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A Focus On Osteoporosis

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Talk about osteoporosis risk in your male patients. Safety concerns with treatments are still being evaluated, but in most cases benefits outweigh the risk of adverse effects. Drug holidays may be appropriate for select patients, but the evidence is limited. Calcium is still required for healthy bones, but intake should be through diet rather than supplements, and more is not better. All adults should take a vitamin D supplement. Smoking cessation and avoiding excessive alcohol intake can reduce the risks of both osteoporosis as well as adverse effects of treatment.

November is osteoporosis awareness month. This Tablet column highlights a few emerging issues.

Osteoporosis in men

Although osteoporosis is more common and occurs earlier in women, men account for 20% of patients with osteoporosis and a disproportionate number of osteoporosis-related fractures.¹⁻⁴ Mortality following fractures of the hip is also two to three times higher compared to women. There is a need for increased awareness of the problem and clinical practice guidelines for assessing and treating osteoporosis in men have recently been published.¹⁻³

Treatment options have not been as thoroughly studied in men as in women, and outcomes have focused mainly on bone mineral density (BMD) rather than fractures. However, many of the same therapies are recommended. Antiresorptive agents like alendronate, zoledronic acid, and risedronate, and anabolic agents such as teriparatide have indications for treating osteoporosis in men.^{2,4}

Hormone therapy in men is not a first-line therapy for osteoporosis alone but testosterone may be considered as an initial treatment for men with osteoporosis who also have symptomatic hypogonadism. Testosterone has been shown to maintain BMD but it has not been shown to reduce fracture rates, so if there is no relief of hypogonadal symptoms after 3-6 months,

discontinue testosterone and use another approved bone therapy.^{1,2}

Treatment related safety issues

Calcium and myocardial infarction (MI)

Many patients do not get enough calcium from their diet and require a supplement to reach the goal of 1000-1200 mg calcium intake. However, recent studies have shown an association between calcium supplement use and increased risk of MI (20-86% increase) and stroke (20% increase).⁵⁻⁷ Dietary calcium was not associated with an increased risk. It has been hypothesized that unlike dietary calcium, supplements produce high peak serum calcium levels that may promote atherogenesis. The findings have elicited much debate, and some feel that cardiovascular concerns are premature. However, patients should try to obtain their calcium requirements through diet, and not exceed 1200 mg/d. If supplements are needed, patients should not take more than 500-600 mg elemental calcium at a time; smaller doses taken more frequently are preferred.

Cancer

Following a warning from the European Medicines Agency,⁸ Health Canada is assessing cancer risks with calcitonin.⁹ Calcitonin is not recommended as a first-line treatment.

There may also be a connection between oral bisphosphonate use and esophageal cancer, but so far the absolute risk is likely to be small - it has been estimated from one study that there would be one additional cancer case per 1000 patients treated for 5 years.^{10,11}

Atypical femoral fractures, osteonecrosis of the jaw

Bisphosphonates suppress bone remodelling that leads to bone loss, but this can also suppress bone repair and lead to increased brittleness. Studies have found an increased risk for atypical femoral fractures associated with use of bisphosphonates for at least several years.¹²⁻¹⁴ The risk appears to be small - about 1 per 1000 users per year.¹² Thigh, hip, or groin pain may precede these fractures.¹⁵

Bisphosphonates have been associated with osteonecrosis of the jaw (ONJ). The risk is greatest with high doses used in cancer patients. While the exact occurrence is not known, it appears to be much lower with oral agents used in osteoporosis (less than 1 per 1000 patients).^{16,17} Prevention is key: counsel patients about maintaining good oral hygiene, smoking cessation, and ask about gum problems, pain or swelling.

Elective drug holidays

Continuous treatment seems to provide the most benefits, but there is evidence (at least in women) that some BMD and fracture-preventing benefits persist for several years after stopping alendronate and zoledronic acid, raising the possibility of drug holidays.

At present, no definite recommendations can be made.¹⁸⁻²³ Some experts recommend that most patients on long-term bisphosphonate treatment be offered a drug holiday,¹⁸ while others recommend that treatment be continued.¹⁴ Concern over the long-term safety of bisphosphonates is probably the strongest reason for considering a drug holiday, but whether or not interrupting therapy reduces treatment-related harms has not been studied.

Based on available evidence, drug holidays may be considered for women who have been compliant with at least 3 years therapy with zoledronic acid or 5 years therapy with alendronate and are not at higher risk for fracture (femoral neck T score <-2.5, or history of vertebral fracture and T-score <-2.0).²⁰

In addition, the following have been suggested for patients with concerns about treatment side effects:²³

- Intermediate fracture risk*: discontinue bisphosphonates after 5 years, monitor BMD every 2 years and bone turnover markers (BTM) yearly; resume therapy if significant declines in BMD or significant increases in BTM or new fractures
- High fracture risk*: continue bisphosphonates for at least 10 years, monitoring oral health and thigh pain. Then consider teriparatide for 2 years as a holiday from bisphosphonates. If teriparatide is not an option, stop bisphosphonates but monitor BMD and BTM as above, and resume therapy if significant declines in BMD or >40% increase in BTM.

*based on the WHO fracture risk assessment tool (FRAX) and clinical assessment (e.g. frailty, fall risk)

Vitamin D for everyone

A recent meta-analysis found that supplementation with at least 800 units/day in patients 65 years and older was associated with a 30% reduction in hip fracture and 14% reduction in any non-vertebral fracture.²⁴ Lower vitamin D doses did not have any protective effect.

Most Canadians are at risk for low vitamin D levels from autumn to spring and it is difficult for adults to obtain sufficient vitamin D from diet alone. Health Canada recommends that all adults over the age of 50 years supplement daily with 400 units of vitamin D,²⁵ but Osteoporosis Canada recommends higher doses: 400-1000 units for adults 19-50 years, and 800-2000 units/d for older adults and those with osteoporosis, fractures, or malabsorption.²⁶

Weekly or monthly dosing may be a more convenient option for some patients.

Resources:

Osteoporosis Canada has more information as well as tools for patients to help assess their risk and calculate their calcium intake and need for supplements. Visit their website at www.osteoporosis.ca.

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by Raymond Li, BSc(Pharm), MSc

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