Ann Med Res

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Annals of Medical Research

journal page: www.annalsmedres.org

The effect of beta-hydroxy beta-methylbutyrate (HMB)/glutamine/arginine support on quality of life and toxicity in patients undergoing pelvic radiotherapy

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ARTICLE INFO

Keywords:
Pelvic radiotherapy
HR-QOL
HMB\Arjinin\Glutamin

Received: Apr 02, 2022
Accepted: Aug 08, 2022
Available Online: 23.11.2022

DOI:
10.5455/annalsmedres.2022.04.120

Abstract

Aim: In this clinical study, beta-hydroxy beta-methyl butyrate (HMB)\Arginine\ Glutamine enriched mixture was administered during pelvic radiotherapy; the effects on the patients' quality of life, treatment-related side effects, and nutritional status were investigated.

Materials and Methods: Forty-nine patients who underwent pelvic radiotherapy were divided into 2 groups according to age, gender, operation status, tumor type, and concomitant chemotherapy status. While HMB\Arginine\Glutamine was administered to 25 patients, no nutritional support was given to 24 patients. Two groups of patients were followed up weekly and compared in terms of quality of life, toxicity, nutritional status, anthropometric measurements, biochemical parameters and moods.

Results: A statistically significant improvement was found in the anxiety and depression scales in the group that used this mixture. Although there was an improvement in weight change, treatment side effects, fatigue, risk of malnutrition, skeletal muscle mass, prealbumin and albumin, this difference was not statistically significant. There was no significant difference between the two groups in terms of quality of life.

Conclusion: HMB\Arginine\Glutamine mixture may improve toxicity, fatigue, anxiety and depression, skeletal muscle mass, prealbumin and albumin levels when used during pelvic radiotherapy.

Introduction

Pelvic chemo/radiotherapy is commonly used in colorectal, gynecologic and other malignancies in cancer treatment to improve local control and survival. The organs at risk especially the intestine and bladder could be affected by treatment and may cause a wide range of side effects. As a result, patient compliance and health-related quality of life (HR-QOL) may deteriorate.

Nutritional problems and malnutrition are also common problems at the time of diagnosis in cancer patients. It's well known that treatment success and HR-QOL are poorly impressed by malnutrition [1, 2]. Gastrointestinal System (GIS) has a very important role in nutritional status and adding another gastrointestinal toxic agent chemotherapy to pelvic radiotherapy usually increases toxicity and malnutrition risk.

In recent years, some nutritional supplements have been investigated on the impact of GIS mucosa and toxicity during radiotherapy +/- chemotherapy [3-6]. Researches have been carried out on the subject that some amino acids create anti-inflammatory effects on intestinal tissue and reduce mucosal damage during applied chemoradiotherapy or radiotherapy. To our knowledge, there is no clinical data in the literature examining the effects of HMB\Arginine\Glutamine on quality of life, toxicity and nutritional status in patients receiving pelvic radiotherapy.

In this trial, we examined the effect of glutamine, arginine and β-hydroxy β-methyl butyrate (HMB) mixture on HR-QOL, treatment toxicity, serum parameters and anthropometric measurements in cancer patients receiving pelvic radiotherapy with or without chemotherapy.

Materials and Methods

Patients and study design

This trial was approved by the Gazi University local ethical committee. All patients gave their written informed

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Table 1. Patients Demographics.

		Group 1 (HMB\ARJ\GLUT)	Group 2 (NORMAL DİET)	p value
Median age (years)		54	61	ns
Sex	Female	12 (55%)	10 (45%)	ns
	Male	13 (48%)	14 (52%)	
RT Time	Preoperative	16 (50%)	16 (50%)	ns
	Postoperative	9 (53%)	8 (47%)	
Concomitant chemotherapy	Yes	22 (51%)	21 (49%)	ns
	No	3 (50%)	3 (50%)	

Abbr: HMB=β-hydroxyβ-methyl butyrate mixture; ARJ= Arginine; GLUT=Glutamine; RT= Radiotherapy ns: not significant.

