Nutrición Hospitalaria

Nutr Hosp. 2015;32(1):202-207
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original/*Nutrición enteral*

Effect on quality of life and handgrip strength by dynamometry of an enteral specific suplements with beta-hydroxy-beta-methylbutyrate and vitamin D in elderly patients

Daniel Antonio de Luis, Olatz Izaola, Pablo Bachiller y José Pérez Castrillon

Svo de Endocrinología y Nutrición Hospital Clínico Universitario de Valladolid, Valladolid, Spain.

Abstract

Aim: **the aim of our study was to investigate the effect on strenght and quality of life of an enhanced specific enteral formula with HMBD and vitamin D in elderly patients.**

Methods: **we conducted an open-label study. General assessment of nutritional status included measurements of body weight, height, body mass index (kg/m^2) and bioimpedance. Handgrrip strength was measured by dynamometry. QOL (quality of life) was assessed using the well validated SF 36 questonnaire. Albumin, prealbumin, transferrin and 25-OH vitamin D were measured. All these parameters were recorded at basal time and after 12 weeks of nutritional intervention.**

Results: **patients were divided in two groups by the median percentage of weight improvement (3.4%); group 1 (percentage of weight improvement <3.4%) and group 2 (percentage of weight improvement >3.4%). In group 1, patients showed an improvement in prealbumin and vitamin D levels. In group 2, patients showed an improvement of BMI, weight, fat mass, fat free mass, prealbumin, vitamin D levels, role physical domain of SF 36 , general health domain of SF 36 and handgrip strength. The volumetric consumption rates of the formula were higher in group 2 than group 1 (group 1: 1.25+0.78 units/day [1.81+/-0.9 g per day of HMBD) vs. group 2: 1.86+0.82 units/day (2.79+/-1.1 g per day of HMBD]).**

Conclusions: **elderly patients with a previous weight loss and with a high consumption of a HMBD and vit D enhanced formula had a significant improvement in anthropometric, biochemical parameters, handgrip strength and quality of life.**

(*Nutr Hosp*. 2015;32:202-207)

DOI:10.3305/nh.2015.32.1.9083

Key words: *Elderly. Handgrip strenght. HMBD. Vitamin D. Quality of life*.

Correspondence: Daniel Antonio de Luis.
Head of Institute of Endocrinology and Nutrition.
Medicine Schooll. Valladolid University.
C/ Los perales 16 (Urb Las Aceñas), Simancas.
47130 Valladolid (Spain).
E-mail: dadluis@yahoo.es

Recibido: 7-IV-2015.
Aceptado: 8-V-2015.

EFECTO EN LA CALIDAD DE VIDA Y EN LA FUERZA MUSCULAR POR DINAMOMETRÍA DE UN SUPLEMENTO ENTERAL ESPECÍFICO ENTRIQUECIDO EN BETA-HYDROXI-BETA-METILBUTIRATO Y VITAMINA D EN PACIENTES ANCIANOS

Resumen

Objetivo: **el objetivo de nuestro estudio fue investigar el efecto sobre la fuerza y la calidad de vida de una fórmula enteral específica enriquecida con HMBD y vitamina D en pacientes de edad avanzada.**

Métodos: **se realizó un estudio de una rama abierto. La evaluación de la situación nutricional incluyó mediciones de peso, talla, índice de masa corporal (kg/m^2) y bioimpedancia. La fuerza se midió mediante dinamometría. La calidad de vida se evaluó mediante el cuestionario SF 36. Se midieron los niveles de albúmina, prealbúmina, transferrina y 25-OH vitamina D. Todos estos parámetros se registraron en el momento basal y después de 12 semanas de intervención nutricional.**

Resultados: **los pacientes fueron divididos en dos grupos por el porcentaje medio de la mejoría de peso (3,4%); grupo 1 (porcentaje <3,4%) y el grupo 2 (porcentaje >3,4%). En el grupo 1, los pacientes mostraron una mejoría en los niveles de prealbúmina y vitamina D. En el grupo 2, los pacientes mostraron una mejoría del índice de masa corporal, peso, masa grasa, masa libre de grasa, prealbúmina, niveles de vitamina D, dominio físico del SF 36, dominio de la salud general del SF 36 y la fuerza de prensión. El consumo de la fórmula enriquecida fue mayor en el grupo 2 que en el grupo 1 [grupo 1: 1,25 + 0,78 unidades/día (1,81 +/- 0,9 g por día de HMBD) vs. grupo 2: 1,86 + 0,82 unidades/día (2,79 +/- 1,1 g diarios de HMBD)].**

