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Original Article

Effect of weight loss on bone metabolism in postmenopausal obese women with osteoarthritis

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ABSTRACT

Background: The choice of hypocaloric diets in obesity can affect bone health.
Aims: The aim of this study is to assess the effect of a hypocaloric diet in postmenopausal obese women and to determine the influence of weight reduction on bone metabolism.
Methods: This was a non-randomised, single-treatment study in 96 postmenopausal women with a body mass index (BMI) greater than 35 kg/m^2 and osteoarthritis. The patients received a formula diet with two intake levels of a normocaloric hyperproteic formula (1035 kcal (25% protein)). Anthropometry and biochemistry with CrossLaps, osteocalcin, parathyroid hormone (PTH) and 25-OH vitamin D were measured. Consumption of protein, calcium and vitamin D were determined at the beginning of and 3 and 6 months into the study. The response to treatment was compared (high-responder (HR): weight loss greater than 15%, and low-responder (LR): weight loss less than 15%).
Results: The mean age was 64.2 (7.5) years. After 6 months of treatment, a weight loss of 10.2% (8.2–13.8) was observed. There was a significant increase in vitamin D (HR: 21.8% (36.2) vs. LR: 22.7% (36.9), p = 0.93) and CrossLaps (HR: 26.8% (19.5–35.2)) vs. LR: 13.3% (−6.1 to 27.9), p = 0.01). The loss of more than 15% of initial body weight was an independent risk factor for an increase in CrossLaps (OR: 4.22 (1.1–16.8), p = 0.04).
Conclusions: In postmenopausal obese women, weight loss was associated with an increase in the biochemical parameters of bone resorption. The increase in resorption parameters was related to the magnitude of weight loss.

Introduction

Obesity is the most prevalent metabolic disease in the developed world and one of the main causes of morbidity and mortality. In 2008, the prevalence of obesity in the world was 12% [1], while in Spain it was 22.9% [2]. The rate of obesity in elderly patients is increasing, reaching 20%–30% of the total population over 60 years of age in Europe [3]. Obesity increases the risk of osteoarthritis, by up to 2-fold in the case of the knee [4].

Osteoporosis and osteoarthritis are two closely related entities since they both appear in elderly patients (usually over 50 years old). In addition, both are associated with an alteration in bone microarchitecture, and these entities are involved in proinflammatory processes that may be exacerbated in situations of altered body composition. There is a chronic, low-grade inflammation in these diseases where adipose tissue seems to have great importance [5]. Altered bone metabolism, osteoporosis and an increased risk of fracture all have a high prevalence in elderly patients.

In degenerative joint pathology, weight loss has a positive influence on disease evolution. In osteoarthritis of the knee, a 10% decrease in body weight was associated with a significant

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reduction in functional disability [6]. Clinical practice guidelines in knee osteoarthritis recommend dietetic treatment and exercise in patients with BMI >25 kg/m^2 and symptomatic knee osteoarthritis [7]. On the other hand, dietary treatment and consequent weight loss can be detrimental to bone mineral density. Some studies relate weight loss with a decrease in bone mass and an increased risk of fracture [8,9]. It is important to know how bone loss can be reduced through changes in the diet.

One type of diet used in weight loss in patients with osteoarthritis is the formula diet. The effect of this diet on weight loss is relative and is conditioned by short-duration studies [10,11]. The use of formula diets has not been associated with greater alterations in bone metabolism in the elderly compared with other similar diets in patients without [12] and with [13] osteoarthritis. In these cases, it is important to consider the factors that most influence the risk of metabolic bone disease: female sex and advanced age, associated with the presence or absence of menopause.

The aims of our study were to assess the effect of a modified hypocaloric diet in postmenopausal obese women in the modification of parameters related to bone metabolism and the influence of weight loss and a change in plasma vitamin D on these parameters.

