Progestogen-only emergency contraception and ectopic pregnancy

Pregnancies that occur in women using daily progestogen-only pills (POPs) are more likely to be ectopic than are pregnancies among users of most other contraceptive methods. This may be due to the mechanism of action of POPs, which reduce the activity of fallopian tube cilia and alter tubal motility. By the same mechanism, it is possible that pregnancies following treatment failure with progestogen-only emergency contraception (POEC) may be more likely to be ectopic.

In the July 2002 issue of the Journal of Family Planning and Reproductive Health Care, the first case report of ectopic pregnancy following failed postcoital POEC was published. During the last few months, medicines regulatory authorities on both sides of the world have also been assessing this issue. The Medicines Control Agency (MCA) in the UK and the Centre for Adverse Reactions Monitoring (CARM) in New Zealand (NZ) have shared data and expertise to assess spontaneous reports of ectopic pregnancy following use of POEC. A summary of the information available to date [which has been presented to both the Committee on Safety of Medicines (CSM) in the UK and the Medicines Adverse Reactions Committee (MARC) in NZ] is given here.

POEC products (containing two tablets of levonorgestrel 0.75 mg) were first licensed for use in the UK in 1999 and in New Zealand in 2000. These authorisations were based largely on data from the World Health Organization (WHO) Task Force comparative study of postcoital contraception. This multicentre study showed the progestogen-only method had better efficacy and fewer side effects than the Yuzpe (oestrogen and progestogen) regimen. There were, however, limited data on the risk of ectopic pregnancy following treatment failure: in 976 women randomised to receive levonorgestrel, 11 pregnancies occurred and all of these were intrauterine. As the risk of ectopic pregnancy is likely to be very small (because emergency contraception is an effective treatment) the clinical trials would have needed to be several times larger to estimate any effect of POEC on the incidence of this rare event.

At the time levonorgestrel emergency contraception was licensed in the UK and NZ, few postmarketing data were available, although there had been extensive use of this method in Eastern Europe since the 1980s. In particular, there were no reports of ectopic pregnancy associated with POEC in the WHO international spontaneous reporting database. This may have been due to underdeveloped (or non-existent) medicines regulatory facilities in these countries at this time, rather than to an absence of cases.

In the 2 years since levonorgestrel emergency contraceptive pills were licensed in the UK and NZ (and other countries including the USA) some postmarketing safety data have become available. Information on cases of ectopic pregnancy has come from spontaneous reports, which health professionals have submitted to either the MCA in the UK or the CARM in NZ in the form of a ‘yellow card’. Each card submitted is individually assessed by professional assessors and added to a national database that stores all adverse events reported. In the UK there have been 12 reports of ectopic pregnancy following use of levonorgestrel emergency contraception. The case reports all suggested the product had been taken as directed, and in 6/12 cases treatment commenced within 24 hours of unprotected intercourse. In NZ, the CARM has received three reports of ectopic pregnancy following use of the progestogen-only emergency pill. In all three cases the treatment was taken as directed and in two cases it was known to have started within 24 hours of unprotected intercourse. In one report the doctor specified that the woman had no known risk factors for ectopic pregnancy and had previously had two normal pregnancies. Analysis of the WHO database identified a further three cases of ectopic pregnancy following treatment with levonorgestrel 0.75 mg for emergency contraception. Two reports were from Sweden and one from the USA.

Whilst spontaneous reports have identified an additional 18 case reports to the one published in this journal, it is not possible to calculate the incidence of ectopic pregnancy from these data. A weakness of spontaneous reporting schemes is that the population exposed to the medicine is not known. Exposure to progestogen-only emergency pills has been high and therefore it could be argued that the incidence of ectopic pregnancy is very low. However, underreporting of adverse events to spontaneous reporting schemes is also well recognised. To calculate an accurate incidence of ectopic pregnancy following POEC, a large postmarketing study would be required where the number of women treated is known. Such a study would be valuable to investigate the efficacy and safety of this method in ‘real life’ use. It would be particularly interesting as in both the UK and NZ, POEC products are now available from pharmacists without a prescription.

For now, we have to draw what information we can from the available data and use this to best inform women requiring emergency contraception. The important message from the worldwide postmarketing data is that ectopic pregnancies have now been reported following treatment with POEC. This might have been expected from the known action of other POPs. It is not possible to estimate the risk of this adverse event, but it is likely to be very small as emergency contraception is effective at preventing pregnancy. However, the clinical trial data showed that the method is not always 100% effective and that efficacy decreases with time from unprotected intercourse. Women therefore need to know that the first tablet should be taken as soon as possible, but also that treatment might fail. Doctors and pharmacists should advise women to have a pregnancy test if they have amenorrhoea (or an unusually light period) following treatment. If pregnancy testing is positive, the possibility of ectopic pregnancy should be considered, especially if the woman has risk factors (e.g. previous ectopic pregnancy) or symptoms such as abdominal/pelvic pain.

