Systematic review of the effects of aromatase inhibitors on pain associated with endometriosis

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CRD summary
This review found that although aromatase inhibitors appeared to have a promising effect on pain associated with endometriosis, but due to the paucity of good quality evidence, the strength of the inference was limited. The review was well conducted and the authors' conclusions are likely to be reliable.

Authors' objectives
To evaluate the effects of aromatase inhibitors in women with symptoms of pain with endometriosis.

Searching
MEDLINE, EMBASE, CINAHL and the Cochrane Library were searched from inception to 2007 for relevant published studies, using a combination of keywords (not reported). Reference lists from the review and primary articles were also searched.

Study selection
Studies that compared aromatase inhibitors with standard medical treatment on pain outcomes in women previously treated for endometriosis; and experiencing symptoms such as dyspareunia, dysmenorrhoea and chronic pelvic pain, were eligible for inclusion.

Most of the patients in the included studies were pre-menopausal women; two studies enrolled post-menopausal women. The mean age of the patients ranged from 20 to 57 years. The aromatase inhibitors evaluated in the studies included letrozole (at a range of doses from 1mg to 2.5mg) and anastrazole (given at a range of doses from 0.25mg to 1.0mg). Concurrent medications for the patients receiving aromatase inhibitors included norethindrone acetate, alendronate, prometrium, levonorgestrel, goserelin, ethinyl E₂ and supplements of calcium and vitamin D. The comparator treatment in the sole trial included was the gonadotrophin-releasing hormone analogue goserelin. Treatment duration ranged between three and 18 months. The outcomes examined were pelvic pain, lesion size, bone mineral density and quality of life.

Two reviewers independently reviewed citation lists and selected the studies for inclusion. Any disagreements were resolved by consensus or arbitration by a third reviewer.

Assessment of study quality
The reviewers assessed methodological quality in terms of the extent to which the design and conduct of the study avoided bias and errors in estimates of effectiveness of treatments.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Two reviewers independently extracted data on pain outcomes and other outcomes as reported in the individual studies; any disagreements were resolved by consensus or by a third reviewer.

Methods of synthesis
The results of the review were summarised narratively, with tables supporting the text.

Results of the review
Eight studies (137 women) were included in the review, including one randomised controlled trial (RCT, n=97 women), one prospective non-randomised study (n=15 women), two non-randomised studies (n=20 women), and four case
reports (n=5 women). The authors reported that the case series were poorly described and were numerically insufficient. The single RCT was characterised by adequate blinding of participants and satisfactory generation of the randomisation sequence. The length of follow-up ranged from six to 24 months.

One RCT (n=97 women) found significantly improved pain scores (p<0.001), and a non-significant trend towards benefits in bone mineral density, with the use of aromatase inhibitors and goserelin compared with the use of goserelin alone.

The remaining case reports and case series showed benefits with the use of aromatase inhibitors alongside progestogens, oral contraceptive pills or gonadotrophin-releasing hormone analogues in mean pain scores, quality of life, lesion size and bone mineral density.

**Authors' conclusions**

Aromatase inhibitors appeared to have a promising effect on pain associated with endometriosis but, due to a paucity of good quality evidence, the strength of the inference was limited.

**CRD commentary**

The review addressed a clear question. Criteria for the inclusion of studies were clearly stipulated. Appropriate databases were searched, although few attempts were made to identify unpublished studies. The search terms were not reported. In addition, it was unclear whether language restrictions were applied, so whether there was potential for language bias. Steps were taken to minimise errors and bias throughout the review process.

The authors correctly acknowledged the limitations of the review in terms of the dearth of good quality studies and the risk of bias in most of the included studies. In general, the review was well conducted and the authors' cautious conclusions are likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that prospective "powerful" randomised controlled trials were required to confirm potential beneficial clinical effects resulting from the use of aromatase inhibitors on pain and other outcomes in women with endometriosis.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.