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Invited critical review

Omega-3 fatty acid effects on biochemical indices following cancer surgery

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Abstract

Epidemiological studies have indicated that a high intake of saturated fat and/or animal fat increases the risk of colon and breast cancer. Laboratory and clinical investigations have shown a reduced risk of colon carcinogenesis after alimentation with omega-3 fatty acids, as found in fish oil. Mechanisms accounting for these anti-tumor effects are reduced levels of PGE_2 and inducible NO synthase as well as an increased lipid peroxidation, or translation inhibition with subsequent cell cycle arrest. Further, omega-3 eicosapentaenoic acid is capable of down-regulating the production and effect of a number of mediators of cachexia, such as IL-1, IL-6, TNF-alpha and proteolysis-inducing factor. In patients with advanced cancer, it is possible to increase energy and protein intake via an enteral or parenteral route, but this seems to have little impact on progressive weight loss. Fish oil administration improved patients' conditions in cancer cachexia and during radio- and chemotherapy. In patients undergoing tumor resection surgery we observed improvement of liver and pancreas biochemical indices when omega-3 fatty acids were administered.

This paper is a review of recent developments in the field of nutrition in cancer patients with emphasis on the acute phase response following cancer surgery and the beneficial aspects of fish oil administration.

Keywords: Cancer; Nutrition; Fish oil; Immunity; Acute phase response; Omega-3 fatty acids

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1. Introduction

1.1. Omega-3 and omega-6 fatty acids

Maritime food sources include two omega-3 polyunsaturated fatty acids (omega-3 FA) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), as opposed to omega-6 polyunsaturated fatty acids (omega-6 FA) found in terrestrial sources (the typical Western diet). Deep-sea fish contain 0.1–1.2% omega-3 FA such as EPA (C20:5) and DHA (C22:5) [1] and therefore are the main omega-3 FA nutritional reservoir for humans. Historically, the intake of saturated FA and unsaturated omega-3 and omega-6 FA was approximately equal. Modern nutritional habits that emphasize industrially produced vegetable oils and animal fats have disturbed this balance, resulting in a proportional decrease of omega-3 FA intake [1]. Intensive research in recent years has broadened our understanding of omega-3 FA effects, uncovering for instance an omega-3 FA dependant formation of eicosanoids with immuno-modulatory characteristics.

When available, EPA is released from membrane sources in states of inflammation and competes with arachidonic acid (AA) for enzymatic metabolism resulting in a reduction of inflammatory and chemotactic derivatives. On the subcellular level, omega-3 FA modulate nuclear factor kappa-B derived upregulation of the acute phase response and, thus, prevent overshooting immune response. As a result, improved outcome after supplementation with omega-3 FA was observed in a broad range of diseases ranging from chronic disorders to cancer and critical patient conditions.

In contrast to numerous studies investigating the effects of long-term (weeks to months) supplementation with omega-3 FA, more recent interest has focused on the question of whether or not omega-3 FA are integrated into the membrane lipid pool even after short-term intravenous application. In a study of patients undergoing major abdominal surgery, incorporation of omega-3 FA was shown in liver and gut mucosa tissue as well as in tumor tissue after a five days of preoperative administration [2].

Following major abdominal surgery we found that short-term intravenous administration of omega-3 FA improved liver function without untoward effects on platelet function and coagulation. Moreover, omega-3 FA helped to maintain the balance of pro- and anti-inflammatory cytokines and thus prevented hyper-inflammatory complications. This was confirmed in 661 patients who received a fish oil infusion during peri-operative intensive care therapy. Fish oil significantly decreased the incidence of co-morbid infections. If at least 5% fish oil was included in daily alimentary intake, patients needed substantially less antibiotics and had shorter length of hospital stay. The two main factors contributing to the length of stay in a multifactor-regression model were the amount of omega-6 FA (+1.6 d/100 g) and the delay of nutrition onset (+1.42 d/day of delay) [3]. Subsequent in-depth diagnosis-related analysis of the same database showed that fish oil had the most favorable effects on survival, infection rates, and length of stay when administered in doses between 0.1 and 0.2 g/kg/day. Multiple quasi-linear regression models revealed that a fish oil dose of 0.23 g/kg/day reduced intensive care unit stay and showed that an inverse linear relationship exists between dosage and intensive care unit stay after major abdominal surgery [4].

In view of clinical consequences, these findings with FA supplementation show prophylactic benefit as well as mitigation of acute effects and were readily achieved by a simple rearrangement of nutritional components.

1.2. Lipid mediators

Lipid mediators are a fundamental part of the complex process leading to inflammation. The inflammatory reaction is characterized by the stimulation of humoral and cellular mediator systems and the release of a wide variety of inflammatory mediators that alter microvascular tone and permeability. Lipid mediators are essentially involved in the regulation of these complex actions. Prostaglandins such as PGE_2 and PGI_2 support the formation of inflammatory edema (tumor) by their vasodilative properties (rubor) and contribute to the development of hyperalgesia at the site of inflammation (dolor). FA peroxides and leukotrienes additionally increase local permeability and are potent chemo-attractants for neutrophil granulocytes resulting in a further accumulation of phagocytes in the microcirculation at the site of action.

The precursors for all lipid mediators are FA as a part of cellular lipid membranes. It should be noted that a fundamental component of membrane lipids is AA, a four-fold polyunsaturated FA consisting of twenty carbon atoms.

1.3. Nomenclature

Unsaturated FA are divided into mono- and poly-unsaturated FA. Depending on the location of the first double bond (as determined from the methyl end of the polyunsaturated FA), these molecules are further classified as omega-3, omega-6 and omega-9 FA. Oleic acid (C18:1) is a mono-unsaturated FA which can be synthesized by mammalians, whereas omega-3 and omega-6 FA are essential for humans [5]. Omega-6 FA, such as linoleic acid (C18:2) and AA (C20:4), are found in plant oils and fatty tissues of mammalians and represent the