Nutrient effects on stress reaction to bone

Marni L. Wesner MD MA FCFP DipSportMed

Pain complaints related to periostitis and stress fractures are common in active individuals. This spectrum of "stress reaction" to bone is usually associated with untrained athletes who are making a lifestyle choice and beginning activity, or conditioned athletes who increase the intensity, frequency, or duration of training.

The role of calcium and vitamin D in bone health is undisputed. Since 1997, the Canadian and American governments have recommended a daily allowance for vitamin D for adults of 600 IU per day. Many experts believe this value is inadequate and continue to advocate for a higher recommended daily allowance for vitamin D.[1] In 2007 the Canadian Cancer Society recommended a daily intake of 1000 IU of vitamin D, advocating for the beneficial effects of vitamin D in the prevention of colorectal, breast, and prostate cancer.[2] Vitamin D is synthesized in the skin; UVB solar exposure converts 7-dehydrocholesterol to vitamin D. In Canada there is a seasonal variation to vitamin D synthesis, with levels at their lowest in the winter months.[3-7] About 20000 IU of vitamin D are produced from a single 15-minute, midday, whole-body exposure to sunlight.[8] However, this is negatively affected by clothing and sunscreen. In winter months, at latitudes beyond 42°N the solar angle is too oblique for vitamin D synthesis,[3] contributing to increased deficiency between October and April. Food-source supplementation has become the main source of vitamin D where solar exposure is limited. Food products provide about 200 IU of vitamin D per day.[9] Health Canada recommends that, in addition to following Canada's Food Guide, those older than 50 years of age should take a daily vitamin D supplement of 400 IU daily.

Vitamin D is required at all phases of skeletal development and is essential for the mediated transport of calcium to produce mineralized bone matrix. Bone resorption markers are detected with vitamin D levels less than 60 nmol/L, and parathyroid hormone (PTH) increases with vitamin D levels less than 78 nmol/L. Inadequate vitamin D results in secondary hyperparathyroidism, increased bone turnover, accelerated bone loss, and increased fracture risk.

Previous research has variably demonstrated both positive and negative relationships between calcium and vitamin D levels and stress fractures. Previous research identified that athletes with stress fractures had lower calcium intake.[10] Calcium supplementation has a positive linear relationship to spinal trabecular bone density in amenorrheic elite athletes.[11] But calcium intake did not correlate with stress fractures and bone mineral density in female army recruits,[12] and calcium in the diet did not alter stress fractures in elite cross-country athletes.[13] Vitamin D levels have been shown to be lower in Israeli military personnel with stress fractures,[14] but calcium and vitamin D levels have not been related to stress fractures in adolescent girls.[15] In 179 Finnish military recruits, stress fractures were associated with high PTH levels but not low vitamin D levels. Because Finnish men have poor vitamin D status, vitamin D supplementation to lower PTH and reduce the incidence of stress fractures was recommended.[16] In another study, serum vitamin D was significantly lower among 756 Finnish military recruits in those with stress fractures (odds ratio=3.6, 95% CI 1.2 to 11.1).[17] More recent studies have identified a 20% decrease in stress fractures in American military recruits using calcium and vitamin D supplementation.[18] The balance of current research provides evidence to suggest that maintaining adequate vitamin D status might reduce stress fracture risk in athletic populations.[19]

This article has been peer reviewed.
Cet article a fait l'objet d'une révision par des pairs.
Can Fam Physician 2012;58:1226-30

EDITOR'S KEY POINTS

- Pain related to periostitis and stress fractures is common among active individuals, particularly untrained athletes becoming active and conditioned athletes increasing the intensity, frequency, or duration of training. Supplementation with calcium and vitamin D aids in optimizing bone health and might reduce the incidence of stress reaction to bones in active individuals.

- The author has been successfully treating patients with periostitis and stress fractures with 1500 mg calcium and 1000 to 2000 IU vitamin D, without regularly altering levels of training or weight-bearing exercise.

POINTS DE REPÈRE DU RÉDACTEUR

- La douleur reliée à une périostite et aux fractures de stress est fréquente chez les personnes actives, en particulier les athlètes qui reprennent l'entraînement après avoir cessé et les athlètes en bonne condition qui augmentent l'intensité, la fréquence ou la durée de leur entraînement. Un supplément de calcium et de vitamine D aide à optimiser la santé des os et pourrait réduire l'incidence d'une réaction de stress aux os des personnes actives.

- L'auteur a traité avec succès des patients souffrant de périostite et de fractures de stress avec 1 500 mg de calcium et de 1000 à 2000 UI de vitamine D, sans avoir à modifier périodiquement l'intensité de l'entraînement ou les exercices de port de poids.

