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Clinical effects of a hypercaloric and hyperproteic oral supplement enhanced with w3 fatty acids and dietary fiber 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 a hypercaloric and hyperproteic oral supplement enriched with w3 FATTY ACIDS and fiber in clinical parameters in head and neck tumor postsurgical ambulatory patients with or without radiotherapy.

Design: A population of 37 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 hypercaloric and hyperproteic oral supplement for a twelve week period.

Results: The mean age was 63.8±7.1 years (16 female/21 males). Duration of supplementation was 98.1±19.1 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: An omega 3 and fiber enriched 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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Key words: *Ambulatory. W3 fatty acids. Fiber. Head and neck cancer.*

EFFECTOS DE UN SUPLEMENTO HIPERCALÓRICO E HIPERPROTÉICO ENRIQUECIDA CON ÁCIDOS GRASOS W3 Y FIBRA 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 hiperenergético e hiperproteico enriquecido en ácidos grasos w3 y fibra en pacientes postquirúrgicos ambulatorios con tumores de cabeza y cuello, con y sin radioterapia.

Diseño: Una muestra de 37 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 hiperproteico e hipercalórico durante 12 semanas.

Resultados: La edad media fue de 63.8±7.1 años (16 mujeres/21 varones). La duración media de la suplementación fue de 98.1±19.1 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: La formula enriquecida en omega 3 y fibra 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 claves: *Ambulatorio. Ácidos grasos w3. Fibra. Cáncer de cabeza y cuello.*

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Introduction

Patients with head and neck cancer undergoing surgery have a high incidence of postoperative complications, based on dysfunction of host homeostasis, defense mechanisms and inflammatory response¹. 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 radiotherapy². Oral supplements (ONS) are useful to treat malnutrition in this type of patients. A recent systematic review shows that ONS significantly reduce hospital (re)admissions, particularly in older patient groups, with economic implications for health care³.

This malnutrition may be modulated by specific nutritional substrates, such as omega 3 fatty acids or dietary fiber⁴. Administration of omega 3 fatty acids or high purity EPA capsules has been associated with weight stabilization in patients with pancreatic cancer⁵. Good tolerance and an improvement on serum proteins have been demonstrated with omega 3-enhanced ONS in patients with head and neck cancer⁶⁻⁷. Omega 3 fatty acids 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 immunosuppressive⁸. Decrease of proinflammatory cytokines has been found in patients with sepsis⁹. Other immunonutrients, as fiber, could play an important role in this type of patients. Fiber has demonstrated immunomodulatory effect in different life-stages¹⁰.

The aim of our study was to investigate the influence of a hypercaloric and hyperproteic oral supplement enriched with w3 and fiber in clinical parameters in head and neck tumor postsurgical ambulatory patients with or without radiotherapy.

Material and methods

Patients

A population of 37 ambulatory postsurgical patients with oral and laryngeal cancer was enrolled. Baseline studies on all patients at the moment of Hospital discharge after surgery consisted of complete history taking and physical examination. Exclusion criteria included; 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 2013 to December 2014, it was approved by ethical committee of our Institution (all patients signed an informed consent).

Nutrition evaluation and support

General assessment of nutritional status included measurements of height, body weight, body mass index (kg/m²), circumferences and tricipital skinfold of the midarm with an additional bipolar bio impedance. At Hospital discharge postsurgical head and neck cancer patients were asked to consume two units per day of a enriched supplement for a twelve week period. Each unit has 125 ml of formula. Table I shows the composition of the supplement Resource support Plus[®]. A dietitian instructed patients on how to record food and beverage intake. 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. 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.

Biochemical 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 gr/dl), prealbumin (18-28 mg/dl), transferrin (250-350 mg/dl), and lymphocytes (1.2-3.5.10³/uL) with an auto analyzer (Hitachi, ATM, Manheim, Ger).

