Randomized control trials

Randomized study of clinical effect of enteral nutrition support during neoadjuvant chemotherapy on chemotherapy-related toxicity in patients with esophageal cancer

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ARTICLE INFO
Article history:
Received 16 July 2011
Accepted 8 November 2011
Keywords:
Esophageal cancer
Chemotherapy
Enteral nutrition
Toxicity
Adverse effect
Neoadjuvant

SUMMARY
Background & aims: Enteral nutrition (EN) is provided for patients with cancer. However, little is known about the clinical efficacy of EN support during chemotherapy in patients with cancer.
Methods: Ninety-one patients who received neoadjuvant chemotherapy (5-fluorouracil, cisplatin, and adriamycin) for esophageal cancer were enrolled to receive either EN (n = 47) or PN (n = 44) at random.
The primary endpoint was the incidence of chemotherapy-related toxicities during chemotherapy.
Results: Total and dietary intake calories during chemotherapy were equal in the two groups. There were no significant differences in serum albumin level and body weight change after chemotherapy between the two groups. There was no significant difference in tumor response to chemotherapy between the two groups (EN: 51%, PN: 55%, p = 0.886). Leukopenia and neutropenia of grade 3 or 4, defined according to the Common Toxicity Criteria of the National Cancer Institute, were significantly less frequent in the EN group than in the PN group (leukopenia: 17% vs 41%, p = 0.01, neutropenia: 36% vs 66%, p = 0.005). Leukopenia and thrombocytopenia tended to be less frequent in the EN group, albeit insignificantly.
Conclusions: Compared with PN support, EN support during neoadjuvant chemotherapy reduced the incidence of chemotherapy-related hematological toxicities in patients with esophageal cancer.
The clinical trial registration number: UMIN000004483
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1. Introduction

Esophageal cancer is the eighth most common incident cancer and sixth most common cause of cancer death.1,2 Surgery is regarded as standard management for esophageal cancer, but the prognosis of patients who receive only surgery is poor.2,3 To improve the survival rate in these patients, chemotherapy with or without radiotherapy followed by surgery has become one of the standard treatment strategies for esophageal cancer.3–8 Indeed, chemotherapy is an important component of treatment of not only esophageal cancers but also other gastrointestinal cancers. However, chemotherapy is associated with a variety of chemotherapy-related toxicities. Bone-marrow suppression, such as leukopenia and anemia, stomatitis, appetite loss, nausea and diarrhea are frequently observed during chemotherapy, and such adverse effects sometimes force the patient to quit treatment. The efficacy of chemotherapy is usually dose-dependent, while the dose is limited by the side effects.9 Therefore, approaches to reduce chemotherapy-related toxicities are needed, not only to relieve pain associated with the above adverse effects but also to maximize the efficacy of chemotherapy.

Recent clinical evidence has supported the benefits of enteral nutrition in cancer patients. Especially in malnourished cancer patients, enteral nutrition maintains quality of life and improves nutritional status by increasing or ensuring nutrient intake.10–12 In patients with moderate or severe malnutrition, especially those who undergo surgery for cancer or peritonitis, perioperative enteral nutrition has been reported to reduce morbidity and mortality related to gastrointestinal surgery and reduce the duration of hospitalization.13–17 In addition to its usefulness in patients on surgery, enteral nutrition during radiotherapy significantly enhances dietary intake, prevents weight loss and promotes adherence to radiotherapy.18–20 However, for patients with
cancers who undergo chemotherapy, effect of enteral nutrition during chemotherapy on chemotherapy-related toxicities or response to chemotherapy has not been established. In esophageal cancer, patients sometimes are malnourished at the initial diagnosis, and cisplatin-based chemotherapy which is a standard chemotherapy for esophageal cancer often cause the reduced dietary intake due to cisplatin-induced anorexia. Therefore, during cisplatin-based chemotherapy for patients with esophageal cancer, enteral nutrition support may be beneficial.

The present study was designed to examine whether enteral nutrition during chemotherapy help reduce chemotherapy-related toxicities. Among the various enteral nutrients, we focused on omega-3 fatty acids-rich nutritional supplements. Omega-3 fatty acids have been reported to have anti-inflammatory effects, improve immune function, and reduce intestinal damage caused by anti-cancer agents. The study compared enteral nutritional support with parenteral nutrition during chemotherapy for advanced esophageal cancer. All chemotherapy-related toxicities were evaluated in both groups.

