



Canadian Geriatrics Society

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## COMMON CONTROVERSIES IN OSTEOPOROSIS THERAPY – HELPING PATIENTS MAKE INFORMED DECISIONS

### Abstract

The media regularly reports scientific articles that are felt to be of general interest. Unfortunately, the contextual content of these reports is not always included, and patients (and health professionals) are subjected to a barrage of often conflicting information. This sometimes results in patients making potentially risky unilateral decisions to discontinue medications, or in numerous unnecessary visits to the Family Practitioner for the latest advice.

To assist with such office visits this article seeks to provide a summary of the common controversies in osteoporosis management for the busy primary care provider, as well as accessing resources to which the patient can be directed that provide accurate and reliable information in order to promote more informed decisions.

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Les médias rapportent régulièrement des articles scientifiques considérés d'intérêt général. Malheureusement, le contexte dans lequel ces données ont été obtenues n'est pas toujours inclus et les patients (ainsi que les professionnels de la santé) sont confrontés à une avalanche d'informations souvent contradictoires. Il en résulte parfois des décisions unilatérales du patient de mettre fin à un traitement, ou de nombreuses visites inutiles chez le médecin de famille pour des conseils à jour.

Pour faciliter la tâche des médecins de première ligne occupés, cet article vise à fournir un résumé des controverses les plus fréquentes dans la prise en charge de l'ostéoporose, et propose des ressources vers lesquelles le patient peut être dirigé afin d'obtenir de l'information précise et fiable et promouvoir des prises de décisions éclairées.

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### Case history 1

Mrs. OP is a 70-year-old woman with a history of a wrist fracture at the age of 60 years. She is new to your practice. What, if any, investigations do you order?

### Osteoporosis management based on fracture risk

#### Before seeing the patient you briefly review:

1. The Osteoporosis Canada (OC) guidelines ([http://www.cmaj.ca/content/early/2010/10/12/cmaj.100771.full.pdf+html?ijkey=edc6c6048e7d4acdc41368fe3f1e622bf5a2deac&keytype2=tf\\_ipsecsha](http://www.cmaj.ca/content/early/2010/10/12/cmaj.100771.full.pdf+html?ijkey=edc6c6048e7d4acdc41368fe3f1e622bf5a2deac&keytype2=tf_ipsecsha))
2. The Osteoporosis Canada Quick Reference Guide [http://www.osteoporosis.ca/multimedia/pdf/Quick Reference Guide October 2010.pdf](http://www.osteoporosis.ca/multimedia/pdf/Quick%20Reference%20Guide%20October%202010.pdf)

You ordered the screening blood work as suggested in the guidelines and Quick Reference Guide. Her blood work is normal, consistent with a diagnosis of postmenopausal osteoporosis.

You also ordered a DXA Bone Mineral Density (BMD) test. This shows a T-score of -2.5 in the femoral neck and -2.8 in the lumbar spine. You discuss the need for osteoporosis medications. She is an avid follower of the news and has been reading and hearing about all the side effects of calcium and osteoporosis drugs. Her neighbour was told that all her teeth would fall out and her jaw would "drop off" if she continued on her bisphosphonate medication!

How would you approach the risk/benefit discussion with your patient?

### 1. Calcium supplementation

#### Key points:

- Recent publications have raised concerns about supplemental calcium intake increasing the risk of myocardial infarction (not all cause cardiac mortality).<sup>1</sup> Subjects were allowed calcium in their diet and were supplemented with 1500 mg calcium citrate daily. Many had total calcium intakes >2000 mg daily.
- The WHI study showed no similar increase, but only all cause mortality and not MI alone was evaluated, and subjects had a much lower dietary intake of calcium.<sup>2</sup> Supplements were calcium carbonate 1000 mg daily. (Of note, bioavailability of calcium citrate is greater than that of calcium carbonate.)
- A large European population study suggests no increased risk with dietary calcium in women or men.<sup>3</sup>
- Canadian data shows calcium supplements, up to 1000 mg/day may be associated with reduced risk of mortality in women (HR 0.75-0.78).<sup>4</sup>
- In a meta-analysis, calcium or vitamin D supplementation did not have an effect on major cardiovascular events (OR, 1.03; 95% CI: 0.94-1.12; P = 0.54), myocardial infarction (OR, 1.08; 95% CI: 0.96-1.22; P = 0.21), or stroke (OR, 1.01; 95% CI: 0.91-1.13; P = 0.80) when compared to placebo.<sup>5</sup> Subgroup analysis indicated that calcium supplementation alone might play an important role in increasing the risk of major cardiovascular events, myocardial infarction and stroke, but this difference was not statistically significant.