consent to attend this study. Forty-nine patients aged between 18 and 70, Karnofsky performance status >70 and histologically proven cancer patients indicated for pelvic RT were considered eligible regardless of whether the primary tumor site and the proposed RT were definitive, post-operative, or pre-operative. Patients who have distant metastases, prior pelvic RT and patients whom were required to use a feeding tube or parenteral feeding were excluded. Forty-nine patients, referred for pelvic RT to Gazi University Faculty of Medicine Radiation Oncology Department, were divided into two groups randomly and stratified by gender, age, prior surgery and existence of chemotherapy. The median age was 57 (range 35-86) years and twenty-two (%38) of the patients were women in the whole cohort (Table 1). In group 1, all of the patients used glutamine, arginine and HMB mixture (Abound©) during RT. In group 2, the patients didn't use any supplements. Diet consultation was given to all patients at the beginning and weekly during the therapy. Nutritional status, anthropometric changes, biochemical parameters like albumin and prealbumin levels, and HR-QOL questionnaires were surveyed at baseline, end of the first week, end of the third week and at the end of RT for each patient. The two groups were compared according to HR-QOL, nutritional status, toxicity, anthropometric changes, biochemical parameters, fatigue and psychological status during pelvic RT.

HMB\Arginine\Glutamine mixture

The mixture that we used during pelvic RT contains 7.4 gr Glutamine, 7.4 gr Arginine as semi-essential amino acids and 1.3 gr HMB, an active metabolite of leucine amino acid, in one package. It's a powder mixture and prepared with water at room temperature. It is recommended to drink in 30 minutes. It's sold as an Abound© market name in Europe. In group 1, all of the patients used this mixture twice a day during RT and were questioned weekly.

Radiotherapy (RT)

The Computerized Tomography (CT) of all the patients was scanned in a supine position with a 5 mm slice thickness. Clinical Target Volume (CTV), Planned Target Volume (PTV) and Organ at Risk (OAR) volumes were described as International Commission on Radiation Units & Measurements (ICRU) 50 and 62 reports (7). Magnetic Resonance Imaging (MRI) is also used to describe these target volumes if they could be obtained. All of the patients received 45-50,4 Gy in 25-28 fractions external beam RT to the primary tumor/tumor bed and draining lymphatic by Saturne 43, Saturne 41(GE Healthcare, USA) and DHX Clinac (Varian Medical Systems, USA) linear accelerators. Treatment plans were performed as conformal radiotherapy with three-field lateral and posterior fields or four-field box technique. The small intestine volume that received 50 Gy was kept lesser than 150 cc in all patients. The median RT dose was 50 Gy.

Chemotherapy

Forty patients (87%) received concomitant chemotherapy with RT. Chemotherapy protocols were different according to the primary tumor, stage and individual preferences. Patients with rectal cancer have received bolus or infusion 5-Fluorouracil (5-FU) 325-500 mg/m^2 + Folinic acid (FA) 20-30 mg/m^2. Weekly 40 mg/m^2 cisplatin was used in cervix cancer if indicated.

Study measures

Quality of life, toxicity and nutritional assessment

The European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire version 3.0 (EORTC QLQ-C30) and its colorectal module (EORTC QLQ-CR38) were used to measure the quality of life in this study. The EORTC QLQ-C30 is the main instrument that covers the general issues of quality of life (QOL). It is designed to be supplemented with disease-specific modules which can assess particular issues of QOL. In this study, we chose the EORTC QLQ-CR38 because it contains scales examining that are relevant to patients undergoing pelvic RT. The Radiation Therapy Oncology Group (RTOG)/EORTC morbidity scoring schema was used to assess acute morbidity. Lower GI systems including pelvis, genitourinary system (GUS) and skin components were evaluated. Nutritional assessment and screening were performed by use of Subjective Global Assessment (SGA), Nutritional Risk Screening 2002 (NRS 2002), Malnutrition Screening Tool (MST) and anthropometric measurements like weight and Body Mass Index (BMI). These nutritional assessment and screening tools were completed for four times during RT [8-11].

