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[Intervention Review]

Interventions for emergency contraception

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ABSTRACT

Background

Emergency contraception (EC) is using a drug or copper intrauterine device (Cu-IUD) to prevent pregnancy shortly after unprotected intercourse. Several interventions are available for EC. Information on the comparative effectiveness, safety and convenience of these methods is crucial for reproductive healthcare providers and the women they serve. This is an update of a review previously published in 2009 and 2012.

Objectives

To determine which EC method following unprotected intercourse is the most effective, safe and convenient to prevent pregnancy.

Search methods

In February 2017 we searched CENTRAL, MEDLINE, Embase, PsycINFO, CINAHL, Popline and PubMed, The Chinese biomedical databases and UNDP/UNFPA/WHO/World Bank Special Programme on Human Reproduction (HRP) emergency contraception database. We also searched ICTRP and ClinicalTrials.gov as well as contacting content experts and pharmaceutical companies, and searching reference lists of appropriate papers.

Selection criteria

Randomised controlled trials including women attending services for EC following a single act of unprotected intercourse were eligible.

Data collection and analysis

We used standard methodological procedures recommended by Cochrane. The primary review outcome was observed number of pregnancies. Side effects and changes of menses were secondary outcomes.

Main results

We included 115 trials with 60,479 women in this review. The quality of the evidence for the primary outcome ranged from moderate to high, and for other outcomes ranged from very low to high. The main limitations were risk of bias (associated with poor reporting of methods), imprecision and inconsistency.

Comparative effectiveness of different emergency contraceptive pills (ECP)

Levonorgestrel was associated with fewer pregnancies than Yuzpe (estradiol-levonorgestrel combination) (RR 0.57, 95% CI 0.39 to 0.84, 6 RCTs, $n = 4750$, $I^2 = 23\%$, high-quality evidence). This suggests that if the chance of pregnancy using Yuzpe is assumed to be 29 women per 1000, the chance of pregnancy using levonorgestrel would be between 11 and 24 women per 1000.

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Mifepristone (all doses) was associated with fewer pregnancies than Yuzpe (RR 0.14, 95% CI 0.05 to 0.41, 3 RCTs, $n = 2144$, $I^2 = 0\%$, high-quality evidence). This suggests that if the chance of pregnancy following Yuzpe is assumed to be 25 women per 1000 women, the chance following mifepristone would be between 1 and 10 women per 1000.

Both low-dose mifepristone (less than 25 mg) and mid-dose mifepristone (25 mg to 50 mg) were probably associated with fewer pregnancies than levonorgestrel (RR 0.72, 95% CI 0.52 to 0.99, 14 RCTs, $n = 8752$, $I^2 = 0\%$, high-quality evidence; RR 0.61, 95% CI 0.45 to 0.83, 27 RCTs, $n = 6052$, $I^2 = 0\%$, moderate-quality evidence; respectively). This suggests that if the chance of pregnancy following levonorgestrel is assumed to be 20 women per 1000, the chance of pregnancy following low-dose mifepristone would be between 10 and 20 women per 1000; and that if the chance of pregnancy following levonorgestrel is assumed to be 35 women per 1000, the chance of pregnancy following mid-dose mifepristone would be between 16 and 29 women per 1000.

Ulipristal acetate (UPA) was associated with fewer pregnancies than levonorgestrel (RR 0.59; 95% CI 0.35 to 0.99, 2 RCTs, $n = 3448$, $I^2 = 0\%$, high-quality evidence).

Comparative effectiveness of different ECP doses

It was unclear whether there was any difference in pregnancy rate between single-dose levonorgestrel (1.5 mg) and the standard two-dose regimen (0.75 mg 12 hours apart) (RR 0.84, 95% CI 0.53 to 1.33, 3 RCTs, $n = 6653$, $I^2 = 0\%$, moderate-quality evidence).

Mid-dose mifepristone was associated with fewer pregnancies than low-dose mifepristone (RR 0.73; 95% CI 0.55 to 0.97, 25 RCTs, $n = 11,914$, $I^2 = 0\%$, high-quality evidence).

Comparative effectiveness of Cu-IUD versus mifepristone

There was no conclusive evidence of a difference in the risk of pregnancy between the Cu-IUD and mifepristone (RR 0.33, 95% CI 0.04 to 2.74, 2 RCTs, $n = 395$, low-quality evidence).

