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Ibandronate

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Bisphosphonates are analogues of pyrophosphate, and like this substance they are strongly bound to hydroxyapatite in bone. Bisphosphonates inhibit osteoclastic bone destruction by a number of means, some of which are not fully understood. Compounds from this group of substances have been used with great success in the treatment of Paget's disease, hypercalcaemia, tumour osteolysis and osteoporosis, and they may also be able to prevent the development of bone metastasis.

Ibandronate is a newly developed third generation bisphosphonate. It acts in the same way as other aminobisphosphonates (e.g. pamidronate, alendronate), but has a much higher affinity for bone matrix. This provides advantages with regard to the tolerability of the substance and its route of administration. At intravenous doses of between 2 and 6mg ibandronate is extremely effective in the treatment of tumour-induced hypercalcaemia. Because of the small amount of drug, damage to the kidney, the most important organ at risk for toxicity, can practically be ruled out, and the dose does not have to be reduced in patients with impaired kidney function (serum creatinine <442 μmol/L). Otherwise, ibandronate is associated with the same adverse effects as other aminobisphosphonates.

Initial experience has shown that ibandronate can be administered as a bolus injection (up to 3mg), thus avoiding the need for lengthy infusions. Proteinuria and haemoglobinuria have been observed at doses above 3mg,[1] and so short term infusions (15 to 30 min) should be used at these dose levels. Ibandronate is currently approved for the treatment of hypercalcaemia, with or without skeletal metastases. According to a clinical trial, in hypercalcaemia ibandronate can be administered at doses of between 2 and 6mg depending on the level of serum calcium.[2] Preclinical and initial clinical investigations into the treatment of osteoporosis are promising, and only 4 bolus injections per year of 0.5 to 2mg may prove to be sufficient for effective therapy and prophylaxis. If initial data from ongoing studies confirm the efficacy of this regimen, it would constitute a paradigm shift in the treatment of osteoporosis with bisphosphonates and could replace oral therapy, which is frequently associated with adverse events affecting the stomach and oesophagus.

In preclinical studies in tumour osteolysis, intravenous ibandronate produced a clear improvement in parameters of metabolism. Phase III studies on prevention of tumour-induced skeletal morbidity have not yet been completed. Intravenous doses of 2 and 6mg and oral doses of 20 and 50mg ibandronate are being investigated in breast cancer, while 2mg intravenously is being studied in multiple myeloma. Although the results of these studies are not yet available, it can be said that ibandronate is a useful extension to the range of bisphosphonates. According to current knowledge, its advantages lie in its high efficacy, low toxicity and its ability to be given by bolus injection. ▲

References

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