Fatigue and Mood assessment

Fatigue and depression are one of the most important components of QOL and can also be seen in cancer patients. We assessed the fatigue and mood with the Cancer Fatigue Scale (CFS) and Hospital Anxiety and Depression Scale (HADS), respectively. Cancer Fatigue Scale is a 15-item brief, feasible and validated scale, composed of 3 subscales (physical, affective and cognitive subscales). It contains seven questions for a physical score, four questions for affective and four questions for cognitive components. This questionnaire uses a five-point response scale (no, a little, somewhat, considerably and very much) to assess each functional or symptom item [12]. Higher scores in all components of fatigue indicate worse fatigue status. If a patient selects "a little" answer to all questions, the physical score occurs as 7, the affective score is 12, the cognitive score is 4 and the total fatigue score is 23. These scores were used in this study as cut-off values. Hospital Anxiety and Depression Scale is developed by Zigmond et al. and evaluates the symptom of mood disturbance [13]. Validity and reliability testing of the Turkish version was performed by Aydemir et al. and a depression cut-off point of 7/8, and anxiety cut-off point of 10/11 were established [14].

Anthropometric and biochemical assessment

Anthropometry means 'the scientific study of the measurements and proportions of the human body'. Many measurements can be used for different purposes but weight, height, Body Mass Index (BMI), Skeletal Muscle Mass (SMM) and Body Fat Mass (BFM) are usually used to assess nutritional status. BMI is defined as the individual's body mass divided by the square of their height - with the value universally being given in units of kg/m^2. Body composition like SMM and BFM can be measured by bioelectrical impedance analysis (BIA) and air displacement plethysmography. In this study, BIA (In Body S20© Body Composition Analyzer, Korea) was used to analyze body composition in addition to weight, height, and BMI measurements for four times during RT. BIA measures body composition by sending a low, safe electrical current through the body. The current passes freely through the fluids contained in muscle tissue but encounters difficulty/resistance when it passes through fat tissue. This resistance of the fat tissue to the current is termed 'bioelectrical impedance'. BIA allows the determination of the fat-free mass (FFM), SMM and total body water [15]. Biochemical parameters like prealbumin and albumin also have been investigated to analyze nutritional changes in this study.

Statistical analysis

SPSS ver 15 (IBM Corp Released 2010. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY) was used for statistical analysis in the study. Significance between qualitative groups was evaluated with the Chi-Square-Fisher Exact test. The Friedman test was used for parameters in multiple dependent groups. In cases where a difference was detected, further evaluation was performed with the Wilcoxon-signed rank test and Bonferroni correction was made. Statistical evaluation of the difference between two independent samples was used with the "Mann-Whitney U" test. Since the patients were evaluated with multiple tests measuring different entities, the p-value was accepted as 0.02 and below, and the type 2 error was reduced.

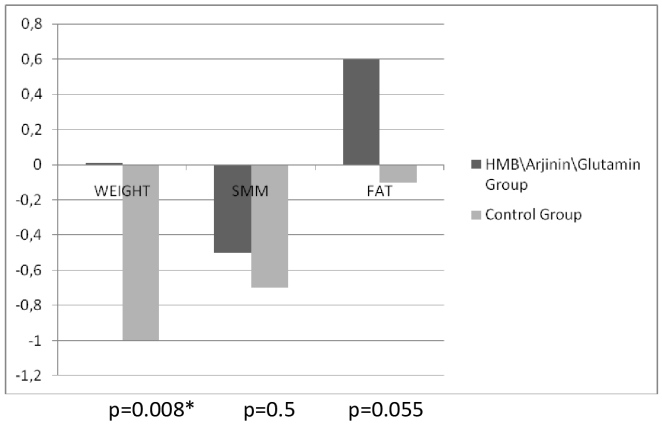

Figure 1. Median weight, Skeletal Muscle Mass (SMM) and fat composition changes (kg) at the end of RT.

