Title	**Bisphosphonate Agents for the Management of Pain Secondary to Bone Metastases: A Systematic Review of Effectiveness and Safety**
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Aim

To examine the effectiveness and safety of specific bisphosphonate agents, compared with placebo and other analgesics, in managing the pain of bone metastases.

Conclusions and results

Fifty articles were found, including studies of mixed quality. The complexity of measuring pain limited interpretation of the results. Bisphosphonates were found to be moderately effective in relieving painful bone metastases compared with placebo when patients were assessed at 12 weeks. No one drug regimen (lower or higher doses of pamidronate, clodronate, or zoledronate) was found to be superior to another, and the effect was not limited to any specific cancer. No studies were found with adequate outcomes to allow comparisons of bisphosphonates with therapies such as other analgesic regimens, palliative radiotherapy, and palliative chemotherapy.

Recommendations

When making treatment choices, the delayed effect (benefit at 12 weeks) and adverse effects of bisphosphonates should be considered.

Methods

This study focused on five bisphosphonates: etidronate, clodronate, pamidronate, zoledronate, and ibandronate. Updating a 2001 Cochrane review, the research literature was searched extensively to identify randomized controlled trials that compared pain outcome with bisphosphonate treatment to 1) placebo, 2) no treatment, 3) other bisphosphonates, or 4) other treatments. Two reviewers independently discarded studies that did not fulfil the inclusion criteria, and then assessed the quality of the randomized controlled trials that were included. The primary outcome of interest was short-term pain relief (within 12 weeks). Secondary outcomes included reductions in analgesic use, mean pain scores, mean analgesic scores, and adverse effects.

Further research/reviews required

Future research should incorporate standard methods of reporting pain outcomes, including measurement of the proportion of patients achieving pain relief. Also, standard deviations should be used when reporting continuous variables, eg, pain score and morphine equivalent.

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