FROM THE CLINICAL EFFECTIVENESS UNIT (CEU)

The members’ enquiry service: frequently asked questions

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(Accepted 29 July 2004)


Background

The Clinical Effectiveness Unit (CEU) presents an illustrative response of a frequently asked question to the Members’ Enquiry Service on whether or not hormonal contraceptive use by women with a history of pregnancy-related cholestasis is safe or associated with recurrence of cholestasis.

Illustrative CEU response

Clinical question

In women with a history of pregnancy-related cholestasis, can hormonal contraception be used safely?

Summary of response

The Summaries of Product Characteristics (SPCs) for combined oral contraceptives (COCs) and progestogen-only pills (POPs) advise against use by women with a history of cholestatic jaundice or with severe pruritis in pregnancy. The World Health Organization (WHO) Medical Eligibility Criteria for Contraceptive Use (WHOMEC), however, recommends that for women with pregnancy-related cholestasis the benefits of COC use outweigh the risks (WHO Category 2) and progestogen-only methods or non-hormonal methods can be used without restriction (WHO Category 1). No evidence was identified to support an increased risk of recurrence of symptoms with hormonal contraceptive use.

The CEU advises that women with a history of pregnancy-related cholestasis should be informed about the unknown risk of recurrence with hormonal contraceptive use. After counselling regarding non-hormonal methods, women with a history of pregnancy-related cholestasis may choose to use hormonal methods (COCs, POPs, progestogen-only injectables, implant or intrauterine system). Women should be informed that the use of COCs and POPs in this situation is outside the product licence.

Evidence-based medicine question (which guided our literature search strategy)


Intervention: Hormonal contraception.

Outcome: Recurrence of cholestasis with hormonal contraceptive use.

Information sources

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

Evidence reviewed

MEDLINE and EMBASE. Pregnancy-related cholestasis complicates between 0.1% and 1.5% of pregnancies. Genetic and environmental factors and hormones, such as oestrogen and progesterone, have been implicated in its aetiology. Up to 60% of affected pregnancies result in premature delivery and 2% result in intrauterine death. Pregnancy-related cholestasis usually presents in the second or third trimester with symptoms of pruritis. Serum bile acids are elevated and in severe cases serum transaminases and bilirubin are also elevated. Within hours of delivery, serum levels of bile acids fall and the pruritis resolves. These symptoms and signs can recur in subsequent pregnancy or when taking hormonal contraception.1 Women with previous pregnancy-related cholestasis are therefore often advised to avoid hormonal contraception due to the risk of recurrence following exposure to oestrogen or progesterogen.2 The SPCs for several COCs3–22 and POPs23–28 advise that their use is contraindicated in women with a history of cholestatic jaundice, or with a history of severe pruritis during pregnancy or with hormonal contraceptive use. The British National Formulary advises that women with a history of cholestasis during pregnancy should avoid COC use.29 The SPCs for a progestogen-only injectable (depot medroxy-progesterone acetate)30 and a progestogen-only implant (Implanon®)31 however, do not suggest use is contraindicated for women with a history of pregnancy-related cholestasis.

WHO publications. WHOMEC32 does not support the avoidance of hormonal contraception for women with a history of pregnancy-related cholestasis. WHOMEC recommends that the benefits of COC use by women with a history of pregnancy-related cholestasis outweigh the risks (WHO Category 2). WHOMEC recommends that women with previous pregnancy-related cholestasis can use progestogen-only contraceptives (pills, injectables, implants and the levonorgestrel-releasing intrauterine system) without restriction (WHO Category 1). WHOMEC acknowledges that a history of pregnancy-related cholestasis might predict an increased risk of developing cholestasis with COC use. WHOMEC recommends that the risks associated with COC use for women with a history of cholestasis related to previous COC use outweigh the benefits (WHO Category 3). However, WHOMEC recommends that the benefits of using progestogen-only methods by women with a history of pregnancy-related cholestasis are therefore often advised to avoid hormonal contraception due to the risk of recurrence following exposure to oestrogen or progesterogen.

Table 1 Sources used in developing the Members’ Enquiry Response

<table>
<thead>
<tr>
<th>Source searched</th>
<th>Information identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>The National Guidelines Clearing House</td>
<td>No relevant information</td>
</tr>
<tr>
<td>Existing FFPRHC and RCOG Guidance</td>
<td>No relevant information</td>
</tr>
<tr>
<td>WHO publications: Medical Eligibility Criteria for Contraceptive Use (2002) and Selected Practice Recommendations for Contraceptive Use (2002)</td>
<td>See text</td>
</tr>
<tr>
<td>The Cochrane Library</td>
<td>No relevant information</td>
</tr>
<tr>
<td>MEDLINE and EMBASE from 1988 to 2004</td>
<td>See text</td>
</tr>
</tbody>
</table>

FFPRHC, Faculty of Family Planning and Reproductive Health Care; RCOG, Royal College of Obstetricians and Gynaecologists; WHO, World Health Organization.
of combined oral contraceptive-related cholestasis outweigh the risks (WHO Category 2). 1,2

The CEU advises that women with a history of cholestasis related to previous COC use should be advised against further COC use. However, women may consider progestogen-only methods if non-hormonal contraception is unacceptable.

The CEU was unable to identify evidence to support an increased risk of recurrence with hormonal contraceptive use. The CEU advises that women with a history of pregnancy-related cholestasis should be informed about the unknown potential for recurrence with COC use. The CEU support the WHOME recommendations that the benefits of COC use outweigh any risks, and progestogen-only methods or non-hormonal methods can be used without restriction for women with a history of pregnancy-related cholestasis. Women should be informed that the use of COCs and POPs in this situation is, however, outside the product licence.

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 results. This response has been prepared as a service to FFPRHC and it may not include all acceptable methods of care aimed at the same

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

The 4-0-8 Sheffield Fund
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For details on how to apply to the 4-0-8 Sheffield Fund visit the Faculty website at www.ffprhc.org.uk. For an application form apply to: Chair of the Education Committee, Faculty of Family Planning and Reproductive Health Care of the RCOG, 27 Sussex Place, Regent’s Park, London NW1 4RG, UK. Closing date: 6 months prior to the event for which funding is applied for.