Results

After stratification, groups were defined as follows; Group 1 (n=25), patients received two packages HMB\Arginine\Glutamine mixture a day in addition to their usual diet, Group 2 (n=24), patients didn't receive any supplement in addition to their usual intake. All patients completed the study and no patients were lost to follow-up. None of the patients used another nutritional supplement during RT according to their discourse.

The median weight and BMI values during RT are listed in Table 2 for the groups. Significant weight changes (p=0.03) and also BMI changes (p=0.004) were determined during RT in group 1.

At the end of RT, compared to the onset, patient numbers who had weight changes are listed in Table 3. According to this, the number of patients who lost weight in group 2 was more than twice than group 1 (p=0.03).

When we compare the groups about body compositions, although we have found a median 0.5 kg decrease in SMM and 0.6 kg increase in fat mass in the mixture group, 0.7 kg decrease in SMM and 0.1 kg fat mass decrease were detected in group 2 (Figure 1).

RTOG GIS, GUS and skin toxicities were noted during the study. The incidence of grade 2 and higher toxicity was not significantly different between the two groups, although a trend for reduced GI symptoms was found in group 1 (Table 4).

Additionally, patients were evaluated and compared for fatigue which has an important role in HR-QOL. The CFS evaluates the physical, affective and cognitive components of fatigue. A cut-off score was determined in each component to compare groups. According to this, although more patients passed the cut-off values in group 2, a significant difference was not seen in all components (Table 5).

Another parameter that affects the HR-QOL is mood change and this was followed with HADS. This scale in-

Table 2. Median Weight and BMI measures during RT.

	Group 1 (HMB\ARJ\GLUT)				Group 2 (NORMAL DIET)			
	Baseline	End of 1stweek	End of 3rd.week	End of RT	Baseline	End of 1stweek	End of 3rd.week	End of RT
Weight (kg)	76	76.2	76.1	76.2	73.6	74	72.9	72.7
BMI (kg\m^2)	28.5	28.6	28.6	28.6	27.3	27.3	27	26.9

Abbr: RT= Radiotherapy; BMI= Body Mass Index; kg=kilogram.

Table 3. Number of patients having weight loss.

	Group 1 (HMB\ARJ\GLUT)	Group 2 (NORMAL DIET)	p value
Weight Loss (n, %)	7 (28%)	15 (62.5%)	0.03
Same or weight gain (n, %)	18 (72%)	9 (37.5%)	

volves anxiety and depression subscales. When we compare the groups, more patients exceeded the anxiety and depression cut-off scores at least one time during RT in group 2 and this difference was statistically different (Table 6).

SGA, NRS-2002 and MST were performed during RT to compare nutritional changes between the groups. Patients who have the risk of malnutrition during RT were determined for each malnutrition screening method. No difference was found between the two groups at the beginning and during RT. Twenty patients according to SGA and 9 patients according to NRS-2002 in each group were found at risk of malnutrition. Nine patients in group 1 and 17 patients in group 2 were found for risk of malnutrition in the malnutrition screening tool, no statistical difference was found between the groups (p=0.03) (Table 7).

The influences of this HMB, glutamine and arginine enriched mixture on biochemical nutritional parameters were also investigated. Serum prealbumin levels at the beginning of RT, at the end of the first and third week and the end of RT were measured in serum plasma. Albumin levels were also measured at the beginning and the end of RT.

Prealbumin and albumin median changes between the start and at the end of the RT were calculated. Serum albumin level decrease was median 0.2 mg/dl in group 1 and 0.3 mg/dl in group 2 (p=0.5). Prealbumin levels were increased median 1.2 mg/dl in Group 1 and decreased 2.2 mg/dl in group 2 (p=0.2) (Table 8).