Case

A healthy, white, 26-year-old female patient presented in March 2004 for a second opinion about exercise-induced pain in her right leg. For 3 years she had been training for a marathon, but she had yet to successfully complete the training owing to recurrent leg pain. In 2 successive years she had been diagnosed with stress fractures in the right and left tibia that curtailed her training. At the time of her presentation, she had been experiencing similar leg pain for the third consecutive year. The pain was only present with running and began after 10 minutes of training. She described the pain as sharp and constant along the anterior right tibia with every foot strike. She was able to run for 90 minutes with pain, but in the month preceding her presentation, the pain escalated in severity and became more focal at the distal aspect of the anterior right tibia. There were no sensory changes or weakness associated with the pain, and she experienced relief with rest. Review of her training log uncovered nothing remarkable and suggested no clinical concerns about the volume of cardiovascular or strength training. Footwear was changed every 500 miles (800 km). She ran outdoors on grass or trails in the summer and on a treadmill in the winter. She did not use nicotine; caffeine consumption was limited to a single cup of coffee in the morning. She menstruated regularly; ate a healthy, balanced diet with adequate dietary sources of calcium; and was not taking any medications or supplements.

Examination findings were relatively unremarkable; the only positive finding was pain on palpation of the anterior medial tibial boarder bilaterally, with more focal pain at the junction of the middle and distal third of the right tibia. Pain in this area was augmented with tuning fork vibration. X-ray films of the tibia and fibula were unremarkable. Nuclear medicine imaging demonstrated a stress fracture at the midshaft of the right tibia. The patient's bone densitometry results were normal for her age, and findings from biochemical investigation for metabolic disease affecting bone were normal save for her total 25-hydroxyvitamin D level, which was 64 nmol/L (normal 80 to 150 nmol/L).

Supplementation with 2000 IU of vitamin D and 1500 mg of calcium daily was initiated, and laboratory values for 25-hydroxyvitamin D normalized in 3 months. Pain complaints and the clinical findings of the stress fracture had resolved 6 weeks after initiating vitamin D and calcium supplementation. Without altering the training program she had previously been following, the patient was able to resume her training schedule without pain and successfully completed her first marathon in August 2005. She continues to take calcium and vitamin D supplements, and she participates in a marathon each summer.

Discussion

Vitamin D deficiency is common in Canada[3-7] and at latitudes above 42°N.[3] Sunscreen and clothing limit vitamin D synthesis in the summer months, and exposure to solar radiation is insufficient in winter months to affect vitamin D production. Normal calcium metabolism is dependent upon adequate intake of calcium and vitamin D, but an excess of one can partially compensate for a deficiency in the other. The effect of calcium and vitamin D on bone metabolism has been confirmed in the osteoporotic population but might be underappreciated in the healthy, active population.

Periostitis and stress fractures are 2 entities along the spectrum of stress reaction to bone. Bone is a specialized form of connective tissue. In the adult, bone comprises 35% organic material that is mainly type 1 collagen; 60% mineral, mainly calcium hydroxyapatite; and 5% water. Like other tissues, bone responds to stress. Weight-bearing activity results in stress-generated potentials that affect the orientation of collagen fibres and the mineral deposition in bone.[20] Bone remodels in response to mechanical stress and is affected by the number of loading cycles, cycle frequency, amount of strain, strain rate, and strain duration per cycle. When bone is loaded, bending of the collagen molecules under compression results in electronegative forces, and the area under tension creates electropositive forces.[21] Osteoclasts dissolve the crystalline and collagen structure of bone and are stimulated by electropositive forces created from tensile forces. Activation of osteoclasts causes microfracture and debonding at the cement lines of the haversian canal in the basic unit of bone. Each loading cycle results in a small amount of strain energy lost through microscopic cracks along the cement lines of the haversian system. Progressive accumulation of microdamage results in bone failure through crack propagation when remodelling and new bone formation cannot keep up with the progressive bony remodeling.[1] With accumulation of stress response to bone, a spectrum exists from normal remodeling of bone to excessive remodeling, which results in weakening of the bony trabeculae and microfracture. Proliferation of periosteum occurs along areas of microfracture. If the stress to the bone is not altered, the progressive microfracture results in macrofracture. Increased levels of unaccustomed activity together with insufficient time for recovery result in the progressive accumulation of microfracture and stress fracturing of bone.

