Comparative efficacy of emergency contraception pills

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As part of the new systematic review, published in Cochrane Database of Systematic Reviews, a comparison was made of the effectiveness of various contraceptive pills.

Note

This article was exposed to the machine translation from Ukrainian.

Background

Unwanted pregnancy is a common problem. So, if you follow the data represented on the official website of the Ministry of Health of Ukraine, in the 2011 year the number of abortions was estimated near 156 thousands when the number of births - near 492 thousands. The standard way of solving this problem is to use primary prevention on form of reliable contraception. For a long time under the contraception understood only the prevention of pregnancy before/during sexual intercourse ("anticipational contraception), but currently this concept also includes contraception after the coitus.

Emergency contraception (EC) is the use of the drug or agent as immediate measures to prevent pregnancy after unprotected sexual act. According to this definition, this method is used to prevent pregnancy after intercourse but prior to pregnancy occurrence.

Today no method of contraception is completely reliable. In addition, not all people use these methods correctly and every time during sexual relationship. In such cases EC can be useful. Another field of EC use is after sexual assault. Moreover, in most developed countries a common practice is to recommend these drugs for women who have experienced sexual assault, along with the prevention of sexually transmitted infections. These recommendations can be found on the WHO website.

How does emergency contraception works?

EC can prevent pregnancy after unprotected sexual intercourse, but these drugs do not always work effectively. Many factors can affect their effectiveness. For example, it was found that women who had had sexual contact on the day before ovulation, are at 4.5 times increased risk of getting pregnant. In addition, there is evidence of less effectiveness of EC in women with obesity, but these data do not have sufficient evidence base.

Among the EC the largest distribution have the following medications and devices:

- **Levonorgestrel.** It is a synthetic progestogen and is used either alone or in combination therapy (Yuzpe method - estrogen + progestogen). The mechanism of action is inhibition of ovulation.
- **Ulipristal acetate.** It is a selective progesterone receptor modulator which also delays or inhibits the ovulation.
- **Mifepristone.** This is a selective progesterone receptor modulator. It has an effect on the endometrium and inhibits implantation and may induce abortion.
- **Intrauterine Device with cooper.** Can prevent oocyte fertilization when inserted before fertilization or implantation - if after.

### Which method is more efficient?

Find the answer to this question tried a group of scientists led by Jie Shen from the Shanghai Research Center. This scientific work had a design of systematic review and meta-analysis and was conducted under the Cochrane collaboration [6]. Such studies are reliable have high level of evidence, because they are conducted by researchers from around the world who have no conflict of interest regarding the theme of the work and on a voluntary basis.

The researchers reviewed all relevant researches on the topic of EC and selected for further analysis 115 best quality studies with a total sample of 60,479. The main purpose of the analysis was to compare the efficacy and safety of drugs and devices for EC. Brief description of the results:

- Levonorgestrel was more effective than combination therapy for the Yuzpe. So, while the first drug using pregnant 17 women for every 1,000 patients treated, when you use the Yuzpe - 29 women for every 1,000 high level of evidence.
- 2 comparison regimen of levonorgestrel (1.5 mg once or 0.75 mg twice) showed no difference in terms of prevented pregnancies.
- Mifepristone in medium dosage (25-50 mg) was more effective than levonorgestrel. Thus, the analyzed studies that compared the efficacy of these drugs has shown that after taking mifepristone pregnancy been registered in 21 cases per 1000 and levonorgestrel - 35 per 1000. The level of evidence was moderate. Note that results on effectiveness of levonorgestrel from these studies are differ from that in previous studies (when compared to the effectiveness of Yuzpe regimens). Because of this and moderate quality of evidence, the researchers inserted a remark that mifepristone «probably» more effective.
- The use of ulipristal acetate was associated with more pregnancies than levonorgestrel.
- Data on the use of the copper intrauterine device was not enough for any conclusions.

Researchers have also analyzed data on safety. It was noted some differences. Thus, comparing Yuzpe regimens vs levonorgestrel showed that the latter causes side effects in 20% less cases (high level of evidence). Although its use cause bleedings by 80% more frequent (moderate level of evidence). Average doses of mifepristone were associated with a lower risk of side effects than levonorgestrel (50% less), and bleeding (39% less), but the level of evidence was low. Comparing these drugs also showed that first often led to early menstruations (28%, a low level of evidence), and the second – to menstruation delay (29% average level of evidence). Regarding the intrauterine device, they significantly more likely than drugs caused abdominal pain.

As an example we give the absolute numbers of adverse effects in the studies, which compared levonorgestrel (L) and medium doses of mifepristone (M):

- All side effects: L - 202 per 1 thousand, M - 111/1000.
- Nausea: A - 80/1000, M - 65/1000.
- Spotting / bleeding: A - 77/1000, M - 47/1000.
- Early menstruation: L - 94/1000, M - 68/1000.
- Delayed menstruation - L - 108/1000, M - 139/1000.

As for the optimal time, the risk of pregnancy while taking levonorgestrel was 49% lower when it was received in the first 72 hours after intercourse than later. As for the Yuzpe drugs, when taken within the first 24 hours the risk of becoming pregnant were 53% and 57% lower than on the 2nd and 3rd day respectively. For other drugs and devices, there was insufficient data for analysis.
Scientists have concluded that levonorgestrel and mifepristone in medium doses (25-50mg) were more effective than other methods of EC, with the possible superiority of the latter drug. They were also associated with lower risk of side effects. Low quality evidence data show less likelihood of side effects in mifepristone than levonorgestrel. For maximum efficiency it should be taken immediately after intercourse, after the first 72 hours their effectiveness decreases significantly.

**References**