LETTERS

Evidence-based reproductive medicine

Madam

I look forward to the arrival of the Journal. It is always a good read, full of relevant and practical information – much more ‘user-friendly’ than most journals I receive these days. July’s edition seems particularly interesting with a number of interesting articles.

However, my interest was quickly replaced by irritation. There is a lot to be said for evidence-based medicine (EBM). It is always worth having a review of the current evidence available in order to provide women with accurate information when discussing contraception. However, it is not sufficient just to provide the ‘evidence’. EBM must consist of clinicians needing practical guidance with decision making.

The Clinical Effectiveness Unit (CEU) product review of the desogestrel-only pill is always worth having a read to have a review of the current evidence available in order to provide women with accurate information when discussing contraception.

In my opinion they are marred by their surprisingly negative conclusions.

What do we do when the evidence from clinical trials and epidemiology is not as complete as we would all like, but we have clients sitting in front of us wanting our help in choosing from the available options? It is then not sufficient just to provide the ‘evidence’ from an ivory tower. A decision has to be made, at present. Pending more data, evidence-based medicine (EBM) must be subjected to informed clinical judgement, based on all available evidence (including the reported pharmacology of the product) and – dare I say it? – clinical common sense.

The statement of the DTB is not inaccurate when it states in broad terms: ‘The CEU? ‘There is insufficient evidence on whether it is the primary mode of action’. Since when was it proposed/approved as a single collaborative bleeding pattern and efficacy trial (discussed below). Yet another study showed that the desogestrel-only pill inhibits ovulation in 97% of cycles and that this is its primary mode of action.

The main collaborative European multicentre study was indubitably underpowered, as regards efficacy, in the levonorgestrel POP comparator arm. However, among more than 600 women in the other (desogestrel) arm, who were not breastfeeding and with known non-contraceptive benefits (as described in the WHO publication 1999), the rate of CI being less than 1, in any clinical study of a POP over 3 years is historically unprecedented. The rate was only 0.17 (CI 0.004-0.928) per 100 woman-years. Such a low rate (with an upper bound of the CI being less than 1), in any clinical study of a POP over 3 years is historically unprecedented. Therefore I consider this product a useful addition to the range of contraceptives, particularly for a young, non-breastfeeding woman wanting a pill method but recommended, or wishing, to avoid the combined oral contraceptive (COC). It is likely highly (though again this is not yet fully established) to be more forgiving of late pill-taking than other POPs. But users will, as usual for all POPs, need forewarning about the occurrence of irregular bleeding. And I see no special reason to use it in those situations where the combination with a cheaper old-type POP is already virtually 100%, such as in lactation, or in older women, especially those aged over 45 years.

One final point refers to the FFPRHC Guidance on Contraceptive Choices for Women with Inflammatory Bowel Disease which includes the repeated comment that WHO 3 implications cannot use, e.g. ‘Women with primary inflammatory bowel disease (IBD) who are breastfeeding should only use a POP which is Category 1 – risks outweigh the benefits’. I am concerned that the CEU is perpetuating this misinterpretation of the WHO 3 category that does not absolutely contraindicate use, although other methods should be the first choice.

Anne MacGregor, MFFP
Medical Adviser, Margaret Pyke Memorial Trust, 73 Charlotte Street, London W1T 4PL, UK

References
1 FFPRHC Clinical Effectiveness Unit. FFPRHC Guidance (July 2003): 162-164.
2 Fry R, Colly M, Berchene S. Evidence-based reproductive medicine

John Guillebaud, FRCS, FCOG
Emeritus Professor of Family Planning and Reproductive Health, University College London, London, UK

CUS New Product Review of the desogestrel-only pill

Madam

The Clinical Effectiveness Unit (CEU)’s product review of the desogestrel-only pill’ and the recent article ‘Is Cerazette the minipill of choice?’ in the Drug and Therapeutics Bulletin (DTB) are both good reviews of the studies. But in my opinion they are marred by their surprisingly negative conclusions.

The recommendation is based on insufficient evidence to support lower failure rates with the desogestrel-only pill. This is despite another study showing that the desogestrel-only pill was sufficient to inhibit ovulation in 97% of cycles and that this is its primary mode of action.