Methods

Study design

This was a non-randomised, single-treatment study with a modified hypocaloric diet with a normocaloric hyperproteic formula. The population selected consisted of postmenopausal women with a BMI greater than 35 kg/m^2 and osteoarthritis of the knee or hip with indications for orthopaedic surgery. The exclusion criteria were active oncological disease and a history of alcohol abuse or drug abuse that could modify bone metabolism.

The study was carried out from January 2014 to July 2017 in patients belonging to the health services catchment area of East Valladolid (Spain). These patients were referred from the Traumatology Service to the Endocrinology and Nutrition Service of the Clinical Hospital of Valladolid for weight loss prior to orthopaedic surgery.

A minimum sample size of 50 patients was calculated as required to detect differences with a 5 kg weight loss in a population with an average weight of 85–90 kg and a deviation of 5–6 kg, assuming a power of 90%, an alpha error of 5% and a rate of 5% loss. We chose weight as the primary outcome for calculating sample size because a minimum weight loss is needed to see changes in bone turnover parameters.

All participants provided informed consent to the protocol, for which ethical approval was obtained from the Valladolid University Clinical Hospital (HCUVA) Ethics Committee. This study was registered in the clinical trial registry of the HCUVA and University of Valladolid with the code FUNGE 061/140242. All procedures involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Therapeutic intervention

After a patient was included in the study, a nutritional assessment and analysis of biochemical markers were carried out. The patients received nutritional education and a hyperproteic, low-fat formula diet: (1) The macronutrient and micronutrient characteristics of the diet in are shown in Table 1. (2) The diet was structured into six meals (breakfast, morning snack, lunch, afternoon snack, dinner and after dinner snack). The lunch and dinner were replaced by an artificial nutritional preparation (VEGEStart Complete®). The formula contains protein in the form of casein and whey. (3) A dietitian consulted with the patient by telephone every 14 days. The different assessments and tests were carried out before the start of the dietary intervention, at 3 months and at 6 months after the beginning of the intervention.

Study variables

Anthropometry

Anthropometric assessment of the subjects was carried out by determination of weight, height and body mass index (BMI). Weight was measured to the nearest 0.1 kg, without clothing, with an accuracy of ±0.5 kg, using a manual scale (Seca, Birmingham, United Kingdom). Height was measured to the nearest centimetre, using a stadiometer (Seca), with the patient in an upright position. BMI was calculated using the following formula: weight (kg)/height × height (m^2). To assess the difference in relative weight, the percentage of weight lost (%PP) was used as follows: (weight before dietary intervention − weight after dietary intervention (kg)/initial weight (kg)) × 100.

We compared patients who lost more than 15% of their initial weight (high-responders) and those who lost less than 15% of the initial weight (low-responders). We selected these patients as high-responders to ensure that there was a significant effect on the mechanical function of bone. An increase in bone resorption markers associated with a weight loss of 13% was seen in a previous study by Brinkworth et al. [14].

Bioelectrical impedance measurement

A bioelectrical impedance analysis (BIA) was performed on all subjects. These measurements were performed before and 3 and 6 months after the start of the intervention. The BIA was performed on all subjects after a fast of at least 5 h. As BIA may be influenced by the degree of hydration, subjects were asked not to exercise or drink alcohol within 48 h prior to the test.

BIA was conducted by means of a four-point single-decubitus device. An alternating current of 0.8 mA at 50 kHz produced by a calibrated signal generator (EFG, Akern Italy) was used and applied to the skin by adhesive electrodes placed on the back of hand and right foot. The body composition was estimated with Bodygram® software.

The parameters analysed by BIA were fat-free mass and fat mass. Both are represented as weight (kg).

Bone metabolism

Bone metabolism was assessed by measurement of biochemical parameters in a blood sample collected at the initial visit and 3 and 6 months into the intervention. The blood sample was collected at 8:00 am after a 12-h fast. The blood samples were transported to the reference laboratory in a cooler filled with ice.

