Impact of EPA nutritional approach on cachexic patients with advanced hypopharyngeal cancer treated by induction chemotherapy

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Abstract

Introduction
Induction chemotherapy is often performed when treating hypopharyngeal cancer in order to preserve organs. A significant problem for treatment is that cachexia usually occurs in advanced hypopharyngeal cancer patients during the induction chemotherapy. Eicosapentaenoic acid (EPA) is reported to modulate the immune function and improve cachexia in cachexic patients with advanced cancer. The aim was to investigate the nutritional effects of induction chemotherapy on patients with hypopharyngeal cancer and to improve prognosis through the use of EPA.

Material and methods
Thirty-one patients with hypopharyngeal cancer received induction chemotherapy during the period of 2011-2012. Nutritional parameters (albumin, total protein, and body weight) were evaluated before and after induction chemotherapy.

Results
All patients experienced varying degrees of malnutrition. Serum albumin levels and total protein levels became significantly worse than those recorded prior to induction chemotherapy. In contrast, our data indicated that EPA significantly improved the condition of cachectic patient after induction chemotherapy. A 71-year-old man with stage IV hypopharyngeal cancer received induction chemotherapy. The response was progressive disease, and cachexia rapidly became worse. EPA enteral nutritional supplementation was adopted in order to improve his cachexia. Within 2 weeks of EPA treatment, the systemic inflammatory response was resolved, and the serum levels of albumin increased. These improvements allowed us to conduct radical surgery. There were no postoperative complications, and no recurrence has been observed. A prospective randomized trial is now being conducted to confirm the effectiveness of EPA nutritional treatment.

Conclusion
In patients with hypopharyngeal cancer who experienced malnutrition after induction chemotherapy, EPA nutritional treatment significantly improved the cachexia and therefore made it possible to conduct radical treatment.

Introduction
Induction chemotherapy is generally performed for organ preservation and preventing distant metastasis for hypopharyngeal cancers. Induction chemotherapy also provides predictive and prognostic information that is useful for determining the suitability of radical treatment such as surgical resection or intensive chemoradiation. Docetaxel, cisplatin, and fluorouracil (TPF) are typically used for the treatment of hypopharyngeal cancer1.

The serum albumin levels are very low in advanced hypopharyngeal cancer patients with cachexia. Saline hydration often causes systemic oedema, pleural effusion, or cardiac insufficiency. Consequently, radical therapy cannot always be implemented. Cachexia results from specific metabolic mechanisms that cause a reduction in energy intake, and also host-derived inflammatory cytokines2,3 including tumour necrosis factor-α (TNF-α), interleukin-6 (IL-6) and tumour-derived factors4,5. EPA is reported to be modulated both directly through eicosanoid production and indirectly through decreased productions of TNF-α, IL-6, and tumour-derived factors6,7. These anticytotoxic properties of EPA have been reported in patients with advanced pancreatic cancer8. There is much evidence suggesting that the use of EPA improves the postoperative immunological response and accelerates the recovery from immunosuppression following surgical trauma. Moreover, the incidence of infectious complications is reduced9,10.

In the following study, we report a case of advanced hypopharyngeal cancer in a patient for whom EPA enteral nutritional supplements improved his cachetic condition after induction chemotherapy. This enabled radical surgery to be conducted.

The objective was to investigate the nutritional effects of induction chemotherapy on patients with hypopharyngeal cancer and to improve the prognosis through the use of EPA.

Material and methods
This work conforms to the values laid down in the Declaration of Helsinki (1964). The protocol of this study has been approved by the relevant ethical committee related to our institution in which it was performed. All subjects gave full informed consent to participate in this study. Thirty-one patients with hypopharyngeal cancer received induction chemotherapy (combining Cisplatin, Docetaxel, and 5-FU) during the period of 2011-2012.

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Results
All 31 patients experienced varying degrees of malnutrition. Serum albumin levels and total protein levels became significantly worse than those recorded prior to induction chemotherapy. However, there was no significant change recorded in body weight (Figure 1). In contrast, our data indicated that EAP significantly improved the cachexia following induction chemotherapy.

Case report
A 71-year-old male had a 6-month history of dysphagia, and was diagnosed as advanced hypopharyngeal cancer with cervical oesophageal invasion. The patient was cachectic, as indicated in the clinical laboratory data on admission: serum albumin 2.6 g/dL, pre-albumin 17.3 mg/dL, transferrin 162 µg/dL and CRP 23 mg/L (Figure 2) as recorded using the Glasgow Prognostic Score (GPS) 3.11,12.

The patient’s body weight had decreased by 8 kg (52.7 kg to 44.7 kg) during 6 months.