Conclusiones: **los pacientes ancianos con una pérdida de peso anterior y con un alto consumo de una fórmula enriquecida en HMBD y vitamina D tuvieron una mejoría significativa en parámetros antropométricos, bioquímicos, fuerza de prensión y calidad de vida.**

(*Nutr Hosp*. 2015;32:202-207)

DOI:10.3305/nh.2015.32.1.9083

Palabras clave: *Anciano. Fuerza en mano. HMBD. Vitamina D. Calidad de vida.*

Introduction

Muscle loss is common throughout the aging process[1]. Approximately 30% of muscle mass is lost between the fifth and eighth decades of life and rates of muscle loss can reach up to 15% per decade by 70 y of age[2]. Moreover, low levels of muscle mass in the elderly have been correlated with decreased quality of life[3], decreased physical function[4], and increased mortality[5]. Therefore, interventions to maintain or potentially increase lean mass in elderly are needed. Recently, Beta-hydroxy-beta-methylbutyrate (HMB) has been researched for its muscle-sparing properties[6].

In the other hand, it has been shown that vitamin D contributes to the improvement of bone health independent of calcium regulation. It is proposed that vitamin D effects on muscle mass may mediate this effect by inducing increased mechanical stress that may improve bone mass[7]. Evidence is accumulating to suggest that optimal vitamin D intake can promote muscle mass accumulation[8]. Vitamin D status is assessed by serum 25-hydroxyvitamin D (25OHD) levels and is linked to changes in muscle mass[9]. For example, low vitamin D status has been associated with muscle weakness and muscle wasting[10] that may be reversed with supplementation. Thus, the potential contribution of vitamin D supplementation to improved muscle growth and function requires further investigation.

The aim of our study was to investigate the effect on strenght and quality of life of an enhanced specific enteral formula with HMBD and vitamin D in elderly patients.

Material and methods

Subjects and research design

We conducted an open-label study. The study was carried out from January 2012 to December 2013. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and approved by the HURH ethics committee. Written informed consent was obtained from all patients and signed.

A total of 35 elderly (>65 years) patients with recent weight loss (>5% during previous 3 months) were included in this study, all patients received two cans per day of an enhanced specific enteral formula with HMBD and vitamin D. Exclusion criteria included; ongoing infections, major gastrointestinal disease, cancer, severely impaired hepatic function (total bilirubin concentration >3.5 mg/dl) and/or renal function (serum creatinine concentration >3 mg/dl), steroids treatment, medication could modulate weight, mineral or vitamin supplementation during the study period.

Baseline studies on all patients consisted of complete history taking and physical examination. General assessment of nutritional status included measurements of body weight, height, body mass index (kg/m^2) and bioimpedance. Handgrip strength was measured by dynamometry. QOL (quality of life) was assessed using the well validated SF 36 questonnaire. Albumin, prealbumin, transferrin and 25-OH vitamin D were measured. All these parameters were recorded after 12 weeks of nutritional intervention.

Procedures

At the initial and after twelve weeks of nutritional intervention, assessment body weight was measured to an accuracy of 0.1 Kg and body mass index computed as body weight/(height^2). Tetrapolar body electrical bioimpedance was used to determine body composition[11] (EFG Akern, Italy). Precautions taken to ensure valid BIA measurements were; no alcohol within 24 hours of taking the test, no exercise or food for four hours before taking the test.

At the initial and after 12 weeks of nutritional intervention, fasting blood samples were drawn for measurement of, albumin (3,5-4,5 gr/dl), prealbumin (18-28 mg/dl) and transferrin (250-350 mg/dl) (Hitachi, ATM, Manheim, Ger). 25-OH Vitamin D was measured by electrochemiluminiscence immunoassay (Roche Diagnostics GmbH, Mannheim, Ger).

QOL (quality of life) was assessed using the well validated SF 36 questonnaire[12]. The SF-36 QOL questionnaire is a self administered questionnaire containing 36 items which takes about five minutes to complete. It measures health on eight multidimensiones, covering functional status, well being, and overall evaluation health.

