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A randomized clinical trial with two omega 3 fatty acid enhanced oral suplements in head and neck cancer ambulatory patients

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Abstract. – The aim of our study was to investigate whether oral ambulatory nutrition of post surgical head and neck cancer patients with recent weight loss, using two different omega 3 fatty acids enhanced diets could improve nutritional variables as well as clinical outcome.

A sample of 65 ambulatory post surgical patients with oral and laryngeal cancer and recent weight loss was enrolled. At Hospital discharge post surgical head and neck cancer patients were asked to consume two cans per day of either a specially designed omega 3 fatty acid enhanced supplement with a high ratio of omega3/omega6 (I) or a omega 3 fatty acid enhanced supplement with a low ratio of omega3/omega6 (II).

Serum albumin, prealbumin and transferrin concentrations improved with both enhanced formula. Weight stabilization was reached with both formulas. Gastrointestinal tolerance (diarrhea episodes) with both formulas was good (6.45 vs 5.88%: ns). The postoperative infectious complications were similar in both groups (29 group I vs 15.7% group II: ns). No local complications were detected in surgery wound.

In conclusion, at dose taken, omega 3 enhanced formulas with different omega3/omega6 ratios improved serum protein concentrations in ambulatory postoperative head and neck cancer patients with good tolerance.

Key Words:

Head and neck cancer, Immunonutrition, Omega 3 Fatty acids.

Introduction

Patients with head and neck cancer undergoing surgery have a high incidence of postoperative complications, such as anastomotic fistula, wound infections, and major complications[1].

It is known that immune system is frequently affected in these patients[2]. The alterations in the host defense mechanism make patients susceptible to above mentioned complications. Although immune dysfunction could be multifactor, this immune system may be modulated by specific nutritional substrates, such as omega 3 fatty acids[3]. Eicosapentaenoic acid (EPA), an omega 3 fatty acid, has been shown to have anticachectic and antitumour effects in murine adenocarcinoma model[4]. Administration of omega 3 fatty acid or high purity EPA capsules has been associated with weight stabilization in patients with pancreatic cancer[5]. Previous studies have demonstrated in head and neck cancer patients an improvement in weight and complications rate with enteral arginine enhanced formulas after surgery[6]. Both immunonutrients could produce benefits in these patients.

The aim of our study was to investigate whether oral ambulatory nutrition of postsurgical head and neck cancer patients with recent weight loss, using two different omega 3 fatty acids enhanced diets could improve nutritional variables as well as clinical outcome.

Material and Methods

Patients

A sample of 65 ambulatory post surgical patients with oral and laryngeal cancer with recent loss weight (> 5% during previous 3 months) were enrolled and randomized (sealed envelops). Exclusion criteria included: severely impaired hepatic function (total bilirubin concentration >

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3.5 mg/dl) and/or renal function (serum creatinine concentration > 2.5 mg/dl), ongoing infections, major gastrointestinal disease, autoimmune disorders, steroids treatment, and medication could modulate metabolism or weight. The study was a prospective randomized trial carried out from November 2004 to December 2006. Baseline studies on all patients at the moment of Hospital discharge after surgery consisted of complete history taking and physical examination. General assessment of nutritional status included measurements of height, body weight, body mass index (kg/m^2), circumferences and triceps skin fold of the midarm with an additional bioimpedance.

Nutrition

At Hospital discharge post surgical head and neck cancer patients were asked to consume two cans per day of either a specially designed omega 3 fatty acid enhanced supplement with a high ratio of omega3/omega6 (I) or a omega 3 fatty acid enhanced supplement with a low ratio of omega3/omega6 (II) for a twelve week period. Table I shows the composition of the two supplements. Three day diet diaries completed at baseline (week 0), and weeks 12 were used to assess the patient's dietary intakes. One weekend day and two week-days were studied to account for potential day of the week effects on dietary intake. A dietitian instructed patients on how to record food and beverage intake. Mean total energy and macronutrient intakes were calculated using country specific computerized dietary analysis packages. Total dietary intake was calculated by adding oral supplement consumption to spontaneous food intake, asking to record the number of cans of supplements or parts therefore.

Table I. Composition of supplement.