2. Materials and methods

2.1. Patients

Patients were entered into the study according to the following eligibility criteria: 1) previously untreated and histopathologically-confirmed thoracic esophageal cancer; 2) clinical stage IIA, IIB, III or IV with distant node involvement; 3) age >20 or <80 years; 4) an Eastern Cooperative Oncology Group performance status (PS) of 0–2; 5) adequate hepatic, renal and bone-marrow reserve (leukocyte count > 3500/mm³, hemoglobin > 10 g/dl, platelet count > 100,000/mm³, AST and ALT not higher than twice the normal levels; total serum bilirubin < 3.0 mg/dl; and creatinine level <1.3 mg/dl); 6) ability of oral intake; 7) oral or written informed consent obtained before randomization. Patients were ineligible if they had severe stenosis of esophagogastrointestinal tract or they had uncontrolled diabetes.

In this study, all patients were staged before treatment according to the criteria of the International Union Against Cancer (UICC). Pretreatment clinical staging was based on endoscopy, computed tomography (CT) scans of the neck, chest and the upper abdomen as continuous 5 mm thick slices and, if at all possible, positron emission tomography (PET) scan. Lymph nodes were diagnosed as metastasis-positive CT scan if they were greater than 1.0 cm in maximum transverse diameter. Lymph nodes visible but smaller than 1.0 cm or the long axis on CT scan were regarded as metastasis-positive only if focal prominent 18-fluorodeoxy glucose (FDG) uptake, compared with normal mediastinal activity, was detected on the PET scan.

The study protocol was approved by the Human Ethics Review Committees of Osaka University Graduate School of Medicine, Osaka Medical Center for Cancer and Cardiovascular Diseases and Kinki University.

2.2. Study design and treatment

Patients were randomly assigned to either the enteral nutrition (EN) group or parenteral nutrition (PN) group. The sizes of the groups were balanced according to institution, gender and serum albumin level. A coordinating center (section of the Department of Gastroenterological Surgery, Graduate School of Medicine, Osaka University) generated the treatment allocation codes using a computer generated randomization table.

In both groups, the enrolled patients received neoadjuvant chemotherapy consisting of cisplatin, adriamycin and 5-fluorouracil (5-FU). Cisplatin was administered at 70 mg/m², adriamycin at 35 mg/m² by rapid intravenous infusion on day 1; and 5-FU at 700 mg/m² administered by continuous intravenous infusion on day 1 through day 7. Supportive therapy and prophylaxis against expected side effects was provided. Antagonists of 5-HT3 receptor were routinely administered prophylactically at day 1–7 in both groups. Adequate hydration was ensured before and after cisplatin infusion. Additional antimetics or steroid preparation were recommended in case of grade-3 or higher anorexia, nausea, and vomiting by the toxicity grading criteria of the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Granulocyte-stimulating factor (G-CSF) was used for febrile neutropenia when deemed necessary. Two courses of chemotherapy were provided, separated by a 4-week interval, except when the tumor did not show any sign of significant regression after the first course of chemotherapy. Patients underwent surgery 3–5 weeks after the completion of neoadjuvant chemotherapy only if complete tumor resection was considered possible.

2.3. Parenteral or enteral nutrition support

In patients assigned to the EN group, omega-3 fatty acid-rich nutritional supplements (Racol, Otsuka Pharmaceuticals, Tokyo, Japan) at 600 mL/day (600 kcal/day) were provided. The composition of the nutritional supplements was 4.38 g protein, 2.23 g lipid (omega-3 fatty acids: omega-6 fatty acids = 1:3) and 16.62 g carbohydrate in 100 mL volume. Omega-3 fatty acid-rich nutritional supplement was administered from 3 days before the start of chemotherapy to 7 days after completion of chemotherapy (for 17 days). Basically, patients drank the supplement or it was administered through a trans-nasal feeding tube when oral intake was not possible due to chemotherapy-related toxicities such as nausea and stomatitis. During that time, patients took oral diet arbitrarily and when oral intake decreased, parenteral nutrition support was instituted to compensate for the reduced calories through oral intake.

