Combined Meeting of the
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SESSION TIME: 0930 - 1100, Thursday 26 Oct 2006

Workshop Abstracts

Workshop D - Treatment - why, whom, when, what drug, how long?

W10 Use of antiresorptives in osteoporosis
John Eisman (Australia)

W11 Osteonecrosis of the jaw in patients on bisphosphonate therapy
Michael Hooper (Australia)

W12 Anabolic therapies for osteoporosis
Peter Ebeling (Australia)

W10

Use of anti-resorptives in osteoporosis

John A Eisman
Bone and Mineral Research Program, Garvan institute of Medical Research, Department of Endocrinology, St Vincent's Hospital and UNSW, Sydney, NSW

Anti-resorptives, which are the most commonly used therapies in osteoporosis, are effective and generally well tolerated. Barriers to initiation of treatment and long-term compliance include limited osteoporosis knowledge and uncertainty of responsibility for treatment. Another major barrier re their optimal use will be the focus of this part of the workshop.

Anti-resorptives, including HRT, SERMs and bisphosphonates, have been well studied in randomised controlled trials with fracture, mostly vertebral fracture-deformity end-points. Most RCTs have not had non-vertebral or hip fracture as primary end-points. Also there have been no head-to-head studies with fracture end-points, so it is not possible to assign superiority for the clinically relevant outcome.

HRT reduces all clinical fractures including hip fractures, but is not recommended in women without menopausal symptoms because of increased breast cancer diagnoses and cardio- & cerebrovascular risk. Oestrogen alone may have a better safety profile. Tibolone reduces fracture risk but may also increase cerebrovascular risk. The SERM, raloxifene, reduces vertebral fracture and possible non-vertebral fracture risk (in a high risk group) but, while not changing cardio- & cerebro-vascular events, may increase post-stroke mortality. Bisphosphonates effectively reduce all types of fracture risk and have few side effects apart from relatively uncommon GI intolerance. High dose IV bisphosphonates in malignancy have been associated with osteonecrosis of the jaw but the relevance to osteoporosis is uncertain.

With this range of agents, there is always an effective therapy available but duration of use, follow-up and drug 'holidays' require careful discussion and explanation to patients.

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W11

Osteonecrosis of the jaw in patients on bisphosphonate therapy

M. Hooper
The University of Sydney and Sydney South West Area Health Service, Sydney, Australia

Osteonecrosis of the jaw is a localised osseous pathology that has been reported since the 19th century. In recent medical literature a rare association between poor healing of the bone of the jaw often related to dental extraction or periodontal disease has been described in patients on bisphosphonate therapy. In brief osteonecrosis of the jaw (ONJ) can be described as a non-healing tooth extraction socket or an area of exposed jawbone that is responding poorly to standard dental therapy. Removal of involved bone is contraindicated, bisphosphonate therapy should be withdrawn and conservative oral medical management continued.

This condition has mostly been reported in cancer patients (on chemotherapy) who have also received intravenous bisphosphonate therapy in higher doses than are usually used in benign bone conditions.

Whilst no cases have been reported in clinical trials in benign bone disease this may be related to its rare occurrence and the relatively small number of patients followed for a long time.

Whilst the definite aetiology and pathogenesis of ONJ remains unclear and the relationship with bisphosphonate therapy needs further clarification risk factors include the underlying malignancy, chemotherapy, corticosteroids and infection.

Iit is prudent to enquire into the dental health of all patients on or starting bisphosphonate therapy, ensure good oral hygiene and regular dental review and ensure any required invasive dental procedures are undertaken before or after withdrawal of bisphosphonates.

Additionally we should review the indication for continuing long-term bisphosphonates especially in those who may be receiving higher doses (i.e. Paget's Disease) to ensure that the intended benefit out-ways any possible risks.

W12

Anabolic therapies for osteoporosis

Peter R. Ebeling
Dept. Medicine (RMH/WH), The University of Melbourne, Western Hospital, Footscray 3011, Victoria, Australia

Therapies for osteoporosis are either anti-catabolic or anabolic. Subcutaneous teriparatide [human PTH (1-34)] injections are the first anabolic therapy for osteoporosis and significantly increases BMD and reduce vertebral and non-vertebral fracture risk. There are no hip fracture data. Its mode of action is differs from anti-catabolic drugs in that it restores trabecular microarchitecture and increases cortical and trabecular bone volume.

Teriparatide increases bone formation before bone resorption, allowing for an early anabolic response. Early increases in type I procollagen propeptides strongly predict the subsequent increase in BMD and bone microarchitecture. However, increases in areal BMD underestimate the effects of teriparatide in increasing bone strength. Results from 3-dimensional micro-computed tomography of biopsies show teriparatide significantly increases trabecular bone volume, connectivity and cortical bone thickness without loss of cortical bone porosity versus placebo. Thus, the increased biomechanical competence may explain the observed reductions of vertebral and non-vertebral fracture incidence of patients treated with teriparatide.

Mild transient hypercalcemia may occur; however, monitoring of serum calcium is not required. Osteosarcoma was observed in a rat oncogenicity study, but no cases of osteosarcoma in response to teriparatide have been reported in human studies and only a handful have been reported associated with hyperparathyroidism. Studies using PTH (1-84) are underway. Combining PTH and anti-catabolic drugs diminishes PTH effects; sequential therapy is preferred. Anti-catabolic therapy should be reinitiated after PTH to maintain or increase BMD.

Another drug, strontium ranelate, reduces vertebral and non-vertebral fracture risk. Although it increases osteoblastic cellular activity, definitive data relating to its effects on bone histomorphometric bone formation are not currently available.