Other articles

Das De et al (JBJS, 2010; 92A (1) 679-686)
A rational approach to management of alendronate-related subtrochanteric fractures

26 low velocity subtrochanteric fractures of a 6-year period, in 20 patients (6 had bilateral fractures). 12 of 20 patients were taking alendronate (for >4 years). Characteristics: transverse or slight oblique fracture line, lateral cortical thickening, and minimal comminution.

Pre-existing ellipsoid thickening of the lateral femoral cortex associated with pain should prompt investigation for occult fracture and prophylactic fixation on contralateral side. Stop bisphosphonate and re-assess osteoporosis risk with bone densitometry and FRAX score – tetraniatide may be a suitable alternative agent if required.

Isaacs et al (CORR, 2010; 468, 3384-3392)
Femoral Insufficiency Fractures Associated with Prolonged Bisphosphonate Therapy

Comparison of low energy subtrochanteric and femoral fractures, over 65 without underlying cancer: pre-bisphosphonates (1995-1997) n=38, post (2007-2009) n=79. Only 55% of pre-group included as imaging available (i.e. 21 patients). In the pre-group there were no patients with an insufficiency type fracture on imaging.

In the post-group, 53 of the 79 patients on long term bisphosphonates, and there were 41 patients with a characteristic insufficiency pattern. All of the 41 insufficiency type fractures were taking bisphosphonates for average 7.1 years. The 12 patients on bisphosphonates without an insufficiency fracture were only taking for an average 3.2 years. 71% of the 41 insufficiency fractures had a prodrome of groin, thigh or knee pain, and nearly half (44%) had bilateral insufficiency femoral fractures on x-ray.

Is there a difference between alendronate (taken by 40 of the 41 with insufficiency fractures) and risedronate? Study only looks at relative risk of bisphosphonates, and not absolute risks. Advice: need to further investigate limiting bisphosphonate use to 5 years, and assessing any patients for insufficiency who complain of prodromal symptoms – prophylactically treating insufficiency, and stopping bisphosphonates or switching to alternative agents.
Insufficiency Fractures

- Atypical insufficiency fractures first reported in 2005 as a case series of 9 patients (Odvina et al)

- Abrahamsen (2010) performed a national register cohort analysis, and found an increased incidence of subtrochanteric fractures amongst bisphosphonate users.

- Wang (2011) also found that with bisphosphonate therapy: for a reduction of 100 neck of femur fractures, there was a subsequent increase of 1 subtrochanteric fracture.

- Women taking bisphosphonates for more than 5 years had a significantly higher relative risk for subtrochanteric or femoral shaft fractures, albeit with a low absolute risk when compared to non-bisphosphonate users.

- Current recommendations made by American Society of Bone and Minerak Research Committee (2010)
  - Investigate patients on bisphosphonate therapy for any history of thigh or groin pain with AP and lateral x-rays of the femur.
  - If high clinical suspicion and x-rays negative, consider bone scan or MRI
  - For a complete fracture – discontinue bisphosphonate and fix with an IM-nail, and then evaluate the other side. Continue calcium & vitamin D supplements
    - For an incomplete fracture – discontinue bisphosphonates, and give calcium & vitamin D supplements
      - If painful, then prophylactic IM nailing
      - If minimal pain, then trial 2-3 months of partial weight bearing and re-assess x-rays before prophylactic fixation
      - If asymptomatic, reduce activity until bone oedema absent on MRI
  - Consider raloxifene or teriparetide in patients with osteoporosis of the spine, but normal or only moderately reduced BMD at the femoral neck.
**Bisphosphonate Use & Controversy**

*Yoon et al (2011), Long-term bisphosphonate usage and subtrochanteric insufficiency fractures a cause for concern?, JBJS, 93-B (10); 1289-1295*

**Osteoporosis Prophylaxis Evidence**

- Alendronate has a propensity for osteoclast over osteoblasts by a ratio of 11:1
  - Lies dormant within mineralised matrix of bone
  - Activated only in the presence of osteoclast to inhibit bone resorption

- 2 subclasses:
  - N-BP (nitrogen containing bisphosphates)
    - alendronate, pamidronate, risedronate, zoledronate
    - induce osteoclast inhibition via melavonate pathway
  - n-BP (non-nitrogen containing)
    - etidronate, tiludronate
    - form toxic ATP analogues through its metabolites
    - induce osteoclast apoptosis

- **FIT trial (fracture intervention trial)**
  - Double-blind RCT assessing alendronate over placebo
  - 6400 women with low bone mineral density (BMD)
  - sustained BMD increase
  - reduced cost of hip fractures by 58%
  - reduced overall fracture care costs by 35%

- **FLEX trial (FIT Long-term Extension)**
  - Over 1000 women already taking bisphosphonates
  - randomised to continued therapy or placebo
  - patients who discontinued therapy maintained their reduced fracture risk, despite slight decreases in BMD (which remained higher than their pre-treatment level)

- **HORIZON trial (Health outcomes and reduced incidence with Zolendronate)**
  - Once yearly infusion
  - Better compliance with similar results to FIT and FLEX data
  - Avoided GI side effects
  - Increase in rates of atrial fibrillation – later deemed not significant (Lyles 2007)

- **HORIZON Recurrent trial** looked at secondary prevention, randomising hip fracture patients to either zolendronate infusions or placebo.
  - Reduced vertebral and non-vertebral fractures
  - Lower associated mortality