Muscles exert a protective effect on bone. Muscle contraction causes a reduction in cortical bone surface bending strain and diminishes the electropositive forces on the bone. With muscle fatigue, the shock-absorbing effect is diminished and more force is transmitted directly to the bone, increasing the microdamage accumulation. Intrinsic factors such as sex, race, age, bone geometry, foot structure, and leg length affect the stress reaction to bone. So do external hip rotation, lower limb biomechanics, hormonal factors, and bone mineral density. Extrinsic factors such as the training regimen, training surfaces, footwear, aerobic fitness and muscle strength, medications, and smoking also factor into the stress reaction to bone. There are also general medical issues, such as the female athlete triad, and the nutritional influences of caffeine, calcium, and vitamin D that play a role in the stress response to bone.

For a number of years, I have been successfully treating patients who have periostitis or stress fractures with 1500 mg calcium and 1000 to 2000 IU vitamin D, without regularly altering levels of training or weight-bearing exercise. Between July 2007 and June 2010, a random sample of 33 patients (8 men and 25 women) presenting with a clinical diagnosis of stress fracture were evaluated for calcium and vitamin D adequacy by measuring serum calcium and vitamin D levels. No one in this sample population demonstrated deficiencies in serum calcium levels, but 4 men (50%) and 11 women (33%) were clinically deficient in vitamin D, with serum levels less than 80 nmol/L. The importance of this is uncertain, as vitamin D deficiency has a high prevalence in the general population. A recent Statistics Canada study identified that 2 out of every 3 people in Canada have levels of vitamin D below the amounts research has associated with reduced health risks. One in 10 Canadians has a level below that needed for bone health, and about 4% of Canadians have levels of vitamin D sufficiently low to be at risk of rickets.[22]

In many areas of Canada, the results of vitamin D investigation are not available in a timely manner. Screening for serum vitamin D levels is not advised for the generally healthy population, and should be restricted to those who are at higher risk of vitamin D deficiency such as elderly individuals, breastfed infants, individuals with dark skin, or those with malabsorption syndromes or limited sun exposure. Athletes with a history of stress fracture, frequent illness, bone or joint injury, skeletal pain, or overtraining syndrome should be screened.[19] Athletes who have restricted eating patterns (eg, vegetarian, vegan) or athletes who spend most of their time training indoors should also be screened for vitamin D deficiency. Monitoring the response of patients who are deficient in vitamin D is appropriate 3 to 4 months after initiating vitamin D therapy, but it is not necessary to monitor routine supplementation in otherwise healthy individuals.

I recommend that all of my patients with periostitis and stress fractures take 1500 mg of calcium and 1000 IU of vitamin D daily in the summer months (2000 IU of vitamin D in the winter months). Excessive calcium can result in constipation, kidney stones, renal insufficiency, and vascular calcification, and can impair iron and zinc absorption. However, these effects are rare from dietary or supplemental calcium intake and are more commonly associated with primary hyperparathyroidism and malignancy.[23] Excessive vitamin D levels result in nonspecific adverse effects of anorexia, weight loss, and polyuria. They can also lead to increased calcium levels and cardiac arrhythmias. However, symptoms of toxicity are unlikely at supplementation levels less than 10000 IU daily.[24]

Conclusion

Supplementation with calcium and vitamin D aids in optimizing bone health and might reduce the incidence of stress reaction to bones in active individuals. However, there are many other factors that contribute to athletic-induced stress reaction to bone, and further large population-based studies are needed to better understand the roles of calcium and vitamin D.

Dr Wesner practises sports medicine at the Glen Sather Sport Medicine Clinic in Edmonton, Alta, and is Chief Medical Officer for Skate Canada.

Competing interests
None declared

Correspondence
Dr Marni L. Wesner, Glen Sather Sport Medicine Clinic, Edmonton Clinic, Level 2, 11400 University Ave, Edmonton, AB T6G 1Z1, telephone 780 407-5160; fax 780 407-5667; e-mail **mwesner@ualberta.ca**

