Drugs reduce bone cancer damage but clinical guidance remains non-specific

May 15 2012

Bone cancer-related fractures and pain can be reduced by drug treatment, but no one drug is superior, according to a review published in The *Cochrane Library*. Researchers undertook a systematic review of the current evidence on bisphosphonate drugs, which are used to prevent bone damage in multiple myeloma.

Multiple myeloma is a type of cancer that grows in and on bones, and can cause fractures in long bones and the spine. Severe back pain is a common symptom. Bisphosphonate drugs may help to reduce the occurrence of fractures and bone pain in myeloma patients. They work by inhibiting the activities of bone cells called osteoclasts, which are involved in the formation of fractures. Many different bisphosphonate drugs are available, but their relative merits are uncertain.

The researchers analysed data from 20 trials involving a total of 6,692 patients who took bisphosphonate drugs including zoledronate, clodronate, pamidronate, ibandronate and etidronate in addition to their myeloma treatments. Bisphosphonates reduced the occurrence of fractures and pain. For all types of fractures, the researchers estimated that between 6 and 15 patients would need to be treated to prevent fractures in one patient. For pain, between 5 and 13 patients would need to be treated to reduce pain in one patient.

Four trials made direct comparisons between different drugs. In the remaining trials, the effects of the drugs were compared to those of placebos or no treatment and the researchers made indirect comparisons

by interrogating the data from these trials. Head-to-head trials suggested that zoledronate was more effective at reducing fractures compared to etidronate, but taken together with the indirect comparisons, the researchers conclude that no one drug can be regarded as superior.

"Whether zoledronate is superior to any other bisphosphonate drug remains an open question," said lead researcher Ambuj Kumar of the Center for Evidence Based Medicine and Health Outcomes Research at the University of South Florida, in Tampa, Florida. "In light of the inconsistencies we see in the data, it is difficult to recommend any drug as a preferential treatment for clinical practice."

Based on the findings of the review, adverse effects of bisphosphonate drugs appear to be rare. Osteonecrosis of the jaw (a disease whereby the jaw bone can appear through lesions in the gum which do not heal) is one potential complication that has been gaining attention in recent years, but the authors report that it is no more common in those taking bisphosphonate drugs than in those receiving placebos or no treatment. "We didn't identify any significant adverse effects, but this work does highlight the need for larger head-to-head trials, which are needed to better compare the safety and effectiveness of the different drugs available," said Kumar.

More information: Mhaskar R, Redzepovic J, Wheatley K, Clark OAC, Miladinovic B, Glasmacher A, Kumar A, Djulbegovic B. Bisphosphonates in multiple myeloma: a network meta-analysis. *Cochrane Database of Systematic Reviews* 2012, Issue 5. Art. No.: CD003188. DOI: 10.1002/14651858.CD003188.pub3