Drugs 1999 Jan; 57 (1): 109-110
0012-6667/99/0001-0109/$02.00/0

Ibandronate

A Viewpoint by Silvano Adami

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Ibandronate is a third generation bisphosphonate with the highest potency, relative to other members of its class, in inhibiting osteoclastic bone resorption. The mechanism of action and the bone pharmacodynamics are likely to be very similar to those of other aminobisphosphonates, such as alendronate or risedronate, which have been somewhat more thoroughly investigated. The drug is still under evaluation for the treatment of osteoporosis and Paget's disease, whereas it has already been registered in some countries for the treatment of hypercalcaemia of malignancy.

The high potency of ibandronate does not seem to offer relevant advantages over the other aminobisphosphonates for the usual therapeutic indications but it might be relevant for its tolerability profile. Oral aminobisphosphonates may lead to serious gastrointestinal adverse effects which depend on the contact of undissolved crystals with the oesophageal or gastric mucosa.[1] These adverse events can be lessened by increasing the speed of dissolution by ingesting the tablet with a large amount of water. The same goal can be theoretically achieved with the smaller amount of substance needed with the more potent compounds. However, the general impression is that the stronger the antiosteoclastic activity of the aminobisphosphonate, the higher the irritating effect on the mucosa. Because of the high clinical relevance of the gastrointestinal tolerability of oral aminobisphosphonates, there is an obvious need for comparative studies in patients in the clinical setting.

The renal clearance of bisphosphonates is even higher than the glomerular filtration rate. Thus, with the high circulating concentrations obtained during intravenous infusion, the concentration at the renal tubule easily reaches toxic levels. These toxic effects[2] are strongly associated with the amount (weight) of compound infused per unit of time and it is strongly recommended not to exceed an intravenous infusion rate of 200 mg/h or 5 mg/min. Because of the very high potency of ibandronate, the highest recommended intravenous dose is 4mg. This dose can be administered as an intravenous bolus, avoiding the need for impractical and expensive slow infusions. This appears to represent the most intriguing 'plus' for ibandronate over the less potent bisphosphonates, particularly for long term intermittent treatment protocols. The treatment of osteoporosis with 2 to 4 intravenous bolus injections of ibandronate per year[3] might represent an interesting alternative to continuous oral therapy for a good proportion of patients. ▲

References

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