#### Bottom line:

- a. Dietary calcium has been universally shown to be safe.<sup>1-4</sup>
- b. The benefits of adequate calcium intake outweigh the risks.
- c. OC guidelines recommend daily dietary PLUS supplemental calcium total of 1000-1200 mg daily in postmenopausal women and men >65years.
- d. All antiresorptive therapy requires adequate intake of calcium and vitamin D for antifracture efficacy.

**Resources:**

1. The OC list of sources of calcium  
<http://www.osteoporosis.ca/osteoporosis-and-you/nutrition/calcium-requirements/>
2. The OC calcium calculator <http://www.osteoporosis.ca/osteoporosis-and-you/nutrition/calculate-my-calcium/>

## 2. Vitamin D supplementation

**Key points:**

- Vitamin D is difficult to get from diet alone (other than from cod liver oil, where 1 tablespoon=1360 IU).
- Serum 25(OH)D levels of at least 80 nmol/L are recommended. Increasing data on non-bone benefits of vitamin D including muscle strength.<sup>6</sup>  
[www.canadiangeriatrics.ca/default/index.cfm/linkservid/BE339FDF-E89F-4ABF-B518C69392D4C5F3/showMeta/0/](http://www.canadiangeriatrics.ca/default/index.cfm/linkservid/BE339FDF-E89F-4ABF-B518C69392D4C5F3/showMeta/0/)

**Bottom line:**

- a. OC recommends 800-2000 IU vitamin D daily.
- b. All osteoporosis medications require adequate serum vitamin D to be effective.

**Resources:**

1. OC Vitamin D [www.osteoporosis.ca/osteoporosis-and-you/nutrition/vitamin-d/](http://www.osteoporosis.ca/osteoporosis-and-you/nutrition/vitamin-d/)
2. OC Vitamin D Review [www.osteoporosis.ca/multimedia/pdf/hp/vitamin\\_D\\_review\\_CMAJ\\_2010.pdf](http://www.osteoporosis.ca/multimedia/pdf/hp/vitamin_D_review_CMAJ_2010.pdf)

## 3. Osteonecrosis of the jaw (ONJ)

Defined as a nonhealing (>8 weeks) area of exposed bone in the maxillofacial region (pictures [www.bing.com/images/search?q=picture+of+osteonecrosis+of+jaw&qpv=picture+of+osteonecrosis+of+jaw&qpv=picture+of+osteonecrosis+of+jaw&FORM=IGRE](http://www.bing.com/images/search?q=picture+of+osteonecrosis+of+jaw&qpv=picture+of+osteonecrosis+of+jaw&qpv=picture+of+osteonecrosis+of+jaw&FORM=IGRE))

**Key points:**

- Rare; rate of 1.03 per 100,000 person-years.<sup>7</sup>
- More likely in multiple myeloma and breast cancer patients on high-dose bisphosphonates (up to 10 times osteoporosis dose).<sup>7</sup>
- Usually associated with a dental extraction.
- Most heal with appropriate medical and surgical management.
- The jaw does not “drop off” nor do teeth spontaneously fall out.

**Bottom line:**

- a. Ensure good dental hygiene for patients already on and starting bisphosphonates.  
See [www.osteoporosis.ca/multimedia/pdf/hp/Recommendations\\_Pamphlet\\_Eng.pdf](http://www.osteoporosis.ca/multimedia/pdf/hp/Recommendations_Pamphlet_Eng.pdf)
- b. Risk of osteoporotic fracture (20% in first year in those who have already fractured) far outweighs ONJ risk.<sup>8</sup>

**Resources:**

1. Osteoporosis Canada (OC) patient and doctor information.  
See [www.ncbi.nlm.nih.gov/pubmed/25414052/?](http://www.ncbi.nlm.nih.gov/pubmed/25414052/?)
2. American Dental Association/Canadian Dental Association position statements  
[www.cda-adc.ca/jcda/vol-74/issue-7/617.pdf](http://www.cda-adc.ca/jcda/vol-74/issue-7/617.pdf)

#### 4. Atypical (subtrochanteric) femoral fracture (AFF)

Defined as an isolated subtrochanteric or femoral shaft fracture, with a specific appearance on radiograph.