Calcium, phosphorus and bone turnover parameters were determined by Cobas 6000e-60 chemiluminescence immunoassay. Total 25-OH vitamin D was obtained with a measurement range between 3.00 and 70.0 ng/mL. The PTH reference level was 15–65 pg/mL with a functional sensitivity of 6.0 pg/mL. The osteocalcin reference level was 13–48 ng/mL. The aminoterminal propeptide reference level of procollagen type I (P1NP) was <76.3 ng/ml. The reference level for β-crosslap was 0.556–1.008 ng/mL with a functional sensitivity of 0.07 ng/mL. All molecules were measured with a chemiluminescence immunoassay using a Roche Diagnostics autoanalyzer (Basel, Switzerland).

Bone turnover parameters vary between 10% and 15% [15]. So, we considered a change of 25% between the start and the end of treatment as a significant effect on bone turnover markers.

Table 1
Composition of intervention diet and change in dietary consumption in the total sample.

n = 96	Intervention diet	Start	p (1–3)	3 months	p (3–6)	6 months	p (1–6)
Caloric value (kcal)	1035	1466 (406)	<0,01	999 (215)	<0,01	1169 (339)	<0.01
Proteins (g)	64.4	20.5 (3.8)	<0,01	25.9 (17.5)	0,11	22.7 (3.8)	<0.01
Proteins (%TCV)	25%	77.6 (19.9)	<0,01	69.2 (16)	0,10	90.8 (114.7)	0.31
Lipids (g)	19.1	58.46 (23.6)	<0,01	25.72 (116.7)	<0,01	37.3 (20)	<0.01
Lipids (%TCV)	17%	35.5 (7.7)	0,35	28.5 (69.5)	0,86	31.1 (39.3)	0.38
Carbohydrates (g)	151.6	159 (54)	<0,01	147 (107)	0,23	143 (44)	0.02
Carbohydrates (%TCV)	59%	43.4 (8.4)	0,03	62.7 (80.8)	0,14	49.4 (9.1)	<0.01
Fiber (g)	15.9	16.04 (6.6)	0,71	16.27 (4.9)	0,28	25.3 (74.5)	0.26
Vitamine D3 (μg)	10	6.4 (14.6)	<0,01	18.5 (43.4)	<0,01	11.6 (17.1)	<0.01
Vitamin D (%RDA)	66.7	42.9 (97.7)	<0,01	123.2 (289.5)	<0,01	77.7 (114.34)	<0.01
Calcium (mg)	1259.2	901.1 (263)	<0,01	1030.2 (207)	<0,01	965.7 (243.1)	0.03
Calcium (%RDA)	105	90.1 (26.3)	<0,01	101.1 (20.7)	<0,01	96.6 (24.3)	0.13
Phosphorus (mg)	2313.4	1170.1 (296.8)	<0,01	982.9 (209.2)	<0,01	1092.8 (326.4)	0.12
Phosphorus (%RDA)	330	167.2 (42.4)	<0,01	140.4 (29.9)	<0,01	156.1 (46.6)	0.12

RDA: recommended dietary allowances; %TCV: total caloric value percentage; Req: requirements; p (1–3): p value between start-3 month; p (3–6): p value between 3 month and 6 month; p (1–6): p-value between start and 6 months. The variables are expressed in mean (Standard Deviation).

The degree of modification in the parameters of bone metabolism (osteocalcin, CrossLaps, P1NP, 25-OH vitamin D, PTH) between the different time points (basal, 3 months and 6 months) was calculated as a percentage change ((initial value – final value/final value) × 100).

Dietary survey

All subjects completed a 48-h dietary record to assess the intake of calories, macronutrients, minerals and vitamins. This record was carried out before the start of the intervention. After the start of the intervention, all participants consumed the same number of calories. A new dietary record was performed at 3 and 6 months to assess adherence to the formula diet.

