Phil Howard asks what exactly happens the morning after the night before

Photo: PA

The morning-after pill

KEY POINTS

Levonelle-2 replaced Yuzpe as the preferred method of 'emergency contraception' on the basis of a 1998 WHO trial. The manufacturers Schering and the government have repeatedly asserted that Levonelle-2 cannot affect an established pregnancy, and yet in the trial it reduced expected pregnancy rates even more than Yuzpe (which is known already to have a post-implantation effect), even when intercourse took place again after the drug was given. This suggests that Levonelle-2 acts mainly by disrupting implantation. And yet, although pregnancy tests were taken on entry to the trial, the percentage of positive tests that didn't lead to established pregnancies was never published. Have vested commercial and political interests led to a suppression of the truth?

'Don't say a prayer for me now, save it till the morning after.' (Save a Prayer, Duran Duran)

The Morning After Pill (MAP) is an umbrella term for various regimens of hormonal emergency contraception. It is licensed for use up to 72 hours after unprotected sexual intercourse, provided the woman's menstrual bleed is not overdue.[1]

In January 2001, amidst much public and medical debate, MAP became available over the counter to women over 16 years of age. Schering Health Care Limited, manufacturers of leading brand Levonelle-2 (Levonorgestrel) and Yvette Cooper, the Public Health Minister, have repeatedly asserted that MAP cannot affect an established pregnancy.[2] However, where is the positive evidence for this?

Theoretically, of course, there are several stages at which MAP could act…

True contraceptive effect?

MAP may have a true contraceptive effect by inhibiting ovulation. This would depend upon its ability to inhibit the LH surge and on the timing of administration in relation to the menstrual cycle. There would still remain a risk of pregnancy if MAP merely delayed, not prevented, ovulation.

Levonorgestrel has only a limited effect on preventing ovulation (less than 15%), even when deliberately administered just before the LH surge.[3,4] In one study, 361 peri-ovulatory women took levonorgestrel 0.75mg after intercourse. Using basal body temperature analysis, only 14.4% showed ovulatory inhibition.[5] Another study looked at levonorgestrel as a postcoital contraceptive. 77 women took 0.4mg per coitus for 1,011 cycles, resulting in seven pregnancies (Pearl index 8.3). 27 women took 0.75mg per coitus for 226 cycles, resulting in two pregnancies, one due to faulty drug administration (corrected Pearl index 5.3).

Pearl index – the number of unwanted pregnancies that occur during one year of 100 normally fertile women having regular coitus.

Thickened mucus?

Two studies have detected sperm in the uterus very soon after intercourse: after 30 minutes and four hours (in eight out of ten women) respectively.[6,7] MAP administration is advised up to 72 hours after intercourse and cervical mucus changes then take another 24 hours.[8] Relying on thickened mucus the next morning is analogous to closing the stable door after the horse has bolted.

Tubal motility

There is a theoretical possibility that MAP may alter tubal motility, altering the passage of sperm up the Fallopian tubes. Alternatively, the transit of the egg or conceptus moving towards the uterine cavity could be affected.

Implantation disruption

Depending upon both dose and timing, MAP can disrupt implantation or cause the loss of a newly implanted embryo. Post-coital studies in post-ovulatory mice have shown that levonorgestrel can cause resorption of already implanted embryos.[9]

The Yuzpe method (ethinyloestradiol 0.1mg and levonorgestrel 0.5mg both given twice 12 hours apart) is thought to have a similar mode of action to

Levonelle (levonorgestrel 0.75mg taken twice 12 hours apart) although it may be less effective. Very recently, the Yuzpe method was shown to be effective between 72 and 120 hours after unprotected intercourse.[10] This provides evidence of a post-implantation effect.

WHO study

1998 women were given either levonorgestrel 0.75mg (repeated 12 hours later) or the Yuzpe regime (0.1mg ethinyloestradiol and 0.5mg levonorgestrel, repeated after 12 hours) starting within 72 hours of a single episode of unprotected intercourse. The primary outcomes were crude (compared with expected) pregnancy rates and side effects.[11] Included women were healthy with regular menses and no recent pregnancy. Women were excluded if they had recently been pregnant, recently taken the oral contraceptive pill or were breastfeeding. Blood or urine samples were taken at entry for pregnancy tests.

Overall levonorgestrel caused an 85% (74-93%) and Yuzpe a 57% (39-71%) reduction in expected pregnancy rates. In both groups, the majority of women did not have further intercourse over the next few days; these women had an 89% reduction in expected pregnancy rate if taking levonorgestrel and a 73% reduction if taking Yuzpe.

However, about one third of the women in both groups did have further intercourse. Assuming that the expected pregnancy rates for these women were between one and two times those for women with a single episode of intercourse, there was a reduction in the pregnancy rates of 79-90% in the levonorgestrel group and 28-64% in the Yuzpe group. Hence in the levonorgestrel group, these pregnancy rates were not significantly higher than those after a single episode of pre-treatment intercourse. This suggests that levonorgestrel acts mainly by disrupting implantation rather than a contraceptive effect on cervical mucus or ovulation.

