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Clinical effects of a w3 enhanced powdered nutritional formula in postsurgical ambulatory head and neck cancer patients

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Abstract

Background: **Patients with head and neck cancer undergoing surgery have a high risk of nutritional complications.**

Objective: **The aim of our study was to investigate the influence of an oral w3 enriched immunoenhanced powdered formula in nutritional and biochemical parameters in postsurgical ambulatory patients with head and neck tumor.**

Design: **A population of 33 ambulatory postsurgical patients with oral and laryngeal cancer was enrolled. At Hospital discharge postsurgical head and neck cancer patients were asked to consume two units per day of a w3 enriched immunoenhanced powdered formula for a twelve week period.**

Results: **The mean age was 61.3 ± 9.1 years (6 female/27 males). Duration of supplementation was 95.9 ± 21.1 days. A significant increase of albumin and transferrin levels was observed, in total group and in patients undergoing radiotherapy and without it. No differences were detected in weight and other anthropometric parameters in total group and in patients with radiotherapy during the protocol. Nevertheless, patients without radiotherapy showed a significant improvement of BMI; weight, fat free mass and fat mass.**

Conclusions: **At dose used, an omega 3 enriched powdered formula improved seric protein levels in ambulatory postoperative head and neck cancer patients. Improvement of weight, fat mass and fat free mass was observed in patients whom not received radiotherapy during the follow up.**

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EFECTOS DE UNA FÓRMULA NUTRICIONAL EN POLVO ENRIQUECIDAD CON W3 EN PACIENTES AMBULATORIOS POSTQUIRÚRGICOS CON CÁNCER DE CABEZA Y CUELLO

Resumen

Antecedentes: **Los pacientes con tumores de cabeza y cuello sometidos a cirugía presentan un alto riesgo de complicaciones nutricionales.**

Objetivo: **El principal objetivo de nuestro trabajo fue evaluar la influencia de un suplemento oral en polvo inmunoenriquecido con ácidos grasos omega 3 en pacientes postquirúrgicos ambulatorios con tumores de cabeza y cuello.**

Diseño: **Una muestra de 33 pacientes postquirúrgicos ambulatorios con tumores de cabeza y cuello fue evaluada. Tras el alta hospitalaria, los pacientes recibieron dos envases al día de un suplemento inmunoenriquecido con omega 3 en polvo durante 12 semanas.**

Resultados: **La edad media fue de 61,3 ± 9,1 años (6 mujeres/27 varones). La duración media de la suplementación fue de 95,9 ± 21,1 días. Se detectó un aumento significativo en los niveles de albúmina y transferrina en los pacientes del grupo global, en los que recibieron radioterapia y en los que no al recibieron. El peso y los parámetros antropométricos no mejoraron en el grupo global ni en los que recibieron radioterapia. Sin embargo los pacientes que no recibieron radioterapia tuvieron un aumento de la masa magra, peso y masa grasa**

Conclusiones: **A la dosis usada, la formula en polvo enriquecida en omega 3 mejoró lo niveles de proteínas séricas. Por otra parte los pacientes que no recibieron radioterapia durante el seguimiento presentaron un aumento del peso, masa grasa y masa magra.**

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Palabras clave: *Ambulatorio. Ácidos grasos w3. Fórmula en polvo. Cáncer de cabeza y cuello.*

Introduction

Significant malnutrition exists up to 35-50% of patients with cancer of the head and neck.[1] Many factors contribute to malnutrition in these patients, including poor dietary practices, alcoholism, catabolic factors secreted by the tumor, anorexia, cancer-induced cachexia, and treatment effects such as surgical procedures or radiotherapy.[2] This nutritional situation may be modulated by specific nutritional substrates, such as omega 3 fatty acids.[3] Administration of n-3 fatty acid or high purity EPA capsules has been associated with weight stabilization in patients with pancreatic cancer.[4] Good tolerance and an improvement on serum proteins have been demonstrated in patients with head and neck cancer.[5] Omega-3 fatty acids are long-chain polyunsaturated acids that appear to have anti-inflammatory effects, possibly by interference with macrophage eicosanoid production.[6] They play a role on the structural and functional integrity of the cell membrane, intercellular signal transduction, and synthesis of eicosanoids. In particular, they lead the production of prostanoids from the dienoic to the trienoic variety, the latter of which are much less immunosuppressive.[7] By replacing other fatty acids with omega 3 fatty acids, membrane flexibility is enhanced, which is essential for phagocytes.[8] Decrease of proinflamatory cytokines has been found in patients with sepsis.[9] Other immunonutrients, as arginine, could play an important role in this type of patients. It has demonstrated in head and neck cancer patients with enteral arginine enhanced after surgery an improvement in weight and complications rate.[10]

