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The Effect of Intravenous Omega 3 Fatty Acids (Omegaven) on Quality of Life and Nutritional Status of Patients with Advanced Cancer

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1. Abstract

1.1. Background: Several studies found omega 3 fatty acids helpful in stabilizing weight or decrease the rate of weight loss in advanced cancer patients. The aim of this study was to evaluate the efficacy of intravenous (iv) omega 3 fatty acids (Omegaven. Fresenius Kabi) on quality of life and weight of patients with advanced and metastatic malignancies with weight loos.

1.2. Methods: In this study 50 patients with advanced cancer were given Omegaven iv once a week. Omegaven includes 10gr highly refined fish oil, 2.82g eicosapentaenoic acid, 3g docosahexaenoic acid and other acids in 100ml emulsion given by iv infusion. Total energy in one infusion is 470kJ/100ml= 112kcal/100ml. Some patients received only omegaven and others received omegaven and chemotherapy sequentially. Clinical and laboratory characteristics of patients before and after omegaven administration were compared.

1.3. Results: Mean duration of treatment was 11 weeks (range: 3-24 weeks). Patients lost a mean of 4.19kg of their weight within the 2-3 months prior to receiving omegaven, while their weight increased by an average of 0.24kg after omegaven treatment (p=0.02). Karnofsky performance status increased from 50% before omegaven to 60% after omegaven. Total protein levels increased by 0.34mg on the average after omegaven and albumin levels increased by 0.24mg compared to baseline levels before omegaven (p=0.04). No side effects were documented.
1.4. Conclusions: Intravenous omigaven significantly increased weight, performance status, proteins and quality of life in advanced and cachectic cancer patients. No side effects were reported. Omegaven given iv is safe and effective in treatment of cancer cachexia.

2. Keywords: Omega 3, cancer, cachexia, weight loss

3. Introduction

The importance of nutritional support in cancer patients is in consensus. Cancer cachexia is a syndrome characterized by progressive involuntary weight loss. Clinical features include host tissue wasting, anorexia, skeletal muscle atrophy, fatigue, anemia, and hypoalbuminemia [1]. It is a major contributor to mortality and morbidity in patients with advanced cancer [2 ,3].

Weight loss in cancer patients appears to result from metabolic changes characterized by relative hypermetabolism, an acute-phase protein response and a failure of anabolism compounded by inadequate food intake [1]. Possible mediators of this process are interleukin-1, interleukin-6, proteolysis inducing factor, neuroendocrine hormones, and tumor necrosis factor [4].

Calories rich diets are not enough to help cancer cachexia patients increase their weight and improve their quality of life. Mostly conventional nutritional supplements increase caloric intake only while cachexia is not addressed [5,6]. In both healthy and cancer patients Eicosapentaenoic acid (EPA) has been shown to have anti-inflammatory properties including downregulation of both proinflammatory cytokine production, leading to improvement of cancer cachexia [7]. There is no consensus in the literature whether EPA can improve cachexia in cancer patients. In a double-blind, placebo-controlled, randomized study on eicosapentaenoic acid diester in patients with cancer cachexia Fearon et al has shown no statistically significant improvement in survival, weight, or other nutritional variables [8]. On the other hand Murphy et al reported that nutritional intervention with 2.2 gr of fish oil per day (which contains EPA) appears to provide a benefit over best supportive care, resulting in the maintenance of weight and muscle mass during chemotherapy [9].

Fish oil (FO) is rich in the n–3 polyunsaturated fatty acid eicosapentaenoic acid (EPA) and DHA. Because EPA and fish oil reduce the production of proinflammatory cytokines it improves cachexia [10, 11]. Several studies of a pure EPA preparation providing 2 g per day EPA or a mixed fish oil preparation with EPA 2 g given every day orally have reported weight stabilization in cachectic cancer patients [12].

Generally oral administration of FO is required for several weeks to produce biological and clinical effects [12]. None the less many cancer patients with advanced disease with or without chemotherapy suffer

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from nausea and vomiting or mechanical difficulties in swallowing. Intravenous administration of fat emulsions enriched with EPA and DHA leads to rapid response and it can be administered to cancer patients with any performance status [13,14].

The aim of our study is to evaluate the efficacy and safety of intravenous omega 3 fatty acids FO (Omegaven. Fresenius Kabi) on quality of life and body weight of patients with advanced and metastatic malignancies.

4. Methods

Fifty eligible patients were included in this prospective observational study from the Ziv Medical Center and the Meir Medical Center in Israel. The study was approved by the Ethics Committee of both Hospitals. Written informed consent was obtained from all patients. Patients received Omegaven; 100 ml fish oil emulsion by intravenous infusion within 30 minutes weekly (Table I). Treatment was done in the daycare of the outpatient clinic. Blood tests were drawn before the first treatment and then repeated every 2 weeks before the iv infusion. The blood tests included complete blood count, liver and kidney function tests, protein and glycerides levels. A questionnaire evaluating Karnofsky performance status (KPS) [15] was filled out by the patients at every treatment. Weight (without shoes and with light cloths) was measured every week. Inclusion criteria included men and women diagnosed with advanced cancer (breast, pancreas, colorectal, lung, and others), age >18 years, patients receiving or not chemotherapy, >10% weight loss while on or after chemotherapy, Karnofsky 40-50, Life expectancy of at least 3 months.

Table I Package insert of Omegaven

Exclusion criteria included BMI>30kg/m2 (BMI=weight (kg) / height (m)2), concomitant treatment with fish-oil supplements, steroids, COX-2 inhibitors, sever hemorrhagic disorder, unstable diabetes, MI/stroke/thromboembolism during the last 3 months, Severe renal dysfunction (estimated GFR<30ml/min), severe liver dysfunction, hypokalemia, known allergy to fish-oil or egg protein, extensive bone marrow involvement. Primary Endpoints: Weight gain during treatment period and improving (Karnofsky) performance status. Secondary Endpoints were improved QOL and improved nutritional status (elevation of plasma proteins).