##### Key points:

- Rare; prevalence of 2-78 per 100,000 person years of bisphosphonate exposure.<sup>9</sup>
- Position statement from American Society for Bone and Mineral Research (ASBMR) with radiographic and clinical definition.<sup>9</sup>  
See <http://onlinelibrary.wiley.com/doi/10.1002/jbmr.1998/epdf>
  - Specific criteria required – radiologically (especially cortical thickening, and transverse or slightly oblique fracture) and clinically (prodromal hip pain prior to fracture).
- Can occur with and without bisphosphonate or denosumab use.
- May be related to duration of antiresorptive therapy or type of bisphosphonate.<sup>9</sup>

##### Bottom line:

- a. Such fractures may not be visible on regular x-ray until the fracture is complete.
- b. In patients presenting with significant ongoing hip pain and nondiagnostic x-rays, a bone scan is the ideal investigation to rule out this fracture.
- c. May be seen prior to complete fracture as a subtrochanteric hot spot on the bone scan.

See Table 1 for relative risks that may lend perspective to the discussion with the patient.

*Management of incomplete fracture (as for any other stress fracture):*

1. Rest;
2. Discontinue bisphosphonate therapy (if they are on it);
3. Teriparatide (Forteo) therapy has been shown to heal the fracture;<sup>9</sup> and
4. Prophylactic surgical repair can also be considered.<sup>9</sup>

##### Resources:

1. ASBMR position statement (doctors) <http://onlinelibrary.wiley.com/doi/10.1002/jbmr.1998/epdf><sup>9</sup>
2. OC doctor and patient information <http://www.osteoporosis.ca/news/position-statements/>

**Table 1.** Relative risk table<sup>7</sup>

	<b>BP and ONJ</b>	<b>2 yr BP and AFF</b>	<b>8 yr BP and AFF</b>	<b>Murder</b>	<b>Motor vehicle accident</b>	<b>Major OP fracture in low risk women</b>	<b>Major OP fracture in moderate risk women</b>	<b>Major OP fracture in high risk women</b>
<b>Per 100,000 person years</b>	1.03	2.00	78	1.62	8.4	650	1600	3100

BP = Bisphosphonate, ONJ = Osteonecrosis of the jaw, AFF = Atypical (subtrochanteric) femoral fracture, OP = Osteoporosis

*Mrs. OP agrees to your suggestions and has started on vitamin D 200 IU daily, calcium 1000-1200 mg in her diet (with supplements if needed) and weekly risedronate.*

*Five years later, now aged 75, she mentions concerns about continuing her bisphosphonate because of further "scary" things she has heard about in the media.*

*You are considering whether she may be a candidate for a "drug holiday."  
What information do you need to help you make this decision?*

**Scenario 1:**

*Adherence: She takes her risedronate every Monday morning with a glass of water first thing in the morning. However, as she eats early in the evening, she is often hungry when she wakes, and her risedronate feels like it gets stuck in her throat so she usually has a cracker with it. If she has a Monday appointment she sometimes misses her dose.*

**Scenario 2:**

*Adherence: She takes her risedronate every Sunday morning with a glass of water. She then sits up and reads the newspaper before having her breakfast 30-45 minutes later. She rarely misses her medication.*

**5. Bisphosphonate drug holiday<sup>7</sup>**

**Key points:**

- Major osteoporotic fracture prevalence in low risk women is 650/100,000 person years, in moderate risk women is 1600/100,000 person years and in high risk women is 3100/100,000 person years.

- Risk level can be calculated using a risk assessment tools:

- CAROC – [www.osteoporosis.ca/multimedia/pdf/CAROC.pdf](http://www.osteoporosis.ca/multimedia/pdf/CAROC.pdf)
- FRAX – [www.sheffield.ac.uk/FRAX/tool.jsp?country=19](http://www.sheffield.ac.uk/FRAX/tool.jsp?country=19)

Comment: CAROC is generally used by radiologists to categorize risk reported on the BMD test. FRAX is useful for clinicians as it includes risk factors for OP and provides an absolute risk score. It can be modified for ethnicity for immigrants. It is helpful for discussion with patients, especially regarding lifestyle modification (e.g., smoking).

**IMPORTANT NOTE:** Neither CAROC nor FRAX are valid tools for assessing fracture risk in patients already on antiresorptive therapy.

- Adherence needs to be 80% to achieve published fracture risk reduction, and to determine anticipated effect of drug discontinuation.
- Ensure adequate adherence BEFORE discussing drug holiday. Eighty percent compliance is required for fracture risk reduction and sustained benefit with bisphosphonate therapy.
- Drug holidays are only a consideration with bisphosphonates but not other antiresorptive drugs (denosumab, raloxifene).
- Consider drug holidays only after 3-5 years of persistent intake in low risk (<10% risk of fracture in next 10 years) or select moderate risk (10-19% risk of fracture in next 10 years) patients.
- Drug holidays should not be considered for high fracture risk (20% or greater) patients (elderly, high fall risk, low BMD) as the benefit of treatment far outweighs the potential risk of side effects.

