

Improving Appetite in Patients with Advanced Cancer: Putting Fish Oil to the Test

Bruera E, Strasser F, Palmer JL, et al. Effect of fish oil on appetite and other symptoms in patients with advanced cancer and anorexia/cachexia: a double-blind, placebo-controlled study. J Clin Oncol 2003;21:129-34.

Study Overview

Objective. To determine whether high doses of fish oil given over 2 weeks improve symptoms in patients with advanced cancer and decreased weight and appetite.

Design. Randomized, double-blind placebo-controlled trial.

Setting and participants. Patients with advanced cancer (recurrent or metastatic) in Canada. Eligibility included the presence of anorexia and weight loss (> 5% of pre-illness weight), ability to maintain oral intake for 2 weeks, and normal cognition.

Intervention. Patients were randomized to 18 gelatin capsules daily containing either 1000 mg of fish oil (180 mg of eicosapentaenoic acid [EPA], 120 mg of docosahexanoic acid, and 1 mg of vitamin E) or 1000 mg of a placebo (olive oil). After complaints of vomiting in approximately 10 patients in both arms, the trial was amended to require 6 capsules a day, with encouragement to take up to 18 per day. Adjunctive therapy included antiemetics, analgesics, steroids, prokinetics, antidepressants, and stimulants. No patient received progesterin. 5 patients received chemotherapy and 4 hormonal therapy.

Main outcome measures. Baseline and day 14 measurements were obtained. Appetite, nausea, tiredness, and well-being were assessed on a visual analogue scale (VAS) of 0 to 100 mm (0 = best, 100 mm = worst). Food intake was recorded. Anthropometric measurements were performed on days 1 and 14.

The primary outcome was appetite as measured on the VAS. Descriptive statistics, summarized baseline characteristics and assessment, and regimen tolerability were secondary outcomes.

Main results. 91 eligible patients were randomized, with 46 allocated to fish oil and 45 to placebo. Approximately 13 patients in each group discontinued treatment because of disease progression or death, gastrointestinal symptoms (11% overall in each group), or loss to follow-up. 30 patients in

each arm were able to complete treatment (60/91; 66%). All side effects subsided on discontinuation of the capsules. The average age of participants was 64 years. Cancer types included genitourinary, breast, gastrointestinal, lung, head and neck, and sarcoma tumors. Baseline weight loss was approximately 16 kg in both groups, whereas baseline appetite was 58 ± 24 mm and 67 ± 19 mm in the fish oil and placebo groups, respectively ($P = \text{NS}$). There were no imbalances in baseline weight, appetite, tiredness, nausea, well-being, caloric intake, performance status measures, lean mass, or arm measurements.

Patients in the fish oil group took a mean of 9.8 ± 4 capsules per day compared with 9.2 ± 3 in the placebo group. No significant differences in symptomatic or nutritional parameters were found. There was no correlation between changes in variables between days 1 and 14 and the fish oil doses. The majority of patients were unable to ingest more than 10 fish oil capsules per day because of burping and aftertaste.

Conclusion. Fish oil did not significantly influence appetite, tiredness, nausea, well-being, caloric intake, nutritional status, or function after 2 weeks compared with placebo in patients with advanced cancer and loss of both weight and appetite.

Commentary

Anorexia and weight loss are common in patients with advanced cancer and other chronic progressive conditions such as AIDS, congestive heart failure, or obstructive lung disease. In patients with cancer, malnutrition (sometimes referred to as cancer cachexia) is associated with increased morbidity and predictive of early mortality [1]. Nutritional counseling probably offers little clinical benefit and parenteral or enteral supplementation often are not feasible. Progestins such as megestrol acetate [2] and corticosteroids have been shown to stimulate appetite and contribute to weight gain (and possibly to well-being) while reducing nausea and vomiting. However, these agents can be associated with toxicity (progestins: thromboembolic events,

adrenal insufficiency; steroids: myopathy, ulcers). Moreover, these effects may be difficult to sustain and have not correlated with improvements in chemotherapy response rates or overall survival. Other agents, such as dronabinol (the active component in marijuana), melatonin, and thalidomide have demonstrated mixed results to date. EPA, an α -3 omega fatty acid found in fish oil, may be a promising new agent because of its immunomodulating effects [3].

In this well-designed trial, Bruera tested a common form of fish oil supplements with placebo capsules in a moderately-sized group of patients with reported advanced cancer and cachexia. No meaningful benefits could be found in the patients who took daily fish oil supplements. The study was randomized, prospective, and baseline characteristics appeared similar. Little information was provided about the prognosis of the participants or extent of prior therapies, but most (if not all) probably met criteria for poor nutritional status and overall performance based on the baseline scores for weight loss, appetite, and functional assessment.

There are several potential explanations for these results worth considering. First, all of the patients were allowed to take other supportive therapies, potentially including steroids; this perhaps explain minimal improvements in appetite and well-being seen in both groups but masks any true benefit of fish oil alone. In addition, these findings may be an effect of being followed closely on a study, with patient contact impacting favorably on the placebo group.

Perhaps 14 days is simply not enough time to assess meaningful improvements in appetite or fatigue that translate into sustained weight gain and functional improvement. Finally, the supplement dose may be too low, or patients were poorly compliant with a supplement associated with belching and a fish aftertaste (compliance rates were not reported.)

Applications for Clinical Practice

The role of fish oil supplements in patients with advanced cancer and cachexia remains unclear. Progestins or corticosteroids remain the agents of choice.

—Review by David R. Spigel, MD

References

1. Dewys WD, Begg C, Lavin PT, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern Cooperative Oncology Group. *Am J Med* 1980;69:491-7.
2. Bruera E, Macmillan K, Kuehn N, et al. A controlled trial of megestrol acetate on appetite, caloric intake, nutritional status, and other symptoms in patients with advanced cancer. *Cancer* 1990;66:1279-82
3. Gogos CA, Ginopoulos P, Salsa B, et al. Dietary omega-3 polyunsaturated fatty acids plus vitamin E restore immunodeficiency and prolong survival for severely ill patients with generalized malignancy: a randomized controlled trial. *Cancer* 1998;82:395-402.

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