Medical management of first-trimester induced abortion and miscarriage

Surgical evacuation is the mainstay of treatment in the UK for first-trimester termination of pregnancy and miscarriage and, although a minor procedure, it has an associated considerable morbidity and mortality. Induced abortion in the UK is now a safe procedure but on a global scale continues to be a major cause of maternal mortality. Medical management would provide a safe and effective alternative. Many women would prefer to be given the choice and avoid the risks associated with anaesthesia and surgery. Recent studies have confirmed high acceptability rates, showing that 84–96% of women would choose medical treatment for a subsequent abortion.

BACKGROUND

The drugs used for medically induced abortion in the UK include an antiprogestosterone, mifepristone, and several prostaglandin analogues, including gemeprost and misoprostol. Mifepristone is the 11β-dimethyl-amino-phenyl derivative of norethindrone and has a high affinity for progesterone and glucocorticoid receptors. Receptor binding in the placenta is followed by inefficient transcription of progesterone genes, so that mifepristone effectively blocks the progesterone receptors in the decidua, myometrium and cervix. This usually results in termination of the pregnancy. When mifepristone is used alone, the success rate is variable and never greater than 88%.

Gemeprost is a prostaglandin E₁ analogue and is effective in 95% of cases in combination with mifepristone at less than 63 days of amenorrhoea. Initial studies were with a dose of 1 mg. The high efficacy is associated with increased adverse effects of bleeding per vaginum, diarrhoea and vomiting. In a randomised trial, where 1 mg versus 0.5 mg of gemeprost was compared, the complete abortion rate was similar for the two groups (98–100%), although the incidence of adverse effects was significantly lower in the latter group.

Misoprostol is a synthetic analogue of prostaglandin E₁, and causes increased uterine contractility with a low incidence of other unwanted effects. The main advantages over gemeprost are that it does not require refrigeration, is cheaper and can be administered orally or vaginally. One gemeprost pessary costs £22, whereas the equivalent dose of misoprostol is just over £1. The uterotonic properties are enhanced if women are pretreated with mifepristone, reflecting the effect of antiprogestones in increasing sensitivity to prostaglandins.

GUIDELINES FOR MEDICAL TERMINATION

Details relating to organisational, clinical and supportive aspects of abortion care are given in the evidence-based guideline produced by the RCOG. The earlier the termination is performed, the more effective is the procedure, with a lower risk of complications. At six to seven weeks, medical termination is the method of choice and is effective in 97.5% of cases. The effectiveness falls to 95% for gemeprost and 89.1% for misoprostol at between seven and nine weeks. The latter induces less powerful uterine contractions at this gestation.

An ultrasound determination of gestational age will help improve efficacy and confirm that the pregnancy is intra-uterine. If the fetus is found to be non-viable, this might help to allay some of the guilt and anxiety felt by women.
undergoing a termination of pregnancy.18

Within the UK, mifepristone must be administered on licensed premises or in a hospital. Prostaglandins are then administered 36–48 hours later, with the patient being kept under observation for four to six hours. Facilities for immediate suction curettage should be available in the event of excessive vaginal bleeding. A two-week follow-up is important, with a repeat pregnancy test and an ultrasound scan if products of conception have not been identified. Women who are rhesus (D) negative should be given anti-D rhesus immunoglobulin simultaneously. Contraindications to medical termination are shown in Table 1.

Table 1. Contraindications to medical termination of pregnancy14

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy of more than 63 days</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Suspected ectopic pregnancy</td>
<td></td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td></td>
</tr>
<tr>
<td>Long-term glucocorticoid therapy</td>
<td></td>
</tr>
<tr>
<td>Haemoglobinopenias or anticoagulant therapy</td>
<td></td>
</tr>
<tr>
<td>Anaemia</td>
<td></td>
</tr>
<tr>
<td>Known allergy to mifepristone or prostaglandin</td>
<td></td>
</tr>
<tr>
<td>Smokers over 35 years of age</td>
<td></td>
</tr>
<tr>
<td>Porphyria</td>
<td></td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td></td>
</tr>
</tbody>
</table>

ADVERSE EFFECTS AND COMPLICATIONS

The most common adverse effects are gastrointestinal and are mainly related to the prostaglandins. Besides nausea and vomiting, headaches, dizziness and tiredness can occur. Haemorrhage requiring transfusion is a recognised complication of both surgical and medical treatment and the risk increases with gestational age. Blood loss before nine weeks of gestation is similar for both methods.18 Significant blood loss necessitating a transfusion occurs in 0.7–1% of cases.19-21

Abdominal pain requiring analgesia, and in particular parenteral analgesia, is greater with medical abortion than with surgical abortion (28.5–35%).19,22 This is not surprising as the woman is fully conscious during medical treatment.

Approximately 5% of women require surgical curettage following medical treatment.19 The continuing pregnancy rate after mifepristone and gemeprost is 0.3%. If oral misoprostol is used, the risk can be as high as 7%.13 Although there has been no reported fetal abnormality with mifepristone, misoprostol has been associated with defective formation of the frontal and temporal regions of the skull and limbs, due to vascular disruption.23,24 In view of this, it is recommended that unsuccessful medical termination should be followed by surgical evacuation.