The main collaborative European multicentre study was indubitably underpowered, as regards efficacy, in the levonorgestrel POP comparator arm. However, among more than 600 women in the other (desogestrel) arm, who were not breastfeeding and with known non-contraceptive benefits (as described in the WHO publication 1999), the rate of CI being less than 1, in any clinical study of a POP over 3 years is historically unprecedented. The rate was only 0.17 (CI 0.004-0.928) per 100 woman-years. Such a low rate (with an upper bound of the CI being less than 1), in any clinical study of a POP over 3 years is historically unprecedented. Therefore I consider this product a useful addition to the range of contraceptives, particularly for a young, non-breastfeeding woman wanting a pill method but recommended, or wishing, to avoid the combined oral contraceptive (COC). It is likely highly (though again this is not yet fully established) to be more forgiving of late pill-taking than other POPs. But users will, as usual for all POPs, need forewarning about the occurrence of irregular bleeding. And I see no special reason to use it in those situations where the combination with a cheaper old-type POP is already virtually 100%, such as in lactation, or in older women, especially those aged over 45 years.

One final point refers to the FFPRHC Guidance on Contraceptive Choices for Women with Inflammatory Bowel Disease which includes the repeated comment that WHO 3 implications cannot use, e.g. ‘Women with primary inflammatory bowel disease (IBD) who are breastfeeding should only use a POP which is Category 1 – risks outweigh the benefits’. I am concerned that the CEU is perpetuating this misinterpretation of the WHO 3 category that does not absolutely contraindicate use, although other methods should be the first choice.

Anne MacGregor, MFFP
Medical Adviser, Margaret Pyke Memorial Trust, 73 Charlotte Street, London W1T 4PL, UK

References
1 FFPRHC Clinical Effectiveness Unit. FFPRHC Guidance (July 2003): 162-164.

Reply

Madam

On behalf of the FFPRHC Clinical Effectiveness Unit (CEU), I thank you for the opportunity to respond to the letter from Anne MacGregor concerning two articles in the July 2003 issue of the Journal relating to the desogestrel-only pill. I am sorry that your correspondent found the New Product Review from our Unit irritating, rather than clinically useful.

We also welcome the opportunity to respond to the letter from John Guillebaud on the same theme.

In my view, our New Product Review provides an utterly objective summary of currently available evidence concerning the desogestrel pill. I stand by our statements that ‘on theoretical grounds and in terms of efficacy, the desogestrel-only pill is more effective than existing progestogen-only pills... but we do not have trial evidence to support this’. The evidence-based reproductive health paper by Foy et al is commended by your first correspondent but reaches the same conclusion as our New Product Review: ‘You cannot tell if the DSG pill is superior or inferior to other POPs’.

Dr MacGregor mentions ‘the suggestion that the data provided by the manufacturers may not be credible’. Nowhere in our New Product Review is an assessment or suggestion made relating to claims or data provided by the manufacturers. She goes on to seek assurance ‘that none of those undertaking the desogestrel-only pill review have any relevant associations with manufacturers of other progestogen-only pills’.

The New Product Review from the CEU does not include an explicit statement of interests. However, the CEU state that their work is guided by a formal code of practice on ‘Relationships with the Pharmaceutical Industry’, which was drawn up in consultation with the FFPRHC Clinical Effectiveness Committee and is now firmly established. This eight-point code of practice includes the following statements: ‘In all aspects of the work of the CEU, staff will be required to appraise the relative benefits made relating to individual contraceptive products and groups of products. Such appraisals will always be conducted in an impartial manner, and be based on available research evidence.’ and ‘CEU staff should not accept any honoraria or consultancy payments from pharmaceutical companies – either for their personal accounts or for CEU funds’.

Dr MacGregor also comments on the FFPRHC Guidance on Contraceptive Choices for Women with Inflammatory Bowel Disease, developed by our Unit and included in the same issue of the Journal. She feels that we have misrepresented ‘Category 3’ (risks outweigh benefits) as described in the WHO publication Medical Eligibility Criteria for Contraceptive Use, 2 giving the impression that ‘Category 3 equates to absolute contraindication’. This is certainly not our intention, and I fully agree with Dr MacGregor’s interpretation that ‘Category 3 indicates that a method should not be advised as a woman’s first choice, but may be used after appropriate counselling. I can only apologise if, in the interests of brevity, this distinction was unclear in this particular FFPRHC Guidance.’