Enteral nutrition</td>
<td>53</td>
<td>T0</td>
<td>13.19±1.68</td>
<td>20.91±2.69</td>
<td>45.41±4.99</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>9.08±0.97</td>
<td>15.09±1.67</td>
<td>38.12±4.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>7.13±0.76</td>
<td>11.08±1.54</td>
<td>32.18±3.62</td>
</tr>
</tbody>
</table>

Note: compared with same group at T0, *P<0.05.

3.2 Th17/Treg immune response indexes

3.3 Inflammatory mediators

Comparison of serum inflammatory mediators hs-CRP (mg/L), PGE (ng/mL) and HMGB1 (pg/mL) contents between the two groups of patients was as follows: at T0, there was no statistically significant difference in serum hs-CRP, PGE and HMGB1 contents between the two groups of patients (P>0.05). At T1 and T2, serum hs-CRP, PGE and HMGB1 contents of both groups were lower than those at T0; serum hs-CRP, PGE and HMGB1 contents of enteral nutrition group were lower than those of parenteral nutrition group (P<0.05), shown in Table 3.

4. Discussion

Elderly patients can't take food independently by the pharynx oralis after esophageal cancer surgery, both the high consumption status of tumors and the surgical trauma cause the body in continuous negative nutritional balance state, timely nutrition supply is the most reliable way to prompt the healing of incision and enhance the immunity, but the specific mode of nutritional support is still questionable. Parenteral nutrition is the preferred way of nutrition support for patients with gastrointestinal dysfunction or temporarily unsuitable for intestinal feeding, it is with simple operation and quick nutrient absorption, and its long-term application can cause gastrointestinal hypofunction and liver dysfunction. Enteral nutrition is the way to directly make the nutrient enter the gastrointestinal tract and be absorbed through the nasogastric tube, the nasal duodenal tube, and so on, and it is suitable for those with normal gastrointestinal function[7,8]. Traditional concept holds that after surgery, enteral nutrition can only be carried out when patients’ gastrointestinal function is back to normal, but the latest fast-track surgery theory believes that early enteral nutrition can promote gastrointestinal peristalsis recovery and protect gastrointestinal barrier function. In this study, the effects of postoperative parenteral nutrition and early enteral nutrition on antitumor immunity, systemic inflammatory response and other aspects were discussed in order to clarify the optimal way of postoperative nutritional support.

Th1/Th2 immunity is an important part of anti-tumor immunity in the body. Th1 cells mainly secrete IFN-γ and IL-12, and mediate the cellular immune response[9,10]; Th2 cells mainly secrete IL-4 and IL-13 and mainly mediate humoral immune response[11,12]. There is Th1/Th2 immune imbalance in patients with esophageal cancer, the Th1 cytokine expression decreases while Th2 cytokine expression increases, the body shows Th2 cell-dominant condition, and the Th2 shifting is more serious with the decrease of tumor cell differentiation[13,14]. Patients with esophageal cancer have preoperative eating disorder and are in a malnutrition state, surgical trauma further consumes more nutrients after surgery, and it will further lead to Th1/Th2 immune imbalance and result in anti-tumor immune dysfunction if the nutrition supply is not restored in time. The study results showed that serum Th1 cytokine contents of both groups of patients at T1 and T2 were higher than those at T0 whereas Th2 cytokine contents were lower than those at T0, and the change in above index contents in enteral nutrition group was larger than that in parenteral nutrition group, confirming that early postoperative enteral nutrition can effectively optimize the Th1 cell function and
suppress the Th2 cell shifting.

Th17/Treg immunity is also involved in the antitumor immunity of esophageal cancer, studies have shown that Th17 cell infiltration is a common feature of malignant tumors, and the IL-6, IL-17 and other cytokines are secreted and accumulate in the tumor microenvironment, which can be used as potential biomarkers that estimate the prognosis of esophageal cancer[15]; Treg cell can inhibit the host’s anti-tumor immune response, and its high expression may be one of the important mechanisms of immune escape of esophageal cancer[16]. In this study, Th17/Treg cell contents were compared between the two groups of patients, and it was found that serum contents of Th17 cytokines and Treg cytokines of both groups of patients at T1 and T2 were lower than those at T0, and the decrease of the above index contents was more significant in enteral nutrition group, indicating that early postoperative enteral nutrition can effectively inhibit the expression of Th17/Treg cytokines and enhance the body's anti-tumor immunity.

There is different degree of systemic inflammatory response in elderly patients after esophageal cancer surgery, and obvious malnutrition can aggravate the inflammatory state and even lead to multiple organ dysfunction, which is one of the important reasons malnutrition can aggravate the inflammatory state and even lead to elderly patients after esophageal cancer surgery, and obvious systemic inflammatory response in elderly patients with esophageal cancer, studies have shown that Th17/Treg cell infiltration is a common feature of malignant tumors, and the IL-6, IL-17 and other cytokines are secreted and accumulate in the tumor microenvironment, which can be used as potential biomarkers that estimate the prognosis of esophageal cancer[15]; Treg cell can inhibit the host’s anti-tumor immune response, and its high expression may be one of the important mechanisms of immune escape of esophageal cancer[16]. In this study, Th17/Treg cell contents were compared between the two groups of patients, and it was found that serum contents of Th17 cytokines and Treg cytokines of both groups of patients at T1 and T2 were lower than those at T0, and the decrease of the above index contents was more significant in enteral nutrition group, indicating that early postoperative enteral nutrition can effectively inhibit the expression of Th17/Treg cytokines and enhance the body's anti-tumor immunity.

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To sum up, it is concluded that compared to traditional parenteral nutrition, early postoperative enteral nutrition support can more effectively enhance the antitumor immunity and reduce the extent of systemic inflammatory response in elderly patients with esophageal cancer, it is a feasible and reliable way of nutritional support, and it is worthy of popularization and application in such patients in the future.

References