All of the patients filled the QLQ-C30 which evaluates general HR-QOL and disease-specific QLQ CR-38 forms which were developed by EORTC at the beginning, end of the first and third week and end of the RT. These forms have a total of 68 questions and measure 27 parameters like functional status, symptom severity and financial parameters.

According to median scores, improvement on future perspective (p=0.002), physical function (p=0.005) and body image (p=0.007) were detected in group 1 during RT. When we compare the groups about the symptoms, amelioration on chemotherapy side effects (p=0.009), micturition problems (p=0), fatigue (p=0.002) and pain (p=0.01) were found better in group 2 and constipation scores were better (p=0.01) in group 1.

Discussion

Advances in technology and the drug industry have made expectations greater in medicine. Today, not only the cure is the main goal but also preserving the HR-QOL has become one of the main objectives in cancer treatment. Thus, in vivo and in vitro trials examining HR-QOL have been practiced within cancer treatment studies. In this study, we examined the effects of the HMB\Arginine\Glutamine mixture on HR-QOL, toxicity, serum parameters, anthropometric measures, fatigue, mood and nutritional changes. To our knowledge, this is the first human study investigating the effect of this mixture on pelvic irradiated patients and it is distinguished from other studies because of its comprehensive design.

Weight loss is one of the elementary malnutrition components and it is related to worse survival in chronically ill patients [16, 17]. In our study, we found a significant improvement in weight changes in the mixture group. The effect of this mixture on weight changes has been also investigated by some authors [18,19] and it has been found effective to decrease weight loss in cachectic cancer and HIV-positive patients. In these studies, body composition changes were also examined and improvements in lean body mass were seen (LBM) with the use of the HMB\Arginine\Glutamine mixture. In our study, we couldn't find any significant change in LBM with usage of this mixture.

Loss of LBM in chronic diseases especially in cancer is thought to have a prognostic significance in survival so it is a research area. In a study, it has been shown that LBM loss in cancer patients decreases physical function, HR-QOL and survival rates [20]. The cause of protein and LBM loss in cancer patients is associated with proteolysis-inducing factor (PIF), produced by tumor cells, and cytokines (TNF alpha, IL-1, etc.) produced by the host immune system to provide more energy with protein and fat degradation [21,22]. Glutamine and arginine increase protein synthesis and HMB reduces protein degradation, so decrease in the total protein loss is expected in cancer patients with the use of this supplement [19]. The RTOG-0122 trial also showed that this mixture may reduce LBM loss in cachectic cancer patients [23]. In our study, we compared the groups by SMM and fat composition changes. Thus, both of the groups had SMM loss at the end of RT. This decrease was greater in the normal diet group without a statistical difference (p=0.5). When we compare the fat changes, an increase was seen in group 1 despite a decrease has been found in group 2. This difference was also not significant (p=0.055). Patient cohorts between our study and

Table 4. Patients having grade 2 and higher toxicity during RT.

	Group 1 (HMB\ARJ\GLUT)	Group 2 (NORMAL DIET)	p value
Grade 2 and over Gastrointestinal toxicity (n,%)	10 (40%)	17 (70%)	0.06
Grade 2 and over Genitourinary toxicity (n,%)	8 (32%)	5 (20%)	0.5
Grade 2 and over Skin toxicity (n,%)	9 (36%)	7 (29%)	0.8

Table 5. Patient numbers and percentages on the Cancer Fatigue Scale.

	Group 1 (HMB\ARJ\GLUT)	Group 2 (NORMAL DIET)	p value
Fatigue-Physical score 8 and over (n,%)	8 (32%)	13 (54%)	0.2
Fatigue-Affective score 13 and over (n,%)	7 (28%)	12 (50%)	0.1
Fatigue-Cognitive score 5 and over (n,%)	3 (12%)	7 (29%)	0.1
Fatigue-Total score 24 and over (n,%)	4 (16%)	14 (58%)	0.05

Table 6. Patient numbers who exceed the Anxiety and Depression cut-off scores during RT at least one time.