	Group I (1 unit 240 ml)	Group II (1 unit 200 ml)
Total energy (Kcal)	295	310
Protein (g)	15.96	18
Total lipid (g)	6.14	10.6
ω3/ω6	3.7	0.99
Linolenic acid	0.12	0.08
EPA	1.01	0.92
DHA	0.45	0.6
Carbohydrate (g)	43.9	35.8
Dietary fiber (g)	2.64	3

Dietary fiber source: (I) oligofructose, (II) guar gum (31% and inuline 69%).

Patient Monitoring

At the initial assessment body weight was measured to an accuracy of 0.1 kg and body mass index computed as body weight/(height^2). Bipolar body electrical bioimpedance was used to determine body composition[7]. An electric current of 0.8 mA and 50 kHz was produced by a calibrated signal generator (Biodynamics Model 310e, Seattle, WA) and applied to the skin using adhesive electrodes placed on right-side limbs. Resistance and reactance were used to calculate total body water, fat and fat-free mass. Regional changes in body mass were estimated by measuring the circumferences and tricep skin fold of the midarm. Ambulatory postoperative complications were recorded as none, general infections (respiratory tract infection and/or urinary tract infection) and local complications such as fistula and/or wound infection, assessed all complications with standard methods by the same investigator. Gastrointestinal problems related to enteral feeding were also recorded (diarrhea).

Assays

Fasting blood samples were drawn for measurement of, albumin (3,5-4,5 g/dl), prealbumin (18-28 mg/dl), transferrin (250-350 mg/dl) (Hitachi, ATM, Mannheim, Germany), and lymphocytes (1.2-3.5.10^3/uL) (Beckman Coulter, Inc, Los Angeles, CA).

Statistical Analysis

The results were expressed as average ±SD. The distribution of variables was analyzed with Kolmogorov-Smirnov test. Quantitative variables with normal distribution were analyzed with two tailed paired or unpaired Student's t-test and analysis of variance (ANOVA) as needed. Non-parametric variables were analyzed with the Friedman and Wilcoxon test. To minimize the potential for introducing bias, all randomized patients were included in the comparisons, irrespective of whether or not and for how long they complied with their allocated regimen (intention-to-treat analysis). A *p*-value under 0.05 was considered statistically significant.

A power calculation based on weight improvement was performed. Thirty patients in each group were necessary to detect an improvement of 5 kg, with a p value < 0.05 and a power of 80%.

Results

Sixty five patients were enrolled in the study. The mean age was 63.7 ± 10.9 years (6 females/69 males). There were 31 patients in the group I (omega 3 fatty acid enhanced supplement with a high ratio ω3/ω6) and 34 patients group II (omega 3 fatty acid enhanced supplement with a low ratio ω3/ω6), without drop-outs during protocol. Characteristics of the patients on enrolment were similar for the two groups, reflecting the homogeneity of the patients. There were no significant differences with regard to gender, mean age, body weight, location and stage of tumor (Table II). Alcohol habit were similar in both groups (group I 32.2 vs group II 32.3%; ns), no differences were detected in smoking habit (group I 38.7 vs. group II 41.1%; ns).

Duration of supplementation in both groups was similar with an average duration of (group I: 85.8 ± 26 vs group II: 88.9 ± 22.6 days).

To assure adherence to study supplementation program, we dispensed enough formula to our patients to provide 2 units per day. The volumetric consumption rates of the formula were identical for the two groups, with an average of taken units (1.6 ± 0.62 units/day). Total calorie and protein consumption, based on both formula and dietary intake with 3 days food records, were similar in both groups, (calories: group I 2041 ± 509 vs group II 1997 ± 527 cal/day: ns) and (protein: group I 94.68 ± 30 vs group II 94.2 ± 29 g/day: ns). As shown in Table III, no significant intergroup differences in the improvement of the three plasma proteins were detected. No differences were detected in anthropometric parameters (Table IV).

Gastrointestinal tolerance (diarrhea episodes) with both formulas was good, without statistical differences (6.45 vs 5.88%: ns). No vomiting episodes were reported. There were no drop-outs due to intolerance.

The postoperative infectious complications were similar in both groups (29 group I vs 15.7% group II: ns). No local complications were detected in surgery wound, in both groups.

Table II. Patient characteristics.