The aim of our study was to investigate the influence of an oral w3 immunoenhanced powdered formula in clinical parameters in postsurgical ambulatory patients with head and neck tumor.

Material and methods

Patients

A population of 33 ambulatory postsurgical patients with oral and laryngeal cancer was enrolled. Exclusion criteria included; severe/moderate impaired hepatic function (total bilirubin concentration > 3 mg/dl) and/or renal function (serum creatinine concentration > 2 mg/dl), ongoing infections, major gastrointestinal disease, autoimmune disorders, steroids treatment, active chemotherapy and medication could modulate metabolism or weight. The study was prospective and carried out from May 2011 to April 2013, it was approved by ethical committee of our Institution (all patients signed an informed consent). 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 tricipital skinfold of the midarm with an additional bipolar bio impedance.

Table I
Composition of supplement (resource support instant®)

	Composition (1 unit 50 g)
Total energy (kcal)	214
Protein (g)	6.5
Total lipid (g)	7.5
W3	1.5
EPA	0.5
MCT	0.25
Carbohydrate (g)	30.0
Dietary fiber (g)	0.75

Dietary fiber: fructoaoligosaccharides.

Nutrition

At Hospital discharge postsurgical head and neck cancer patients were asked to consume two units per day of a w3 enriched inmunoenhanced powdered supplement for a twelve week period. Each unit has 50 g of formula. Table I shows the composition of the supplement Resource support instant®. 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 weekdays 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. In order to improve monitoring of treatment, patients received a phone call from the dietitian every 14 days. Mean total energy and macronutrient intakes were calculated using country specific computerized dietary analysis packages (http://www.ienva.org). Total dietary intake was calculated by adding oral supplement consumption to spontaneous food intake, asking to record the number of units of supplements or parts therefore.

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.[11] An electric current of 0.8 mA and 50 kHz was produced by a calibrated signal generator (Akern EFG, Pisa, It) 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. Precautions taken to insure valid BIA measurements were; no alcohol within 24 hours of taking the test, no exercise or food for four hours before taking the test. Regional

Table II
Patients characteristics

	Group (n = 33)
Age (years)	61.3 ± 9.1
Men/women	22/6
Body weight (kg)	67.8 ± 9.3
Disease Stage	
I	0
II	0
III	12
IV	16
Diagnosis of disease	
Oral cavity	8
Larynx	20

changes in body mass were estimated by measuring the circumferences and tricipital skinfold of the midarm. Radiotherapy treatment was recorded. Gastrointestinal problems related to enteral feeding were also recorded (diarrhea or vomiting).

Assays

Samples were assayed in duplicate in one day by the same investigator to avoid inter-investigator variability. 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), and lymphocytes (1.2-3.5.10^3/uL) with an auto analyzer (Hitachi, ATM, Manheim, Ger).

Statistical analysis

The results were expressed as mean ± standard deviation. The distribution of variables was analyzed with Kolmogorov-Smirnov test. Quantitative variables with normal distribution were analyzed with two tailed paired Student s t-test. Non-parametric variables were analyzed with Wilcoxon test. The analysis was performed in the all group and a posthoc analysis was realized in two groups (patients received radiotherapy and patients without this treatment during protocol). A p-value under 0.05 was considered statistically significant.

Results

33 patients were enrolled in the study. The mean age was 61.3 ± 9.1 years (6 female/27 males). Epidemiological data of population are shown in table II. Duration of supplementation was 95.9 ± 21.1 days. Patients were evaluated in three groups; a total group with all patients (n = 33) , patients with radiotherapy during the protocol as indicated by standard protocols (n = 15) and patients without undergoing radiotherapy (n = 18). The mean age of patients undergoing radiotherapy was 63.1 ± 10.1 years (2 female/13 males), with a duration of supplementation of 99.1 ± 20.8 days. The mean age of patients without radiotherapy was 61.0 ± 8.1 years (4 female/14 males), with a supplementation of 93.1 ± 18.1 days.