	Group 1 (HMB\ARJ\GLUT)	Group 2 (NORMAL DIET)	p value
HADS-A score 11 and over (n,%)	2 (8%)	10 (41%)	0.01*
HADS-D score 8 and over (n,%)	7 (28%)	17 (70%)	0.007*

*: statistically significant, Abrr: HADS-A= Anxiety score; HADS-D= Depression score.

Table 7. Number of patients who exceeded the cut-off levels in three malnutrition screening tests during RT.

	Group 1 (HMB\ARJ\GLUT)	Group 2 (NORMAL DIET)	p value
SGA B and over (n,%)	20 (80%)	20 (83.3%)	ns
NRS 3 and over (n,%)	9 (36%)	9 (37.5%)	0.9
MST 2 and over (n,%)	9 (36%)	17 (70.8%)	0.03

Abbr: SGA=Subjective Global Assessment; NS=Not significant; NRS=Nutritional Risk Screening; MST=Malnutrition Screening Tool.

Table 8. Albumin and prealbumin changes (median) between the start and the end of RT (mg/dl).

	Group 1 (HMB\ARJ\GLUT)	Group 2 (NORMAL DIET)	p value
Albumin change (mg/dl)	-0.2	-0.3	0.5
Prealbumin change (mg/dl)	+1.2	-2.2	0.2

the other studies may be the reason for the discrepancy in SMM and LMB changes. Despite newly diagnosed cancer patients being included in our trial, cachectic cancer patients were investigated in other studies. Evaluation with different body composition assessment instruments such as Air Displacement Plethysmography may also cause this difference.

Gastrointestinal system is affected by RT and chemotherapy widely because of its constantly dividing epithelium. It's thought that glutamine is the major energy source of GIS epithelium. Diestel et al. found that glutamine ameliorates the injury of epithelium in rats [24]. In a clinical trial, Huang et al. showed that oral swished glutamine decreases the severity and duration of objective mucositis [25]. An increase in mucosal regeneration and intestinal microperfusion with arginine also has been shown [26, 27]. Most of the studies in the literature are about the effects of micronutrients on histological and pathological changes. There is a lack of clinical data about toxicity and HR-QOL. One of the most important clinical studies is a randomized, double-blinded, phase 3 study, investigating the effects of glutamine on toxicity, in patients receiving pelvic radiotherapy. This study has shown that 8 mg orally taken daily glutamine does not affect the prevention of acute diarrhea [28]. In another study by Sari et al., the effect of this HMB\Arginine\Glutamine mixture on toxicity and QOL has been examined in head and neck cancer patients undergoing chemoradiotherapy [29]. The investigators found that using this mixture during treatment may ameliorate the oral mucositis, pain and dysphagia and improve QOL. In another study, amelioration of radiation-induced acute inflammation and mucosal atrophy with HMB\Arginine\Glutamine mixture in rats was shown [30]. In our trial, patients who had grade 2 and higher GIS toxicity were lesser in the mixture group (10 pts. vs. 17 pts.) but a statistical difference wasn't determined (p=0.06). There wasn't also a statistical difference in GUS grade 2 toxicity (8 pts. vs. 5 pts.) (p=0.5) and skin grade 2 toxicity (9 pts. vs 7 pts.) (p=0.8). A correlation between our clinical trial and studies showing

pathological and histological improvement with these micronutrients in irradiated mucosa was seen. Further studies with larger cohorts may show significant differences in GIS toxicity.

Detecting malnutrition is important because adding nutritional support to malnourished patients decreases the length of hospital stay, and complications and provides better treatment results [31]. So biochemical parameters and protein levels have been investigated to assign malnutrition earlier. Albumin is one of the most emphasized proteins historically, but studies showed that it isn't very sensitive to detect malnutrition and nutritional changes. Also, prealbumin has been investigated and the relation between prealbumin levels and nutritional status has been found concordant in various studies [32]. In our trial, albumin levels decreased median of 0.2 mg/dl in the mixture group and decreased to 0.3 mg/dl in the control group at the end of RT. Prealbumin levels were also evaluated and a median 1.5 mg/dl increase in the mixture group and 2.2 mg/dl decrease in the control group were found. These differences may become significant with larger cohorts and this study may lead to future trials.