After demonstrating the technique to the patient, the HGS measurements were carried out by the Jamar hydraulic dynamometer (Sammons Preston Inc. Illinois USA) as it demonstrates the highest calibration accuracy[13].If necessary, the instrument was adjusted to the size of the patients' hand. The patient was sitting in a chair, his upper arm by his side of the body and the forearm stretched to an angle of 90º, with the elbow unsupported. The HGS by dynamometry was expressed in kilograms (round down) and carried out three times by both hands. Brief pauses were taken between each measurement. The patient was encouraged to squeeze the dynamometer as hard as possible. For all four algorithms the highest of three measurements was recorded for both the right and the left hand.

Gastrointestinal problems related to enteral feeding were recorded (diarrhea, nausea, cramps, abdominal distension, or vomiting).

Nutritional intervention

At basal time, elderly patients were instructed to consume two cans per day of an enhanced supplement with HMBD and vitamin D. Table I shows the composition of this specific supplement Ensure Plus

Advance® (Abbott, Abbott Park, USA). 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. Two weekdays and one weekend day were studied to account for potential day of the week effects on dietary intake. Mean total energy and macronutrient intakes were calculated using a 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.

Statistical analysis

A power calculation based on weight improvement was performed. Thirty five patients were necessary to detect an improvement of 1,5 kg, with a error type I <0.05 and a statistical power of 80%. Statistical tests were two-tailed and conducted at the 0.05 significance level, and p-values were rounded to four decimal places. Quantitative variables with normal distribution were analyzed with two tailed paired or unpaired Student's t-test. Non-parametric variables were analyzed with Wilcoxon test. The statistical package used was (SPSS 15.0, IL, USA).

Results

Overall, 35 subjects were enrolled and completed the study. The mean age was 79.1+7.5 years (19 females/16 males).

The 35 subjects treated with Ensure Plus Advance® basal assessment of nutritional intake with a 3 days written food record showed a calorie intake of 1532.6+381.1 kcal/day, a carbohydrate intake of 171.7+59.5 g/day, a fat intake of 63.3+20.5 g/day, a protein intake of 68.6+19.1 g/day and a vitamin D3 of 2.8+5.3 mg/day. During the intervention, these patients reached the next dietary intakes; calorie intake of 2224.5+446.2 kcal/day, carbohydrate intake of 242.1+48.5 g/day, fat intake of 89.9+21.6 g/day, protein intake of 111.39+27.7 g/day and vitamin D3 of 23.1+7.3 ug/day. Statistical differences were observed between basal and postreatment in all dietary intakes.

Table II shows the differences in anthropometric and biochemical variables. BMI (0.97+/-1.0 kg/m^2), weight (2.5+/-2.2 kg), fat mass (1.5+/3.3 kg) and fat free mass (-7.2+/-4.4 cm) increased. Prealbumin (1.5+/-4.1 mg/dl) and vitamin D levels increased (11.9+/-10.1 ug/dl), too.

Table III shows the differences in SF-36 questionnaire and handgrip strength. Role physical domain of SF 36 (0.76+/1.7 points) and general health domain

Table I
Composition of supplement

	(1 unit 220 ml)
Total energy(Kcal)	330
Protein (g)	18 (22,14%)
Total lipid (g)	11 (28.81%)
HMB (g)	1.5
Vitamina D3 (ug)	12
Carbohydrate (g)	39 (46.95%)
Dietary fiber (g)	1.7

HMB: Hydroximethil butyrate. Dietary fiber source: oligofructose.

Table II
Basal and post dietary intervention anthropometric parameters (average ± standard deviation) in all group

Parameters	*Basal*	*3 months*
BMI (kg/m^2)	22.6±3.4	23.5±3.3*
Weight (kg)	55.1±9.3	57.5±9.0*
FFM (kg)	40.5±4.2	41.1±5.2*
FM (kg)	15.1±5.6	16.6±4.8*
Albumin (mg/dl)	3.5±0.7	3.6±0.5
Prealbumin (mg/dl)	19.6±6.6	21.1±8.1*
Transferrin (mg/dl)	242.9±78.1	246.8±63.9
Vitamin D3 (ug/dl)	19.8±9.4	31.8±14.3*

BMI: Body mass index. FFM: fat free mass. FM: fat mass.
(*) p<0,05.