Dietary consumption, based on both formula and dietary intake with 3 days food records improved; in total group and in patients treated with radiotherapy and without it. Calories, proteins, carbohydrates, lipids, w3 fatty acids, EPA and dietary fiber intakes increased in a significant way. The increases of these parameters were similar in the three groups. And the nutritional powdered formula represent a 9.6% of the total daily calories, a 14.1% of protein intakes, 14.5% of fat intakes and 9.85 of dietary fiber intakes.

As shown in table IV, a significant increase of albumin and transferrin levels was observed, in total group and in patients treated undergoing radiotherapy and without it.

No differences were detected in weight and other anthropometric parameters in total group and in patients with radiotherapy during the protocol (table V). Nevertheless, patients without radiotherapy showed a significant improvement of BMI; weight, fat free mass and fat mass.

Table III
Dietary intakes

Nutrients	*Total group (n = 33)*		*No radiotherapy group (n = 18)*		*Radiotherapy group (n = 15)*	
	Baseline	*3 month*	*Baseline*	*3 month*	*Baseline*	*3 month*
Calories(kcal/day)	1,570.3 ± 586.1	2,228.2 ± 638.2*	1,543.3 ± 803	2,341.1 ± 448.2*	1,570.2 ± 586.2	2,228.5 ± 638.2*
Carbohydrates(g/day)	149.8 ± 63.4	256.8 ± 80.4*	128.4 ± 46.2	265.3 ± 55.2*	149.8 ± 63.3	256.8 ± 80.9*
Fats (g/day)	73.8 ± 35.4	92.7 ± 30.4*	78.1 ± 55.7	98.7 ± 22.7*	73.8 ± 35.4	92.7 ± 30.4*
w3 (g/day)	0.49 ± 0.2	3.79 ± 1.1*	0.38 ± 0.1	3.41 ± 1.8*	0.41 ± 0.1	3.52 ± 1.8*
EPA (g/day)	0.08 ± 0.15	1.19 ± 0.51*	0.07 ± 0.21	1.13 ± 0.41*	0.09 ± 0.31	1.16 ± 0.51*
Proteins(g/day)	73.2 ± 35.4	89.4 ± 24.7*	73.0 ± 48.7	92.3 ± 21.9*	75.1 ± 24.4	88.4 ± 28.1*
Dietary fiber (g/day)	11.9 ± 7.2	15.2 ± 5.4*	9.4 ± 6.1	15.1 ± 6.8*	12.9 ± 7.7	15.1 ± 5.1*

*($p < 0.05$) with basal values.

Table IV
Visceral serum protein and lymphocytes

Parameters	Total group (n = 33)		No radiotherapy group (n = 18)		Radiotherapy group (n = 15)	
	Baseline	3 month	Baseline	3 month	Baseline	3 month
Albumin (g/dl)	3.2 ± 0.4	4.1 ± 0.4*	3.3 ± 0.5	4.3 ± 0.4*	3.1 ± 0.4	3.8 ± 0.3*
Prealbumin (mg/dl)	22.5 ± 7.3	22.1 ± 6.3	24.1 ± 10.1	25.7 ± 4.5	21.2 ± 5.7	18.9 ± 6.1
Transferrin (mg/dl)	215.7 ± 43.4	265.5 ± 50.7*	222.1 ± 54.4	275.2 ± 66.4*	209.8 ± 33.4	257.4 ± 32.4*
Lymphocytes (103 uL/mm^3)	1,426.1 ± 681.1	1,526.7 ± 426.2	1,473.1 ± 529.1	1,521.2 ± 543.8	1,326.1 ± 541.1	1,428.1 ± 413.2

*($p < 0.05$) with basal values.