References

1. McClung JP, Karl JP. Vitamin D and stress fracture: the contribution of vitamin D receptor gene polymorphisms. *Nutr Rev* 2010;68(6):365-9.
2. Canadian Cancer Society [website]. *Canadian Cancer Society announces vitamin D recommendation.* Toronto, ON: Canadian Cancer Society; 2007. Available from: **www.cancer.ca/Canada-wide/About%20us/Media%20centre/CW-Media%20releases/CW-2007/Canadian%20Cancer%20Society%20Announces%20Vitamin%20D%20Recommendation.aspx?sc_lang=en**. Accessed 2012 Oct 5.
3. Webb AR, Kline L, Holick MF. Influence of season and latitude on the cutaneous synthesis of vitamin D3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D3 synthesis in human skin. *J Clin Endocrinol Metab* 1988;67(2):373-8.
4. Vieth R, Cole DE, Hawker GA, Trang HM, Rubin LA. Wintertime vitamin D insufficiency is common in young Canadian women and their vitamin D intake does not prevent it. *Eur J Clin Nutr* 2001;55(12):1091-7.
5. Gozdzik A, Barta JL, Wu H, Wagner D, Cole DE, Vieth R, et al. Low wintertime vitamin D levels in a sample of healthy young adults of diverse ancestry living in the Toronto area: associations with vitamin D intake and skin pigmentation. *BMC Public Health* 2008;8:336.
6. Vecino-Vecino C, Gratton M, Kremer R, Rodriguez-Manas L, Duque G. Seasonal variance in serum levels of vitamin D determines a compensatory response by parathyroid hormone: study in an ambulatory elderly population in Quebec. *Gerontology* 2006;5(1):33-9.
7. Rucker D, Allan JA, Gick GH, Hanley DA. Vitamin D insufficiency in a population of healthy western Canadians. *CMAJ* 2002;166(12):1517-24.
8. Barger-Lux MJ, Heaney RP. Effects of above average summer sun exposure on serum 25-hydroxyvitamin D and calcium absorption. *J Clin Endocrinol Metab* 2002;87(11):4952-6.
9. Freedman DM, Looker AC, Chang SC, Graubard BI. Prospective study of serum vitamin D and cancer mortality in the United States. *J Natl Cancer Inst* 2007;99(21):1594-602.
10. Myburgh KH, Hutchins J, Fataar AB, Hough SF, Noakes TD. Low bone density is an etiologic factor for stress fractures in athletes. *Ann Intern Med* 1990;113(10):754-9.
11. Wolman RL, Clark P, McNally E, Harries MG, Reeve J. Dietary calcium as a statistical determinant of spinal trabecular bone density in amenorrhoeic and oestrogen-replete athletes. *Bone Miner* 1992;17(3):415-23.
12. Cline AD, Jansen GR, Melby CL. Stress fractures in female army recruits: implications of bone density, calcium intake and exercise. *J Am Coll Nutr* 1998;17(2):128-35.
13. Laker SR, Saint-Phard D, Tyburski M, van Dorsten B. Stress fractures in elite cross-country athletes. *Orthopedics* 2007;30(4):313-5.
14. Givon U, Friedman E, Reiner A, Vered I, Finestone A, Shemer J. Stress fractures in the Israeli defense forces from 1995-1996. *Clin Orthop Relat Res* 2000;(373):227-32.
15. Loud KJ, Gordon CM, Micheli LJ, Field AE. Correlates of stress fractures among preadolescent and adolescent girls. *Pediatrics* 2005;115(4):e399-406.
16. Välimäki VV, Alfthan H, Lehmuskallio E, Loyttyniemi E, Sahi T, Souminen H, et al. Risk factors for clinical stress fractures in male military recruits: a prospective cohort study. *Bone* 2005;37(2):267-73.
17. Ruohola JP, Laaksi I, Ylikomi T, Haataja R, Mattila VM, Sahi T, et al. Association between serum 25(OH)D concentrations and bone stress fractures in Finnish young men. *J Bone Miner Res* 2006;21(9):1483-8.
18. Lappe J, Cullen D, Haynatzki G, Recker R, Ahlf R, Thompson K. Calcium and vitamin D supplementation decreases incidence of stress fractures in female Navy recruits. *J Bone Miner Res* 2008;23(5):741-9.
19. Larson-Meyer DE, Willis KS. Vitamin D and athletes. *Curr Sports Med Rep* 2010;9(4):220-6.
20. Treharne RW. Review of Wolff's law and its proposed means of operation. *Orthop Rev* 1981;10:35-47.
21. Reid DC. Bone: a specialized connective tissue. In: *Sports injury assessment and rehabilitation*. New York, NY: Churchill-Livingstone Inc; 1992. p.103-28.
22. Statisitics Canada. *Canadian Health Measures Survey: cholesterol and vitamin D levels.* Ottawa, ON: Statisitics Canada; 2009. Available from: **www.statcan.gc.ca/daily-quotidien/100323/dq100323a-eng.htm**. Accessed 2012 Oct 5.
23. Office of Dietary Supplements. *Dietary supplement fact sheet: calcium*. Bethesda, MD: National Institutes of Health; 2012. Available from: **http://ods.od.nih.gov/factsheets/calcium**. Accessed 2012 Oct 5.
24. Office of Dietary Supplements. *Dietary supplement fact sheet: vitamin D*. Bethesda, MD: National Institutes of Health; 2011. Available from: **http://ods.od.nih.gov/factsheets/vitamind**. Accessed 2012 Oct 5.