	Group I N = 31	Group II N = 34
Age (years)	63.9 ± 11.2	62.8 ± 11.4
Women/men	4/27	2/32
Body weight (kg)	70.3 ± 13.	69.4 ± 15.5
BMI	24.7 ± 4.2	24.7 ± 5.7
Disease Stage		
I	0	0
II	2	3
III	9	9
IV	20	22
Diagnosis of disease		
Oral cavity	9	8
Larynx	22	26

No statistical differences.

Table III. Serum protein concentrations and limphocyte count.

Parameters	Baseline	3 months
Albumin (g/dl)		
Group I	3.14 ± 0.9	4.1 ± 0.66*
Group II	2.98 ± 0.6	4.12 ± 0.43*
Prealbumin (mg/dl)		
Group I	20.7 ± 7.1	27.2 ± 5.7*
Group II	23.4 ± 7.5	28.5 ± 4.2*
Transferrin (mg/dl)		
Group I	184.4 ± 41.1	245.39 ± 44.4*
Group II	189.4 ± 50	252.8 ± 48*
Lymphocytes (103 uL/mm^3)		
Group I	1538 ± 454	2090 ± 1158
Group II	1644 ± 520	1790 ± 541

* ($p < 0.05$) with basal values in each group. No statistical differences between groups.

Discussion

Our present finding shows that both omega 3 enhanced enteral formulas improved blood protein concentrations with a weight stabilization in postsurgical head and neck cancer patients.

Malnutrition and immunosupression were two factors of head and neck cancer patients[8,9]. In these tumor patients, malnutrition is due to reduced dietary intake secondary to dysphagia and alcohol consumption[10] and interleukins secreted by tumor with catabolic action played a dominant role[11]. Immunosupression are related to surgery and immunosuppressive capacity of the tumor[12]. There is evidence suggesting that oral nutrition, supplemented with omega 3 fatty acids, improves immune function and reduce postoperative complications, in different group of patients such as pancreatic surgery[13], surgery of stomach

Table IV. Evaluation of anthropometric parameters.

Characteristics	Group I		Group II	
	Baseline	*3 month*	*Baseline*	*3 month*
Weight (kg)	70.3 ± 13.5	70.8 ± 12.9	69.4 ± 15.5	69.8 ± 15.4
Fat free mass (kg)	53.7 ± 8.7	52.7 ± 8.6	51.1 ± 8	49.4 ± 8.4
Fat mass (kg)	15.8 ± 6.6	18.1 ± 8.4	16.7 ± 5.7	17.5 ± 6.5
TS (mm)	11.5 ± 4.7	11.8 ± 6.1	11.6 ± 6.5	11.3 ± 5.6
CA (cm)	27.7 ± 3.4	27.6 ± 4.4	27.7 ± 3.2	27.9 ± 3.3

CA: Circumference arm. TS: Triceps skin fold. (*) $p < 0.05$, differences between time 0 and at 3 months in each group.

and colon-rectum cancer[14], bone marrow transplantation[15], critically ill patients[16], and cancer cachexia[17,18].

However, all these studies[6,7,18] have been performed during hospital stay, with a short period of enteral nutrition. In our study, we analyzed ambulatory patients during three months of oral supplementation, with a significant increase in serum protein concentrations in both groups (formula enhanced with omega 3 fatty acids), without improvement in weight or other anthropometric parameters. Recently, Fearon et al[19] has demonstrated, with an omega 3 enhanced formula with a high ratio ω3/ω6, weight stabilization in patients with pancreatic cancer as our group I. Previous studies in cachectic pancreatic patients suggested that EPA alone at a dose of 2 g/day was associated with weight stability[20], with net gain of lean body mass and an average can consumption of 1.9 cans/day (a dose of 2.1 g/day of EPA). Average units consumption in our study was 1.6 units per day (containing 1.6 g EPA in group I and 1.5 g EPA in group II), with a weight stabilization in both groups. It therefore remains to be tested if compliance can be improved whether there would be an increase in net anabolism with secondary increase in lean body mass and weight.

Few studies in this topic area have been published. Perhaps other factors such as taste of formula, other inmunonutrients such as arginine[21] and genetic background[22] could improve the nutritional results in these patients.

In conclusion, at dose taken, omega 3 enhanced formulas with different omega3/omega6 ratios improved blood protein concentrations in ambulatory postoperative head and neck cancer patients.

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