MINI-REVIEW

Impact of Omega-3 Fatty Acid Supplements on Gastrointestinal Cancer Patients after Surgery: Beneficial or Useless?

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Abstract

Omega-3 polyunsaturated fatty acids (ω-3 PUFAs) are essential nutrients for human beings and their potential roles against cancer development and progression have become of wide concern recently. Some studies have suggested that perioperative supplementation with omega-3 fatty acids may have beneficial effects in gastrointestinal cancer patients undergoing surgery, while other researchers reported contrary results. This paper reviews recent research to establish therapeutic effects as well as possible underlying mechanisms of ω-3 PUFA actions, and to help explain possible reasons for inconsistent results from different institutions.

Keywords: Omega-3 polyunsaturated fatty acids - gastrointestinal cancer - perioperative patients

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Introduction

Omega-3 polyunsaturated fatty acids (ω-3 PUFAs) are essential for human, which can only synthesize a little in mammal and must obtained from dietary sources. Marine fish oil contains high level of ω-3 PUFA including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) which are of particular interest. EPA is a long-chain ω-3 PUFA that has 20 carbon atoms and 5 double bonds (20 : 5), similarly, DHA has 22 carbon atoms and 6 double bounds (22 : 6).

Increasing number of studies have suggested that ω-3 PUFA has beneficial effects on chronic diseases such as cardiovascular disease (Kar and Webel, 2012; Xin et al., 2012), diabetes (Rudkowska, 2010), autoimmune diseases such as rheumatoid arthritis (Calder, 2007; Chapkin et al., 2009; Miles and Calder, 2012), and cancer (Cockbain et al., 2012; Vaughan et al., 2013). Despite of ongoing advances in surgical technique and patient care, malnutrition and immunity reduction are still common in patients after gastrointestinal surgery. ω-3 PUFA have potent anti-inflammatory properties by incorporating in membrane structure and function, suppressing proinflammatory transcription factors, and modulating the production of eicosanoid. These effects may play important roles in suppressing generalized inflammatory response and then lead to subsequent immunosuppression and capillary leakage after major surgery.

Here we reviewed recent researches of ω-3 PUFAs to assess their therapeutic effects in gastrointestinal cancer patients undergoing surgery, and discussed the possible reasons for inconsistent results reported by different institutions.

Pre-operative Infusion of ω-3 PUFAs

Patients with GI cancer always have severe malnutrition and associated suppression of immunological function preoperatively which can be aggravated by operation and trauma, thus greatly increasing the risk of postoperative complication such as poor wound healing, infection and prolonged hospital stay (Senkal et al., 1999).

In a randomized, double-blind, and controlled clinical trial, Torrinhas et al used parenteral infusion of isolated fish oil as an adjuvant pharmacological agent for the preoperative treatment of gastrointestinal cancer patients, and found this treatment favorably modulated postoperative immune mediators, which was accompanied by the preservation or improvement in leukocyte phenotype (Torrinhas et al., 2013). Nakamura et al also found that oral administration of omega-3 fatty acids for 5 days before surgery may improve not only preoperative nutritional status but also pre- or post-operative inflammatory and immune responses in patients who have cancer (Nakamura et al., 2005). Tsekos et al showed greater benefit, including a lower mortality rate, was found in surgical patients receiving PN with fish oil LE infused perioperatively than those given postoperatively (Tsekos et al., 2004). Caglayan et al found that in the colorectal cancer patients who had nutrition in the 7-day preoperative period, except for the standard enteral nutrition group, there were significantly increasing infiltration of CD56 (+) cells in the mucosal part of the tumor tissue within the CD4 (+) and CD8 (+) cell populations. When the different post-nutrition values were compared, there was foudn to be a marked increase of CD8(+) cells in the immunonutrition group (Caglayan et al., 2012).

