

Opinion

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Post-coital Intervention over the Counter

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Recently, the Australian *Therapeutic Goods Authority* proposed that the post-coital intervention *Postinor-2* be issued over the counter by pharmacists without prescription. The proposal seemed to be based on the grounds that women might be more inclined to use it if they did not also have to undergo a medical consultation in order to obtain a prescription. The TGA did not rule out the fact that there are precautions and contraindications that would otherwise have warranted a prescription-only status.

This seemed to be a pragmatic decision by the TGA, sought by the family planning associations, and it is a decision that involves some danger. It also involves a lack of regard for the legal and ethical obligation to ensure that women are provided with information about the use of *Postinor-2*, in their particular circumstances, that could only be provided after clinical history taking and assessment by a medical practitioner.

The active ingredient of *Postinor-2* is Levonorgestrel, an artificial progesterone. *Postinor-2* differs from what had been commonly used for post-coital intervention, the so-called *Yupze regimen*. The latter involved two large doses of the combined contraceptive pill containing both oestrogen and progesterone and taken twelve hours apart.

The *Yupze regimen* normally causes a shedding of the endometrium resulting in loss of the embryo if fertilisation occurs in that cycle. The *Yupze regimen* may also suppress or delay ovulation. This latter contraceptive effect would, of course, be ineffective in preventing fertilisation, if ovulation was occurring or had already occurred at the time. In that case, the regimen's effect would be on nidation.¹

It is unlikely that the *Yupze regimen* would cause changes to the cervical mucus sufficient to completely prevent sperm from reaching the fallopian tube. Even the normal natural rise in progesterone, which begins eight hours before ovulation, does not prevent residual channelling in the cervix which is capable of allowing the passage of sperm on the third day after the rise in progesterone and the peak day of mucus.²

¹ Stewart DC. "Contraception" In: Hofmann AD, Greydanus DE, eds. *Adolescent Medicine*, 3rd ed. Stamford, Conn: Appleton & Lange; 1997:566-588.

Hewitt G, Cromer B. "Update on adolescent contraception" *Obstet Gynecol Clin North Am*. 2000;27:143-162. Committee on Adolescence "Contraception and adolescents" *Pediatrics*. 1999;104:1161-66.

² Eric Odeblad cf. Evelyn L Billings and John J Billings *Teaching the Billings Ovulation Method Part 2* Melbourne: Ovulation Method Research and Reference Centre 1997, p.45

The progestogen-only (levonorgestrel) regimen in Postinor-2 is favoured because it is thought to be more effective and have fewer side effects than the combined (Yuzpe) regimen used since the 1980s³

However, medically it is unsafe to issue Postinor-2 over the counter. In relation to the manufacturer's (Schering Pty Ltd) prescribing information for Postinor-2, note the following contraindications and precautions⁴ that would require history taking, medical examination and testing.

- Possibility of pregnancy (from another act of intercourse more than 72 hours before)
- Severe hypertension (BP>180+/110+),
- Diabetes mellitus with nephropathy,
- Retinopathy,
- Neuropathy
- Vascular disease,
- Ischaemic heart disease,
- Stroke,
- History of breast cancer
- Unexplained vaginal bleeding,
- Hypersensitivity to any of the ingredients of the preparation.
- Possibility of ectopic pregnancy if pregnancy occurs.
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It is unlikely that a pharmacist spending the time to do take blood pressure and a detailed history. Also it is unlikely that a woman would want a pharmacist to do so in the over the counter circumstances of a busy pharmacy, especially such protracted discussion, including about recent sexual activity. The circumstances would not be conducive to the openness and candour needed.

Note also that in 2001 Schering opposed making Postinor-2 available to women under the age of 16⁵.

.There are also some drug interactions that warrant knowledge of other medications that the patient is taking, including:

- barbiturates,
- primidone,
- phenytoin,
- carbamazepine,
- phenylbutazone,
- rifampicin,

³ World Health Organization Task Force on Post-Ovulatory Methods of Fertility Regulation. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet* 1998; 352: 428-433.

⁴ MIMIS Annual 2003 18-1428

⁵ Katie D Schenck *Emergency Contraception: The UK Experience* Reproductive Health Alliance 2003 www.rhalliance.org/images/rhaemer.pdf

- ritonavir,
- ampicillin
- griseofulvin.
- The requirement for oral anti-diabetics and insulin can change as a result of an effect on glucose tolerance.

There is also a manufacturer's recommendation for follow-up medical consultation - immediately in the event of vomiting or nausea or other side effects, and routinely three weeks later. There would be significant danger that without a prescribing doctor involved in the first instance, such follow-up would not happen or would happen without the doctor being informed of the Postinor-2 event, given the sensitivity of the issue. Note that there is the possibility of an ongoing pregnancy (Postinor-2 is only 85% effective) that raises questions not only about the woman's health but that of her child following Postinor-2 administration.

