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[Intervention Review]

Combined hormonal contraceptives for heavy menstrual bleeding

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ABSTRACT

Background

Menorrhagia or heavy menstrual bleeding (HMB) is an excessive blood loss that impairs a woman's quality of life, either physical, emotional, social or material. It is benign and not associated with pregnancy or any other gynaecological or systemic disease. Medical treatments used to reduce excessive menstrual blood loss (MBL) include prostaglandin synthetase inhibitors, antifibrinolytics, oral contraceptive pills, and other hormones. The combined oral contraceptive pill (COCP) is claimed to have a variety of beneficial effects, inducing a regular shedding of a thinner endometrium and inhibiting ovulation, thus having the effect of both treating HMB and providing contraception. More recently, a contraceptive vaginal ring (CVR) has been trialled to investigate whether this treatment can provide similar benefits to COCP while lessening hormonal systemic exposure. This review is an update of a review which originally focused on COCP alone. The scope of the review has been widened to consider other types of delivery of combined hormonal contraceptives for reduction of MBL.

Objectives

To determine the efficacy of combined hormonal contraceptives (pills, vaginal ring or patch) compared with other medical therapies, placebo, or no therapy in the treatment of HMB. A secondary objective was to compare the COCP with the CVR.

Search methods

We searched the Gynecology and Fertility Group trials register, MEDLINE, Embase, CENTRAL, CINAHL and PsycINFO (search dates: Oct 1996, May 2002, June 2004, April 2006, June 2009, July 2017 and September 2018) for all randomised controlled trials (RCTs) of COCP and CVR for the treatment of HMB. We also searched trial registers and the reference lists of retrieved studies for additional trials.

Selection criteria

We included randomised controlled trials (RCTs) of the use of COCP or CVR compared with no treatment, placebo, or other medical therapies for women with HMB and regular menstrual cycles.

Data collection and analysis

All assessments of trial quality and data extraction were performed unblinded by at least two review authors. Our primary review outcomes were treatment success, menstrual bleeding (assessed objectively, semi-objectively or subjectively), and participant satisfaction with treatment. Secondary outcomes were adverse events, quality of life, and haemoglobin level.

Main results

We identified eight RCTs involving 805 participants. Two trials comparing COCP with placebo were considered to be moderate quality and the remaining studies were low to very low quality, mainly because of serious risk of bias from lack of blinding and concerns over precision.

COCP versus placebo

COCP, with a step-down oestrogen and step-up progestogen regimen, improved response to treatment (return to menstrual 'normality') (OR 22.12, 95% CI 4.40 to 111.12; 2 trials; 363 participants; I^2 = 50%; moderate-quality evidence), and lowered MBL (OR 5.15, 95% CI 3.16 to 8.40; 2 trials; 339 participants; I^2 = 0%; moderate-quality evidence) when compared to placebo. The results suggested that, if the chance of 'successful' treatment was 3% in women taking placebo, then COCP increased this chance from 12% to 77% in women with unacceptable HMB. Minor adverse events, in particular breast pain, were more common with COCP. No study in this comparison reported semi-objectively assessed MBL or participant satisfaction with treatment.

COCP versus other medical treatments

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

There was insufficient evidence to determine whether the COCP reduced MBL when compared to NSAIDs (mefenamic acid and naproxen). No study in this comparison reported semi-objectively assessed MBL, subjectively assessed MBL, participant satisfaction with treatment or adverse events.

Levonorgestrel-releasing intrauterine system (*LNG IUS)*

The LNG IUS was more effective than COCP in reducing MBL (OR 0.21, 95% CI 0.09 to 0.48; 2 trials; 151 participants; I^2 = 0%; low-quality evidence) but it was not clear whether satisfaction with treatment or adverse effects varied according to which treatment was used. No study in this comparison reported semi-objectively assessed MBL or subjectively assessed MBL.

Contraceptive vaginal ring (CVR) versus other medical treatments

COCP

COCP was compared with CVR in two trials. There were discrepancies between some of the findings and there was no evidence of a benefit for one treatment compared to the other for response to treatment, MBL or participant satisfaction with treatment. There was a greater likelihood of nausea with COCP. No study in this comparison reported objectively assessed MBL or subjectively assessed MBL.

Progestogens

CVR was compared to long course progestogens in one trial. It is possible that CVR increased the odds of satisfaction; but we are uncertain whether CVR improved MBL. The evidence was based on small numbers of participants and was very low quality, so definitive conclusions could not be reached. No study in this comparison reported objectively assessed MBL, subjectively assessed MBL, or adverse events.

Authors' conclusions

Moderate-quality evidence suggests that the combined oral contraceptive pill over six months reduces HMB in women with unacceptable HMB from 12% to 77% (compared to 3% in women taking placebo). When compared with other medical options for HMB, COCP was less effective than the LNG IUS. Limited evidence suggested that COCP and CVR had similar effects. There was insufficient evidence to determine comparative efficacy of combined hormonal contraceptives with NSAIDs, or long course progestogens.

PLAIN LANGUAGE SUMMARY

Combined hormonal contraceptives for heavy menstrual bleeding

Review question

Researchers in the Cochrane Gynaecology and Fertility Group reviewed the evidence about the effects of combined hormonal contraceptives versus no treatment, placebo (sham treatment), or other medical treatments for women with heavy menstrual bleeding (HMB).

Background

HMB can cause anaemia (too few red blood cells) and interfere with a woman's quality of life and well-being. This means that premenopausal women may often consult with their own doctor or seek referral to gynaecology specialists to treat their menstrual bleeding. Combined oral contraceptive pills (COCP) can provide control of the menstrual cycle by thinning the endometrium (the lining of the womb that is shed during menstruation). It is possible that contraceptives delivered in other ways (via a vaginal ring or patch on the skin) may also act in a similar way and reduce menstrual blood loss.

Study characteristics

Eight studies, which included 805 women, were identified that compared combined hormonal contraceptives (mostly, the combined contraceptive pill) with either no treatment, placebo or other medical treatments. The studies assessed the effects of interventions on menstrual bleeding, satisfaction, quality of life, adverse events, and haemoglobin levels (protein in red blood cells that carries oxygen throughout the body). The evidence is current to September 2018.

Key results

Two studies found that a type of COCP, containing estradiol valerate and dienogest, reduced HMB and improved quality of life and haemoglobin levels when compared with placebo, but at the expense of some minor side effects. There was insufficient evidence to compare contraceptives with other treatments, such as nonsteroidal anti-inflammatories or progestogens. Two studies found that the levonorgestrel-releasing intrauterine system (LNG IUS) was more effective than the COCP at reducing menstrual blood loss. Two trials found no evidence of different effects between the oral contraceptive pill or the hormonal vaginal ring. We found no studies that assessed the effects of the combined hormonal patch (transdermal patch).

Quality of the evidence

The quality of the evidence that compared the oral contraceptive pill with placebo was moderate, but the evidence for the other comparisons was either low or very low in quality. The LNG IUS is more effective than the COCP at reducing menstrual bleeding but evidence was insufficient for the other treatment comparisons. This means that, although it is likely that combined hormonal contraceptives can reduce HMB, we cannot be absolutely certain how they compare with other medical treatments for reducing HMB (although LNG IUS appears to be more effective).