The records were reviewed by a dietitian and analysed by using the programme Dietsource (Nestlé, Geneva, Switzerland). Nutritional intake was measured in absolute values (kilocalories, grams, milligrams or micrograms) and also in percentages of the Reference Daily Intake (RDI). The RDIs established for the Spanish population by the Federación Española de Sociedades de Nutrición, Alimentación y Dietética (FESNAD) [16] were used. The values of vitamin D and calcium intake were classified according to the current recommendations of 2011 of the Institute of Medicine (IOM) and the Endocrine Society Workshop [17].

Statistical analysis

The data were analysed using the statistical package SPSS (SPSS for Windows version 15.0, 2008 SPSS Inc., Chicago, IL, USA). An intention-to-treat analysis was performed.

The continuous variables were described as mean (standard deviation) in the case of a normal distribution or as median and interquartile range (p25–p75) if the distribution was not normal. The qualitative variables were described by absolute and relative frequencies (percentages).

In the case of quantitative variables, the Kolmogorov–Smirnov test was used to determine the normality of the distributions. To study the differences between independent means, the parametric or nonparametric statistical tests required by the application conditions (Student's *t*- or Mann–Whitney U test) were used. To study the differences between paired variables, the Student's *t*-test for paired variables and Wilcoxon signed-rank test were used. A multivariate analysis was performed using a binary logistic regression. The level of significance was conventionally set at $p \leq 0.05$.

Results

We recruited 109 women with obesity and osteoarthritis of the knee, hip or both, pending orthopaedic surgery between January 2014 and July 2017; 13 of these did not meet the inclusion criteria. A total of 96 women were allocated to the intervention and 16 (16.7%) patients discontinued treatment with modified diet (Fig. 1). No adverse symptoms related to the intervention were reported. The average age of the patients was 64.2 (7.5) years.

Evolution of parameters

Anthropometry

The percentage weight reduction at 6 months was 10.2% (8.2–13.8). The evolution of weight and BMI are shown in Table 2.

Bone metabolism

After the start of the formula diet, there was an increase in the dietary intake of calcium and vitamin D and the relative protein content of the diet, as well as a decrease in phosphorus. Table 1 shows the content of the diet before and at 3 and at 6 months after the start of the intervention.

In this study, we detected an increase in CrossLaps; 33 patients (34.4% of the total) experienced a 25% increase in the initial CrossLaps value 6 months after the start of the diet. We also observed a decrease in PTH levels and an increase in the level of 25-OH vitamin D; 46 patients (47.9%) achieved an increase of more than 30% in vitamin D at 6 months after the beginning of the diet. The modification of the biochemical values of bone metabolism and the modification in dietary patterns is observed in Table 2.

Differences between responders and non-responders

Frequencies

A comparison was made of two groups that we named high-responders (HR) (those who lost more than 15% of their initial weight) and low-responders (LR) (those who lost less than 15% of their initial weight). There were no differences in age between the two groups (HR: 62.9 (6.7) years vs. LR: 64.5 (7.6) years, p = 0.43).

Of the 96 patients who started the study, 15 (15.8%) achieved a 6-month weight loss greater than 15% (HR).

Significant differences were observed between high responders and low responders in terms of protein consumption and fat free mass loss (Tables 2 and 3).