4.1. Statistical analysis: All analyses were carried out using SPSS Data Analysis Program (ver. 17.1). A Students T test was used to assess for differences in serum protein levels and weight. Chi-squared test was used to assess the association among clinical–pathological features and omegaven intake.

5. Results

Mean age of patients was 58 years (range 39-82). Among the 50 treated patients 27 were males and 23 were females. Primary tumor site was breast, lung, stomach and other malignancies (Table II). Most common site of metastases was liver and bones. KPS was 40-50%. Most patients (90%) were treated with chemotherapy. Omegaven 100 ml emulsion contains Eicosapentaenoic acid (EPA) 2.82g, Docosahexaenoic acid (DHA) 3.09g, highly refined fish oil 10.0g and other nutritional components (Table I). Mean duration of treatment was 11 weeks (range: 3-24 weeks). Patients lost on average 4.19kg of their weight during 3 months prior to receiving omegaven, while their weight increased on an average of 0.24kg after omegaven treatment (p=0.02) (Table III). Performance status increased from 40-50% before omegaven to 60% KPS after omegaven. Total protein levels increased by a mean of 0.34mg after omegaven treatment and albumin increased by a mean of 0.24mg compared to baseline levels prior to omegaven therapy (p=0.04) (Table 3). No side effects were documented. A fishy taste in the mouth during treatment was documented by 48% of patients, disappearing after few hours. Patients reported better

quality of life and increased appetite resulting in improvement of their nutritional status.

6. Discussion

Weight loss and cachexia are main problems in patients with advanced and poor prognostic malignancies. Stabilization of additional weight loss and even a small gain in weight of 1 to 2 kg, is likely to be clinically important to these patients. Uncontrolled studies of either a mixed fish oil preparation providing approximately 2 g per day EPA or a pure EPA preparation providing 6g per day have reported weight stabilization in cachectic pancreatic cancer patients when treated over a period of 8 weeks [16, 17]. Fearon et al found that although of marginal statistical significance, the mean weight of the patients who received 2g EPA per day over 8 weeks increased by 1.2 kg (95% CI, 0 kg to 2.3 kg) [8].

In this prospective study 50 patients from 2 cancer centers were given omigaven which includes fish oil, EPA, DHA and other supplements (table1). All patients were in poor performance status, with advanced and metastatic disease. All were in different degrees of cachexia. After a mean of 11 weekly treatments with omegaven patients achieved a minimal weight gain of 0.24 kg. The same patients suffered an average of 4.19 kg weight loss within 2-3 months before omegaven administration. Although most patients in this study were receiving chemotherapy treatment which was accompanied by nausea in the majority of them they maintained muscle mass and weight. Patients also showed elevation of total protein, albumin and globulin. Similar to other studies in the medical literature [18] this improvement allowed patients to continue chemotherapy, other molecular targeting therapies and hormonal treatments [18].

Oral administration of FO for several weeks is required to produce biological effects and weight gain or stabilization [19]. Metastatic cancer patients may have nausea and vomiting due to many reasons in addition to chemotherapy. This leads to cachexia, weakness and decrease in their performance status. Patients in this status have difficulty receiving drugs orally. Intravenous administration of FO and/or EPA is an easy and sure way to take FO. It was observed that intravenous administration of fat emulsions enriched with n-3 PUFA leads to rapid incorporation of n-3 fatty acids into phospholipids of platelets or monocytes [20].

Previous studies have reported controversial results when FO or EPA were used. Some of the studies failed to show increased body weight with the use of EPA compared to control groups [21, 22]. Other studies showed a median increase in weight of 2 kg over 7 weeks and an increase in physical activity when EPA was given; with or without a high-protein, calorie rich oral nutritional supplement [23, 24]. According to these studies an optimum net dose of EPA as marine triglycerides is suggested to be at least 2g per day when given in combination with oral nutritional supplements [25]. In the recent study EPA was given in mean dose of 2g intravenously. This dose is equivalent to more than the 2g dose given orally.

Some interventional therapies that have been proposed, including nutritional (dietary, omega-3 fatty acid supplementation), hormonal (insulin), pharmacological (clenbuterol), and nonpharmacological (physical exercise) therapies. Omega-3 (n-3) polyunsaturated fatty acids (PUFAs), especially eicosapentaenoic acid (EPA) and docosahexaenoic acid, are recognized for their anti-inflammatory properties and have been used in therapeutic approaches to treat or attenuate cancer cachexia [26].

All cancer patients treated in this study were in advanced or metastatic stages of the disease. Although we have no control group, patients included in this study had lost an average of 4.19kg of their weight during the 2-3 months prior to omegaven. The purpose of this study was to intervene in cancer cachexia by increasing or maintaining patient's weight and thus improving quality of life. Both aims were achieved.

7. Conclusion

Nutritional intervention with intravenous FO given weekly appears to provide a benefit over supportive care, resulting in significant weight increase, improved performance status, elevated proteins and better quality of life in advanced cancer patients. No side effects were reported. Omegaven given iv seems safe and effective in cancer cachectic patients.

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9. Authors' contributions

Jamal Zidan conducted research, wrote manuscript, analyzed data, performed statistical analysis, and had primary responsibility for the study. Sigalit Tamam, Amira Abzah performed data collection and revision of nursing procedures. Osama Hussein conducted data analyses and revised the manuscript. All authors critically reviewed and approved the final manuscript.