Table V
Evolution of anthropometric parameters

Parameters	Total group (n = 33)		No radiotherapy group (n = 18)		Radiotherapy group (n = 15)	
	Baseline	3 month	Baseline	3 month	Baseline	3 month
BMI (kg/m^2)	24.8 ± 4.2	24.7 ± 4.6	25.6 ± 4.7	26.3 ± 5.2*	24.1 ± 4.2	23.9 ± 4.2
Weight (kg)	67.1 ± 11.1	67.5 ± 12.7	70.1 ± 7.4	72.2 ± 9.2*	65.9 ± 11.1	64.7 ± 10.8
Fat free mass (kg)	52.4 ± 9.4	51.3 ± 9.1	53.7 ± 9.9	54.5 ± 8.1*	50.6 ± 8.8	49.9 ± 9.1
Fat mass (kg)	15.6 ± 7.3	16.4 ± 8.4	15.9 ± 5.2	17.4 ± 9.5*	15.3 ± 9.1	14.9 ± 8.1
Tricipital skinfold(mm)	12.1 ± 5.3	11.7 ± 4.2	12.1 ± 5.1	12.8 ± 3.1	12.2 ± 5.7	11.3 ± 4.1
Circumference arm (cm)	24.5 ± 3.2	24.6 ± 3.1	25.1 ± 3.1	25.5 ± 2.8	23.3 ± 3.0	23.8 ± 2.5

No statistical differences between time 0 and at 3 months.

Gastrointestinal tolerance (diarrhea and vomiting) was good, without cases during the protocol follow up. There were no dropouts due to intolerance.

Discussion

Malnutrition and immunosupression were two factors of head and neck cancer patients.[12] There is a body of evidence suggesting that enteral feeding; supplemented with w3 fatty acids reduce postoperatively complications.[10] However, most of the studies have been performed with tube feeding and few outpatients through oral supplements.[5,13] Our present finding shows that this powdered omega 3 fatty acids diet improved blood protein concentrations in postsurgical head and neck cancer outpatients and in the subgroup of patients without radiotherapy, a significant increase in anthropometric parameters was reached.

There is evidence suggesting that oral nutrition, supplemented with omega 3 fatty acids, improve immune function and reduce postoperative complications, in different group of patients such as pancreatic surgery,[14] surgery of stomach and colon-rectum cancer,[15] bone marrow transplantation,[16] cancer cachexia,[17] critically ill patients[18] and head and neck cancer.[19] All these studies have been performed during hospital stance, with a short period of enteral nutrition by tube.

In our study, we analyze ambulatory patients during three months of oral supplementation, with a significant improvement in albumin, prealbumin and transferrin concentrations, with an improvement in weight in patients without radiotherapy. Our data agree with 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 dose of 2.1 g/day of EPA. In our patients, the average consumption produced the next EPA intakes (1.13 g EPA in patients without radiotherapy and 1.16 g EPA in patients undergoing radiotherapy). In other study with head and neck cancer patients without radiotherapy,[13] an intake of an omega 3 enhanced supplements (0.6 g EPA per day) improved protein levels without effect on weight. As we can see the concomitant treatments and the dose of EPA have an important role in the benefits of these patients.

The interest in head and neck cancer patients is increased. In a recent systematic review,[21] the authors examined 10 trials that investigated the effects of immunonutrition in patients treated surgically for head and neck cancer. Where stated, all the studies looking at in-hospital postoperative nutrition used arginine and a mix of other immunonutrient (w3 fatty acids, nucleotides, and so on), a main result an improvement in postsurgical complications was reported. The specific efficacy and potential benefits of enteral nutrition support with w3 fatty acids (enteral tube feeding or specifically oral nutrition supplements) are limited. However, in cancer patients undergoing radiotherapy, meta-analysis[22] showed that oral nutritional supplements significantly increase dietary intake compared to routine care and in patients undergoing surgery, meta-analyses

showed significantly shorter length of hospital stay, lower incidence of any complications, infectious complications and lower sepsis cores, but not difference in mortality. Therefore, new studies are needed to evaluate the usefulness of specific immunoenhanced formulas with w3 fatty acids in outpatients with cancer and different treatments.

In conclusion, at dose taken, omega 3 enhanced powdered nutritional formula improved blood protein concentrations in ambulatory postoperative head and neck cancer patients. In patients without radiotherapy this specific formula improved weight, fat mass and fat free mass, too.

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