There have also been reports of ectopic pregnancy following *Postinor-2* use⁶. Low-dose daily progestogen-only oral contraceptive pills are effective at preventing pregnancy but if this method fails, pregnancies are more likely to be ectopic than those occurring among users of other contraceptive methods.⁷

Apart from the safety issues, there are some other ethical issues. Ethically, women have a right to know how Postinor-2 works. The manufacturer is vague about the method of action of the main ingredient, Levonorgestrel. There are several possibilities that are listed:

- Altering the lining of the uterus so that the embryo when it reaches the uterus at about 6days old cannot implant
- Preventing ovulation (likely to be less than a 33% chance of preventing ovulation and may be as low as 19%⁸)
- Preventing the sperm from reaching the ovum by altering the production of mucus-carrying sperm in the cervix (the neck of the womb)
- Altering the function of the fallopian tube so as to prevent sperm reaching the egg. These effects may also be a cause of ectopic pregnancy, as they would also interfere with the passage of the embryo along the fallopian tube after fertilisation. By the same mechanism, ectopic pregnancies might occur following treatment failure with a progestogen-only emergency contraceptive pill (ECP). The ECP is indicated for the prevention of pregnancy if taken within 72 hours of unprotected intercourse⁹.

⁶ Dr Mira Harrison-Woolrych, Senior Research Fellow, "Progestogen-Only Emergency Contraception and Ectopic Pregnancy" Centre for Adverse Reactions Monitoring, Dunedin *Prescriber Update* 2002;23(3):40-41

⁷ McCann M, Potter L. Progestin-only oral contraception: a comprehensive review. *Contraception* 1994;50(6):S44-S49.

⁸ I. Aref, F. Hefnawi, O Kandl, T AbdelAziz "Effect of Minipills on Physiologic Responses of Human Cervical Mucus, Endometrium and Ovary" *Journal of Fertility and Sterility* August 1973 Vol 24 no. 8 pp 578-583

⁹ Dr Mira Harrison-Woolrych, Senior Research Fellow, "Progestogen-Only Emergency Contraception and Ectopic Pregnancy" Centre for Adverse Reactions Monitoring, Dunedin *Prescriber Update* 2002;23(3):40-41

The first is not a contraceptive effect but an abortifacient effect. When the effect occurs the embryo has already formed and reached the stage at which differentiation of the cells into organs has just begun (at least 4-6 days old). This anti-nidation or anti-abortifacient effect is thought to be the major effect¹⁰.

Preventing ovulation will not happen in most women following *Postinor-2* use. The main ingredient in the combined contraceptive pill that prevents ovulation is oestrogen. *Postinor-2* is progesterone only (Levonorgestrel) and has a reduced effect on preventing ovulation¹¹. In fact, if preventing or delaying ovulation was all that was wanted, then a moderate dose of oestrogen is all that would be required. This was tried in the early research on the pill and there is good data available on the ovulation delaying effects of oestrogens. That would be sufficient to prevent pregnancy from occurring from an act the night before, provided that ovulation and fertilisation had not already occurred.

Preventing the sperm from reaching the ovum by altering the production of mucus-carrying sperm in the cervix is a known effect of progesterone if it is administered on a daily basis ahead of sexual intercourse. However, if intercourse happened the night before it is a little late to try to prevent the passage of sperm if the woman is at a fertile time. The mucus channels that transport the sperm will already have been formed¹². Sperm can be found within the fallopian tube within twenty minutes of sexual intercourse.

Unlike the other actions of the oral contraceptives, the effect on the function of the fallopian tube has not been established, though the reports of ectopic pregnancy would indicate some kind of complication in the function of the fallopian tube as a result of *Postinor-2* use.

From this it would appear that the abortifacient or anti-nidation effect is the most likely effect of *Postinor-2*. This would happen at the time that the embryo was about six days old when it reached the endometrium and the latter had been altered by the anti-nidation effect of *Postinor-2* so that the embryo could not implant into an environment that it needed to survive.

It is important to note also that since a woman is infertile most of the cycle, there is an issue whether most use of post-coital intervention is in fact unnecessary.

If it is possible to identify that:

- (a) an act of intercourse in the previous twenty four hours could not have resulted in fertilization,

¹⁰ RJ Pepperell "The Physiologic Basis of Human Fertility Control"
[www.obsgyn.unimelb.edu.au/.../Undergrad/med5/Lecturers/LECTURE - 20FERTILITY%20CONTROL%202003%20RPepperell.pdf](http://www.obsgyn.unimelb.edu.au/.../Undergrad/med5/Lecturers/LECTURE-20FERTILITY%20CONTROL%202003%20RPepperell.pdf)

¹¹ Ibid. Note that there has been little research interest since early on in the OCP development in identifying the precise effects. The manufacturers have been content to be vague and not to distinguish between anti-nidation and contraceptive effects.

¹² Discussion with Professor James Brown 23 6 02

- (b) ovulation and hence possible fertilization might yet occur in the near future unless there is intervention, or
- (c) ovulation had already occurred and the ovum already likely to have been exposed to sperm, and that fertilization, if it was to occur had already occurred,

then this would seem to be useful information to determine whether any intervention were necessary and to allow the woman to make an informed choice. For at least some women, distinguishing between contraception and abortifacience is significant.

Some GPs, rather than subject the women to unnecessary medication, offer women requesting post-coital intervention, the opportunity to identify whether their fear of pregnancy is warranted. By history taking and by offering a test for serum ovarian hormone levels, if it is indicated, they can usually reassure the women that pregnancy is most unlikely. It is also an important time to discuss with them their sexual health and to inform them of the dangers. The serum test for ovarian hormones takes no longer to achieve a result than the pregnancy tests that would be required. Postinor-2 is contraindicated in pregnancy.