MEDICAL MANAGEMENT

Miscarriage commonly occurs in 15–20% of pregnancies within the first trimester. The routine management of such cases is still surgical evacuation. Although medical management of miscarriage with herbal remedies was known before the 19th century, only in the last decade of the 20th century has interest in this field been rekindled.25 As well as avoiding complications of surgery, it is also less expensive than surgery, with a saving of £50 per case.26

Various efficacy rates for medical treatment of miscarriages have been cited. Factors determining success are the type of miscarriage, the gestation, the type, dose and route of administration of medication and whether an ultrasound scan is used to assess completion.

The efficacy of medical treatment for silent miscarriage varies from 52% to 92%, depending on the doses of mifepristone and misoprostol.27,28 Nielsen et al.27 used lower oral doses of both and defined success objectively using transvaginal ultrasound to detect retained products. Vaginal misoprostol is effective in 88% of cases.29 In silent miscarriage the progesterone level is already low and therefore the antiprogesterone may be omitted. This has important implications in countries where mifepristone is unavailable. Further studies in the UK indicate that the success rate with mifepristone and vaginal misoprostol is similar to that seen in induced abortion.

In the case of incomplete miscarriage, use of either oral misoprostol (400 mg) alone or intramuscular sulprostone (0.5 mg) has been shown to be effective in 95% of cases. Sulprostone was withdrawn after three cases of myocardial infarction.30 Subsequent studies have shown a lower success rate of misoprostol in incomplete miscarriages (13.9–70.6%).31,32 The discrepancy between these two studies (de Jonge et al.21 and Chung et al.32) can be explained by the difference in the mean duration of amenorrhoea (80 and 66 days, respectively) and the use of pelvic ultrasound. The morbidity in those treated medically was lower than in those requiring surgery (1.7% versus 6.6%).31

In the only published patient-centred partially randomised controlled trial comparing the medical method with surgical evacuation, different regimens of misoprostol and mifepristone were used for silent and incomplete miscarriage.25 Complete evacuation of the uterus was assessed by history and clinical examination, without resorting to pelvic ultrasound. The overall success rate was 93% for the medical method and 98% for surgery (P = 0.004). In the case of silent miscarriage, the efficacy was greatest for those pregnancies of less than ten weeks or with a sac diameter of less than 24 mm (92–94%) and was not statistically significantly different from that of surgery. In women with incomplete miscarriage, the success rate for both methods was 100%.

Gemeprost used alone for miscarriage is effective in 77% of cases at gestations of less than 13 weeks.33 The disadvantages of using gemeprost rather than misoprostol have already been mentioned.

The proportion of women requesting medical treatment for miscarriage is the same as the proportion requesting medical termination (20%),3,25 although with experience this is likely to increase. The main reasons stated were avoidance of general anaesthesia or surgery (57%) and feeling ‘more natural’ and ‘in control’ of the process (36%). The acceptability of medical treatment over surgery was the
same for both incomplete and silent miscarriages of less than ten weeks. Both these trials (Henshaw et al.3 and Hinshaw et al.5) were based on the Brewin and Bradley design, which allows the effect of patient choice on various outcomes to be assessed and yet maintains a randomised group for comparing two interventions.34

Medical management of miscarriage may be less suitable for those women with heavy vaginal bleeding, anaemia (haemoglobin less than 10 g/dl) or who are pyrexial and have contraindications to medical therapy (Table 1). In those cases where the products of conception have not been passed, an ectopic pregnancy must be excluded.

Expectant management appears to be a suitable alternative to medical management in cases of spontaneous miscarriage although, again, varying rates of efficacy have been quoted.35-37

CONCLUSIONS
In these days of patient choice, the onus is on health professionals to provide the option of medical treatment for all indications for uterine evacuation, irrespective of gestation. Both surgical and medical methods should be viewed as having complementary rather than alternative roles. Further patient-centred randomised controlled trials are required to establish the optimal dose of mifepristone and which prostaglandin should be used.

AUTHOR DETAILS
Shamim Amis MRCOG, Specialist Registrar in Obstetrics and Gynaecology, Whipps Cross Hospital, Whipps Cross Road, London E11 1NR, UK (corresponding author)
Jonathon Evans-Jones FRCOG, Lead Clinician and Consultant, Department of Obstetrics and Gynaecology, Colchester General Hospital, Colchester, UK

References
2 Ewan WR, Winniford B. Towards safe and effective medical abortion. Science 1998;281:520–1
15 Royal College of Obstetricians and Gynaecologists Clinical Effectiveness Support Unit. The Care of Women Requesting Induced Abortion. London: RCOG Press, 2000 (Evidence-based guideline no 7)
17 Creinin MD, Vittinghoff E, Galbraith D, Klaes C. A randomized trial comparing misoprostol three and seven days after methotrexate for early abortion. Am J Obstet Gynecol 1995;173:1578–84
18 Rodger MW, Baird DT. Induction of abortion using mifepristone (RU486) and a prostaglandin analogue (gemeprost). Contraception 1989;40:439–47
19 UK Multicentre Study – final results. The efficacy and tolerance of mifepristone and prostaglandin in termination of pregnancy of less than 63 days gestation. Contraception 1987;31:1
21 El-Refay H, Templeton AA. Early induction of abortion by a combination of oral mifepristone and misoprostol administered by the vaginal route. Contraception 1994;49:111–4
31 de Jonge EDM, Marijn JD, Manefeldt E, de Wet GH, Pattison RC. Randomised clinical trial of medical evacuation and surgical curettage for incomplete miscarriage. BMJ 1995;311:662