Modern management of miscarriage

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Key content:
• Miscarriage has traditionally been treated by surgical evacuation, on the assumption that any retained tissue increases the risk of infection and haemorrhage.
• Over the last decade, effective non-surgical alternatives have been advocated to minimise unnecessary surgical intervention while maintaining low rates of morbidity and mortality.
• Improved access to early pregnancy assessment units and greater awareness among women has led to increasing demand for more conservative management of miscarriage.

Learning objectives:
• To learn about the use of appropriate miscarriage terminology.
• To learn about the advantages and disadvantages of expectant, medical and surgical management.
• To understand that women’s choice is paramount in planning treatment.

Ethical issues:
• Guidance on the sensitive disposal of fetal remains is essential.

Keywords early pregnancy assessment units / expectant management / medical management / miscarriage / surgical evacuation
Introduction

Miscarriage accounts for approximately 50,000 inpatient admissions in the United Kingdom annually (Department of Health statistics, 2005). It is common, occurring in 15–20% of all pregnancies, and can have both medical and psychological consequences. While maternal death is rare after miscarriage, particularly in the first trimester, on which this review focuses, it has featured in previous Confidential Enquiries into Maternal Deaths in the UK, particularly after surgical procedures in association with sepsis. Ectopic pregnancy, recurrent miscarriage, gestational trophoblastic disease and pregnancy of unknown location are not discussed.

Early pregnancy assessment units

The benefits of an early pregnancy assessment unit service were first described by Bigrigg and Read in 1991. Thorough assessment can occur in the presence of a supportive multidisciplinary team, with a confirmed diagnosis made at the first visit in most cases. The admission time was reduced for women requiring evacuation of the uterus from 3 days (range 1.5–3.0) to 1 day and from 1.5 days (range 0.5–3.0) to 2 hours in those requiring no treatment. Women were no longer separated from their families for long periods and the reduced use of inpatient beds produced significant economic benefits for the National Health Service.

According to the Association of Early Pregnancy Units (AEPU) 2004 guidelines, an effective unit should be located in a dedicated area with good-quality ultrasound equipment, easy access to laboratory facilities (for rhesus grouping, sensitive urine pregnancy testing and β-hCG assay with results within 24 hours) and gynaecological procedures. The National Chlamydia Screening Programme recommends opportunistic screening for all women under 25 years of age attending early pregnancy assessment units. Although the gold standard would be to have a unit open 7 days a week, from 8 am to 5 pm, the minimum requirement would be a unit open 5 mornings only. Staffing varies between units but the multidisciplinary team should ideally include doctors, nurses, midwives, ultrasonographers and support staff. Clear and consistent verbal and written information should be available. Direct access to an appointment system should be available to all women and practitioners in the primary care setting (including general practitioners, nurses, midwives and health visitors), as well as other hospital departments (for example, accident and emergency departments, wards). The AEPU recommends using clinical guidelines to standardise management of early pregnancy problems, record keeping and data collection.

Speculum examination

A prospective study published in 2004 of 236 women with early pregnancy bleeding found that, after speculum examination, 3 (1.3%) women had a change of management plan but only 10 (4.2%) women had a change of diagnosis, suggesting that it contributes to a minority of management decisions. The need for speculum examination should be assessed on a case-by-case basis, depending on whether the findings on bimanual examination are conclusive.

The role of ultrasound

The use of transvaginal ultrasound has revolutionised the management of early pregnancy problems. Along with the development of highly sensitive urinary β-hCG assays, early pregnancy ultrasound has resulted in women presenting earlier but with the knock-on effect of an increase in the number of inconclusive scans and the requirement for repeat assessments. Knowledge of the typical ultrasound appearances of normal early pregnancy development and a good understanding of its pitfalls are essential for the diagnosis and management of early pregnancy problems.

It is vital to describe clinical and ultrasound findings in early pregnancy using appropriate terminology (Table 1). The word ‘miscarriage’

<table>
<thead>
<tr>
<th>Recommended term</th>
<th>Previous term</th>
<th>Ultrasound appearance</th>
<th>Clinical presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threatened miscarriage</td>
<td>Threatened abortion</td>
<td>Intrauterine gestation sac</td>
<td>Vaginal bleeding ± abdominal pain; closed cervix</td>
</tr>
<tr>
<td>Complete miscarriage</td>
<td>Complete abortion</td>
<td>Fetal pole with cardiac activity seen Endometrial thickness &lt; 15 mm</td>
<td>Cassation of vaginal bleeding and abdominal pain; closed cervix</td>
</tr>
<tr>
<td>Incomplete miscarriage</td>
<td>Incomplete abortion</td>
<td>No evidence of retained products of conception</td>
<td>Passage of some pregnancy-related tissues ± bleeding and/or abdominal pain; open cervix</td>
</tr>
<tr>
<td>• Missed miscarriage</td>
<td>• Missed abortion</td>
<td>Heterogenous tissues ± sac Distorting midline endometrial echo Any endometrial thickness</td>
<td>Minimal vaginal bleeding or pain; loss of pregnancy symptoms; closed cervix</td>
</tr>
<tr>
<td>• Delayed miscarriage</td>
<td>• Anembryonic pregnancy</td>
<td>Fetal pole &gt; 6 mm with no fetal heart activity Distal sac diameter &gt; 20 mm with no fetal pole or yolk sac</td>
<td></td>
</tr>
<tr>
<td>• Silent miscarriage</td>
<td>• Blighted ovum</td>
<td>(These reflect different stages in the same process) Intrauterine abortion</td>
<td></td>
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<tr>
<td>Early fetal demise</td>
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<td>(These reflect different stages in the same process) Intrauterine abortion</td>
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<td>Inevitable miscarriage</td>
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<td>Miscarriage with infection</td>
<td>Septic abortion</td>
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<td>Septic abortion</td>
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</table>