Table III
Quality of life and handgrip strength, basal and post dietary intervention anthropometric parameters (average ± standard deviation) in all group

Parameters	*Basal*	*3 months*
Sf 36 (points)	96.0±9.1	97.6±9.2
Physical function (points)	15.1±5.4	16.0±5.9
Role physical (points)	5.4±1.7	6.1±1.7*
Bodily pain (points)	6.3±3.3	5.1±2.4
General health (points)	19.7±1.7	21.1±1.5*
Vitality (points)	38.7±4.3	39.6±4.4
Social function (points)	5.6±1.2	5.9±0.7
Role emotional (points)	5.1±1.3	5.3±1.3
Handgrip strength		
Right HS (kg/cm^2)	13.3±9.1	17.1±10.2*
Left HS (kg/cm^2)	13.5±8.9	16.8±10.4*

SF-36: Short Form-36, HS handgrip strength

of SF 36 (1.4+/-1.9 points) improved. Right handgrip strength (3.7+/-9.1 kg/cm^2) and left handgrip strength (3.1+/-9.8 kg/cm^2) improved, too.

In order to assess the effect of weight improvement on quality of life, handgrip strength and metabolic parameters, patients were divided in two groups by the median percentage of weight improvement (3.4%); group 1 (percentage of weight improvement <3.4%) and group 2 (percentage of weight improvement >3.4%). The epidemiological characteristics of group 1 (8 males, 9 females; with an average age of 79.3+10.2 years) was similar than group 2 (8 males, 10 females; with an average age of 79.0+10.0 years). Table IV shows the differences in anthropometric variables and biochemical parameters in group 1 and 2. In group 1, patients showed an improvement of vitamin D levels (-13.1+/-10.8 ug/dl). In group 2, patients showed an improvement of BMI (1.1+/-1.4 kg/m^2), weight (4.9+/-2.8 kg), fat mass (1.9+/3.7 kg) and fat free mass (2.2+/-4.4 kg). Prealbumin (1.9+/-3.1 mg/dl) and vitamin D levels increased (14.8+/-11.1 ug/dl), too.

Table V shows the differences in SF-36 questionnaire and handgrip strength. In group 1, patients did not reach statistical differences in these tests. In group 2, role physical domain of SF 36 (0.91+/1.2 points) and general health domain of SF 36 (1.6+/-1.2 points) improved. Right handgrip strength (3.9+/-7.1 kg/cm^2)

Table IV

Basal and post dietary intervention anthropometric parameters (average ± standard deviation) in group I (patients with percentage of weight improvement <3.4%) and group II (patients with percentage of weight improvement >3.4%)

Parameters	*Group I*		*Group II*	
	Basal	*3 months*	*Basal*	*3 months*
BMI (kg/m^2)	23.9±3.6	24.2±3.8	22.1±4.4	23.9±3.4*
Weight (kg)	56.2±9.4	56.6±9.8	53.9±7.8	58.4±7.9*
FFM (kg)	45.0±10.1	44.6±5.2	46.3±3.1	49.0±2.7*
FM (kg)	15.1±7.5	16.1±9.5	15.1±4.7	16.8±4.4*
Albumin (mg/dl)	3.5±0.6	3.6±0.5	3.6±0.4	3.7±1.1
Prealbumin (mg/dl)	19.9±6.3	21.1±6.5*	19.3±42.7	12.0±41.1*
Transferrin (mg/dl)	231.0±32	228.2±26.5	244.6±66.7	265.8±59
Vitamin D3 (ug/dl)	3.2±7.5	16.3±9.4*	7.3±6.7	30.1±15.4*

BMI: Body mass index. FFM: fat free mass. FM: fat mass. (*) p<0,05 in each group.