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Postoperative Infusion of ω-3 PUFAs

Jiang and colleagues randomized 206 patients with gastrointestinal cancer and perceived need for postoperative nutrition in a double-blind study to receive intravenous infusions of soybean oil (1-2 g per kg bodyweight per day) or soybean oil plus fish oil emulsion (1.0 and 0.2 g per kg bodyweight per day) for 7 days after surgery (Jiang et al., 2010) . The group receiving fish oil had a significantly reduced length of hospital stay and systemic inflammatory response syndrome, but no significant difference was found in the frequency of infectious complication. Marano and co-workers included 109 patients with gastric cancers (either colorectal carcinoma or gastric carcinoma) in a prospectively randomized trial to receive early postoperative enteral immunonutrition (formula supplemented with arginine, omega-3 fatty acids and ribonucleic acid [RNA]) or an isocaloric-isonitrogenous control (Marano et al., 2013). Postoperative infection, anastomotic leak rate, and length of hospitalization were evaluated. Early postoperative enteral immunonutrition significantly improves clinical and immunological outcomes in gastric cancer patients undergoing gastrectomy. Similar results were also reported in a meta-analysis which concluded that intravenous fish oil was likely to reduce infections, the length of hospital stay and liver dysfunction, but no significant change in mortality and postoperative medical cost in post-surgery patients (Li et al., 2014).

Liver Protective Effects of ω-3 PUFAs

Researchers found the increase of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) was to a lesser extent in the intervention group and stayed within the normal range, although they increased in most patients after surgery (Wei et al., 2014). This indicated that ω-3 fish oil fat emulsion may alleviate the hepatic damage resulting from gastric cancer surgery, which may be attributed to the role of ω-3 fatty acids in increasing liver blood perfusion, reducing intestinal bacterial translocation (Pscheidl et al., 2000), reducing the release of prostaglandin E2 (PGE2), leukotriene B4 (LTB4) and platelet activating factor which inhibit mRNA expression of L-1β, IL-2 and TNF-α, thereby blocking the excessive inflammatory response to protect the function of vital organs (Koch and Heller, 2005).

Negative Results of ω-3 PUFAs Supplements

On the other side, some studies didn't get positive results when administrating ω-3 PUFA. In Sorensen's study, ω-3 PUFA-enriched oral nutritional supplement did not alter postoperative complications (infectious and/or non-infectious), length of hospital stay, need for intensive care, blood loss during surgery or readmission rates in patients undergoing surgery for colorectal cancer, even there was a higher content of ω-3 PUFAs and a lower content of the ω-6 PUFA arachidonic acid in granulocytes (Sorensen et al., 2014). And they even found a lower serum haemoglobin level after surgery in patients who received 7 days' oral supplementation with 3 g EPA plus DHA daily. Fortunately, this decrease in haemoglobin concentration was not associated with blood loss or need for blood transfusion. The ω-3 PUFA scould inhibit platelet aggregation and decrease haemoglobin levels that may increase bleeding risk (Schmidt, 1997; Sorensen et al., 2014). But Harris concluded that the benefits of ω-3 PUFAs outweigh the theoretical risk of increased bleeding (Harris, 2007).

Similarly, Sultan and co-workers found an increase in plasma concentrations of ω-3 PUFA in those patients who received an ω-3 PUFA-containing enteral immune enhancing diet for 7 days before or after operation for oesophagogastric cancer, but no differences in the total number of infective complication, intensive care unit stay, hospital stay or mortality (Sultan et al., 2012). Thus, despite an increase in plasma concentrations of ω-3 PUFA, no effect on clinical outcome measures was found. Recently, the negative results of ω-3 PUFA were also reported in patients with cerebrovascular disease (Risk et al., 2013), Alzheimer's disease (Quinn et al., 2010), and macular degeneration (Age-Related Eye Disease Study 2 Research, 2013).

Differences between these studies could be caused by the difference in study populations: only patients with colorectal carcinoma compared with a mix of surgical patients. Jiang et al provided supplements only after surgery and as an intravenous treatment [14]. The latter ensures a quicker incorporation of the presumed active substances (ω-3 PUFA) into the cell membranes of immune active cells and perhaps better promotes a positive impact on clinical outcome. Furthermore, the range of complications reported in the present study exceeds that in the other two studies. The rather high infection rate in the present study could be explained by the inclusion of some minor infections such as positive culture of fungi. Lack of enhanced recovery pathway could also account for the high infection rate.

Conclusions

Only few studies have examined the potential therapeutic benefit of ω-3 PUFAs in patients with gastrointestinal cancer following surgery, and no clear evidence for recommending specific treatment with ω-3 PUFA in these patients. However, data are encouraging and more clinical studies are required in order to clarify these potential therapeutic effects.

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