In patients assigned to the PN group, parenteral nutrition support at 600 kcal/day was provided from 3 days before the start of chemotherapy to 7 days after the completion of chemotherapy (for 17 days). The composition of the intravenous infusion which was provided as basal parenteral nutrition support was 130.0 g glucose, 50 mg Na, 22 mg K, 50 mg Ca, and 20.0 g free amino acids in 1000 mL volume. As in the EN group, patients took oral diet arbitrarily and when oral intake decreased, parenteral nutrition support was instituted to compensate for the reduced calories through oral intake. Thus, the treatment protocol was arranged to maintain the total intake calories during the study period in both groups (Fig. 1). Food intake calories based on the food weight measured by the patient, including standard meal and extra foods, were calculated by dietitians using a calorimeter. In both groups, the desired total intake calories was set at 40–50 kcal/kg/day.

2.4. Evaluation of response to chemotherapy

The clinical response was categorized according to the following criteria [based on the Response Evaluation Criteria in Solid Tumors (RECIST) guideline and the criteria of the Japanese Society for Esophageal Diseases]. A complete response (CR) was defined as clinical complete regression of the disease. A CR of the primary tumors was determined when the tumors disappeared on CT scan and/ or PET scan and endoscopy. If further ulceration and presence of cancer cells in biopsy samples was confirmed by endoscopy, the case was excluded from the CR group. A partial response (PR) was defined as more than 30% reduction in maximum transverse diameter of the primary tumor, on the CT scan. Progressive disease (PD) was defined as more than 20% increase in maximum transverse diameter of the

primary tumor or the appearance of new lesions. Cases that did not meet the criteria of PR and PD were defined as stable disease (SD).

The degree of histopathological tumor regression in surgical specimens was classified into five categories. The percentage of viable residual tumor cells within the total cancerous tissue was assessed as follows: Grade 3, no viable residual tumor cells; Grade 2, less than 1/3 residual tumor cells; Grade 1b, 1/3–2/3 residual tumor cells; Grade 1a, more than 2/3 residual tumor cells; Grade 0, no significant response to chemotherapy.

2.5. Evaluation of chemotherapy-related toxicities and blood sampling

Toxicity was evaluated and scored by the most severe toxicity in the first cycle by toxicity (days 1–28) grading criteria of CTCAE version 3.0. Blood examination was performed at least once a week during the course of chemotherapy. Non-hematological adverse events such as nausea, vomiting, diarrhea and stomatitis were assessed daily during the entire course of chemotherapy. Dose modifications in the second cycle were based on treatment-related adverse events recorded in the first cycle. The dose of cisplatin and Adriamycin was reduced by 20% for grade 4 neutropenia lasting for more than 7 days, febrile neutropenia grade 3 or higher, and thrombocytopenia grade 3 or higher.

The lipid profile and fatty acids in blood were examined before treatment and at days 14 and 42. The ratio of omega-3 fatty acids to omega-6 fatty acids was defined as the ratio of eicosapentaenoic acid (EPA) to arachidonic acid (AA).

2.6. Statistical analysis

The primary endpoint was frequency of chemotherapy-related adverse effects. The secondary endpoints were nutritional status including body weight and serum albumin. The rate of grade 3 or 4 toxicities such as leukopenia, neutropenia and nausea in the PN group was expected to be 50%, based on our previous results. We planned initially to recruit 90 patients, a number that would allow detection of 30% decrease in the incidence of grade 3 or 4 toxicities in the EN group, with two-sided alpha error of 0.05 and statistical power of 80%.

The baseline characteristics and response to chemotherapy were compared using chi-square test or Mann-Whitney U test. Comparison of intake calories between the treatment groups was tested by the Student t-test, and comparison of adverse effects between the groups were evaluated by the Mann-Whitney U test. The Cox proportional hazards regression model was used to identify variables significantly associated with occurrence of chemotherapy-related neutropenia. Continuous variables were expressed as mean ± standard deviation unless otherwise stated. P values less than 0.05 were considered to indicate statistical significance. All analyses were carried out using the StatView software package version 5.0 (SAS Institute Inc., Cary, NC).
3. Results

3.1. Patient characteristics

During the period from December 2007 to February 2010, 91 patients who received neoadjuvant chemotherapy for esophageal cancer were enrolled in this study, and 47 patients were randomly assigned to the EN group and 44 patients to the PN group (Fig. 2). Table 1 summarizes the pretreatment characteristics of all 91 patients enrolled in this study. The baseline prognostic variables, such as age, gender, body mass index, CT, cN, cM and cStage were well balanced between the two groups.

