Editorial

Pharmacological treatment of osteonecrosis

The 2005 Nobel laureates in physiology or medicine won the prize for discovering the bacterium behind gastric ulcer. Their findings are an example of simple observations leading to dramatic change in medicine, once someone has been able to realize their potential.

In orthopedics also, there may be simple facts sitting right in front of our eyes without us really appreciating their importance. The ability of bisphosphonates to inhibit bone resorption was described in 1969 (Fleisch et al. 1969), but interest in this did not catch on amongst orthopedic researchers until the use of bisphosphonates against osteoporosis became popular. Bisphosphonates are potential tools in the hands of orthopedic surgeons for all cases in which bone resorption is involved.

Recently, a group from Taiwan showed in a randomized but unblinded clinical study that bisphosphonates can prevent collapse of osteonecrotic bone (Lai et al. 2005). They had 40 patients (54 hips) with early non-traumatic osteonecrosis of the femoral head. Oral alendronate reduced the number of collapsing femoral heads from 19/25 in the control group to 2/29 in the treatment group. The number of patients requiring THR was reduced from 16 to 1. The alendronate dose was the usual for osteoporosis prophylaxis, and duration of treatment was 6 months. A previous uncontrolled study from India showed similar results (Agarwala et al. 2002).

It remains to be demonstrated that osteonecrotic collapse can also be prevented after fractures. There is still a risk of collapse in undisplaced and nailed femoral neck fractures (Damany et al. 2005), and for dislocated fractures of the talar neck the risk is very high (Vallier et al. 2004). Considering that the cause of collapse is osteoclastic bone resorption, bisphosphonates may turn out to be efficacious regardless of the etiology of the osteonecrosis. The same could be true for Perthe's disease (Little et al. 2005, Ward et al. 2005).

One reason why there has been limited interest in trying out bisphosphonates for orthopedic indications is a misconception that bone formation is always coupled to resorption, so that reduced resorption would lead to a reduced formation. If that were always true, little would be gained by reducing resorption in orthopedic situations. Coupling is an important concept in normal bone remodeling, and a prerequisite for the existence of the bone remodeling units. However, in orthopedic situations such as fracture repair, prosthesis loosening or osteonecrosis, it is obvious that bone resorption and formation can occur independently of each other, either stochastically distributed or organized in different parts of the site. Thus, inhibition of osteoclast activity by the use of bisphosphonates could possibly lead to a net increase in bone mass and strength in these sites. Moreover, in orthopedic conditions it is often possible to apply the drug locally. This will give a much higher local concentration, and because of the unique pharmacokinetics of bisphosphonates, they will remain at the site for a long time.

This field of research is a challenge to the orthopedic community. We can only expect limited economic support from the drug industry, considering the low number of patients and short treatment compared to osteoporosis. On the other hand, the type of study that Lai et al. performed should be simple and reasonably cheap. The study is an eye-opener.

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DOI 10.1080/17453670610045894

Agarwala S, Sule A, Pai B U, Joshi V R. Alendronate in the treatment of avascular necrosis of the hip. Rheumatology (Oxford) 2002; 41 (3): 346-7.

Damany D S, Parker M J, Chojnowski A. Complications after intracapsular hip fractures in young adults. A meta-analysis of 18 published studies involving 564 fractures. Injury 2005; 36 (1):131-41.

Fleisch H, Russell R G, Simpson B, Muhlbauer R C. Prevention by a diphosphonate of immobilization "osteoporosis" in rats. Nature 1969; 223 (202): 211-2.

Lai K A, Shen W J, Yang C Y, Shao C J, Hsu J T, Lin R M. The use of alendronate to prevent early collapse of the femoral head in patients with nontraumatic osteonecrosis. A randomized clinical study. J Bone Joint Surg (Am) 2005; 87 (10): 2155-9.

Little D G, McDonald M, Sharpe I T, Peat R, Williams P, McEvoy T. Zoledronic acid improves femoral head sphericity in a rat model of perthes disease. J Orthop Res 2005; 23 (4): 862-8.

Vallier H A, Nork S E, Barei D P, Benirschke S K, Sangeorzan B J. Talar neck fractures: results and outcomes. J Bone Joint Surg (Am) 2004; 86 (8): 1616-24.

Ward K, Cowell C T, Little D G. Quantification of metaphyseal modeling in children treated with bisphosphonates. Bone 2005; 36 (6): 999-1002.