Reducing fracture risk in osteoporosis with Zoledronic Acid

History of bisphosphonate research

Bisphosphonates are a group of compounds that were first developed as water softeners for use in washing powders. They strongly bind calcium and are hard to break down, so are perfect to stop scale developing.

Original investigations for medical use hoped that bisphosphonates could similarly stop the unwanted deposition of calcium in the body. Research discovered, however, that at lower doses bone resorption is inhibited – useful in diseases characterised by high bone resorption such as Paget’s disease, malignant bone disease and osteoporosis.

Researchers from the University’s Medical School, Department of Molecular Biology and Biotechnology, and Department of Chemistry have studied bisphosphonates for some time, exploring how they work at a cellular level and which ones work best. They found that zoledronic acid was the bisphosphonate with the most useful properties. It had a favourable ratio of inhibiting bone mineralisation and bone resorption, and its effects last a long time.

Contact the Healthcare Gateway
E. healthcare.gateway@sheffield.ac.uk
T. 0114 271 1634
sheffield.ac.uk/shg
Zoledronic acid trials and licensing

Pharmaceutical company Novartis sponsored a Phase III clinical trial of an annual dose of zoledronic acid for osteoporosis treatment. Over three years, the trial investigated the impact of zoledronic acid on reducing fracture risk in degenerative bone disease. It was very effective. Zoledronic acid was shown to reduce spine fracture risk by 70 per cent and hip fracture risk by 40 per cent. The drug was licensed in 2007 and the study continued for a further six years to monitor longer-term effects.

Professor Richard Eastell has been involved in the development of the drug since the start of the trial. As Director of the Mellanby Centre for Bone Research at the University of Sheffield, he is an expert in bone mineralisation and a long-term consultant to Novartis. Results of the extended study are about to be published.

The current situation

Zoledronic acid is now widely used as a treatment for osteoporosis and malignant bone disease, and is the treatment of choice in Paget’s disease. The Novartis patent will soon expire, reducing the price of this already cost-effective treatment.

The treatment is popular with patients, as Professor Eastell pointed out: “People quite often don’t want tablets that give them stomach pain, that are a nuisance to take and that can easily be missed. The zoledronic acid is an intravenous infusion once a year. It only takes 15 minutes and we can ensure complete compliance.”

Follow-on research continues to look for other potential uses for the drug. There are questions about its use in halting the growth of malignant tumours, and studies attempting to combine it with other drugs for even more beneficial effects.

Professor Eastell’s current research adds knowledge to support the use of zoledronic acid. Measuring bone turnover markers enables him to assess how the drug affects the skeleton in individuals. His work also tries to understand how the change in bone density relates to the fracture risk, how different compartments of bone are affected, and why these drugs have such a good effect on particular bones.