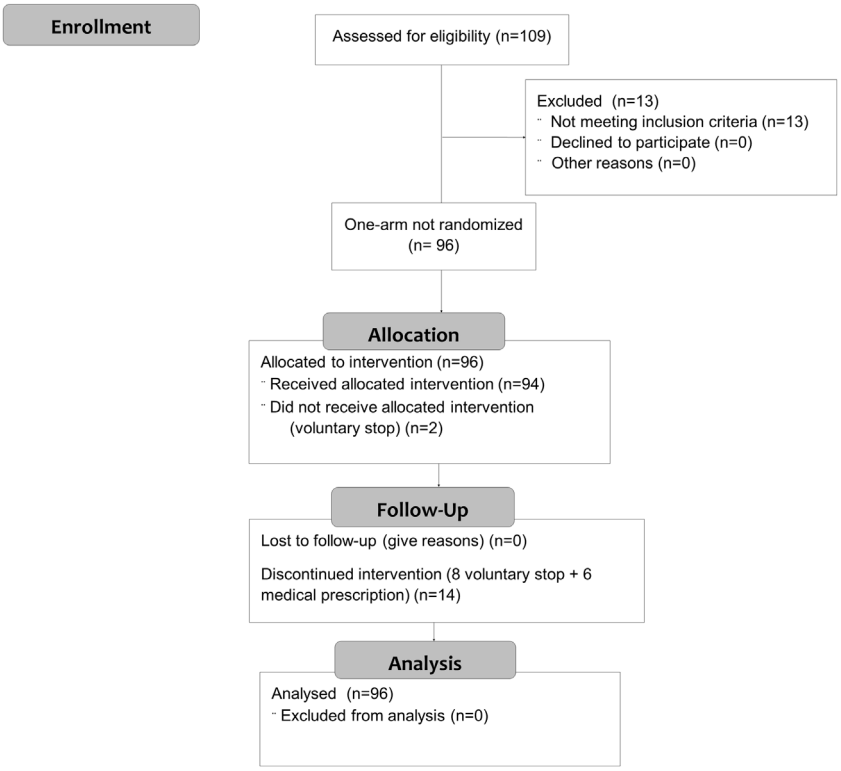

Fig. 1. CONSORT diagram for intervention study.

Table 2
Change in anthropometric parameters, biochemical values dietary consumption in the total sample.

n = 96	Start	p (1–3)	3 months	p (3–6)	6 months	p (1–6)
Anthropometry						
Weight (kg)	96.4 (12.9)	<0.01	88.6 (12.1)	<0.01	85.1 (14.9)	<0.01
BMI (kg/m^2)	40.7 (4.4)	<0.01	37.3 (4.2)	<0.01	36.2 (4.6)	<0.01
Fat free mass (kg)	49.9 (6.5)	<0.01	47.3 (5.6)	0.06	47.7 (5.5)	<0.01
Bioquimic parameters						
PTH (pg/dL)	60.4 (16.9)	<0.01	51.9 (15.6)	0.97	51.8 (18.9)	<0.01
25OHvitaminD (ng/mL)	15.1 (9.4	<0.01	20.9 (16.2)	0.07	24.9 (22.4)	<0.01
Calcium (g/dL)	9.6 (1.3)	0.77	9.6 (0.45)	0.82	9.6 (0.4)	0.72
Phosphorus (mg/dL)	4 (6.1)	0.34	3.4 (0.4)	0.19	3.5 (0.4)	0.41
CrossLaps (ng/mL)	0.40 (0.1)	<0.01	0.45 (0.2)	0.02	0.67 (1.8)	<0.01
P1NP (ng/mL)	48.5 (18.2)	0.57	47.2 (21.4)	0.09	48.7 (20.5)	0.54
Osteocalcin (ng/mL)	21.8 (9.4)	0.05	22.1 (7.9)	0.58	22.5 (8.3)	0.12

BMI: body mass index; PTH: parathyroid hormone; P1NP: procollagen type I; p (1–3): pvalue between start-3 month; p (3–6): p value between 3 month and 6 month; p (1–6): p-value between start and 6 months. The variables are expressed in mean (Standard Deviation).

Table 3
Change (Δ) in anthropometric and biochemical parameters stratified by response to dietary treatment and differences between groups.

