Authors' objectives
To investigate the efficacy of progestogens compared with other hormone therapies in women with breast cancer and bone metastasis.

Searching
Cancerline (1982-1996) was searched for relevant European literature.

Study selection
Study designs of evaluations included in the review
Comparative studies in which at least one of the evaluated treatments was a progestogen. It is unclear if included studies had to be randomised controlled trials (RCTs).

Specific interventions included in the review
Progestogens (medroxyprogesterone acetate 900-2000 mg/day; megestrol acetate 80-160 mg/day) compared with alternative progestogens or hormone antagonists (tamoxifen 20-40 mg/day; aminoglutethimide 250-500 mg/day with hydrocortisone 40-50 mg/day).

Participants included in the review
Breast cancer patients with bone metastases (measurable and/or evaluable) were included. Neither menopausal status nor level of hormonal receptors was a selection criterion.

Outcomes assessed in the review
Bone lesions were assessed by skeletal x-ray or bone scans every three months or after six weeks of treatment. Response to treatment was classified according to published criteria (see Other Publications of Related Interest), as follows: complete remission (complete clearance of all lesions, assessed with two examinations, four weeks apart), partial remission (partial decline of lytic lesions, recalcification of lytic lesions, or a reduction in density of shrinking lesions), stability (to be assessed after a minimum of eight weeks of treatment), or progression (increase in size of existing lesions, or appearance of new lesions). Most of the included studies used global response rates, i.e. complete/partial remission combined, and stability/progression combined.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative review.

How were differences between studies investigated?
The studies were grouped according to the comparison being made.

Results of the review
Ten studies were included overall (n=562). Four studies compared medroxyprogesterone acetate with tamoxifen (n=186), three compared megestrol acetate with tamoxifen (n=208), and there was one comparison each for medroxyprogesterone acetate versus megestrol acetate (n=43), megestrol acetate versus aminoglutethimide (n=66), and medroxyprogesterone acetate versus aminoglutethimide (n=59).

Results from all four studies comparing medroxyprogesterone acetate with tamoxifen showed a statistically significantly difference in terms of global response rates in favour of medroxyprogesterone acetate (p=0.05 or less, for all 4 studies). No statistically significant differences between groups were found in three studies comparing megestrol acetate with tamoxifen. In one evaluation of medroxyprogesterone acetate versus megestrol acetate, a statistically significant effect was found in favour of medroxyprogesterone acetate (p<0.05), and another study showed a statistically significant difference in favour of aminoglutethimide, when this was compared with megestrol acetate. A single study of medroxyprogesterone acetate versus aminoglutethimide, showed no statistically significant difference between treatments.

Authors’ conclusions
Whatever the method of assessment, these data show that medroxyprogesterone acetate (900-2000 mg/day) is more effective than tamoxifen. However, it was not possible to determine the effect on survival because survival data from trials were reported globally and not stratified according to presence of bony metastasis. There was no difference between megestrol acetate and tamoxifen; aminoglutethimide proved to be better than megestrol acetate.

CRD commentary
The research question is clearly explained. The selection criteria for primary studies were mostly clear, however, more information concerning the eligible study designs would have been useful. The search strategy was limited to one source; it is possible that had other databases been accessed, and relevant materials handsearched, further relevant studies may have been identified. There was no attempt to search for unpublished data. No details of search terms are provided and therefore it would not be possible to replicate the search strategy from the information given. There is no reported validity assessment of primary studies and so the reliability of findings cannot easily be assessed. Some details of included studies are provided in tables and text, however, more details relating to participant characteristics would have been helpful. The authors do not explain why they did not attempt to pool study results using statistical techniques. The narrative summary would have been more informative if more information about the methodological quality of primary studies had been presented. There are no details of the review process (i.e. how many reviewers involved, how decisions about inclusion were made, how data were extracted, and how disagreements were resolved). The authors’ conclusions appear to follow-on from the data, however, they do not mention the methodological limitations of this review.

Implications of the review for practice and research
The authors state that, at present, it is not known whether medroxyprogesterone acetate prolongs survival in breast cancer patients with localised bone metastases. It would be of interest to conduct a randomised trial comparing the effectiveness of the three classes of hormone therapy on the development of bone metastases in patients with breast cancer.

Bibliographic details

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