Athropometrical evaluation

At the initial assessment body weight was measured to an accuracy of 0.1 Kg and body mass index com-

Table I
Composition of supplement (Resource support Plus[®])

	<i>Composition (1 unit 125 ml)</i>
Total energy(Kcal)	251
Protein (g)	11.5
Total lipid (g)	7.5
W3	1.9
EPA	1.0
Carbohydrate (g)	25.4
Dietary fiber (g)	3.1

Dietary fiber: fructooligosaccharides and oligosaccharides.

puted as body weight/(height²). Bipolar body electrical bioimpedance was used to determine body composition¹¹. 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 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).

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

37 patients were enrolled in the study. The mean age was 63.8+/-7.1 years (16 female/21 males). Epidemiological data of population are shown in table II. Duration of supplementation was 98.1±19.1 days. Patients

Table II Patients characteristics	
	Group N=37
Age (years)	63.8+/-7.1
Men/women	21/16
Body weight (kg)	62.3 ±15.5
Disease Stage	
I	0
II	0
III	18
IV	19
Diagnosis of disease	
Oral cavity	9
Larynx	28

were evaluated in three groups; a total group with all patients (n=37), patients with radiotherapy during the protocol as indicated by standard protocols (n=13) and patients without undergoing radiotherapy (n=24). The mean age of patients undergoing radiotherapy was 63.2+/-10.9 years (6 female/8 males), with a duration of supplementation of 99.9±20.1 days. The mean age of patients without radiotherapy was 64.0+/-10.1 years (10 female/14 males), with a supplementation of 95.1±18.8 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 (Table III). The increases of these parameters were similar in the three groups. And the nutritional formula represent a 9.5% of the total daily calories, a 14.0% of protein intakes, 14.6% of fat intakes and 9.2% of dietary fiber intakes.

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

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

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

Discussion

Malnutrition and immunosuppression were two factors of head and neck cancer patients¹². There is a body of evidence suggesting that enteral feeding; supplemented with w3 fatty acids, arginine and other immunonutrients reduce postoperatively complications¹³. A limitation of these studies is that most of the studies have been performed with tube feeding and few outpatients through oral supplements¹³⁻¹⁴. Our present finding shows that this hypercaloric and hyperproteic oral supplement improved blood protein concentrations in postsurgical head and neck cancer outpatients and in the subgroup of patients without radiotherapy, a significant increase in weight was observed.

Supplementation with omega 3 fatty acids has been shown a reduction in postoperative complications. This improvement has been demonstrated in different group of patients such as pancreatic surgery¹⁵, surgery of stomach and colon-rectum cancer¹⁶, bone marrow transplantation¹⁷, cancer cachexia¹⁸, critically ill patients¹⁹ and head and neck cancer¹³. A limitation of all these studies it is the setting during hospital stance, with a short period of enteral nutrition by tube. In

Table III
Dietary intakes

Nutrients	Total group (n=37)		No Radiotherapy group (n=24)		Radiotherapy group (n=13)	
	Baseline	3 month	Baseline	3 month	Baseline	3 month
Calories (kcal/day)	1479.3±523.1	2027.2+300.2*	1443.2±503.1	2140.1+421.9*	1510.1±523.2	2001.2+683.1*
Carbohydrates (g/day)	129.3±52.4	236.1+81.4*	128.8±46.2	245.3+52.1*	139.1±60.3	230.8+70.1*
Fats (g/day)	43.2±33.4	87.7+22.4*	40.1±25.1	88.1+20.2*	48.8±31.4	90.1+29.4*
w3 (g/day)	0.41±0.2	3.49+1.0*	0.40±0.1	3.45+1.3*	0.42±0.1	3.53+1.2*
EPA (g/day)	0.07±0.12	1.16+0.50*	0.06±0.11	1.12+0.40*	0.09±0.21	1.18+0.50*
Proteins (g/day)	61.2±32.1	73.4+22.1*	60.0±38.2	72.9+20.9*	65.1±14.2	78.1+22.1*
Dietary fiber (g/day)	15.9±7.1	19.8+5.2*	15.4±9.1	20.1+4.8*	15.9±7.1	19.9+5.2*

* (p<0.05) with basal values.

