15 Effect of Dried Plum on Bone Biomarkers in Men

Shirin Hooshmand

Introduction

Osteoporosis in men is an overlooked yet increasingly important clinical problem that, historically, has not received the same degree of awareness as with women. Epidemiologic studies demonstrate that male osteoporosis contributes significantly to the burden of osteoporotic fractures, especially among the aging population. In particular, men have higher morbidity and mortality associated with osteoporotic fractures compared with women [1]. Typically thought of as a disease impacting women, increasing attention is being paid to osteoporosis in men; however, little research has been conducted to address the situation. About 47% of men older than 50 years have osteopenia [1], and as many as one in four men over the age of 50 years will develop at least one osteoporosis-related fracture in their lifetime [2, 3]. Each year, about 80,000 men in the USA will break their hip [2]; of these, one in three will die in the first year after a hip fracture, and another one-third will fracture again [4]. In light of these statistics, male osteoporosis is recognized as a growing public health concern, and many clinical guidelines now address the evaluation and treatment of osteoporosis in males. Despite this guidance, male osteoporosis remains an underdiagnosed and undertreated condition [5]. Overall, treatments for osteoporosis in men are less defined than in women, mainly due to (a) the fact that there are fewer randomized clinical trials performed in male populations, (b) the relatively smaller sample sizes in the few studies available, and (c) the lack of long-term studies [6].

S. Hooshmand
School of Exercise and Nutritional Sciences, San Diego State University, San Diego, CA, USA
e-mail: shooshmand@sdsu.edu

C. M. Weaver et al. (eds.), *Nutritional Influences on Bone Health*,
https://doi.org/10.1007/978-3-319-98464-3_15

Effects of Dried Plum on Bone

Dried plum is the most effective fruit in both preventing and reversing bone loss. Bone-protective properties of dried plum have been shown in ovariectomized [7, 8] and orchidectomized [9, 10] animal models of osteoporosis and in postmenopausal women [11, 12]. The beneficial effects of dried plum were also tested on male young adult with normal bones vs. old mice with bone loss. The results demonstrated that dried plum increased bone volume above basal levels by nearly 50% in the young adults and 40% in the old mice. Dietary dried plum not only prevented bone loss but also replaced bone that had already been lost due to aging. The magnitude of the changes in bone volume was similar to those in gonadal hormone-deficient male (+36%) and female (+50%) rats fed diets supplemented with dried plum [9]. The effects of the dried plum diet were greatest in the young adult mice, suggesting that although both adult and old mice can respond to dried plum, the effects are somewhat blunted in the aged mice. In almost all cases, the response of adult mice to lower doses of dried plum was similar to the response to higher doses of dried plum, whereas old mice showed little or no response to lower doses of dried plum [13]. Although several animal studies have demonstrated bone-protective effects of dried plum, no human study has evaluated the effect of dried plum on bone metabolism in men.