On the advice of the CSM in the UK and the MARC in NZ, the regulatory authorities have checked that these messages are included (and strengthened where appropriate) in both the prescription-only and pharmacy product information. It is therefore helpful to encourage women to read the patient/consumer leaflet provided with each packet. It is important that the benefits and risks of hormonal emergency contraception are appropriately communicated to women using this method. At this time,
the essential message is that the benefits of POEC far outweigh the risks, which remain very small indeed.

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References


Homeopathy: a potent alternative

Have you ever wished you could offer your patients an additional form of treatment? Acquiring the skills of complementary medicine gives a practitioner another string to their bow. Homeopathy is one such string. When used by a doctor it can be fully integrated with conventional medicine and can be useful when conventional treatment fails. In this issue Dr Angela Jones discusses the use of homeopathy for premenstrual symptoms, including premenstrual syndrome (PMS) (pages 25–28). The value of conventional medicine is debatable for such conditions. She describes how homeopathy has many medicines to offer, including medicines to treat some of the unusual symptoms women describe such as specific food cravings or emotional symptoms.

Homeopathy was first described 200 years ago by a German physician, Dr Samuel Hahnemann (1755–1843). Hahnemann sought a system of medicine that was gentle, reliable and free of harmful effects.1 The principles of homeopathy and the concept of illness differ from those of conventional medicine. The cardinal principle of ‘treating like with like’ was first mentioned by Hippocrates. However, modern homeopathic doctors work in the same way as conventional colleagues. History, examination, investigation and diagnosis form part of the patient management. Prescribing is based on all aspects of the patient’s condition including lifestyle and personality. Hahnemann developed homeopathy using detailed observations and early forms of clinical trials. Present day opponents of homeopathy argue that any beneficial effects (and they have to agree that these exist) must be due to placebo effect. There are difficulties conducting research in homeopathy. Randomised controlled trials (RCTs) present a particular difficulty as homeopathic treatment is individualised. Two patients with the same diagnosis may require entirely different medicines. In RCTs, patient groups are usually assigned to a standardised treatment while the control group receives placebo. However, some researchers have tested the effects of a single remedy on a particular condition, even though in practice practitioners would use a variety of different medicines. One example is Reilly’s trial of homeopathy for hayfever, where subjects were randomised to receive either a single homeopathic medicine or placebo.2 Another is a double-blind RCT to evaluate the efficacy of a homeopathic medicine for influenza where nearly 500 patients received either Oscillococcinum® or placebo.3 Three meta-analyses4–6 have shown a positive response for homeopathy.

Funding is always a problem in research, and particularly so for complementary medicine. Despite the difficulties current research continues.

Having started in Germany, homeopathy continues to be popular there today. It is popular in other European countries including The Netherlands, Belgium, Austria, Greece, France and the UK. European royalty have supported homeopathy since it began. It is even more popular in India where it is often used as the primary method of treatment. There are many thousands of homeopathic doctors in India and over 100 homeopathic colleges. Mother Teresa embraced homeopathic medicine and set up her first homeopathic dispensary in Calcutta in 1950.

Homeopathy is becoming increasingly popular with patients and over-the-counter sales are increasing by 15–20% each year. People are more concerned about drug toxicity, side effects and antibiotic resistance. They recognise the benefits of a holistic approach to care, time to tell their story, and an individual prescription.

Within the field of gynaecology and reproductive health care, homeopathy has many applications both in primary and secondary care. Treatment of PMS is just one of many conditions where homeopathy can be beneficial. Homeopathy can be used in addition to conventional medicine and may reduce the use of conventional drugs. Homeopathic medicines also have the advantage of being inexpensive. For example, the use of homeopathy to treat dysmenorrhoea may lead to a reduction in the use of analgesia or non-steroidal anti-inflammatory drugs (NSAIDs). Appropriate homeopathic medicines for dysmenorrhoea include Sepia (ink of the cuttle fish), Cuprum metallicum (copper) and Nux vomica (poison nut). Homeopathy can be used as an alternative treatment in non-serious conditions when a diagnosis has been established. Ipecacuanha (Ipecac-root), Belladonna and Sepia are three
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