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[Intervention Review]

Oral contraceptives for pain associated with endometriosis

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ABSTRACT

Background

Endometriosis is a common gynaecological condition which affects many women of reproductive age worldwide and is a major cause of pain and infertility. The combined oral contraceptive pill (COCP) is widely used to treat pain occurring as a result of endometriosis, although the evidence for its efficacy is limited.

Objectives

To determine the effectiveness, safety and cost-effectiveness of oral contraceptive preparations in the treatment of painful symptoms ascribed to the diagnosis of laparoscopically proven endometriosis.

Search methods

We searched the following from inception to 19 October 2017: the Cochrane Gynaecology and Fertility Group Specialised Register of Controlled Trials, the Cochrane CENTRAL Register of Studies Online (CRSO), MEDLINE, Embase, PsycINFO, CINAHL (Cumulative Index to Nursing and Allied Health Literature), and the trial registers ClinicalTrials.gov and the World Health Organization Clinical Trials Registry Platform (WHO ICTRP). We also handsearched reference lists of relevant trials and systematic reviews retrieved by the search.

Selection criteria

We included randomised controlled trials (RCT) of the use of COCPs in the treatment of women of reproductive age with symptoms ascribed to the diagnosis of endometriosis that had been made visually at a surgical procedure.

Data collection and analysis

Two review authors independently assessed study quality and extracted data. One review author was an expert in the content matter. We contacted study authors for additional information. The primary outcome was self-reported pain (dysmenorrhoea) at the end of treatment.

Main results

Five trials (612 women) met the inclusion criteria. Only three trials (404 women) provided data that were suitable for analysis.

Combined oral contraceptive pill versus placebo

Two trials compared COCP with a placebo. These studies were at high risk of bias. For GRADE outcomes (self-reported pain (dysmenorrhoea) at the end of treatment), the quality of the evidence very low. Evidence was downgraded for imprecision as it was based

on a single, small trial and for the visual analogue scale data there were wide confidence intervals (CIs). There appeared to have been substantial involvement of the pharmaceutical company funding the trials.

Treatment with the COCP was associated with an improvement in self-reported pain at the end of treatment as evidenced by a lower score on the Dysmenorrhoea verbal rating scale (scale 0 to 3) compared with placebo (mean difference (MD) -1.30 points, 95% CI -1.84 to -0.76; 1 RCT, 96 women; very low quality evidence), a lower score on the Dysmenorrhoea visual analogue scale (no details of scale) compared with placebo (MD -23.68 points, 95% CI -28.75 to -18.62, 2 RCTs, 327 women; very low quality evidence) and a reduction in menstrual pain from baseline to the end of treatment (MD 2.10 points, 95% CI 1.38 to 2.82; 1 RCT, 169 women; very low quality evidence).

Combined oral contraceptive pill versus medical therapies

One underpowered trial compared the COCP with another medical treatment (goserelin). The study was at high risk of bias; the trial was unblinded and there was insufficient detail to judge allocation concealment and randomisation. For GRADE outcomes (self-reported pain (dysmenorrhoea) at the end of treatment), the quality of the evidence ranged from low to very low.

At the end of treatment, the women in the goserelin group were amenorrhoeic and therefore no comparisons could be made between the groups for the primary outcome. At six months' follow-up, there was no clear evidence of a difference between women treated with the COCP and women treated with goserelin for measures of dysmenorrhoea on a visual analogue scale (scale 1 to 10) (MD -0.10, 95% CI -1.28 to 1.08; 1 RCT, 50 women; very low quality evidence) or a verbal rating scale (scale 0 to 3) (MD -0.10, 95% CI -0.99 to 0.79; 1 RCT, 50 women; very low quality evidence). At six months' follow-up, there was no clear evidence of a difference between the COCP and goserelin groups for reporting complete absence of pain as measured by the visual analogue scale (risk ratio (RR) 0.36, 95% CI 0.02 to 8.43; 1 RCT, 50 women; very low quality evidence) or the verbal rating scale (RR 1.00, 95% CI 0.93 to 1.08; 1 RCT, 49 women; low quality evidence).

Authors' conclusions

Based on the limited evidence from two trials at high risk of bias and limited data for the prespecified outcomes for this review, there is insufficient evidence to make a judgement on the effectiveness of the COCP compared with placebo and the findings cannot be generalised.

Based on the limited evidence from one small trial that was at high risk of bias, there is insufficient evidence to make a judgement on the effectiveness of the COCP compared with other medical treatments. Only one comparison was possible, with the medical intervention being goserelin, and the findings cannot be generalised.

Further research is needed to fully evaluate the role of COCPs in managing pain-related symptoms associated with endometriosis. There are other formulations of the combined hormonal contraception such as the transdermal patch, vaginal ring or combined injectable contraceptives which this review did not cover but should be considered in future updates.

PLAIN LANGUAGE SUMMARY

Modern combined oral contraceptives for treatment of pain associated with endometriosis

Review question

The combined oral contraceptive pill (COCP) is commonly used to treat pain associated with endometriosis but how well it works is unclear.

Background

Endometriosis is a common women's healthcare condition where the endometrium (lining of the womb) grows at sites outside the womb, such as the ovaries (which produce eggs). Endometriosis is commonly found in women with painful periods, pain with sexual intercourse, pelvic pain and infertility (difficulty in having a baby). Hormonal treatments, including COCPs and medicines called gonadotrophin-releasing hormone analogues (for example, goserelin) are used to relieve the pain symptoms associated with endometriosis. However, many of the hormonal treatments have side effects which limit their acceptability and duration of use.

Study characteristics

Cochrane authors searched for clinical studies on 19 October 2017. We found five trials, including 612 women, that met the inclusion criteria. The studies took place in Egypt, the US, Japan and Italy.

Key results

Only three of the included studies provided data in a format that could be analysed in this review.

Combined oral contraceptive pill versus placebo

We found two trials including 354 women that compared the COCP with a placebo (pretend treatment). The evidence was at high risk of bias. There was very low quality evidence that treatment with the COCP was associated with an improvement in self-reported dysmenorrhoea (period pain) at the end of treatment measure on a verbal rating scale (where the woman rates her pain as (for example) "no

pain," "slight pain," "moderate pain," "severe pain" and "unbearable pain") and low quality evidence for an improvement in self-reported dysmenorrhoea pain at the end of treatment using a visual rating scale (where the woman marks her pain visually on a line) compared with placebo. There was very low quality evidence that there was a reduction in menstrual pain from the beginning to the end of treatment in the COCP group compared with women having a placebo.

Combined oral contraceptive pill versus other medical treatment

We found one trial of 50 women that compared the COCP with another medical treatment (goserelin).

The study was at high risk of bias. At the end of treatment, the women in the goserelin group were not having a period and therefore we could not compare the groups.

Six months after the end of treatment, there was very low quality evidence that there was no clear difference between women treated with the COCP and women treated with goserelin for self-reported dysmenorrhoea, using a visual rating scale or a verbal rating scale. Six months after the end of treatment, there was very low quality evidence that there was no clear evidence of a difference between the COCP and goserelin groups for reporting complete absence of pain, as measured by a visual rating scale and low quality evidence using a verbal rating scale.

Quality of the evidence

The quality of the evidence was very low quality. The main reasons for downgrading the evidence were because the data were based on a single small trial with wide variation in results and lack of details about how the study had been designed. There were some concerns with two of the studies that were funded by a pharmaceutical company that also had input into the design of the trial, data collection and the analysis of data. This means that we cannot be confident about the results.