Bisphosphonate Induced Osteonecrosis of the Jaw

In April 2006 radio media highlighted problems experienced overseas, predominantly the USA. The interview caused such widespread concern that a second interview was required the following day to provide balanced information relevant to New Zealand.

So far, in New Zealand osteonecrosis of the jaw has only been associated with high doses of intravenous bisphosphonates used to treat cancer or high calcium levels associated with cancer.

“The risks of developing osteonecrosis of the jaw with much lower doses of bisphosphonates as used in the treatment of osteoporosis is much lower”, says Dr Brandon Orr-Walker, chair of the Scientific Committee of Osteoporosis New Zealand. “Exactly how low that risk is remains a little uncertain due to the rarity of the problem, but clearly needs to be balanced with the benefit of these medications in reducing the risk of osteoporotic fracture in patients of high risk”.

There is absolutely no concern for osteoporosis sufferers in New Zealand who are encouraged to maintain their low dose bisphosphonate treatment for osteoporosis. If anxious they should consult their medical practitioner.

Bisphosphonate Action on Bone

Normal bone remodelling consists of osteoclastic activity that promotes bone resorption and osteoblastic activity that promotes bone growth.

Bisphosphonates obstruct bone resorption by inhibiting osteoclastic activity.

In bone disorders with increased osteoclastic activity, such as osteoporosis, multiple myeloma, hypercalcemia of malignancy and bone metastases, bisphosphonates are beneficial in preventing skeletal fractures and reducing bone pain and bony complications. In osteoporosis, low doses (usually given orally) have been are effective in reducing fractures, but for the other conditions, generally higher doses (usually in the order of ten fold) are needed. This is usually done with intravenous treatment.

What is Osteonecrosis?

Osteonecrosis results from temporary or permanent loss of blood supply to the bones.

The condition can be caused by trauma or damage to the blood vessels that supply blood to the bones, blockage by air or fat embolisms, hyper-coagulable states or vasculitis. A loss of blood supply causes minute bone fractures, with ultimate bone collapse.

Studies suggest that approximately 80% of patients with osteonecrosis of the jaw have undergone dental extraction.

It has been suggested that high dose bisphosphonates as used in the treatment of bone cancers inhibit new vessel formation, thereby impairing healing. The jaw bone seems more susceptible to this problem than any other bone in the body. Pre-existing dental or periodontal disease may increase this risk, and healing after an extracted tooth may be impaired, or integration of a dental implant may be unsuccessful.

How common is Osteonecrosis of the jaw in people treated with bisphosphonates?

“Osteonecrosis of the jaw is overwhelmingly a problem of patients treated with very high doses of bisphosphonate drugs for bone cancers”, states Professor Ian Reid, Assistant Dean of the Auckland Medical School, physician and endocrinologist and internationally acclaimed researcher. “Of the 20 million patient years of use of Fosamax (alendronate)

over the last 11 years worldwide there are approximately 100 reported cases of osteonecrosis of the jaw."

"Most of these cases were documented as taking the wrong (high) dose or taking it for too long…well over 90 percent of the cases are patients taking very high doses of bisphosphonates for cancer". Professor Reid says "In the case of osteoporosis, the actual frequency of osteonecrosis is not known - because is to so rare. It is thought to be between one in 100,000 and one in a million."

There are no known cases of osteonecrosis of the jaw caused by Fosamax in New Zealand

There is a handful cases of osteonecrosis of the jaw in New Zealand caused by high dose injectable bisphosphonates used for treating bone cancers.

Is the risk worth it?

In New Zealand, funded treatment with potent bisphosphonates has been limited to those with severe osteoporosis until October 2005. Those criteria were widened by Pharmac at that time.

"Treatment is still only recommended for people with established osteoporosis, or in those with a high risk of developing osteoporosis due to medical side effects", says Dr Orr-Walker.

Risks need to be balanced with clinical effectiveness, like any other intervention.

Based on a large number of studies, Fosamax reduces the risk of fractures by approximately 50%. Similar effectiveness is seen for other bisphosphonates but they are not currently available for use in New Zealand.

"For example, postmenopausal women with osteoporosis and a vertebral fracture qualify for Fosamax under the new criteria. Taking Fosamax for just 3 years halves the fracture rate to just under 5%", says Dr Orr-Walker. "That means for every 22 women taking Fosamax for 3 years there will be one less significant fracture requiring treatment and possibly hospitalisation."

"And a 70 year old woman with no osteoporotic fracture but a bone density score of -3.0 also qualifies for treatment. She can halve her risk of developing a vertebral fracture over the next 5 years, which for most people is a meaningful level of protection," says Dr Orr-Walker.

Currently in New Zealand there are few other funded treatment options.

Apart from bisphosphonates, hormone replacement therapy may be an option for some people. Again the overall risk and benefits need to be considered closely by the patient and doctor.

It is important that patients do not stop their treatment without discussion with their doctors and carefully weighing up the risks and benefits

Osteoporosis is a severe and common disease. The reported link between osteonecrosis of the jaw and oral bisphosphonates is a very rare event. Unfortunately there is no known effective therapy for it.

Attention to dental hygiene and perhaps having dental procedures performed before bisphosphonate treatment is advisable. However the risk of osteoporotic fracture in some people is very high and delaying or avoiding the most effective treatment option we currently have comes with real risks which are far more common and much more serious and intrusive to a person's quality of life.

Conclusion

Osteonecrosis of the jaw is a very rare complication associated with IV bisphosphonate treatment for bone cancers, not osteoporosis.

In the very isolated and extremely rare situations where it has occurred with oral bisphosphonate use it has been due to long term use (patient not being monitored correctly), over use (treatment of low bone density - not osteoporosis) or over dose (patients not following instructions).

The situation in New Zealand is different to the USA where Fosamax is used for prevention of osteoporosis - by people with a low, but not osteoporotic bone density. In New Zealand Pharmac's selective access criteria for Fosamax have limited its use, until October 2005, very few people qualified for it. The access criteria have eased significantly since then, but still ensure its use is not abused.

Osteoporosis New Zealand is very concerned - people on Fosamax should continue to take their medication because they are taking it for a very good reason - to prevent fractures and the effects of osteoporosis.

Prepared by the Scientific Committee on behalf of Osteoporosis NZ Inc.

Further information available at www.anzbms.org.au/resources/policies/jaw_osteo.htm