Where is the positive evidence that levonorgestrel does not work after implantation and affect an established pregnancy? Disruption of implantation is clearly abortifacient as the early human embryo is expulsed from the womb, leading to its inevitable death.

Ethical constraints

Was the WHO study ethical? Nearly 2,000 women were given MAP after blood or urine had been taken for a pregnancy test at enrolment. However, pregnancy was not an exclusion to participation in the study. Of the women later found to be pregnant, almost 10% (four out of 42) were discovered to have been pregnant before taking MAP. How many of the women who did not sustain a pregnancy had actually been pregnant at admission into the trial? The study would have provided data on precisely this point but the results were not published.

Recently, I debated Dr Graham Barker, Schering's deputy medical director, at the Royal Society of Medicine. He conceded that levonorgestrel often acted post-fertilisation and that the WHO study probably was unethical.

Does it matter?

Distinguishing between a true contraceptive and an abortifacient effect is of importance to many women as well as their doctors. Indeed, in America, it is feared that some women may sue their doctors for failing to give adequate information for consent prior to taking MAP. 'Without accurate information presented before prescribing, patients may experience emotional distress from an unanticipated result, an unforeseen side effect or the later discovery of a mechanism of action that is in conflict with their value system.'[12]

Doctors with a Judeo-Christian ethic have even more reason to be informed about MAP's exact mechanism of action. The above evidence shows clearly that MAP often does work after fertilisation and strongly suggests that it can disrupt implantation. It is therefore imperative to be clear on the status of the human embryo.

The evidence shows clearly that the Morning After Pill often does work after fertilisation and strongly suggests that it can disrupt implantation

The Bible does not give any simple proof-texts. Christian thought has identified several stages at which human life could begin: for instance, fertilisation, implantation and physical formation.[13] Whilst there are various reasons for each of these suggestions, it is only at fertilisation that a completely new genetic being is formed. The other stages merely represent points along a continuum of development from fertilisation to birth.

Biblically it is clear that God's care for each human starts at a very early stage. Psalm 139 tells us, 'Your eyes saw my unformed body. All the days ordained for me were written in your book before one of them came to be'.[14] Similarly, Jeremiah was told: 'Before I formed you in the womb I knew you, before you were born I set you apart'.[15] All human life is made in the image of God: this sets it apart and gives it special status.[16]

Bearing all this in mind, Christians should be very wary of sanctioning a drug that is known to act after fertilisation. God has special concern for humans who are vulnerable and cannot speak for themselves.[17] The popular 1980s song 'Save a prayer' talks of a one night stand, requesting that prayer be kept back until the next morning.[18] With increasing use of MAP, this is highly appropriate: newly formed embryos need our prayer and protection.

Phil Howard is a Consultant Physician and Senior Lecturer in medicine in London.

Photo: Wellcome

References

1. *British National Formulary*. London: BMA/Royal Pharmaceutical Society of Great Britain, March 2001:383
2. *Hansard* 2000, 19 July:221W
3. Shi YE, Zheng SH, Shu Yhm He CH, Yu PP, Fortherby K. Pharmaco-kinetic study of levonorgestrel used as a post-coital contraceptive. *Contraception* 1988;37(4):359-369
4. Hapangama D, Glasier AF, Baird DT. The effects of peri-ovulatory administration of levonorgestrel on the menstrual cycle. *Contraception* 2001; 63:123-129
5. He CH, Shi YE, Xu JQ, VanLook PF. A multicenter clinical study on two types of levonorgestrel tablets administered for postcoital contraception. *Int J Gynaecol Obstet* 1991; 36(1):438
6. Rubenstein BB *et al*. Sperm survival in women. *Fertil Steril* 1951;2:51-19
7. Williams M *et al*. Uterine flushing: a method to recover spermatozoa and leucocytes. *Human Reproduction* 1993;8:2019-2026.
8. Cyclic changes of cervical mucus in normal and progestin-treated women. *Fertil Steril* 1966; 17:63.
9. Shriley B, Bundren JC, McKinney S. Levonorgestrel as a postcoital contraceptive. *Contraception* 1995; 52(2):277-81
10. Rodrigues I, Grou F, Jolly J. Effectiveness of emergency contraceptive pills between 72 and 120 hours after unprotected sexual intercourse. *Am J Obstet Gynecol* 2001;184:531-7).
11. Von Hertzen H *et al*. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet* 1998; 352:428-422
12. McGaughran A. Informed consent and emergency contraception. *Am Fam Phys* 2000;62:2219 (15 November)
13. McFarlane G, Moore P. *What is a person?* CMF File 10. London: CMF, 2000
14. Psalm 139:16
15. Jeremiah 1:5
16. Genesis 1:26
17. Psalm 82:3-4; Proverbs 31:8-9
18. Duran Duran. *Save a prayer*, from the album *Decade*. EMI records, 1989