**Case history 1 (continued)**

**Scenario 1 management:**

*She has NOT been adherent so has no residual bisphosphonate benefit. The discussion should focus on means to improve adherence, which may necessitate switching to another oral agent (that may be better tolerated) or Actonel DR (delayed release risedronate that can be taken with breakfast). Other options include injectable twice yearly subcutaneous (denosumab), intravenous once yearly (zoledronate) or subcutaneous daily (teriparatide) alternatives. Risk of fracture needs to be reinforced to encourage adherence.*

**Scenario 2 management:**

*She has been compliant but, at the age of 75, she is at high fracture risk because of her risk of falls and her low BMD. Encourage her to continue her weekly medication or discuss with her whether she would prefer an alternative to oral therapy (e.g., Prolia [denosumab], Aclasta [zoledronate] or Forteo [terapeptide]).*

Reinforce her high hip fracture risk and need for continued therapy. Remind her about continued intake of dietary calcium and vitamin D supplements.

### Case history 2

Mrs. AF, aged 65, has been on long acting alendronate for five years. She takes her medication every Saturday morning on an empty stomach, with water only, before she walks the dog. When she returns she has her morning coffee and breakfast. She denies ever missing her medication. Prior to the alendronate she was on HRT until the age of 60. Her most recent BMD shows she has a T score of -2.0 in her femoral neck and -2.2 in her lumbar spine (an improvement from baseline of -2.5). She has no other medical issues, and walks for at least 30 minutes daily and attends exercise classes at the YMCA twice weekly.

You are considering whether she may be a candidate for a "drug holiday."

What information do you need to help you make this decision?

**See above section on bisphosphonate drug holiday**

### Case history 2 management

She has been adherent, and as such has decreased her fracture risk. Her fall risk is low (due to minimal co-morbid diseases), and her BMD is now in the osteopenic range. A drug holiday may be considered. She needs to be followed closely (accurate height, +/- bone turnover markers such a C-telopeptide (if available), repeat BMD 1-3 years) as the benefit of her alendronate starts to decrease after 12 months. Plan to reassess her in 12 months. If her BMD starts to decline (evaluated by absolute reduction in g/cm<sup>2</sup> in femoral neck BMD greater than least significant change of the facility [usually 2-5%]), restarting a bisphosphonate or denosumab are options.

#### Bottom Line:

- a. OP is a chronic disease therefore treatment is lifelong. However, because of the unique mode of action of bisphosphonates and their long half life (six months for risedronate, 12 months for alendronate. [Data based on brand name and not generic bisphosphonate]) the possibility of a drug holiday can be considered. This discussion has arisen because of concerns with the risk for AFF and ONJ perhaps being increased with prolonged BP exposure, although there is not yet direct evidence of this.
- b. Drug holiday is only to be considered in bisphosphonate adherent, low fracture or select moderate risk cases.

#### Resources:

For a recent Canadian publication that discusses in detail the risks and benefits of a bisphosphonate drug holiday see <http://www.cfp.ca/content/60/4/324.full.pdf+html>.<sup>7</sup>

#### Key points

- OP is a chronic disease, with significant mortality and morbidity.
- Encourage appropriate exercise and nutrition in all patients.
- Adequate calcium and vitamin D intake is required for bone health and drug efficacy.
- In appropriate patients, the benefits of antiresorptive therapy far outweigh the risks.

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USEFUL LINKS:

<http://www.osteoporosis.ca/osteoporosis-and-you/nutrition/calculate-my-calcium/>

[http://www.osteoporosis.ca/multimedia/pdf/Quick Reference Guide October 2010.pdf](http://www.osteoporosis.ca/multimedia/pdf/Quick_Reference_Guide_October_2010.pdf)

[http://www.osteoporosis.ca/multimedia/pdf/Osteoporosis Guidelines 2010 Background And Technical Report.pdf](http://www.osteoporosis.ca/multimedia/pdf/Osteoporosis_Guidelines_2010_Background_And_Technical_Report.pdf)

[http://www.osteoporosis.ca/multimedia/pdf/oc\\_executivesum\\_0410.pdf](http://www.osteoporosis.ca/multimedia/pdf/oc_executivesum_0410.pdf)

<http://www.osteoporosis.ca/osteoporosis-and-you/too-fit-to-fracture/>

<http://www.osteoporosis.ca/osteoporosis-and-you/nutrition/>