3.2. Calorie intake and nutritional status

Dietary intake calories during chemotherapy were almost similar between the EN and PN groups (Table 2). Among the 47 patients of the EN group, EN supplementation was discontinued during the first course of chemotherapy in 6 patients who refused to continue EN treatment because of adverse events such as nausea and vomiting. In the EN group, patients consumed an average of 530 kcal of omega-3 fatty acid-rich nutritional supplements per day. Thus, the ratio of omega-3 to omega-6 fatty acids on day 14 was significantly higher in the EN group than PN group (Average value of EPA and AA in EN group was 21.1 % and 5.7 % of total fatty acids before treatment and 1.6 % and 5.4 % of total fatty acids at day 14. Average value of EPA and AA in PN group was 21.1 % and 5.9 % of total fatty acids before treatment and 1.3 % and 5.6 % of total fatty acids at day 14) (Fig. 3). On the other hand, the caloric content of administered parenteral nutrition was higher in the PN group than EN group. Thus, total intake calories during chemotherapy were almost similar between the EN and PN groups.

There were no significant differences in serum albumin level and body weight at day 14 between the two groups (Table 2).

3.3. Compliance and response to chemotherapy

Among the 47 patients of the EN group, 5 received the first course of chemotherapy only; because of renal dysfunction in one patient, no apparent tumor regression in the remaining four during that period. Among the 44 patients of the PN group, 5 received the first course of chemotherapy only; because of renal dysfunction in one patient, no apparent tumor regression in the remaining four.

Table 1

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>EN group</th>
<th>PN group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>47</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>62.4</td>
<td>63.2</td>
<td>0.643</td>
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<tr>
<td>Gender</td>
<td>Male</td>
<td>Female</td>
<td>0.410</td>
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<tr>
<td>Body mass index</td>
<td>21.3</td>
<td>20.9</td>
<td>0.550</td>
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<tr>
<td>Histology</td>
<td>SCC</td>
<td>Others</td>
<td>0.130</td>
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<tr>
<td>Tumor depth</td>
<td>CT1</td>
<td>CT2</td>
<td>0.650</td>
</tr>
<tr>
<td>Lymph node involvement</td>
<td>cN0</td>
<td>cN1</td>
<td>0.922</td>
</tr>
<tr>
<td>Distant metastasis</td>
<td>cM0</td>
<td>cM1</td>
<td>0.185</td>
</tr>
<tr>
<td>Stage</td>
<td>Stage II</td>
<td>Stage III</td>
<td>0.199</td>
</tr>
</tbody>
</table>

Table 2

| Food intake calories per day for 17 days (from 3 days before the start of chemotherapy to 7 days after the completion of chemotherapy) and nutritional status at day 14. |
|---|---|---|---|
| EN group (n = 47) | PN group (n = 47) | P value |
| Internal nutrition (kcal) | 530 ± 147 | 0 | <0.0001 |
| Parenteral nutrition (kcal) | 434 ± 328 | 925 ± 311 | <0.0001 |
| Dietary intake calories (kcal) | 942 ± 436 | 843 ± 439 | 0.286 |
| Total intake calories (kcal) | 1906 ± 322 | 1768 ± 303 | 0.211 |
| Serum albumin at day 14 (mg/dL) | 3.3 ± 0.7 | 3.2 ± 0.6 | 0.282 |
| Change in body weight at day 14 (%) | 99.4 ± 3.0 | 99.9 ± 3.2 | 0.175 |

Data are mean ± standard deviation. EN: enteral nutrition group, PN: parenteral nutrition group.

During that period. The drug dose was reduced in the second course of chemotherapy in the 5 patients of the EN group and 4 patients of the PN group. In each group, 2 patients achieved clinical complete response (4.3% in EN group and 4.5% in PN group, Table 3). The response rate to chemotherapy was not different between the two groups (EN group: 51%, PN group: 55%). Among the 47 patients of the EN group, 44 (including 3 patients who received chemoradiotherapy after neoadjuvant chemotherapy) underwent surgical resection while 3 patients did not undergo surgery due to bone metastasis in one patient, chemotherapy-related failure in one and tumor growth in one. In the PN group, 40 of 44 patients, including one who received chemoradiotherapy after neoadjuvant chemotherapy, underwent surgical resection while 4 patients did not undergo surgery due to bone metastasis in two patients, and tumor growth in two. The histopathological response after neoadjuvant chemotherapy followed by surgery was almost similar between the two groups.

