Endometriosis: an overview of Cochrane Reviews

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RHL summary

Findings of the review: The prevalence of endometriosis in the general population is as high as 10%. Its main clinical manifestations include pain and infertility. This overview aimed to summarize the effectiveness and side-effects of various treatments for pain and infertility associated with endometriosis. It includes 17 Cochrane reviews: 14 covering pain-relief treatments and eight fertility outcomes.

Gonadotrophin-releasing hormone (GnRH) analogues, levonorgestrel-releasing intrauterine system (LNG-IUD), danazol, progestogens and anti-progestogens, and laparoscopic surgical treatment were found to be effective for pain relief in women with endometriosis. Three-month treatment with GnRH analogues increased pregnancy rate in women with subfertility associated with endometriosis who had undergone assisted reproductive treatment (ART). Excisional surgery was better than ablative surgery in spontaneous pregnancy rate at nine to 12 months after surgery. Laparoscopic surgery gave higher pregnancy and live birth rates compared with diagnostic laparoscopy alone. GnRH analogues and danazol had higher side-effects than placebo. Depot-progestagens were associated with higher adverse effects compared with other treatments.

Implementation: GnRH analogues, LNG-IUD and danazol appear to be beneficial for pain relief in women with endometriosis. Laparoscopic treatment of endometriosis and excision of endometrioma are positively associated with pain control and should be considered. No medical treatments were found to improve natural fertility in women with endometriosis. Subfertile women with endometriosis undergoing ART should receive three month’s treatment with GnRH analogues. Laparoscopic surgery, rather than diagnostic laparoscopy alone, should be used as it appears to improve pregnancy and live birth rates.


Abstract

This overview reports on interventions for pain relief and for subfertility in pre-menopausal women with clinically diagnosed endometriosis.

The objective of this overview was to summarise the evidence from Cochrane systematic reviews on treatment options for women with pain or subfertility associated with endometriosis.
Published Cochrane systematic reviews reporting pain or fertility outcomes in women with clinically diagnosed endometriosis were eligible for inclusion in the overview. We also identified Cochrane reviews in preparation (protocols and titles) for future inclusion. The reviews, protocols and titles were identified by searching the Cochrane Database of Systematic Reviews and Archie (the Cochrane information management system) in March 2014.

Pain-related outcomes of the overview were pain relief, clinical improvement or resolution and pain recurrence. Fertility-related outcomes were live birth, clinical pregnancy, ongoing pregnancy, miscarriage and adverse events.

Selection of systematic reviews, data extraction and quality assessment were undertaken in duplicate. Review quality was assessed using the AMSTAR tool. The quality of the evidence for each outcome was assessed using GRADE methods. Review findings were summarised in the text and the data for each outcome were reported in 'Additional tables'.

Seventeen systematic reviews published in The Cochrane Library were included. All the reviews were high quality. The quality of the evidence for specific comparisons ranged from very low to moderate. Limitations in the evidence included risk of bias in the primary studies, inconsistency between the studies, and imprecision in effect estimates.

**Pain relief (14 reviews)**

*Gonadotrophin-releasing hormone (GnRH) analogues*

One systematic review reported low quality evidence of an overall benefit for GnRH analogues compared with placebo or no treatment.

*Ovulation suppression*

Five systematic reviews reported on medical treatment using ovulation suppression. There was moderate quality evidence that the levonorgestrel-releasing intrauterine system (LNG-IUD) was more effective than expectant management, and very low quality evidence that danazol was more effective than placebo. There was no consistent evidence of a difference in effectiveness between oral contraceptives and goserelin, estrogen plus progestogen and placebo, or progestogens and placebo, though in all cases the relevant evidence was of low or very low quality.

*Non-steroidal anti-inflammatory drugs (NSAIDS)*

A review of NSAIDs reported inconclusive evidence of a benefit in symptom relief compared with placebo.

*Surgical interventions*

There were two reviews of surgical interventions. One reported moderate quality evidence of a benefit in pain relief following laparoscopic surgery compared to diagnostic laparoscopy only. The other reported very low quality evidence that recurrence rates of endometriomata were lower after excisional surgery than after ablative surgery.

*Post-surgical medical interventions*

Two reviews reported on post-surgical medical interventions. Neither found evidence of an effect on pain outcomes, though in both cases the evidence was of low or very low quality.

*Alternative medicine*
There were two systematic reviews of alternative medicine. One reported evidence of a benefit from auricular acupuncture compared to Chinese herbal medicine, and the other reported no evidence of a difference between Chinese herbal medicine and danazol. In both cases the evidence was of low or very low quality.

**Anti-TNF-α drugs**

One review found no evidence of a difference in effectiveness between anti-TNF-α drugs and placebo. However, the evidence was of low quality.

**Reviews reporting fertility outcomes (8 reviews)**

**Medical interventions**

Four reviews reported on medical interventions for improving fertility in women with endometriosis. One compared three months of GnRH agonists with a control in women undergoing assisted reproduction and found very low quality evidence of an increase in clinical pregnancies in the treatment group. There was no evidence of a difference in effectiveness between the interventions in the other three reviews, which compared GnRH agonists versus antagonists, ovulation suppression versus placebo or no treatment, and presurgical medical therapy versus surgery alone. In all cases the evidence was of low or very low quality.

**Surgical interventions**

Three reviews reported on surgical interventions. There was moderate quality evidence that both live births or ongoing pregnancy rates and clinical pregnancy rates were higher after laparoscopic surgery than after diagnostic laparoscopy alone. There was low quality evidence of no difference in effectiveness between surgery and expectant management for endometrioma. One review found low quality evidence that excisional surgery resulted in higher clinical pregnancy rates than drainage or ablation of endometriomata.

**Post-surgical interventions**

Two reviews reported on post-surgical medical interventions. They found no evidence of an effect on clinical pregnancy rates. The evidence was of low or very low quality.

**Alternative medicine**

A review of Chinese herbal medicine in comparison with gestrinone found no evidence of a difference between the groups in clinical pregnancy rates. However, the evidence was of low quality.

**Adverse events**

Reviews of GnRH analogues and of danazol reported that the interventions were associated with higher rates of adverse effects than placebo; and depot progestagens were associated with higher rates of adverse events than other treatments. Chinese herbal medicine was associated with fewer side effects than gestrinone or danazol.

Three reviews reported miscarriage as an outcome. No difference was found between surgical and diagnostic laparoscopy, between GnRH agonists and antagonists, or between aspiration of endometrioma and expectant management. However, in all cases the quality of the evidence was of low quality.

For women with pain and endometriosis, suppression of menstrual cycles with gonadotrophin-releasing hormone (GnRH) analogues, the levonorgestrel-releasing intrauterine system (LNG-IUD) and danazol were beneficial interventions. Laparoscopic treatment of endometriosis and excision of endometriomata were also associated with improvements in pain. The evidence on NSAIDs was inconclusive. There was no evidence
of benefit with post-surgical medical treatment.

In women with endometriosis undergoing assisted reproduction, three months of treatment with GnRH agonist improved pregnancy rates. Excisional surgery improved spontaneous pregnancy rates in the nine to 12 months after surgery compared to ablative surgery. Laparoscopic surgery improved live birth and pregnancy rates compared to diagnostic laparoscopy alone. There was no evidence that medical treatment improved clinical pregnancy rates.

Evidence on harms was scanty, but GnRH analogues, danazol and depot progestagens were associated with higher rates than other interventions.

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