	Baseline			Δ 6 months		
	High responders	Low responders	p-value	High responders	Low responders	p-value
Weight (kg)	97.7 (15.4)	95.9 (12.4)	0.63	−12.09 (0.42)	−6.99 (2.88)	<0.01
BMI (kg/m^2)	41.4 (5.2)	40.5 (4.3)	0.44	−5.18 (1.69)	−2.97 (1.09)	<0.01
Fat free mass (kg)	50.5 (7.7)	49.7 (6.3)	0.66	−4.25 (3.79)	−2.31 (4.12)	<0.01
PTH (pg/dL)	57.3 (15.2)	61.6 (17)	0.54	−8.71 (14.16)	−9.19 (13.95)	0.93
Calcium (g/dL)	9.5 (0.5)	9.7 (1.4)	0.56	0.17 (0.63)	−0.08 (1.39)	0.10
Phosphorus (mg/dL)	3.4 (0.5)	4.1 (6.6)	0.68	0.13 (0.40)	−0.78 (6.82)	0.23
25OHvitaminD (ng/mL)	16.2 (10.3)	15 (9.2)	0.65	4.39 (3.49)	5.42 (16.09)	0.33
CrossLaps (ng/mL)	0.38 (0.08)	0.41 (0.15)	0.45	0.11 (0.12)	0.03 (0.14)	0.01
P1NP (ng/mL)	48.9 (10.3)	48.5 (19.4)	0.93	−2.43 (12.73)	−0.52 (18.11)	0.98
Osteocalcin (ng/mL)	21.3 (5.9)	21.9 (10)	0.80	1.99 (4.08)	0.72 (4.25)	0.33
Dietary calcium (mg/day)	854.9 (241.8)	914.3 (266.7)	0.43	−400 (355)	−483 (420)	0.48
Dietary vitamin D (μg/day)	5.7 (15)	6.6 (14.8)	0.82	9.18 (0.91)	13.01 (47.71)	0.10
Protein (%TVC)	21.2 (2.9)	20.4 (4)	0.48	2.87 (3.23)	6.03 (20.36)	0.42

BMI: body mass index; PTH: parathyroid hormone; %TCV: total caloric value percentage. The variables are expressed in mean (Standard Deviation).

Differences in bone metabolism

The modification of anthropometric parameters and bone metabolism was evaluated, and decreases were observed in weight and BMI in both groups. Moreover, a significant increase in the consumption of dietary vitamin D in both groups (Table 3).

There was no correlation between the loss of lean body mass and changes in bone metabolism (osteocalcin: $r = -0.03$; P1NP: $r = -0.05$; CrossLaps: $r = -0.17$; $p > 0.05$) in all patients. When the markers of bone metabolism were analysed, an increase in CrossLaps was observed, which was greater in the group of high-responders (HR: 26.8% (19.5–35.2) vs. LR: 13.3% (−6, 1–27.9), $p = 0.01$). No differences were observed at the level of osteocalcin or P1NP (Fig. 2). These differences occurred despite the increase in vitamin D and the decrease in PTH (Fig. 2).

Multivariate analysis

A multivariate analysis was carried out to evaluate the risk of an increase in CrossLaps above 25% of the initial value at 6 months. An increase in the risk of CrossLaps elevation was observed in those patients with a weight loss greater than 15% at 6 months (OR 4.5 (CI95%: 1.1–18.1); $p = 0.03$), adjusting for protein consumption (OR 1.99 (CI95%: 0.6–7.1); $p = 0.28$), age (OR 1.04 (CI95%: 0.9–1.1); $p = 0.29$) and the change in vitamin D (OR 0.7 (CI95%: 0.2–2.0); $p = 0.51$).

Discussion

The main finding of this study was the relationship between a significant weight loss and an increase in bone resorption parameters despite a more striking increase in plasma vitamin D and a greater increase in the protein content of the diet. A previous study carried out by our group showed that a formula diet could result in weight loss. This weight loss can induce an improvement of pain, disability and quality of life in postmenopausal women with osteoarthritis [18].