Table V

Quality of life and and handgrip strength basal and post dietary intervention (average ± standard deviation) (patients with percentage of weight improvement <3.4%) and group II (patients with percentage of weight improvement >3.4%)

Parameters	*Group I*		*Group II*	
	Basal	*3 months*	*Basal*	*3 months*
SF36	95.3±11.5	95.7±7.1	96.6±8.2	99.2±5.7
Physical function	13.3±4.1	13.1±4.3	16.6±5.2	18.5±5.8
Role physical	5.0±1.5	5.4±1.4	5.5±1.6	6.5±1.4*
Bodily pain	6.3±2.4	5.5±3.3	6.2±2.3	4.8±2.3
General health	21.6±1.2	20.5±1.6	19.2±1.7	20.6±1.3*
Vitality	38.5±4.2	40.3±4.1	38.8±2.4	39.0±3.1
Social function	5.6±0.8	5.7±0.9	5.6±1.2	6.1±0.9
Role emotional	5.1±1.2	5.3±1.4	4.9±1.1	5.2±1.4
Handgrip strength				
Right HS (kg/cm^2)	13.2±11.1	16.5±10.2	13.3±6.1	17.5±7.2*
Left HS (kg/cm^2)	13.3±8.9	15.6±10.4	13.4±6.1	17.1±9.2*

SF-36: Short Form-36

and left handgrip strength (3.3+/-6.8 kg/cm^2) improved, too.

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 higher in group 2 than group 1 (group 1: 1.25+0.78 units/day (1.81+/-0.9 g per day of HMBD) vs. group 2: 1.86+0.82 units/day (2.79+/-1.1 g per day of HMBD)). The dietary intake of vitamin D (13.2+4.3 ug/day vs 35.8+4.3 ug/day:p<0.05) was higher in the group 2

Gastrointestinal tolerance (diarrhea episodes) with this formula was good. No subjects experienced diarrhea, nausea, cramps, abdominal distension, or vomiting. There were no dropouts due to intolerance.

Discussion

The results of the present study have confirmed the beneficial effects on weight, handgrip strength, some domains of quality of life and vitamin D status of an enhanced enteral formula with vitamin D and Beta-hydroxy-beta-methylbutyrate (HMB) in elderly patients.

HMB is a metabolite of the ketogenic amino acid leucine. Although HMB can be synthesized endogenously from leucine, approximately 60 g of leucine would need to be consumed daily to reach the HMB dosage of 3 g/d[14]. Therefore, to obtain 60 g of leucine from the diet, one would have to consume 600-700 g of protein from a high-leucine protein source daily, such as dairy, meats and eggs[15]. With these previous data, this consumption is not easy to reach and to obtain HMB 3 g/d, supplementation of HMB is mandatory. This recommendation that the optimal dosage of HMB is 3 g/d comes from previous research by Nissen *et al*.[16], who showed that HMB supplementation at 3 g/d in healthy subjects increased strength in a dose-dependent manner.

Intervention studies in elderly patients with HMBD are heterogeneous and with contradictories results. For example, Vukovich *et al*.[17] compared the effects of 8 wk of HMB supplementation on body composition and strength in 70-y-old subjects. Subjects were assigned to HMB 3 g/d (n=14) or a placebo (n=17) and all subjects participated in 5 day of supervised exercise per week. At the end of 8 wk, upper body strength increased by nearly 15% and lower body strength was increased approximately 20% in the two groups; however, there was no difference in strength changes between the groups. A near significant 0.8-kg increase in lean mass was observed in the HMB group measured by skinfold calipers, whereas no change was observed in the placebo group. However, no difference was observed between the groups.

Hsieh *et al*.[18] investigated the effects of HMB in elderly subjects receiving tube feeding. The subjects were assigned to usual care (n=40) or HMB 2 g/d (n=39) for 28 d ays. After 28 d, HMB supplementation increased weight, body mass index, and waist, hip, and calf circumferences. In addition, HMB supplementation resulted in a decrease in nitrogen excretion, suggesting that HMB decreased protein breakdownand/or increased protein synthesis. A limitation of this study, is that this study did not measure body composition to determine if the increases in weight were from lean or fat mass.

Our study was realized without exercise program like the study of Flakoll *et al*.[19]. Flako *et al*.[19] investigated the effects of 12 wk of HMB supplementation in subjects older than 62 y. Subjects were randomly assigned to HMB 2 g/d, arginine 5 g/d, and lysine 1.5 g/d (n=27) or a placebo (n=23). A near significant 0.7-kg increase in lean mass was observedas measured by bioelectrical impedance and Bod Pod, whereas no changes in lean mass were observed in the placebo group. Baier *et al*.[20] investigated the effects of 1 year of HMB supplementation in subjects > 65 year. Subjects were given HMB 2 to 3 g/d, arginine 5 to 7.5 g/d, plus lysine 1.5 to 2.25 g/d (n=40) or an isonitrogenous control made up of non-essential amino acids (n=37). This supplementation increased lean mass by 0.88 kg as measured by bioelectrical impedance, whereas no significant changes in lean mass were observed in the control group. In our study, patients in the group 2 with a high intake of HMBD) increased lean mass above 2 kg during 12 weeks of treatment.