3.4. Chemotherapy-related adverse events

Data on 47 patients of the EN group including 6 patients who could not continue EN supplementation during chemotherapy and 44 patients of the PN group were analyzed for adverse events during the first course of neoadjuvant chemotherapy. Leukopenia and neutropenia were significantly less frequent in the EN group than the PN group (Table 4). Lymphopenia and thrombocytopenia tended to be less common in the EN group, compared with the PN group, although this difference did not reach statistical significance. On the other hand, there were no significant differences in non-hematological side effects such as nausea, diarrhea and stomatitis, between the two groups, with the exception that elevated

Table 3
Effect of enteral nutrition support on response to chemotherapy.

<table>
<thead>
<tr>
<th>Response to chemotherapy</th>
<th>EN group</th>
<th>PN group</th>
<th>P value</th>
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<tbody>
<tr>
<td>CR</td>
<td>64</td>
<td>22</td>
<td>0.067</td>
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<tr>
<td>PR</td>
<td>22</td>
<td>22</td>
<td>1.00</td>
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<tr>
<td>SD/DPD</td>
<td>23</td>
<td>20</td>
<td>0.525</td>
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<tr>
<td>Surgery</td>
<td>yes</td>
<td>44</td>
<td>40</td>
</tr>
<tr>
<td>no</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Histopathological tumor regression</td>
<td>Grade 3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Grade 4</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Grade 0-1a</td>
<td>31</td>
<td>24</td>
</tr>
</tbody>
</table>

EN: enteral nutrition group. PN: parenteral nutrition group.

Table 5
Multivariate analysis for occurrence of grade 3/4 neutropenia.

<table>
<thead>
<tr>
<th>Variables</th>
<th>HR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Female</td>
<td>1.35</td>
<td>0.51–3.89</td>
</tr>
<tr>
<td>Age</td>
<td>≥70</td>
<td>1.61</td>
<td>0.51–5.42</td>
</tr>
<tr>
<td>Body mass index</td>
<td>&lt;18.5</td>
<td>1.04</td>
<td>0.32–3.31</td>
</tr>
<tr>
<td>Albumin</td>
<td>&lt;3.5 mg/dl</td>
<td>0.30</td>
<td>0.42–0.50</td>
</tr>
<tr>
<td>Tumor stage</td>
<td>Stage IV</td>
<td>0.94</td>
<td>0.20–1.48</td>
</tr>
<tr>
<td>Oral intake calories</td>
<td>&lt;1000 kcal</td>
<td>2.23</td>
<td>1.01–5.32</td>
</tr>
<tr>
<td>Enteral nutrition support</td>
<td>Performed</td>
<td>0.28</td>
<td>0.11–0.88</td>
</tr>
</tbody>
</table>

HR: hazard ratio. 95% CI: 95% confidence interval.

In this study, we demonstrated that EN support during chemotherapy for patients with esophageal cancer reduces chemotherapy-related hematological adverse events, in particular, leukopenia and neutropenia, although it affected neither tumor response to chemotherapy nor body weight change during chemotherapy.

Several studies have shown the clinical efficacy of perioperative EN support in patients with cancer scheduled for surgery, but little information is available on the clinical efficacy of EN support during chemotherapy. Klein and Koretz analyzed 7 randomized controlled trials that examined the use of EN support in patients receiving chemotherapy. They concluded that these studies did not allow full assessment due to differences in the formula composition, timing, and duration of nutrition therapy. In addition, several studies were of low quality because either the sample size was small or EN support was not properly provided to patients randomized to receive EN therapy, and no obvious therapeutic benefit was noted with respect to survival, tumor response, or chemotherapy-related toxicity. Current results clearly showed that EN support during chemotherapy reduced the incidence of chemotherapy-related hematological adverse events such as leukopenia and neutropenia. Recently, as chemotherapy regimen which is used in the treatment for gastrointestinal cancers including esophageal cancer and gastric cancer become more powerful, hematological toxicities such as leukopenia and neutropenia become more common while the response rate is getting higher. Therefore, we think that current result that EN support during chemotherapy may have the potential of reducing hematological toxicities is of clinical importance in the treatment for esophageal cancer.

