Coll. Antropol. **32** (2008) 3: 737–740
Original scientific paper

Effects of Nutritional Support in Patients with Colorectal Cancer during Chemotherapy

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A B S T R A C T

Nutritional support, addressing the specific needs of this patient group, is required to help improve prognosis, and reduce the consequences of cancer-associated nutritional decline. Early intervention with nutritional supplementation has been shown to halt malnutrition, and may improve outcome in some patients. In our study we tried to assess the influence of nutritional support (counseling, oral liquids, megestrol acetate) on nutritional status and symptoms prevalence in patients with colorectal cancer during chemotherapy. Group I consisted of 215 (55%) patients with medium age 68 ± 2.6 years who were monitored prospectively and were given nutritional support. Group II included 173 (45%) patients (medium age 67 ± 2.9 years) without the proper nutritional counseling, in whom the data were collected retrospectively during a 6 years period of time. After evaluation Nottingham Screening Tool Score, Appetite Loss Scale and Karnofsky Performance Status) all patients in the group I received nutritional counseling, 153 of them (72%) were taking form of enteral food supplement and 103 (48%) patients were using megestrol acetate. Evaluating the initial risk measurements according to BMI, decrease in weight gain and NST, we did not find any significant difference between the two groups. After chemotherapy completion, patients in group I had a 15.3% drop of those who's BMI was <20,65% patients increased their body weight, with an average weight gain of 1.5 kg (0.6–2.8 kg). Contrary, in group II we found increase in weight loss ≥2 kg/month in 39% of patients. The appetite improvement was detected on Appetite Loss Scale from 3.1 (pre-chemotherapy) to 4.7 (post-chemotherapy) in group I, especially in those receiving megestrol acetate. In both groups Karnofsky Performance Status didn't change significantly reflecting the impact of the disease itself and chemotherapy procedures to the patient's condition. Nutritional counseling, supplemental feeding and pharmacological support do temporarily stop weight loss and improve appetite, social life and quality of life in those groups of patients. However, this improvement have no implications on patients KPS and course of their disease.

Key words: *nutritional support, colorectal cancer, chemotherapy*

Introduction

Colorectal cancer is the significant cause of morbidity and mortality in the developed countries with approximately equal number of new cases annually in men and women[1]. Despite deep knowledge concerning morphogenesis and spread of colorectal carcinoma as well as vast achievements in surgery, chemo- and radiotherapy, the percentage of 5-year-survivals is still poor and reaches 15%. According to the most authors, there are four risk factor categories: epidemiological, intestinal, dietetic, and mixed. It is well known that colorectal cancer is a disease, in which genetic mutations of somatic cells are the molecular base of the disease. The inner innervation of the colon seems to play an important role in carcinoma pathogenesis and spread[2,3]. Today, about 50% of colorectal carcinomas are diagnosed in the advanced stage, with infiltration exceeding the intestinal wall or spreadng to neighboring organs, which gives full clinical symptoms. The prognosis for the survival after disease progression is usually poor[4].

Received for publication July 21, 2008

Tumor growth is associated with profound metabolic and neurochemical alterations, which can lead to the onset of anorexia-cachexia syndrome. Anorexia is defined as the loss of the desire to eat, while cachexia results from progressive wasting of skeletal muscle mass, and to a lesser extent adipose tissue, occurring even before weight loss becomes apparent. Cancer anorexia-cachexia syndrome is highly prevalent among cancer patients, has a large impact on morbidity and mortality, and on patient quality of life[5]. According to clinical studies, increasing caloric intake does not reverse cachexia. The pathophysiology of cachexia involves more complex mechanisms than simply caloric deficiency. The process appears to be mediated by circulating catabolic factors, either secreted by the tumor alone or in association with host-derived factors, such as Tumor necrosis factor-α (TNF-α), interleukins (IL-1, IL-6), interferon-γ (IFN-γ) and Leukemia inhibitory factor (LIF)[6].

The consequences of malnutrition include impairment of immune functions, performance status, muscle function, and quality of life. In addition, responses to chemotherapy are decreased, chemotherapy-induced toxicity and complications are more frequent and severe, and survival times are shortened[7].

Nutritional support, addressing the specific needs of this patient group, is required to help improve prognosis, and reduce the consequences of cancer-associated nutritional decline[8]. Because weight loss shortens the survival time of cancer patients and decreases performance status, effective therapy would extend patient survival and improve quality of life[9].

Early intervention with nutritional supplementation has been shown to halt malnutrition, and may improve outcome in some patients. However, increasing nutritional intake is insufficient to prevent the development of cachexia, reflecting the complex pathogenesis of this condition[10].

In our study we tried to assess the influence of nutritional support (counseling, oral liquids, megestrol acetate) on nutritional status and symptoms prevalence in patients with colorectal cancer during chemotherapy.