In the other hand associations between vitamin D status and muscle function are well documented in both epidemiological as well as small intervention studies[21]. However, the impact of vitamin D intake on the attainment of muscle mass or enhancement of muscle function is not clear. Previous studies suggest that vitamin D supplementation may contribute to lean mass accumulation and improved muscle function. For example, a one year vitamin D supplementation (2000 IU/day) study in premenarcheal girls revealed an increase in lean mass accumulation, without exercise training, compared to placebo[22]. However, the results in the literature are contradictories. In Bunout, *et al*.[23] study, older adults consumed a vitamin D supplement (400 IU/day) during participation in an exercise training program for 9 months and no synergistic effects of vitamin D supplementation on muscular strength and physical function were reported. In our study both groups increased vitamin D levels and intakes.

Finally the quality of life is not typically assessed in the work with HMBD supplementation. We only found a study[24] in the literature to analyze this aspect, but it was realized in a cancer population and no effects on lean mass and quality of life was detected with HMBD.

Limitations of our study include lack of a control group and the small sample size. However, as studies in the literature are scarce, these types of designs are interesting intervention to treat sarcopenia[25-27]. Our design shows as patients with a higher intake of vitamin D have HMBD and greater weight gain, muscle stren-

gth and quality of life in relation to physical parameters and general health.

In conclusion, elderly patients with a previous weight loss, treated with a high consumption of a HMBD and vit D enhanced formula, had a significant improvement in anthropometric, biochemical parameters, handgrip strength and quality of life.

Disclosure Statement section

Authors should declare any financial support or relationship that may pose conflicts of interest

"No potential conflicts of interest were disclosed".