Dried Plum Improves Bone Biomarkers in Men

To determine whether the addition of 100 g dried plum to the diets of men, regardless of their bone status, can positively influences their indices of bone turnover in comparison with their corresponding baseline values and the control regimen, we conducted a controlled randomized trial in which 66 men (50–79 years of age) received either 100 g dried plum/day or a control regimen for 6 months. All participants received 500 mg of calcium carbonate plus 10 μg (400 IU) of vitamin D_3 (cholecalciferol) daily. The rationale for choosing the dried plum dose (100 g/day) was that this amount has been used in previous studies [11, 12] and has been found effective in preventing bone loss in postmenopausal women. Even though we recently showed that 50 g/day dried plum is as effective as 100 g/day dried plum in preventing bone loss in postmenopausal women [14], we proposed to use 100 g/day dose for this study: (1) because men on average have a bigger body size and (2) because this is the first human study evaluating the bone-protective properties of dried plum in men; therefore, starting with a higher dose increases the probability of detecting significant effects. Subjects treated with any prescription medications known to alter bone and calcium metabolism such as calcitonin, bisphosphonates, raloxifene, and/or anabolic agents such as parathyroid hormone, growth hormone, or steroids within 3 months before the start of the study were excluded. In addition, subjects with metabolic bone disease, renal disease, cancer, cardiovascular disease, diabetes mellitus, respiratory disease, gastrointestinal disease, liver disease or other chronic diseases, and heavy smokers (>20 cigarettes/day) were excluded. Men who regularly consumed dried plum or prune juice were not included in the study. A complete medical history and a dietary vitamin D and calcium questionnaire (SCQ2002) were obtained from the subjects before initiating the treatments. The subjects were advised to maintain their usual physical activity and diet pattern throughout the duration of the study. The subjects completed a 3-day food record and physical activity (IPAQ) questionnaire at baseline, 3 months, and 6 months. Anthropometric data were collected at baseline and 6 months, and height and weight were used to calculate BMI (kg/m^2). Characteristics of study participants are displayed in Table 15.1. Bone density was assessed at the beginning and at the end of the treatment by dual-energy X-ray absorptiometry (LUNAR Prodigy Advanced, GE Healthcare Lunar, Madison, WI, USA) equipped with appropriate software for whole-body, lumbar spine, hip, and forearm BMD. To better understand bone structure changes and to differentiate between cortical and trabecular bone changes, bone structure was assessed using high-resolution peripheral quantitative computed tomography (pQCT, Stratec XCT3000 scanner, Bone Diagnostics, Inc.). The distal tibia was scanned at baseline and final visits. Venous blood samples were obtained after an overnight fast from each subject at baseline, 3 months, and 6 months of the study for various analyses. Blood samples were centrifuged at 1200 × *g* for 15 min at 4 °C, and serum samples were separated, divided into aliquots, and stored at −80 °C until analyses. Changes in bone-specific alkaline phosphatase (BAP) and tartrate-resistant acid phosphatase 5b (TRAP-5b) were analyzed at baseline, 3 months, and 6 months using ELISA kits from Quidel Corporation (San Diego, CA, USA).

Forty men (21 on 0 g/day dried plum and 19 on 100 g/day dried plum) completed the baseline, 3-month, and 6-month visits so far (Fig. 15.1). As expected, baseline characteristics were not significantly different by group for men enrolled in the study (Table 15.1). Age, height, body weight, and BMI were similar at baseline and between the two treatment groups. The 40 participants who completed the study so far adhered to the regimens, as indicated by a self-monitoring calendar provided to them on a monthly basis. Overall, the dried plum treatment was well accepted and considered to be palatable, as stated by the subjects. Mean serum concentrations of biomarkers of bone metabolism, BAP, and TRAP-5b are presented in Table 15.2. Dried plum consumption resulted in a reduction in serum TRAP-5b levels, a marker of bone resorption, at 3 months compared to baseline, while there were no significant changes in serum TRAP-5b levels in the control group (0 g/day dried plum). BAP, a marker of bone formation, did not change after 3 months in either group.

Table 15.1 Characteristics of study participants

	Control	Dried plum	*P* value
Age (years)	64 ± 6	63 ± 7	0.713
Height (cm)	178 ± 7	175 ± 6	0.081
Weight (kg)	88.5 ± 15	88.5 ± 13	0.469
BMI (kg/m^2)	27.5 ± 3.6	27.8 ± 3.6	0.743

Values are mean ± standard deviations, there were no statistically significant differences observed between baseline values of two groups. *BMI* body mass index

