



BONE DENSITY & OSTEOPOROSIS:

An Update for Manitoba Physicians

No. 2: May 5, 2000

Re: MONITORING OSTEOPOROSIS WITH BONE DENSITOMETRY

The Manitoba Bone Density Committee has recommended *at least a three year interval in performing follow-up bone density testing* (except in individuals on high-dose systemic steroids in which case a one year interval is preferred). This position differs from the Osteoporosis Society of Canada which recommends that "for following a patient without pharmacologic intervention...the earliest consideration of a follow-up measurement should be at least 2 years". Others have advocated annual follow-up testing, both to detect treatment response and to reinforce adherence to therapy.

The Manitoba Bone Density Committee recently debated these positions and reviewed the scientific data supporting them. We concluded that the available scientific data strongly favours the Manitoba guidelines. In this newsletter we will briefly summarize this data so that health practitioners in Manitoba are aware of the scientific basis for the current guidelines.

Monitoring patients not receiving pharmacologic therapy: The optimal time interval for follow-up measurements is a function of machine precision and the expected rate of bone loss. Manufacturers frequently cite test precision as 1.0% for modern instruments. This significantly underestimates the imprecision when the instrument is used in nonresearch, clinical patient populations. In routine clinical settings the following error (CV) have been reported: lumbar spine 1.8%, femoral neck 3.2-3.6%, total hip 2.5%. Our own program performed 125 short-term reproducibility scans and found spine error (CV) 1.4-1.9% and femoral neck 2.2-2.7%. These values translate into minimum detectable change of 5.4% for the spine and 7.6% for the femoral neck.

In the large clinical trials of postmenopausal osteoporosis, the average rate of bone loss from the hip in the control subjects has been 0.4% per year while spine density has actually increased (thought to reflect degenerative artifact). At the time of menopause bone loss is more rapid, and for the first two years averages 2% per year for the hip and 3% per year for the spine.

Measurement imprecision makes it much more difficult to accurately assess loss rates in individuals. For example, if a subject loses bone mass at a rate of 1% per year then it would take 6 years for this to exceed with (95% confidence) the precision limits of a machine with "typical" performance (CV 2%). For subjects with bone loss of 2% per year, it will again take 3 years for this point to be reached.

Monitoring patients receiving pharmacologic therapy: Currently approved pharmacologic therapy for osteoporosis operates by suppressing osteoclastic bone resorption and usually leads to a small increase in bone density (2.5-4.2% after one year of treatment, 3.1-7.0% after three years of treatment). Only a small number of individuals continue to lose bone mass despite taking treatment, and even these show slowing in the rate of loss. Therefore, if the objective of follow-up testing is to identify individuals with continued rapid bone loss then the interval must be at least as long as in individuals not receiving treatment. An additional factor that is not widely appreciated is an apparent disconnection between the anti-fracture effect of these medications and their effect on bone density. That is, the anti-fracture effect greatly exceeds what would be predicted in the small increment in bone density. Some analysis has suggested that over 80% of anti-fracture effect is not mediated through changes in bone density. Therefore, the definition of "treatment failure" becomes complex to say the least. Finally, a recent study (JAMA 2000; 283: 1318) has looked at the ability of bone densitometry measured one year after starting therapy to predict changes in the second year of continuing the same treatment. This analysis of alendronate and raloxifene clinical trials showed that year 1 repeat bone densitometry was unhelpful in predicting year 2 responses. In fact, women with the greatest bone density loss during the first year had the greatest gains during the second year, whereas those with the greatest gains during the first year had the greatest losses during the second year. The authors concluded that this reflected "regression to the mean" due to relative imprecision in bone densitometry measurements. The simple message is that year 1 repeat bone density measurements should not be the basis for judging treatment failure in osteoporosis.

Bone densitometry to reinforce adherence to treatment: The Bone Density Committee was unable to find any data that proves that bone densitometry will enhance adherence to therapy. Since most problems with adherence occur during the initial three months of starting treatment, long before any follow-up bone densitometry would be performed, it is expected that such testing would be of limited value at best. It is hoped that biochemical bone markers will one day find a role in monitoring adherence since they typically respond within weeks of starting treatment. Unfortunately, they are currently limited by poor reproducibility. For the present, a physician that asks patients about their medication use on a regular basis is probably the best method to maintain adherence.