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Effects of Flaxseed (*Linum usitatissimum*) on Bone Health in Experimental Models

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Mini Review

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ABSTRACT

Previous studies have showed protective effects of flaxseed intake. Nevertheless, little data are available about flaxseed effects on the bone health in experimental models. The review presents results of studies that evaluated the bone parameters of wistar rats fed flour or flaxseed oil during lactation (21 days), until adulthood (90 days), in lactating rats and as treatment of malnutrition after early weaning. These experimental studies suggest a beneficial effect of flaxseed in bone parameters.

INTRODUCTION

The Latin name of the flaxseed is *Linum usitatissimum*, which means "very useful". Flaxseed is made up of 30% lipids (50-55% as alpha linolenic acid - ALA and 15-18% as linoleic acid), 28% fibers, 21% protein and 6% carbohydrates distributed among phenolic acids, sugars, lignin and hemicelluloses. Flaxseed contains a high calcium concentration (236 mg per 100 g of seed) and various edible forms of flax are available in the food market - flour or oil for example [1-3]. Previous experimental studies have showed protective effects of flaxseed intake, such as: to cardiovascular system, reducing serum cholesterol and triglycerides, increasing HDL-cholesterol levels and improving endothelial function [1,4-6]; In the adjuvant treatment of obesity with anti-obesogenic action [7]; In better cerebral development and made less stressed animals [8-11]. Nevertheless, little data are available about flaxseed effects on the bone health in experimental models.

In a first moment was evaluated whether maternal flaxseed intake during lactation period has effects on bone structure of male rats at weaning (21 days). Costa et al. [12] with flaxseed flour and Pereira et al. [13] with flaxseed oil diet observed higher body length and, in Dual-energy X-ray absorptiometry (DXA) test, bone mineral density (BMD), bone mineral content (BMC) and bone area. Femur analysis showed higher mass, distance between epiphysis, BMD and, in biomechanical test, resistance to bone fracture. In addition, these rats showed higher osteoprotegerin and osteocalcin levels. These results demonstrated that ALA provided by flour or flaxseed oil during lactation period plays an important role in bone parameters of pups at weaning.

In a second moment was evaluated the continuity of flaxseed diet since lactation period until adulthood. Costa et al. [14] observed that, at 90 days, experimental group fed with flaxseed flour diet showed no differences (vs. control group) to body BMD, BMC, bone area and osteocalcin levels. However, to femoral structure, flaxseed flour intake was associated with higher mass, BMD, in computed tomography (CT) test, proximal epiphysis radiodensity and resistance to bone fracture. Here, flaxseed flour contributes to lower risk of developing bone fragility in young male rats.

Mothers face, during lactation period, an increase in the rate of bone resorption with daily loss of calcium to produce milk. When lactation ceases, BMC reduces by 20-30%, and the skeleton is normally restored to the prior BMD level within 6-12 months after weaning, however it is not clear whether this bone loss is completely recovered [15,16]. In this context, Ribeiro et al. [3,17] evaluated the bone parameters of lactating rats treated with flaxseed flour diet during post-weaning period. After 30 days of treatment, its female rats showed similar results (vs. control group) to osteoprotegerin, osteocalcin, body, femur and lumbar vertebra (LV4) BMD, BMC and bone area. However, by CT and biomechanical test, femur showed higher radiodensity of proximal

epiphysis and resistance to fracture, respectively. These evidences suggest that flaxseed flour may contribute to bone quality in post-weaning period.

The malnutrition in early period of life is as risk factor for bone health. Given the prevalence of precocious interruption of breastfeeding in humans [18], an study was perfomed by Boueri et al. [19] and Pessanha et al. [20] to compared the effects of flaxseed flour (vs. flaxseed oil) on bone fragility in male rats subjected to early weaning (EW). In fact, precocious lactation interruption, at 14 days, promotes lower body length, BMD, BMC and bone area at 21 and 60 days, respectively. Flaxseed flour (vs. flaxseed oil), after 21 days until 60 days, contributes to recovery of body and femoral BMD, BMC and bone area. Probably, alpha linolenic acid associated with calcium and protein present in flaxseed flour, abbreviates the bone fragility secondary to early weaning, when compared to flaxseed oil.

The mechanism of action of flaxseed on bone structure is complex and involves several signaling pathways. ALA is related to the recruitment and maturation of pre-osteoblasts, thus promoting bone formation. Furthermore, ALA helps maintain osteocalcin, osteoprotegerin levels, secreted by the osteoblast, and decrease receptor activator of nuclear factor kappa-B (RANK) levels, a receptor found in osteoclast binding to nuclear factor kappa-B ligand receptor activator (RANKL). Therefore, ALA is associated with lower maturation, osteoclast lifespan and lower bone resorption [21]. In addition, ALA increases calcium (a key component for the formation of hydroxyapatite crystals and bone matrix mineralization) absorption in the gut, promoting mineral deposition in bone [22]. Another possible explanation is about protein composition of the diet. The literature reported that high animal protein intake produces an increase in organic acids and metabolic acidosis, with bone demineralization and bone loss [23]. In control diet, protein source was casein [24], an animal protein, whereas in flaxseed flour diet, a part of proteins was derived from the seed, which may have contributed to the deposition of organic matrix, including bone specific proteins such as type 1 collagen and to bone tissue rigidity and resistance. Costa et al. [12], Pereira et al. [13] and Ribeiro et al. [3] observed that flour and flaxseed oil were associated with higher HDL-cholesterol and lower concentrations of cholesterol. Experimental studies have reported that cholesterol interferes directly in osteoblast differentiation, by decreasing bone formation and increasing osteoclast bone resorption [25]. Meanwhile, Jeong et al. [26] have found a positive correlation between HDL-cholesterol and BMD, favoring bone formation.