Enteral nutrition through a nasogastric tube was administered before induction chemotherapy. The nutritional supplementation consisted of energy- and protein-dense products (2000 kcal/day) without EPA.

The patient received induction chemotherapy (docetaxel, cisplatin, and fluorouracil). Saline hydration was required to prevent renal impairment during the induction chemotherapy, but it caused systemic oedema, and the body weight increased from 44.7 kg to 49.7 kg. Induction chemotherapy indicated progressive disease (PD), and the performance status declined as can be seen in the clinical laboratory data: serum albumin 1.8 mg/dL, pre-albumin 20.2 g/dL, transferrin 135 µg/dL, and CRP 9 mg/L. The cachexia progressively became worse. EPA enteral nutritional supplementation with ProSure® (two containers of supplement daily supply 2.2g) was adopted in order to improve the cachexia. Within 2 weeks after EPA treatment, the systemic inflammatory response was resolved, and the serum levels of albumin increased. That patient’s body weight decreased from 49.7 kg to 47.9 kg. The clinical laboratory data improved as follows: serum albumin 2.3 g/dL, pre-albumin 25.7 mg/dL, transferrin 204 µg/dL, and CRP 5 mg/L (Figure 2). These improvements immediately enabled to conduct a radical surgery immediately. After surgery, the patient recovered uneventfully, and oral intake was initiated on the 10th postoperative day. There were no postoperative complications, and no recurrence has been observed.

Discussion
Significant malnutrition exists in up to 35-50% of head and neck cancer patients.13,14,15. Many factors contribute to malnutrition in these patients.
including poor dietary practices, alcoholism, local tumour effects, anorexia, and treatment effects. Induction chemotherapy also has emetogenicity usually, worsens the cachectic condition. In the past, we used nutritional supplementation with energy- and protein-dense products without EPA for advanced hypopharyngeal cancer patients, but for most patients, this could not prevent cachexia.

EPA is a long chain polyunsaturated fatty acid (PUFA) of the omega-3 family. When sufficient EPA is taken, it replaces arachidonic acid, n-6 PUFA, in cell membrane phospholipids, and is a substrate for the synthesis of the 3-series prostaglandins and the 5-series leukotrienes. These products are less immunoinflammatory than the respective 2- and 4-analogs normally synthesized from arachidonic acid. EPA may modulate this both directly through eicosanoid production and indirectly through decreased production of TNF-α, IL-6, and tumour-derived factors. This anti-inflammatory property of EPA has been reported in patients with advanced pancreatic cancer.

There is evidence suggesting that enteral feeding supplemented with immune-modulatory agents improves the postoperative immunological response, accelerates recovery from the immunosuppression following surgical trauma and reduces the incidence of infectious complications. The administration of an EPA-enriched oral nutritional supplement to patients with advanced pancreatic cancer appears to be associated with reversal of the body weight loss, increase of the lean body mass, and improvement in the quality of life. For this reason, we used EPA enteral nutritional supplements for a cachectic patient with progressive hypopharyngeal cancer.

EPA enteral nutritional supplements positively impact patients, as indicated in the improvement of specific nutritional markers (serum level of albumin, pre-albumin and transferrin) and the reduction of reliable markers of the inflammatory status (CRP). As a result, the body weight decreased from the reduction of whole body oedema since, with the elevation of the serum albumin level, the extravascular fluid water could re-enter the circulation and be excreted. As changes in the total body weight can be due to changes in the body’s content of water, fat, or lean body mass, it is important to measure the composition as well as total body weight when evaluating the effects of nutritional therapy in patients with cancer-associated weight loss.

Patients undergoing head and neck cancer surgery have a 20-50% incidence of postoperative complications. These complications, including major wound infections, fistula, anastomotic leakage, and respiratory insufficiency, may lead to not only prolonged hospital stay but also to a poorer prognosis. Snyderman et al. reported that postoperative infectious complications in head and neck cancers were significantly decreased in the patient groups that received an enriched diet with arginine, RNA and omega-3 fatty acids. In our case there were no postoperative complications.

EPA enteral nutritional supplements modulate the immune function and limit catabolism in patients with advanced hypopharyngeal cancer during induction chemotherapy, and may promote patient compliance with radical therapy including chemoradiotherapy and surgery. To confirm the effectiveness of EPA enteral nutritional supplements, we are conducting a prospective randomized clinical trial.

Conclusion

Patients with hypopharyngeal cancer experienced malnutrition after induction chemotherapy. EPA nutritional treatment may increase the opportunity for radical therapy by improving the cachexia.

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References