Adverse effects

Nausea and vomiting were the main adverse effects associated with emergency contraception. There is probably a lower risk of nausea (RR 0.63, 95% CI 0.53 to 0.76, 3 RCTs, $n = 2186$, $I^2 = 59\%$, moderate-quality evidence) or vomiting (RR 0.12, 95% CI 0.07 to 0.20, 3 RCTs, $n = 2186$, $I^2 = 0\%$, high-quality evidence) associated with mifepristone than with Yuzpe. levonorgestrel is probably associated with a lower risk of nausea (RR 0.40, 95% CI 0.36 to 0.44, 6 RCTs, $n = 4750$, $I^2 = 82\%$, moderate-quality evidence), or vomiting (RR 0.29, 95% CI 0.24 to 0.35, 5 RCTs, $n = 3640$, $I^2 = 78\%$, moderate-quality evidence) than Yuzpe. Levonorgestrel users were less likely to have any side effects than Yuzpe users (RR 0.80, 95% CI 0.75 to 0.86; 1 RCT, $n = 1955$, high-quality evidence). UPA users were more likely than levonorgestrel users to have resumption of menstruation after the expected date (RR 1.65, 95% CI 1.42 to 1.92, 2 RCTs, $n = 3593$, $I^2 = 0\%$, high-quality evidence). Menstrual delay was more common with mifepristone than with any other intervention and appeared to be dose-related. Cu-IUD may be associated with higher risks of abdominal pain than mifepristone (18 events in 95 women using Cu-IUD versus no events in 190 women using mifepristone, low-quality evidence).

Authors' conclusions

Levonorgestrel and mid-dose mifepristone (25 mg to 50 mg) were more effective than Yuzpe regimen. Both mid-dose (25 mg to 50 mg) and low-dose mifepristone (less than 25 mg) were probably more effective than levonorgestrel (1.5 mg). Mifepristone low dose (less than 25 mg) was less effective than mid-dose mifepristone. UPA was more effective than levonorgestrel.

Levonorgestrel users had fewer side effects than Yuzpe users, and appeared to be more likely to have a menstrual return before the expected date. UPA users were probably more likely to have a menstrual return after the expected date. Menstrual delay was probably the main adverse effect of mifepristone and seemed to be dose-related. Cu-IUD may be associated with higher risks of abdominal pain than ECPs.

PLAIN LANGUAGE SUMMARY

Methods of emergency contraception

Review question

The aim of this Cochrane Review was to evaluate the effectiveness and safety of different methods of emergency contraception to prevent pregnancy following unprotected intercourse.

Background

Emergency contraception (EC) is using a drug or copper intrauterine device (Cu-IUD) to prevent pregnancy shortly after unprotected intercourse. Several interventions are available for EC. Information on the comparative effectiveness, safety and convenience of these methods is crucial for reproductive healthcare providers and the women they serve. Researchers in Cochrane collected and analyzed all relevant studies to answer this question.

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Study characteristics

We searched 10 English-language and three Chinese-language databases for published studies in any language, in February 2017. We also searched grey literature databases and websites and contacted experts and authors for eligible studies. Studies had to report information on interventions to prevent pregnancy after a single act of unprotected intercourse. We included 115 randomized controlled trials with 60,479 women in this review. Ninety-two trials were conducted in China. The evidence is up-to-date to February 2017.

Key results

The studies compared 25 different interventions of different types of emergency contraception. The studies showed the following.

Levonorgestrel and mifepristone were more effective than Yuzpe regimen (estradiol-levonorgestrel combination). Our findings suggest that if 29 women per 1000 become pregnant with Yuzpe, between 11 and 24 women per 1000 will do so with the levonorgestrel, and that if 25 women per 1000 become pregnant with Yuzpe, between one and 10 women per 1000 will do so with mifepristone.

Mid-dose mifepristone (25 mg to 50 mg) was probably more effective than levonorgestrel. Low-dose mifepristone (less than 25 mg) was probably less effective than mid-dose mifepristone, but both were more effective than levonorgestrel (two doses of 0.75 mg). Ulipristal acetate (UPA) was also more effective than levonorgestrel.

Levonorgestrel users had fewer side effects than Yuzpe users, and might be more likely to resume menstruation before the expected date. UPA users were probably more likely to resume menstruation after the expected date. Menstrual delay was probably the main adverse effect of mifepristone and seemed to be dose-related. Cu-IUD may be associated with higher risks of abdominal pain than mifepristone.

Quality of the evidence

The quality of the evidence for the primary outcome (observed number of pregnancies) ranged from moderate to high, and for other outcomes ranged from very low to high. The main limitations were risk of bias (associated with poor reporting of methods), imprecision and inconsistency.