However, the effect of diet and associated weight loss has an important implication in the activation of bone metabolism. In postmenopausal women, an increase in bone turnover and a decrease in bone mineral density are observed at 1 year after starting a diet low in dairy products [19] and similarly with a weight loss diet [20]. This effect on bone metabolism was observed with an increase in CrossLaps in premenopausal women who followed a weight loss diet [21]. In our study, an increase in the parameters of resorption (CrossLaps) was seen in those patients who lost the most weight. This situation confirms the negative effect of weight loss on bone remodelling.

A weight loss of 10% is associated with a loss of bone mass of 1%–2% in the spine and hip and 3%–4% in trabecular areas such as the trochanter and radius [22,23]. In elderly men and women, the rate of bone loss is double these values [24]. Thus, weight reduction and age have an additive effect on bone turnover. In our sample we observed that obese, postmenopausal women who lost more weight could experience activation of bone metabolism. This fact may affect bone mineral density related to the hormonal environment and the persistence of some functional disability. Bone loss has been demonstrated in elderly men and women but not in younger people, which may be related to better maintenance of muscle mass in the young [25]. Likewise, there is a greater loss of bone mass in women than in men, which may be due to differences in hormonal characteristics [26].

This decline in bone mass may be associated both with the loss of the positive mechanical effect of weight and with the change in body composition. A relationship has been shown between a decrease in body fat percentage and a decrease in bone mineral density [27]. Also, it has been observed that a decrease in muscle mass is associated with a loss of bone mass [28]. In this study we did not observe a relationship between loss of fat-free mass and an increase in bone metabolism parameters.

The greatest deterioration in turnover parameters was related to the sudden initial weight loss, but these parameters remained high as the weight stabilised. In the long term, the most important effect of this decrease in bone mass is the risk of fracture. In this regard, two studies on 11,000 and 7500 patients showed an increase in non-vertebral fracture in 10 and 17 years of follow-up, with ORs of 1.7 and 3.3, respectively. This shows that voluntary or involuntary weight loss can induce a loss of bone mass and an increased risk of fracture [8,9]. If we examine the data on bone metabolism, we can demonstrate that in the first 3 months of treatment, the patients experienced the greatest weight loss and the most marked change in bone turnover parameters. In the next 3 months, patients experienced slow weight loss, but CrossLaps increased in those who lost more weight.

The hyperproteic composition of the diet suggests a more favourable bone profile than with other types of diets. However, this dietary pattern failed to prevent the increase in resorption parameters. In fact, those patients who lost more weight followed a diet richer in protein; even so, a greater deterioration of bone resorption parameters was observed.

The improvement in bone resorption parameters with the use of hyperproteic and/or calcium-enriched diets has been postulated to control the effect of weight loss on bone [29] and to stop the loss of bone mineral density [30], although bone metabolism has not been shown to increase with the use of diets of this type [31].

The calcium recommendations according to the American Guidelines for Healthy Eating and Postmenopausal Osteoporosis are between 1200 and 1500 mg per day, preferably from a food source, for the prevention of osteoporosis [32,33]. In the case of calcium, an increase in calcium intake of more than 100 mg per day was observed, especially in those patients who lost less weight. Despite this improvement, the calcium content in both groups was below the requirements for the prevention of osteoporosis in this age group (1200–1500 mg) [34].

The vitamin D content is much higher in post-intervention than in pre-intervention diets. The vitamin D levels of the diet in our sample were far below the recommendations [16,32,33]. Despite this change, we did not see an improvement in bone metabolism. This situation is probably associated with the low blood levels of vitamin D obtained in the sample.

The effect of calcium combined with vitamin D in preventing a decrease in bone mass is well known [33]. However, it is not yet well established that this association could have a net beneficial effect as part of a hypocaloric diet: small elevations of bone formation parameters such as osteocalcin have been observed [35], and clear evidence of improvement with supplementation is lacking [36]. Given that vitamin D deficiency is associated with obesity, it seems necessary to increase the intake of vitamin D in obese patients to avoid damage to the bone [37]. It seems that this supplementation is more difficult in obese patients obtaining lower elevations of 25-HO vitamin D in serum with similar amounts to those of patients with BMI <25 kg/m^2 [38]. For this reason, oral supplementation of calcium and vitamin D would be necessary with a hypocaloric diet, perhaps less so than before the diet [33].

