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[Intervention Review]

Bisphosphonates for advanced prostate cancer

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ABSTRACT

Background

Prostate cancer is the most common cancer in men in many western countries. It is characterized by its propensity for bone metastases which occur in more than 80% of patients with advanced disease. Patients are at risk of complications including pain, hypercalcaemia, bone fracture and spinal cord compression. Hormonal treatment is the mainstay of treatment for these patients but most of them will then become hormone refractory. Bisphosphonates act by inhibiting osteoclast activities and are a potential therapeutic option for metastatic prostate cancer. In addition, they have been shown to reduce pain in patients with bone metastases as a consequence of multiple myeloma. Early uncontrolled studies of bisphosphonates in metastatic prostate cancer patients have shown encouraging results.

Objectives

The objective of this review was to determine the effectiveness of bisphosphonates in relieving pain in patients with bone metastases from prostate cancer.

Search methods

Studies were identified by electronic search of bibliographic databases including MEDLINE, EMBASE, CancerLit and the Cochrane Controlled Trials Register. Handsearching included *Proceedings of American Society of Clinical Oncology* and reference lists of all eligible trials identified.

Selection criteria

Randomised controlled studies comparing the effectiveness of bisphosphonates with placebo or open control for pain relief in patients with bone metastases from prostate cancer.

Data collection and analysis

Data were extracted from eligible studies and included study design, participants, interventions and outcomes. Comparable data were pooled together for meta-analysis with intention-to-treat principle. Outcomes included pain response, analgesic consumption, skeletal events (including pathological fractures, spinal cord compression, bone radiotherapy, bone surgery), prostate cancer death, disease progression, radiological response, PSA response, adverse events, performance status, quality of life and comparisons between different routes, doses and types of bisphosphonates.

Main results

One thousand nine hundred and fifty-five patients from ten studies were included in this review. The pain response rates were 27.9% and 21.1% for the treatment group and the control group, respectively, with an absolute risk difference of 6.8%.The OR for pain response was

1.54 (95% CI 0.97 to 2.44, P = 0.07), showing a trend of improved pain relief in the bisphosphonate group, although this was not statistically significant. The rates for skeletal events were 37.8% and 43.0% for the treatment group and the control group, respectively, with an absolute risk difference of 5.2%. The OR for skeletal events was 0.79 (95% CI 0.62 to 1.00, P = 0.05). A significant increase in nausea was observed in patients who received bisphosphonates compared to placebo. No increase in other adverse events was observed. There was no statistically significant difference between the bisphosphonate group and the control group in terms of prostate cancer death, disease progression, radiological response and PSA response. There are insufficient data to guide the choice of bisphosphonates or the dose and the route of administration .

Authors' conclusions

Bisphosphonates should be considered for patients with metastatic prostate cancer for the treatment of refractory bone pain and prevention of skeletal events. More research is needed to guide the choice of bisphosphonates, optimal treatment schedule as well as cost-benefit comparisons. Combining results from different studies is difficult because different tools were used to assess pain, and also, bisphosphonates vary considerably in potency. This review highlights the need for standardisation and co-ordination among researchers in cancer pain studies.

PLAIN LANGUAGE SUMMARY

Bisphosphonates for advanced prostate cancer

Prostate cancer is the most common cancer in men in many western countries and is characterized by its propensity to spread to bone which occurs in more than 80% of patients with advanced disease. Patients are at risk of complications including pain, hypercalcaemia, bone fracture and spinal cord compression. The role of bisphosphonates for the palliation of symptoms associated with advanced prostate cancer, was evaluated in this review. Pain relief was improved, and the incidence of skeletal events was reduced in patients receiving bisphosphonates compared to control patients. A significant increase in nausea was observed in patients who received bisphosphonates compared to placebo. Bisphosphonates do not appear to influence disease progression or patient survival, however, they should be considered as a palliative option in advanced prostate cancer.