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)

Population: Women with a history of pregnancy-related cholestasis.

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.[1] 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 progestogen.[2] The SPCs for several COCs[3–22] and POPs[23–28] 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 medroxyprogesterone 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. WHOMEC[32] 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

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	No relevant information
WHO publications: *Medical Eligibility Criteria for Contraceptive Use (2004)* and *Selected Practice Recommendations for Contraceptive Use* (2002)	See text
The Cochrane Library	No relevant information
MEDLINE and EMBASE from 1988 to 2004	See text

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).[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 WHOMEC 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 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 Milkiewicz P, Elias A, Williamson C, et al. Obstetric cholestasis. *BMJ* 2002; **324**: 123–124.
2 Lindberg MC. Hepatobiliary complications of oral contraceptives. *J Gen Intern Med* 1992; **2**: 199–209.
3 Schering Health Care Ltd. Microgynon 30. 2000. http://www.medicines.org.uk.
4 Schering Health Care Ltd. Dianette. 2003. http://www.medicines.org.uk.
5 Schering Health Care Ltd. Eugynon 30. 2002. http://www.medicines.org.uk.
6 Schering Health Care Ltd. Femodene. 2002. http://www.medicines.org.uk.
7 Schering Health Care Ltd. Femodene ED. 2002. http://www.medicines.org.uk.
8 Schering Health Care Ltd. Femodette. 2002. http://www.medicines.org.uk.
9 Schering Health Care Ltd. Microgynon 30 ED. 2002. http://www.medicines.org.uk.
10 Schering Health Care Ltd. Logynon ED. 2002. http://www.medicines.org.uk.
11 Schering Health Care Ltd. Logynon. 2004. http://www.medicines.org.uk.
12 Janssen-Cilag Ltd. Cilest. 2002. http://www.medicines.org.uk.
13 Janssen-Cilag Ltd. Ovysmen. 2002. http://www.medicines.org.uk.
14 Janssen-Cilag Ltd. BiNovum. 2002. http://www.medicines.org.uk.
15 Janssen-Cilag Ltd. TriNovum. 2004. http://www.medicines.org.uk.
16 Wyeth Pharmaceuticals. Ovranette. 2003. http://www.medicines.org.uk.
17 Wyeth Pharmaceuticals. Minulet. 2004. http://www.medicines.org.uk.
18 Wyeth Pharmaceuticals. Tri-Minulet. 2004. http://www.medicines.org.uk.
19 Pharmacia Ltd. Brevinor. 2002. http://www.medicines.org.uk.
20 Pharmacia Ltd. Norimin. 2004. http://www.medicines.org.uk.
21 Organon Laboratories Ltd. Marvelon. 2002. http://www.medicines.org.uk.
22 Organon Laboratories Ltd. Mercilon. 2002. http://www.medicines.org.uk.
23 Schering Health Care Ltd. Norgeston. 2001. http://www.medicines.org.uk.
24 Schering Health Care Ltd. Neogest. 2000. http://www.medicines.org.uk.
25 Janssen-Cilag Ltd. Micronor Oral Contraceptive Tablets. 2001. http://www.medicines.org.uk.
26 Wyeth Pharmaceuticals. Microval. 2003. http://www.medicines.org.uk.
27 Pharmacia Ltd. Femulen Tablets. 2002. http://www.medicines.org.uk.
28 Pharmacia Ltd. Noriday Tablets. 2003. http://www.medicines.org.uk.
29 *British National Formulary*, No. 47, March 2004. London, UK: British Medical Association and the Royal Pharmaceutical Society of Great Britain, 2004. http://www.bnf.org.uk.
30 Pharmacia Ltd. Depo-Provera 150 mg/ml Injection. Pharmacia Ltd. 1-6. 2002. http://www.medicines.org.uk.
31 Organon Laboratories Ltd. Implanon. 1-13. 2004. http://www.medicines.org.uk.
32 World Health Organization (WHO). *Medical Eligibility Criteria for Contraceptive Use* (3rd edn). Geneva, Switzerland: WHO, 2004. http://www.who.int/reproductive-health/publications/MEC_3/index.htm.

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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.