Table IV
Evolution of anthropometric parameters

Parameter	Total group (n=37)		No Radiotherapy group (n=24)		Radiotherapy group (n=13)	
	Baseline	3 month	Baseline	3 month	Baseline	3 month
BMI (kg/m ²)	23.6±2.2	24.1+2.6	23.6±4.1	24.0+4.2*	23.9±4.1	24.1+4.2
Weight (kg)	62.2±12.1	63.8+9.7	62.1±7.4	64.1+9.1*	62.9±10.1	63.2+9.8
Fat free mass (kg)	46.7+8.4	47.2+8.1	46.3+8.1	47.5+8.1*	47.1+8.1	47.0+9.0
Fat mass (kg)	16.2+5.3	16.8+5.4	16.0+5.0	16.6+8.1*	16.3+9.1	16.9+8.4
Tricipital skinfold(mm)	12.0+5.1	11.8+5.2	11.9+5.0	11.3+3.1	12.2+5.7	12.3+1.1
Circumference arm (cm)	24.4+3.1	24.7+3.3	24.2+3.1	24.4+3.1	25.3+3.1	25.9+2.1

No statistical differences between time 0 and at 3 months.

Table V
Visceral serum protein and lymphocytes

Parameters	Total group (n=37)		No Radiotherapy group (n=24)		Radiotherapy group (n=13)	
	Baseline	3 month	Baseline	3 month	Baseline	3 month
Albumin (g/dl)	3.4±0.3	4.3+0.2*	3.4±0.5	4.4+0.4*	3.1±0.4	3.8+0.3*
Prealbumin (mg/dl)	25.7±4.3	27.9+6.4	25.9±5.1	26.9+4.1	21.2±5.7	18.9+6.1
Transferrin (mg/dl)	210.7±57.4	254.5+40.7*	182.1±37.4	230.2+46.4*	209.8±33.4	257.4+31.4*
Lymphocytes (10 ³ uL/mm ³)	1439.1±582.0	1506.2+421.9	1433.1±519.1	1501.2+523.8	1526.2±511.1	1528.9+400.2

* (p<0.05) with basal values.

our study, we use other design. Firstly, we evaluated ambulatory patients and secondly we treated these patients during three months of oral supplementation. In all patients, a significant improvement in albumin, prealbumin and transferrin concentrations were observed and an improvement in weight in patients without radiotherapy were detected, too Our data agree with previous studies in patients with cancer pancreas suggested that EPA alone at a dose of 2 g/day was as-

sociated with weight stability²⁰, 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 radiotherapy²¹, an intake of an omega 3 enhanced supplements (0.6 g EPA per day) improved protein levels without effect on weight. With a powe-

red formula in head and neck cancer surgical patients, an improvement in proteins and weight was observed with a intake over 1 g per day of EPA in patients without radiotherapy, too²². This latest study is in line with the work with high doses of omega-3.

The interest in nutritional support of head and neck cancer patients is increased. In a two systematic reviews^{13,23}, the authors examined 10 trials that investigated the effects of immunonutrition in patients treated surgically for head and neck cancer. The specific efficacy and potential benefits of enteral nutrition support with w3 fatty acids (enteral tube feeding or specifically oral nutrition supplements) are limited. A mix of immunonutrient such as arginine, w3 fatty acids and nucleotides showed an improvement in postsurgical complications. In cancer patients undergoing radiotherapy, meta-analysis²⁴ showed that oral nutritional supplements significantly increase dietary intake compared to routine care and in patients undergoing surgery, meta-analyses showed better results in length of hospital stay, incidence of any complications and infectious complications.

In conclusion, at dose taken, omega 3 and fiber enhanced nutritional formula improved blood protein concentrations in ambulatory postoperative head and neck cancer patients. In patients without radiotherapy this formula improved weight, fat mass and fat free mass, too. Further studies are needed in this entity with a high prevalence of malnutrition²⁵⁻²⁶ and with important metabolic implications²⁷.

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