References

1. Janssen I, Heymsfield SB, Wang ZM, Ross R. Skeletal uscle mass and distribution in 468 men and women aged 18–88 yr. *J Appl Physiol* 2000;89:81–8.
2. Grimby G, Saltin B. The ageing muscle. *Clin Physiol* 1983;3:209–18.
3. Reid KF, Naumova EN, Carabello RJ, Phillips EM, Fielding RA. Lower extremity muscle mass predicts functional performance in mobilitylimited elders. *J Nutr Health Aging* 2008;12:493–8.
4. Frontera WR, Suh D, Krivickas LS, Hughes VA, Goldstein R, Roubenoff R. Skeletal muscle fiber quality in older men and women. *Am J Physiol Cell Physiol* 2000;279:C611–8.
5. Landi F, Liperoti R, Fusco D, Mastropaolo S, uattrociocchi D, Proia A, *et al*. Sarcopenia and mortality among older nursing home residents. *J Am Med Dir Assoc* 2012;13:121–6.
6. Fitschen P, Wilson G, Wilson J, Wilund K. Efficacy of Beta-hydroxy-beta-methylbutyrate supplementation in elderly and clinical populations. *Nutrition* 2013;29:29-36.
7. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. *Am J Clin Nutr* 2006;84:18e28.
8. El-Hajj FG, Nabulsi M, Tamim H, Maalouf J, Salamoun M, Khalife H, *et al*. Effect of vitamin D replacement on musculoskeletal parameters in school children:a randomized controlled trial. *J Clin Endocrinol Metab* 2006;91:405e12.
9. Siddiqui SM, Chang E, Li J, Burlage C, Zou M, Buhman KK, *et al*. Dietary intervention with vitamin D, calcium, and whey protein reduced fat mass and increased lean mass in rats. *Nutr Res* 2008;28:783e90.
10. Sato Y, Iwamoto J, Kanoko T, Satoh K. Low-dose vitamin D prevents muscular atrophy and reduces falls and hip fractures in women after stroke: a randomizedcontrolled trial. *Cerebrovasc Dis* 2005;20:187e92.
11. Lukaski H, Johson PE. Assessment of fat-free mass using bioelectrical impedance measurements of the human body. *Am J Clin Nutr*. 1985 Apr;41(4):810-7.
12. Brazier JE, harper R, Jones NMB. Validating the SF 36 health survey questionnaire:new outcome measure for primary care. *BMJ* 1992;305:160-162.
13. Mathiowetz V, Weber K, Volland G, Kashman N. Reliability and validity of grip and pinch strength evaluations. *J Hand Surg Am* 1984;9:222e6.
14. Wilson GJ, Wilson JM, Manninen AH. Effects of beta-hydroxy-betamethylbutyrate (HMB) on exercise performance and body composition across varying levels of age, sex, and training experience: a review. *Nutr Metab* 2008;5:1.
15. United States Department of Agriculture. National nutrient database for standard reference [database on Internet]. Beltsville, MD: United States Department of Agriculture; 2011. Available at: http://www.ars.usda.gov. Accessed December 1, 2011.
16. Nissen S, Sharp R, Ray M, Rathmacher JA, Rice D, Fuller JC Jr, *et al*. Effect of leucine metabolite beta-hydroxy-beta-methylbutyrate on muscle metabolism during resistance-exercise training. *J Appl Physiol* 996;81:2095–104.
17. Vukovich MD, Stubbs NB, Bohlken RM. Body composition in 70-year-old adults responds to dietary beta-hydroxy-beta-methylbutyrate similarly to that of young adults. *J Nutr* 2001;131:2049–52.
18. Hsieh LC, Chow CJ, Chang WC, Liu TH, Chang CK. Effect of beta-hydroxybeta-methylbutyrate on protein metabolism in bed-ridden elderly receiving tube feeding. *Asia Pac J Clin Nutr* 2010;19:200–8.
19. Flakoll P, Sharp R, Baier S, Levenhagen D, Carr C, Nissen S. Effect of betahydroxy-beta-methylbutyrate, arginine, and lysine supplementation on strength, functionality, body composition, and protein metabolism in elderly women. *Nutrition* 2004;20:445–51.
20. Baier S, Johannsen D, Abumrad N, Rathmacher JA, Nissen S, Flakoll P. Year-long changes in protein metabolism in elderly men and women supplemented with a nutrition cocktail of beta-hydroxy-betamethylbutyrate (HMB), L-arginine, and L-lysine. *JPEN J Parenter Enteral Nutr* 2009;33:71–82.
21. Ceglia L. Vitamin D and its role in skeletal muscle. *Curr Opin Clin Nutr Metab Care* 2009;12:628e33.
22. El-Hajj FG, Nabulsi M, Tamim H, Maalouf J, Salamoun M, Khalife H, *et al*. Effect of vitamin D replacement on musculoskeletal parameters in school children: a randomized controlled trial. *J Clin Endocrinol Metab* 2006;91:405e12.
23. Bunout D, Barrera G, Leiva L, Gattas V, de la Maza MP, Avendaño M, *et al*. Effects of vitamin D supplementation and exercise training on physical performance in Chilean vitamin D deficient elderly subjects. *Exp Gerontol* 2006;41:746e52.
24. Berk L, James J, Schwartz A, Hug E, Mahadevan A, Samuels M, Kachnic L; RTOG. A randomized, double-blind, placebo-controlled trial of a beta-hydroxyl beta-methyl butyrate, glutamine, and arginine mixture for the treatment of cancer cachexia (RTOG 0122). *Support Care Cancer*. 2008 Oct;16(10):1179-88.
25. Padilla Colon CJ, Sanchez Collado P, Cuevas MJ. Benefits of **strength** training for the prevention and treatment of sarcopenia. Nutr Hosp. 2014;29:979-88.
26. Velázquez Alva Mdel C, Irigoyen Camacho ME, Delgadillo Velázquez J, Lazarevich I. The relationship between sarcopenia,undernutrition, physical mobility and basic activities of daily living in a group of elderly women of Mexico City. *Nutr Hosp*. 2013;28:514-21.
27. Muñoz-Arribas A, Mata E, Pedrero-Chamizo R, Espino L, Gusi N, Villa G, Gonzalez-Gross M, Casajús JA, Ara I, Gómez-Cabello A [Sarcopenic obesity and physical fitness in octogenarians: the multi-center EXERNET Project]. *Nutr Hosp*. 2013;28:1877-83.