Patients and Methods

Three hundred and eighty-eight patients were included in the study in the period of time from January 2001. to December 2007. The study took place at Gastroenterology department, Clinical Hospital Centre Rijeka. According to the given nutritional support, patients were divided in the two groups. Group I consisted of 215 (55%) patients who were monitored prospectively and were given nutritional support. Group II included 173 (45%) patients without the proper nutritional counseling, in whom the data were collected retrospectively during a 6 years period of time. Seventy-four (43%) patients in group II and 80 (37%) in group I had locally advanced and/or metastatic disease before chemotherapy initiation.

Four weeks after operation (if needed) and one week before chemotherapy initiation, we undertook initial evaluation of the patient's nutritional status (visit 0). Nutritional status was evaluated according to body weight change. BMI was calculated for all patients by using the standard procedure dividing weight in kg by height in m^2. Patients were also evaluated through three questionnaires: Nottingham Screening Tool Score (NST score, 0–7) (Table 1), Appetite Loss scale (0–10) and Karnofsky Performance Status (KPS, 0–100%). Patients who were considered to have nutritional risk, were those with BMI<20, decrease in weight gain>2 kg/month and NST score ≥5.

Nutritional and pharmacological support was given to all patients in group I. Support included nutritional counseling, prescription of megestrol acetate 400 mg daily and supplementary/adjuvant enteral nutrition. Nutritional counseling included interview with physician, instructions for food preparation during chemotherapy, encouraging patients to eat more meals a day and to change bad eating habits.

All patients in the group I received nutritional counseling, 153 of them (72%) were taking form of enteral food supplement and 103 (48%) patients were using megestrol acetate.

All patients with locally advanced (TNM – T_3 or T_4) and/or metastatic disease (TNM – M_1) were treated with the standard first line-treatment, receiving a standard regime combinations of FOLFIRI/XELIRI or FOLFOX protocol.

TABLE 1
NOTHINGAM SCREENING TOOL QUESTIONNAIRE

Nothingam Screening Tool Questionnaire
0 – BMI > 20
1 – BMI 18–20
2 – BMI <18
Has the patient unintentionally lost weight during last 3 months?
0 – no
1 – a little, up to 3 kg
2 – a lot, more than 3 kg
Food intake – has this increase during the last month prior the estimation?
0 – 0
1 – yes
Stress factor/severity of illness?
0 – none
1 – moderate (uncomplicated operation, chronic disease, infection, etc.
2 – severe (multiple fractures and wounds, sepsis, cancers, major operation, etc)

Score 0–2 Patient do not need nutritive support
Score 3–4 Patient had to be monitored once more in week
Score ≥ 5 Patient has malnutrition and need nutritive counseling and support

During the follow-up, we performed 12 visits according to chemotherapy schedule. On each consecutive visit, before chemotherapy initiation, patient's nutritional status was re-evaluated using above mentioned evaluation tools.

Results

Evaluating the initial risk measurements according to BMI, decrease in weight gain and NST, we did not find any significant difference between the two groups (42% vs. 48%, 42% vs. 45% and 45% vs. 52%, respectively).

After chemotherapy completion, patients in group I had a 15.3% drop of those who's BMI was < 20. An opposite 12.1% raise in patients with BMI < 20 was noted in the group without nutritional support.

Similar direction was observed between the two groups when we monitored weight loss > 2 kg/month. In group I 65% patients increased their body weight, with an average weight gain of 1.5kg (0.6–2.8kg). Weight gain was mostly expressed in group I in patients receiving megestrol acetate after 4 weeks-therapy. Contrary, in group II we found increase in weight loss ≥2 kg/month in 39% of patients. The appetite improvement was detected on Appetite Loss Scale from 3.1 (pre-chemotherapy) to 4.7 (post-chemotherapy) in group I, especially in those receiving megestrol acetate (Table 2, Table 3).

In group I no significant difference in KPS score was observed, from 74.2% before chemotherapy to 80.4% after the chemotherapy completion. Also in group II, KPS score was 70.4% before chemotherapy and didn't change significantly – 70.2% after chemotherapy.

Most obvious side effects of enteral food supplementation was diarrhea in 12% (19) of patients, followed by abdominal pain in 9% (14) and bad taste occurring in 5% of patients (8). Water retention with resultant edema was the main side effect experienced in 20% of patients receiving megestrol acetate.

TABLE 2
NUMBER OF PATIENTS IN GROUP I (N=215) WITH BMI<20, NTS≥5, LOSS OF APPETITE AND DECREASED WIGHT GAIN (>2KG/MONTH)

	Visit 0 (Before chemotherapy)	Visit 12 (After chemotherapy)
BMI <20	105 (48.84%)	72 (33.49%)
NTS ≥5	112 (52.10%)	75 (34,88%)
Loss of appetite	168 (78.14%)	81 (37,67%)
Decreasing in weight gain (>2kg/month)	97 (45.12%)	56 (26.05%)

TABLE 3
NUMBER OF PATIENTS IN GROUP II (N=173) WITH BMI<20, NTS≥5, LOSS OF APPETITE AND DECREASED WIGHT GAIN (>2KG/MONTH)

	Before chemotherapy	After chemotherapy
BMI <20	71 (41.04%)	92 (53.18%)
NTS ≥5	78 (45.09%)	101 (58.38%)
Loss of appetite	115 (66.47%)	156 (90.17%)
Decreasing in weight gain (>2kg/month)	72 (41.62%)	140 (80.92%)

Discussion

The role of nutrition therapy is often assumed to be less important than pharmacologic interventions as outcomes are less clear in literature. There is general failure to recognize weight loss early enough and to implement effective nutrition interventions[11,12,13].

