Anabolic Agents:

New Approaches to Osteoporosis Treatment

Aliya Khan, MD, FRCPC, FACP

As presented at the Endocrine Citywide Rounds, McMaster University, Hamilton, Ontario (May 2005)

Osteoporosis is a common condition associated with significant morbidity and mortality. Until recently, the only treatment options were antiresorptive agents, which decrease bone turnover by decreasing osteoblast activity. These agents include the bisphosphonates, raloxifene, calcitonin and hormone replacement therapy. Antiresorptive agents do not have any anabolic skeletal effects.

Anabolic agents

Anabolic agents increase osteoblastic function. They also increase the production of bone matrix by osteoblasts.

A number of anabolic agents have been evaluated (Table 1). Currently the Health Protection Branch has approved teriparatide as the first anabolic agent osteoporosis treatment.

Teriparatide is the 1-34 amino acid fragment of human parathyroid hormone (PTH). It was approved in Canada in June 2004, for an 18-month treatment period of postmenopausal osteoporosis and for the improvement of bone density in men.

Intermittent PTH administration increases bone formation, whereas, continuously elevated PTH levels result in bone catabolism. Teriparatide is given in 20 mg subcutaneously daily for 18 months. The peak concentrations in the plasma are seen at 30 minutes after injection and are undetectable in three to four hours.

Teriparatide results in an increase in the lumbar spine bone mineral density by 9% in comparison to placebo. Femoral and whole body bone mineral density is also improved. A reduction in vertebral fracture was seen in 65% of women treated with teriparatide in comparison to place-

Marge's case

- Marge, 68, is 18 years postmenopausal.
- She presents with her second episode of back pain in two years.
- The spinal films show compression fractures of T8 and T10.
- There are no secondary causes of osteoporosis.
- Marge has lost 5 cm from her best height.
- Marge's mother suffered a hip fracture.
- Marge's T-scores:
  - lumbar spine -3.7,
  - total hip -3.0 and
  - femoral neck -2.5.
- Marge has severe osteoporosis.

bo. Nonvertebral fragility fractures have been reduced by 53% in comparison to placebo.[1]

Teriparatide is well tolerated, and side-effects are minor (nausea and headaches). Mild hypercalcemia may be noted on a transient basis.

Rat studies have shown an increased risk of osteosarcoma in rats receiving teriparatide in doses equivalent to more than 10 times the dose given to humans. There have been no cases of osteosarcoma in humans or in the monkey studies. Also, primary hyperparathyroid patients do not have an increased risk of osteosarcoma.

Teriparatide improves bone strength and reduces the risk of fractures. It is a welcome addition to the therapy currently available for postmenopausal osteoporosis. Dx

Reference

1. Neer RM, Arnaud CD, Zanchetta JR, et al: Effect of parathyroid hormone on fractures and bone mineral density if potmenopausal women with osteoporosis. N Engl J Med 2001: 344(19):1434-41.

Table 1

Anabolic agents

Agent	Comment
Fluoride	Not approved for postmenopausal osteoporosis due to the increased risk of hip fractures and possibility of impaired bone mineralization.
Growth hormone	Currently being further evaluated. Have limited utilization due to the high risk of side-effects (weight gain, carpal tunnel syndrome, glucose intolerance and edema).
Statins	Data evaluating statins has been conflicting with some studies documenting a reduction in fracture, while other studies have not confirmed fracture benefits. Current evidence does not warrant statin use.
Teriparatide	Approved for postmenopausal osteoporosis and low bone density in men.
Strontium ranelate	This element is incorporated into the bone due to its similarities to calcium. Has shown to be effective in reducing bone loss and also effective in stimulating new bone formation. Reduction in vertebral fracture confirmed in phase three clinical trials. Reduction in hip fractures has been confirmed in the high-risk subgroup population.

Dr. Khan is an Associate Clinical Professor of Medicine, Divisions of Endocrinology and Geriatrics, McMaster University, and Chair, Canadian Panel of the International Society of Clinical Densitometry, Hamilton, Ontario.