The members' enquiry service: frequently asked questions

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Background

It is accepted clinical practice to use an increased dose of progestogen-only emergency contraception (POEC) for women using liver enzyme-inducing drugs.[1] The latest volume of the *British National Formulary* (*BNF*) suggests that POEC, marketed as Levonelle® and Levonelle-2® (Schering Health Care Ltd), can be given as a single regimen of three 0.75 mg tablets for women using liver enzyme-inducing drugs.[2] The Clinical Effectiveness Unit (CEU) received several enquiries from Faculty Members regarding the use of POEC in the weeks following this publication and the response to these enquiries is given here.

Illustrative CEU response

Clinical question

For women who are using liver enzyme-inducing drugs, what dose of POEC is advised?

Summary of response

The Faculty of Family Planning and Reproductive Health Care (FFPRHC) CEU Guidance on emergency contraception advises that women using liver enzyme-inducers should take two tablets (total dose 1.5 mg) at first presentation followed by one tablet (0.75 mg) 12 h later and be advised regarding the alternative use of an intrauterine device (IUD). The recently published *BNF* (Volume 48) suggests that for women using liver enzyme-inducers the dose of levonorgestrel can be taken as three 0.75 mg tablets as a single dose. The CEU was unable to identify any new data on efficacy or side effects, such as nausea, vomiting or abnormal bleeding, to support this single regimen of three tablets for women taking liver enzyme-inducers. Until evidence is available, the existing CEU recommendation for POEC use by women taking liver enzyme-inducers remains unchanged. Women should be informed about the lack of data on efficacy of POEC when using liver enzyme-inducers and be offered an IUD as an alternative. Pragmatically, however, neither regimen of POEC (two tablets at first presentation followed by one tablet 12 h later or the three tablets single regimen) are within the product licence for Levonelle and Levonelle-2.[3] Clinicians may consider using the regimen that is most acceptable to an individual woman using liver enzyme-inducers but acknowledge that the evidence base for such practice is limited.

Evidence-based medicine question (which guided our literature search strategy)
Population: Women who are using liver enzyme-inducing drugs.
Intervention: Progestogen-only emergency contraception (POEC).
Outcome: Efficacy and side effects.

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Table 1 *Sources used in developing the Members' Enquiry Response*

Source searched	Information identified
The National Guidelines Clearing House	No relevant information
Existing FFPRHC and RCOG Guidance	See text
WHO publications: *Medical Eligibility Criteria For Contraceptive Use* (2004) and *Selected Practice Recommendations For Contraceptive Use* (2002)	No relevant information
The Cochrane Library	No relevant information
MEDLINE and EMBASE from 1996 to 2004	See text

FFPRHC, Faculty of Family Planning and Reproductive Health Care; RCOG, Royal College of Obstetricians and Gynaecologists; WHO, World Health Organization.

Information sources

The CEU searched the sources listed in Table 1 in developing this Members' Enquiry Response.

Evidence reviewed

Existing FFPRHC and Royal College of Obstetricians and Gynaecologists Guidance. The FFPRHC CEU Guidance on emergency contraception[1] provides evidence-based recommendations on the use of POEC. The CEU recommends that POEC should be started as soon as possible and within 72 h of unprotected sexual intercourse. This Guidance recommends that for women using liver enzyme-inducers the dose of POEC should be increased by 50%. Women using liver enzyme-inducers should take two tablets (1.5 mg) at first presentation followed by one tablet (0.75 mg) 12 h later. Women should also be advised on the use of an IUD as this is unaffected by liver enzyme-inducers. The CEU recommended that in routine practice, for women not using liver enzyme-inducers, one tablet containing 0.75 mg levonorgestrel should be given and be repeated 12 h later.

PubMed and EMBASE. A large, randomised controlled trial published by the World Health Organization showed that a single regimen of POEC (two tablets at initial presentation) was equivalent to the usual divided regimen when taken within 72 h of unprotected sex.[4] In October 2004, the Medicines and Healthcare products Regulatory Agency agreed a new product licence for Levonelle and Levonelle-2. Currently, women may use a single 1.5 mg dose of POEC as soon as possible and within 72 h of unprotected intercourse.[4] No data on the use of POEC by women using liver enzyme-inducing drugs was identified and the CEU advised no change in the recommendations regarding POEC from previous guidance.[5]

Other sources. Volume 48 of the *BNF*[2] states that the effectiveness of POEC is reduced by liver enzyme-inducers and that an IUD may be offered, otherwise the dose of levonorgestrel should be increased to 2.25 mg (three 0.75 mg tablets) taken as a single dose. The CEU was unable to identify any new data to support the recommendation for a single regimen of three tablets for women taking liver enzyme-inducers. No evidence was identified on the efficacy, compliance or side effects, such as nausea or vomiting, which may occur with this regimen. Until more evidence is available, the CEU recommendation for POEC use by women taking liver enzyme-inducers remains unchanged.[5]

The CEU recommends that women should be informed about the lack of data on the efficacy of POEC when using liver enzyme-inducers and be offered an IUD as an alternative. Neither regimens of POEC (two tablets at first presentation followed by one tablet 12 h later or the three tablets single regimen) are within the product licence for Levonelle and Levonelle-2.[3] Clinicians may consider using the regimen that is most acceptable to individual women using liver enzyme-inducers but acknowledge the lack of an evidence base for this.

Disclaimer

The advice given in this Members' Enquiry Response has been prepared by the FFPRHC Clinical Effectiveness Unit team. It is based on a structured search and review of published evidence available at the time of preparation. The advice given here should be considered as guidance only. Adherence to it will not ensure a successful outcome in every case and it may not include all acceptable methods of care aimed at the same results. This response has been prepared as a service to FFPRHC members, but is not an official Faculty Guidance product; Faculty Guidance is produced by a different and lengthier process. It is not intended to be construed or to serve as a standard of medical care. Such standards are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances. Members are welcome to reproduce this Response by photocopying or other means, in order to share the information with colleagues.

References

1 Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. FFPRHC Guidance. Emergency contraception (April 2003). *J Fam Plann Reprod Health Care* 2003; **29**(2): 9–16.

2 *British National Formulary,* Vol. 48, September 2004. London, UK: British Medical Association and the Royal Pharmaceutical Society of Great Britain, 2004. http://www.bnf.org.

3 Schering Health Care Ltd. New dose instructions for Levonelle-2. 2003. http://www.medicines.org.uk.

4 von Hertzen H, Piaggio G, Ding J, Chen J, Song Si, Bartfai G, *et al*. Low dose mifepristone and two regimens of levonorgestrel for emergency contraception: a WHO multicentre randomised trial. *Lancet* 2002; **360**: 1803–1810.

5 de Souza A, Brechin S, Penney G. The members' enquiry service: frequently asked questions September 2002–August 2003 and an illustrative CEU response. *J Fam Plann Reprod Health Care* 2004; **30**: 111–113.

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