Our study showed that early nutritional intervention and adequate counseling can decrease or even reverse course of weight deterioration in the early course of locally advanced or metastatic CRC.

Sixty-five percent of patients increased weight and additional 9% maintained weight during chemotherapy. All patients receiving megestrol acetate were weight gainers.

Studies that analyzed progestational agents, such as megestrol acetate and medroxyprogesterone, showed appetite improvement and weight increase in advanced cancer patients with slight increase in risk of thrombophlebitis[14,15].

Megestrol acetate induced edemas in some patients, but didn't cause any other serious side effect. It seemed that improved social life due to the better appetite was more important for patients than discomfort caused by edema. Even though we have found a difference in KPS between the two groups, our result was not statistically significant, leading us to conclusion that nutritional support had no implications on patients KPS and disease course.

Karnofsky Performance Status didn't change significantly reflecting the impact of the disease itself and chemotherapy procedures to the patient's condition.

We have concluded that nutritional counseling, supplemental feeding and pharmacological support do temporarily stop weight loss and improve appetite, social life and quality of life in those groups of patients. However, this improvement have no implications on patients KPS and course of their disease. Due to a small number of patients and short follow up, we are unable to evaluate the impact of improved nutritional status on a patient's survival.

To achieve compliance, nutrition therapy should be implemented in an aggressive manner. The clinician is therefore faced with the need to recognize nutrition-related issues and to implement effective strategies that will lead to positive outcome for patients.

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UČINCI NUTRITIVNE POTPORE U BOLESNIKA S RAKOM DEBELOG CRIJEVA ZA VRIJEME KEMOTERAPIJE

SAŽETAK

Nutritivna potpora, usmjerena prema specifičnim potrebama ove grupe bolesnika poboljšava prognozu i umanjuje posljedice nutritivnog propadanja povezanog s karcinomom. Rana nutritivna potpora smanjuje mogućnost nastanka malnutricije i može poboljšati ishod bolesti u nekih bolesnika. U našoj studiji nastojali smo ocijeniti učinak nutritivne potpore (savjetovanje, tekući peroralni pripravci, megestrol acetat) na nutritivni status i učestalost simptoma u naših bolesnika s rakom debelog crijeva za vrijeme kemoterapije. Prva grupa bolesnika se sastojala od 215 (55%) bolesnika srednje životne dobi 68 ± 2,6 godina koji su promatrani u prospektivnoj studiji i koji su primili nutritivnu potporu. Druga grupa se sastojala od 173 (45%) bolesnika (srednje životne dobi 67 ± 2,9 godina) bez pravilnog nutritivnog savjetovanja, za koje su se podaci prikupili za razdoblje od 6 godina retrospektivno. Nakon evaluacije Nottingham Screening Tool bodovanjem, skale za gubitak apetita i Karnofsky Performance stanja, svi bolesnici iz prve grupe su »nutritivno« savjetovani; 153 (72%) bolesnika je dobilo tekuće enteralne nadomjesne pripravke a 103 (48%) bolesnika je počelo uzimati megestrol acetat. Između navedene dvije grupe nije bilo statistički značajnih razlika u indeksu tjelesne mase, smanjenju tjelesne težine i Nottingham Screening *Tool* bodovanju. Po završetku ciklusa kemoterapije, u 65% bolesnika iz prve grupe zabilježen je porast tjelesne težine od 1,5 kg (0,6–2,8 kg). Nasuprot tome, u drugoj grupi zabilježili smo smanjenje u tjelesnoj težini >2 kg na mjesec u 39% bolesnika. U prvoj grupi zabilježeno je poboljšanje apetita (na skali za apetit) od 3,1 (prije kemoterapije) na 4,7 (poslije kemoterapije) i to naročito u grupi bolesnika koji su primali megestrol acetat. Karnofsky Performance Status se nije značajno mijenjao u obje grupe, odražavajući tako utjecaj bolesti »same za sebe« i postupka kemoterapije na stanje bolesnika. Nutritivno savjetovanje, nadomjesna ishrana i farmakološka potpora privremeno zaustavljaju gubitak tjelesne težine i popravljaju apetit, socijalnu komponentu života i kvalitetu života u tim grupama bolesnika. Ipak, to poboljšanje nema implikacija na sam status bolesnika i tijek njihove bolesti.