FROM THE CLINICAL EFFECTIVENESS UNIT (CEU)

The members’ enquiry service: frequently asked questions

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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. 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. The SPCs for several COCs advise against use by women with a history of severe pruritis in pregnancy or with hormonal contraceptive use. The British National Formulary advises that women with a history of cholestasis during pregnancy should avoid COC use. The SPCs for a progestogen-only injectable (depot medroxy-progesterone acetate) and a progestogen-only implant (Implanon), however, do not suggest use is contraindicated for women with a history of pregnancy-related cholestasis.

WHO publications. WHOMEC does not support the avoidance of hormonal contraception for women with a history of pregnancy-related cholestasis.

WHOMECE recommends that the benefits of COC use by women with a history of pregnancy-related cholestasis outweigh the risks (WHO Category 2). WHOMECE recommends that women with previous pregnancy-related cholestasis can use progesterogen-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. WHOMECE 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 greater than the risks.

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 FFP/RHC and RCOG Guidance</td>
<td>No relevant information</td>
</tr>
<tr>
<td>WHO publications: Medical Eligibility Criteria for Contraceptive Use (2004) 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>
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</tbody>
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ITFPRHC, 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).32

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.

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References

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