Hormonal treatment for endometriosis associated pelvic pain

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CRD summary
The review concluded that it appeared that combined oral contraceptive pills, gonadotrophin-releasing hormone analogues and progestogens were all effective and well tolerated by patients in treating endometriosis-associated pain, but side effects had to be considered. The review had some methodological problems and data limitations that limit the reliability of the authors' conclusions.

Authors' objectives
To evaluate the effectiveness of hormonal treatments of endometriosis associated pain in women of reproductive age.

Searching
MEDLINE and Cochrane Database of systematic reviews were searched from 1995 to 2009 for articles in English. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) of medical treatments aimed at improving symptomatic endometriosis-associated pain in women aged 18 to 40 years were eligible for inclusion. Endometriosis-associated pain symptoms were dysmenorrhoea, non-menstrual pelvic pain, deep dyspareunia and chronic pelvic pain. Treatments with any progestogens, combined oral contraceptive pills and gonadotrophin-releasing hormone analogues (GnRHa) were all considered, irrespective of dosage, route of administration or duration of treatment. Medical treatments for painful symptoms after conservative surgery were eligible for inclusion. Studies had to measure pain improvement as an outcome. Secondary outcomes were adverse events. Studies where participants were asymptomatic or presented with infertility alone were not considered.

The included trials studied progestogen versus GnRHa, combined oral contraceptive pills versus control versus progestogen or Implanon versus Depot Medroxyprogesterone Acetate (DMPA). Mean duration of treatment was seven months (range three to 12 months). Endometriosis was staged according to the American Fertility Society classification (original or revised) form in three studies (the other studies did not perform staging of endometriosis). Most studies used objective scales to measure pain severity.

The authors did not state how many reviewers performed study selection.

Assessment of study quality
Study validity was assessed using the Jadad scale of randomisation, allocation concealment, blinding and drop-outs to give a maximum score of 5.

The authors did not state how many reviewers performed validity assessment.

Data extraction
Data were extracted on pain outcomes and adverse events and used to calculate mean differences and relative risks (RRs), together with 95% confidence intervals (CIs).

Two reviewers extracted data. Disagreements were resolved by discussion with the senior author.

Methods of synthesis
Meta-analysis was used to calculate pooled standardised mean differences and risk ratios, together with 95% CIs.

Results of the review
Seven RCTs (1,096 participants) were included in the review. Three trials scored the maximum 5 on the Jadad scale, three trials scored 3 and one trial scored 2. The study sample size ranged from 41 to 300 women.
Progestogen versus GnRHa: There was no statistically significant difference in relieving endometriosis-associated pain (three trials). GnRHa appeared to cause more bone mineral density loss than progestogens. Progestogens were associated with a higher incidence of spotting.

Implanon versus DMPA: There was no statistically significant difference in relieving endometriosis-associated pain (two trials). Patients in both treatment groups experienced similar side-effects such as acne, weight gain, hair loss, and breast tenderness.

Combined oral contraceptive pills versus control versus progestogen: There was no statistically significant difference in relieving endometriosis-associated pain (three trials). Progestogen was associated with more bloating and spotting than combined oral contraceptives.

Authors’ conclusions
It appeared that combined oral contraceptive pills, GnRHa and progestogens were all effective and well tolerated by patients in treating endometriosis associated pain, but side effects had to be considered.

CRD commentary
Inclusion criteria for the review were clearly defined. Two relevant data sources were searched. There was the potential for language bias, as only articles in English were included. Publication bias was not assessed and could not be ruled out. Attempts were made to reduce reviewer error and bias during data extraction; whether or not the same methods were used for study selection and quality assessment was unclear. Quality assessment indicated that the quality of the included studies was variable. Studies were combined using meta-analysis, although the full methods were not explained. None of the comparisons had more than three trials. It was unclear whether statistical heterogeneity was considered.

The review had some methodological problems and data limitations which limit the reliability of the authors’ conclusions.

Implications of the review for practice and research
Practice: The authors stated that combined oral contraceptive pills and progestogens were relatively cheap and more suitable for long-term use as compared to GnRHa.

Research: The authors stated that longer-term follow-up studies of Mirena and Implanon were required to look at long-term effects on endometriosis associated pain.

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