The composition of the diet in the proposed intervention, despite having a high protein content and an increased calcium content, did not seem to have a positive effect on the different parameters of bone metabolism beyond the increased intake of vitamin D. The use of diets modified with artificial products in one or two meals has not shown greater alterations in bone metabolism in the elderly than other diets similar in content in patients without osteoarthritis [19] and with osteoarthritis [17].

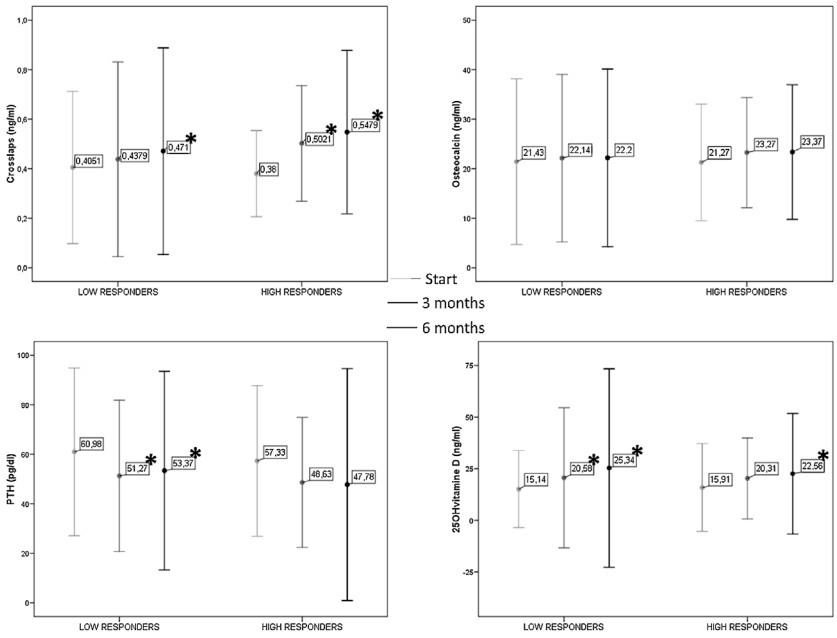

Fig. 2. Changes of dietary treatment at start, 3 and 6 months in bone turnover markers (crosslaps and osteocalcin), parathyroid hormone (PTH) and 25 hydroxivitamin D (25OHvitaminD). * Statystical Signification (p < 0,05).

The main limitation of the study is the absence of a control group to assess the qualitative effect of diet on the deterioration of bone metabolism parameters. It would be interesting to have a direct assessment of the change in bone mass using imaging techniques such as densitometry and, on the other hand, to assess whether this intense weight loss influences the real risk of fracture. This study does not measure physical activity in patients, which could also influence bone mineral density.

Conclusions

In conclusion, the administration of a formula diet in postmenopausal obese women with osteoarthritis pending orthopaedic surgery caused significant weight loss and increased levels of circulating vitamin D. Among patients who lost more weight, there was an increase in bone resorption parameters despite the more marked increase in vitamin D in plasma and a greater increase in the protein content of the diet.

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Conflict of interests

All authors have no conflicts of interest.

Author contributions

Juan José López-Gómez conceived and designed the experiments; analyzed and interpreted the data and wrote the paper.

Olatz Izaola-Jauregui, **David Primo-Martín**, **Beatriz Torres-Torres**, **Emilia Gómez-Hoyos**, **Ana Ortolá Buigues** performed the experiments.

José Luis Pérez-Castrillón, **Miguel Ángel Martín-Ferrero** contributed reagents, materials, analysis tools or data.

Daniel A. De Luis Román conceived and designed the experiments and wrote the paper.

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