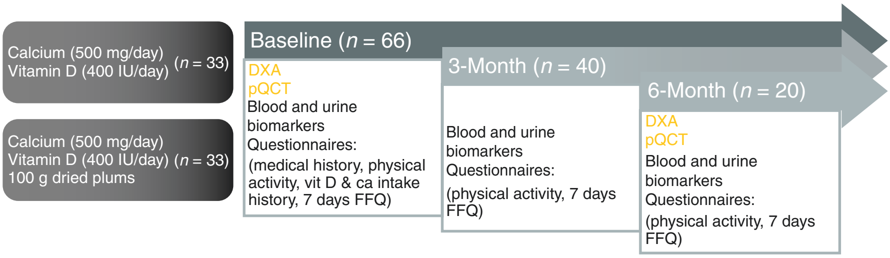

Fig. 15.1 Flowchart of the study design and study participant

Table 15.2 Effect of dried plum on bone biomarkers

Biomarkers	Control (*n* = 21)		*P* value	Dried plum (*n* = 19)		*P* value	*P* value (group × time)
	Baseline	3-month		Baseline	3-month		
BAP (U/L)	24.9 ± 4.1	23.9 ± 4.0	0.12	25.5 ± 8.1	24.3 ± 8.1	0.29	0.08
TRAP5b (U/L)	3.2 ± 1.4	2.9 ± 0.9	0.1	2.7 ± 0.9	2.4 ± 0.7	0.006	0.8

Values are mean ± SD. *BAP* bone-specific alkaline phosphatase, *TRAP-5b* tartrate-resistant acid phosphatase-5b

Conclusions

Dried plum has potent effects on bone in terms of bone mass, microarchitecture, and strength in osteopenic male rats. In our clinical study we have seen suppression of bone resorption marker, TRAP5b, after 3 months of dried plum consumption in men. These findings suggest that dried plum bone-protective effects mediated in part through suppression of bone resorption.

References

1. Lambert JK, Zaidi M, Mechanick JI. Male osteoporosis: epidemiology and the pathogenesis of aging bones. Curr Osteoporos Rep. 2011;9(4):229–36.
2. National Osteoporosis Foundation [webpage on the Internet] Just for Men. Accessed 10 Dec 2017. http://nof.org/articles/236.
3. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int. 2006;17(12):1726–33.
4. von Friesendorff M, McGuigan FE, Besjakov J, Akesson K. Hip fracture in men-survival and subsequent fractures: a cohort study with 22-year follow-up. J Am Geriatr Soc. 2011;59(5):806–13.
5. Willson T, Nelson SD, Newbold J, Nelson RE, LaFleur J. The clinical epidemiology of male osteoporosis: a review of the recent literature. Clin Epidemiol. 2015;7:65–76.
6. Giusti A, Bianchi G. Treatment of primary osteoporosis in men. Clin Interv Aging. 2014;30(10):105–15.
7. Deyhim F, Stoecker BJ, Brusewitz GH, Devareddy L, Arjmandi BH. Dried plum reverses bone loss in an osteopenic rat model of osteoporosis. Menopause. 2005;12(6):755–62.
8. Arjmandi BH, Lucas EA, Juma S, Soliman A, Stoecker BJ, Khalil DA, Smith BJ, Wang C. Dried plums prevent ovariectomy-induced bone loss in rats. JANA. 2001;4(1):50–6.

9. Bu SY, Lucas EA, Franklin M, Marlow D, Brackett DJ, Boldrin EA, Devareddy L, Arjmandi BH, Smith BJ. Comparison of dried plum supplementation and intermittent PTH in restoring bone in osteopenic orchidectomized rats. Osteoporos Int. 2007;18(7):931–42.
10. Franklin M, et al. Dried plum prevents bone loss in a male osteoporosis model via IGF-I and the RANK pathway. Bone. 2006;39(6):1331–42.
11. Arjmandi BH, Khalil DA, Lucas EA, Georgis A, Stoecker BJ, Hardin C, Payton ME, Wild RA. Dried plums improve indices of bone formation in postmenopausal women. J Womens Health Gend Based Med. 2002;11(1):61–8.
12. Hooshmand S, Chai SC, Saadat RL, Payton ME, Brummel-Smith K, Arjmandi BH. Comparative effects of dried plum and dried apple on bone in postmenopausal women. Br J Nutr. 2011;106(06):923–30.
13. Halloran BP, Wronski TJ, VonHerzen DC, Chu V, Xia X, Pingel JE, Williams AA, Smith BJ. Dietary dried plum increases bone mass in adult and aged male mice. J Nutr. 2010;40(10):1781–7.
14. Hooshmand S, Kern M, Metti D, Shamloufard P, Chai SC, Johnson SA, Payton ME, Arjmandi BH. The effect of two doses of dried plum on bone density and bone biomarkers in osteopenic postmenopausal women: a randomized, controlled trial. Osteoporos Int. 2016;27(7):2271–9.