These experimental studies suggest a beneficial effect of flaxseed in bone parameters. However, further experimental studies are necessary to elucidate the effects of flaxseed intake in bone parameters in adult rats (at 180 days) and in glucocorticoid-induced osteoporosis models.

REFERENCES

1. Cardozo LFMF, et al. Exposure to flaxseed during lactation does not alter prostate area or epithelium height but changes lipid profile in rats. Nutr Hosp. 2010;25:250-255.
2. Goyal A, et al. Flax and laxseed oil: An ancient medicine & modern functional food. J Food Sci Technol. 2014;51:1633-1653.
3. Ribeiro DC, et al. Assessments of body composition and bone parameters of lactating rats treated with diet containing flaxseed meal (*Linum usitatissinum*) during post-weaning period. Nutr Hosp. 2014;30:366-371.
4. Daleprane JB, et al. Dietary flaxseed supplementation improves endothelial function in the mesenteric arterial bed. Food Res Int. 2010;43:2052-2056.
5. Pacheco JT, et al. Impact of dietary flaxseed (*Linum usitatissimum*) supplementation on biochemical profile in healthy rats. Nutr Hosp. 2011;26: 798-802.
6. Ribeiro ICA, et al. Effects of flaxseed flour on the lipid profile of rats submitted to prolonged androgen stimuli. Nutr Hosp. 2014;30:825-830.
7. Brant LHC, et al. Impact of flaxseed intake upon metabolic syndrome indicators in female wistar rats. Acta Cir Bras. 2012;27:537-543.
8. Almeida KCL, et al. Influence of omega-3 fatty acids from the flaxseed (*Linum usitatissimum*) on the brain development of newborn rats. Nutr Hosp. 2012;26: 991-996.
9. Leite CDFC, et al. Flaxseed and its contribution to body growth and brain of wistar rats during childhood and adolescence. Nutr Hosp. 2011;26:415-420.
10. Meneses JA, et al. Behavioral analysis of wistar rats fed with a flaxseed based diet added to an environmental enrichment. Nutr Hosp. 2011;26:716-721.
11. Pessanha CR, et al. Brain development in male rats subjected to early weaning and treated with diet containing flour or flaxseed oil after 21 days until 60 days. J Dev Orig Health Dis. 2015;6:268-271.
12. Costa CAS, et al. Body adiposity and bone parameters of male rats from mothers fed diet containing flaxseed flour during lactation. J Dev Orig Health Dis. 2015;7: 1-6.

13. Pereira AD, et al. Maternal flaxseed oil during lactation enhances bone development in male rat pups. Lipids. 2016;51:923-929.

14. Costa CAS, et al. Effects of diet containing flaxseed flour (*Linum usitatissimum*) on body adiposity and bone health in young male rats. Food Funct. 2016;7:698-703.

15. Kovacs CS. Calcium and bone metabolism disorders during pregnancy and lactation. Endocrinol Metab Clin North Am. 2011;40:795-826.

16. Miller SC, Bowman BM. Rapid inactivation and apoptosis of osteoclasts in the maternal skeleton during the bone remodeling reversal at the end of lactation. Anat Rec. 2007;290:65-73.

17. Ribeiro DC, et al. Flaxseed flour (*Linum usitatissinum*) consumption improves bone quality and decreases the adipocyte area of lactating rats in the post-weaning period. Int J Food Sci Nutr. 2016;67:29-34.

18. World Health Organization. Global strategy for infant and young child feeding. Geneva, Switzerland. 2003.

19. Boueri BFC, et al. Body composition in male rats subjected to early weaning and treated with diet containing flour or flaxseed oil after 21 days until 60 days. J Dev Orig Health Dis. 2015;6:553-557.

20. Pessanha CR, et al. Flaxseed flour, compared to flaxseed oil, contributes to femoral structure in male rats subjected to early weaning. Food Funct. 2016;7: 1296-1300.

21. Kruger MC, et al. Long-chain polyunsaturated fatty acids: selected mechanisms of action on bone. Prog Lipid Res. 2007;49:438-449.

22. Lau BYY, et al. Investigating the role of polyunsaturated fatty acids in bone development using animal models. Molecules. 2013;18:14203-14227.

23. Silva ZN, et al. Effect of “protein diet” and bone tissue. Nutr Hosp. 2014;29:140-145.

24. Reeves PG. Components of the AIN-93 diets as improvements in the AIN-76A diet. J Nutr. 1997;127:838-841.

25. You L, et al. High cholesterol diet increases osteoporosis risk via inhibiting bone formation in rats. Acta Pharmacol Sin. 2011;32:1498-1504.

26. Jeong I, et al. Lipid profiles and bone mineral density in pre- and postmenopausal women in Korea. Calcif Tissue Int. 2010;87:507-512.