Various screening methods have been used to detect malnourished patients. In this trial, we used three different tests to detect patients at risk and compared the two groups. Our purpose was to observe any relation in nutritional risk status with the usage of this mixture. At the beginning of RT, any difference between the groups was not found. A gold standard screening method, laboratory, or anthropometric test does not exist so comparing the methods is not a proper approach. It can be interpreted that the patients who had weight loss during pelvic RT were less in the mixture group and the number of patients at risk of malnutrition with the MST screening tool during RT was lesser in the HMB\Arginine\Glutamine group, and these results were consistent with each other.

Fatigue is not only one of the most common symptoms in cancer patients but also usually underestimated by clinicians. Fatigue has lots of components like physiological and psychological problems and often can not be found in any of them. This may be the reason for disregarding this symptom. Fatigue is directly related to weight loss, negative mood, prolonged stress and pain in cancer patients [33,34]. With RT, fatigue may be aggravated and can continue up to 3 months after treatment [35,36]. Weight loss due to radiation enteritis and dysphagia in patients receiving pelvic and head and neck RT is closely related to fatigue syndrome [37]. We also evaluated patients with Cancer Fatigue Scale during RT. The number of patients was lesser in the mixture groups that exceeded the mild total fatigue score and also in physical, affective, and cognitive components but these differences were not significant. That can be related with fewer patients having grade 2 and over GIS toxicity in the mixture group. With larger cohorts, this distinction between the groups may become significant and the relationship between fatigue, GIS toxicity and weight loss may become closer. During pelvic RT, patients with higher anxiety and depression scores were observed significantly less in the mixture group, and these results were consistent with fatigue and toxicity results favors to group 1.

A pronounced difference was not determined between the two groups in EORTC C-30 and CR-38 HR-QOL questionnaires. In some components of these scales like future project, physical function and body image were significantly better in the mixture group. These results were concordant with the existing smaller number of patients with anxiety and depression and having weight loss, in the mixture group. Micturition problems, pain and fatigue were significantly worse in the mixture group. Chemotherapy side effects were significantly worse in the normal diet group. A discrepancy was observed in fatigue symptoms between CFS and QLQ questionnaires. There hasn't been a gold standard method and a cut-off score to detect fatigue. Cancer Fatigue Scale is a more detailed scale with 15 questions examining fatigue. QLQ-30 examines fatigue with only one question. So, comparing the scales may not be a proper approach but we think CFS is more specific to evaluating fatigue.

Although a clear disparity in GU toxicity was not determined between the groups, a significantly worsening quality of life about micturition in group 1 was found. The variety between toxicity assessment and HR-QOL questionnaires was reported in several studies [38,39]. During the assessment process, evaluation of the toxicity and patient-reported symptoms together is recommended and clinicians must pay attention to patient complaints about symptoms.

Conclusion

As a result, the HMB\Arginine\Glutamine mixture may prevent weight loss and develop amelioration in treatment-related toxicity nevertheless this improvement did not reflect the HR-QOL. Positive impacts were seen on fatigue, nutritional status, anxiety and depression with the usage of this mixture. Improvement in prealbumin levels was also seen in the mixture group.

In the literature, there is scarce data concerning the effects of the HMB\Arginine\Glutamine mixture on nutritional status, toxicity and HR-QOL undergoing pelvic radiotherapy. Because of the improvement in nutritional parameters, toxicity, mood changes and laboratory findings, this combination may be used during pelvic radiotherapy with or without chemotherapy. This trial is important in terms of leading large patient-participated randomized placebo-controlled studies.

Ethics approval

Ethical approval was obtained from Gazi University Clinical Research Ethics Committee (Date: 12.10.2011, Decision No: 297).

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