One possible reason of positive result in this study is that we designed the current study to examine the effect of EN support in combination with neoadjuvant chemotherapy after ensuring the inclusion of two otherwise homogeneous groups with respect to patient background. Neoadjuvant setting may allow this study to make a significant difference in chemotherapy-related toxicities between enteral nutrition and parenteral nutrition. Another possible

reason of current positive result is that we conducted the current study for patients who received cisplatin-based chemotherapy. Among various anti-cancer drugs, cisplatin is well-known to be one of the most highly emetic drugs. Patients who receive cisplatin-based chemotherapy often can not take adequate nutrition orally due to cisplatin-induced nausea, and nutrition support during chemotherapy is required for those patients. This decreased dietary intake caused by cisplatin-based chemotherapy may be responsible for current result that enteral nutrition support reduced chemotherapy-related hematological toxicities. Indeed, in subgroup analysis, enteral nutrition support during chemotherapy decreased occurrence of grade 3/4 neutropenia in patients who consumed less than 1000 kcal of dietary intake whereas enteral nutrition support did not have a significant influence on occurrence of grade 3/4 neutropenia in patients who consumed more than 1000 kcal of dietary intake.

It is commonly believed that poor nutritional status, such as body weight loss, is associated with increased treatment-related adverse reactions. However, in this study, the indicators used for nutritional status such as body weight and serum albumin level were almost similar during chemotherapy between the EN and PN groups. The reason for this finding may be related to the study design: both groups received similar total intake calories during therapy. In fact, there was no significant difference in dietary intake calories and total intake calories between the two groups. In the PN group, however, the intake caloric of EN supplementation in the EN group was equal to that provided to patients on parenteral nutrition. The differences in the incidences of hematological adverse events between the two cannot be due to differences in nutritional status between the two, but probably due to differences in the type of intake calories, enteral or parenteral. In fact, in the 6 patients of the EN group who could not continue taking EN supplementation, the frequencies of leukopenia and neutropenia of grade 3 or 4 were 33% and 50%, which were almost comparable to those in patients of the PN group.

In this study, enteral nutrition during chemotherapy did not affect tumor response to chemotherapy. Many previous studies investigated whether nutrition support in patients with cancer undergoing chemotherapy or radiotherapy affect tumor response to treatment or patients survival. The majority of those studies did not show a positive effect for nutrition support on survival or tumor response, although nutrition support significantly increased energy intake and reduced therapy-associated weight loss. Our results of tumor response showed no improvement with EN support is consistent with the above previous studies. Regarding effect of enteral nutrition support on survival, we could not conclude whether EN support improves patient survival or not mainly because of the short follow-up time.

One limitation of the present study is that the possibility that the reduced toxicity in EN group was due to the omega-3 fatty acids, which were abundantly present in enteral nutritional supplement used in this study, cannot be ruled out. The treatment protocol was arranged to equalize intake calories of nutritional support (enteral or parenteral) between EN group and PN group, but the composition of EN support and PN support was not identical. While EN support contains less carbohydrate and less amino acids than PN support, EN support contain more fatty acids including omega-3 fatty acids. In mice, omega-3 fatty acids are reported to reduce the chemotherapy-related toxicities including intestinal damage and hematological toxicities. Moreover, recent study showed that nutritional intervention with fish oil appear to prevent deterioration of weight and muscle mass during chemotherapy in patients with non-small lung cancer. Thus, omega-3 fatty acids in enteral nutritional supplement may contribute to the reduced incidence of hematological toxicities. In fact, the ratio of omega-3 fatty acids to omega-6 fatty acids at day 14 was significantly higher in patients of the EN group, compared to those of the PN group. To examine whether enteral nutrition support or omega-3 fatty acids supplementation is important in terms of reducing chemotherapy-related hematological toxicities, we now plan to conduct prospective randomized study comparing enteral nutrition containing omega-3 fatty acids with enteral nutrition without omega-3 fatty acids in patients who receive cisplatin-based chemotherapy for esophageal cancer.

In conclusion, the present study demonstrated that enteral nutritional support using omega-3 fatty acids-rich nutritional supplements during neoadjuvant chemotherapy reduced chemotherapy-related hematological toxicities such as leukopenia and neutropenia without affecting tumor response to chemotherapy in patients with esophageal cancer. Further studies are required to determine the mechanism of action of EN support on chemotherapy-related hematological toxicities.

Grants/funding

This study is supported in part by a grant from Osaka Foundation for the Prevention of Cancer and Cardiovascular Diseases.

Statement of authorship

The authors' responsibilities were as follows: HM and YD: design of the study, collection and analysis of data, and writing of the manuscript; MY, TY, RH, MY, EH, MM, OS, KT and MM: design of the study, collection and analysis of data. All authors read and approved the final manuscript.

Conflict of Interest

There is no conflict of interest from authors related this study.

Acknowledgments

We would like to thank Dr Motohiro Hirao and Dr Yutaka Kimura for data analysis.

References