Table 1: Clinical correlates of ultrasound appearances.**

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should replace ‘abortion’ in clinical practice. The use of the term ‘indeterminate’ in relation to location or viability is confusing and should be replaced by the terms ‘pregnancy of unknown location’ (positive pregnancy test but no signs of intra- or extrauterine pregnancy or retained products of conception) and ‘pregnancy of uncertain viability’ (intrauterine sac < 20 mm mean diameter with no obvious yolk sac or fetus, or fetal echo > 6 mm crown-rump length with no obvious fetal heart activity). In these circumstances a repeat scan at a minimum interval of 1 week is necessary. 7

No single ultrasound measurement of the different anatomical features in the first trimester has been shown to have a high predictive value for determining early pregnancy outcome. Similarly, Doppler studies and 3D ultrasound have failed to predict those pregnancies that will subsequently end in miscarriage and are, therefore, unlikely to have a clinical role. 10, 11

**Treatment**

See Figure 1. 14, 16

**Viable intrauterine pregnancy**

(threatened miscarriage)

Ninety percent of women in whom fetal heart activity is detected at 8 weeks will not miscarry. The therapeutic value of progesterone in preventing or treating threatened miscarriage has not yet been established. 7 There is also insufficient evidence to support the use of uterine muscle relaxants 12 or a policy of bed rest. 13 A small study published in 2005 14 showed no evidence of a difference in the outcome of threatened miscarriage when treated with hCG in the first trimester.

**Non-viable pregnancy**

The term non-viable pregnancy includes incomplete, silent, delayed and missed miscarriage and early fetal demise.

**Expectant management**

Up to 70% of women will choose expectant management if given the choice. 16 A review by Butler 7 showed that expectant management is successful within 2–6 weeks without increasing complications in 80–90% of women with incomplete spontaneous miscarriage and 65–75% of women with delayed miscarriage or an empty sac. Women’s experiences with expectant management revealed a mean worst pain of 5.9 on an 11-point scale. 7 The satisfaction rates were 92.9% with family physician care and 84.6% with hospital care. Bleeding varied, but was often very heavy. The median daily levels of bleeding and pain were highest during the first 8 days from the start of bleeding and decreased thereafter in the 188 women managed expectantly. 7

Expectant management can be continued as long as the woman is willing and provided there are no signs of infection. The duration can sometimes be as long as 6–8 weeks; this is reflected in the higher success rates with prolonged follow-up. An increasing bleeding pattern at inclusion 7 and ultrasound findings such as blood flow within intervillous spaces 7 can be used to predict the likelihood of successful expectant management. Biochemical markers (including serum hCG, prostegorone, inhibit A and inhibit pro-alpha C RI) also show significant differences in those pregnancies that resolve spontaneously (P < 0.05). 20 Other ultrasound parameters such as endometrial thickness and the presence or absence of a gestational sac did not add any further information to the likely outcome. 7

**Medical management**

**Incomplete miscarriage**

A variety of equally effective prostaglandin regimens have been described, including gemeprost 0.5–1 mg, vaginal misoprostol 800 µg and oral misoprostol 400 µg. 21 Single and repeated doses of oral misoprostol 600 µg (with the dose repeated after 4 hours to a total of 1 200 µg) have been shown to be equally effective, although with a lower incidence of diarrhoea in the single dose group. 22 However, vaginal misoprostol is as effective as oral misoprostol, with a significant reduction in the incidence of diarrhoea. 22 Success rates varied from 61–95%, mild–moderate bleeding lasted 4–6 days, side effects were tolerable in 96% and satisfaction rates were 95%. 20, 22 Misoprostol has the advantage of being cheap and not requiring refrigeration, although it is not licensed for use in the management of miscarriage.

**Silent, delayed, missed miscarriage or early fetal demise**

A confusing number of alternative regimens have been described using prostaglandin alone (oral, sublingual or vaginal misoprostol, 400, 600 or 800 µg in single or repeated doses), or the anti-progestogen mifepristone (200, 400 or 600 mg orally) followed 36–48 hours later by either misoprostol or gemeprost (0.5–1mg vaginally). Mifepristone 200 mg, in combination with oral misoprostol, was equally effective and better tolerated than mifepristone 600 mg. 22 Sublingual misoprostol 400 µg appears to be a safe, effective alternative to the oral or vaginal routes. 22 Success rates with mifepristone and misoprostol varied from 70–84%, the median induction to miscarriage interval was 8 hours, overall the satisfaction rate was 91% and bleeding stopped, on average, by 8 days. 24, 25

Since progesterone levels are low in non-viable pregnancy, in contrast to medical termination of pregnancy, mifepristone can be avoided and
Figure 1
Algorithm for management of miscarriage

**THREATENED**
- Active bleeding
- Admit for reassurance
- Follow up if:
  1. Haematoma
  2. liquor volume decreased
  3. Fetal bradycardia
- To report if bleeding persists >2/52
- Rescan may be offered 2/52

**COMPLETE**
- ET <15 mm
  - Expectant: Provided bleeding not heavy
  - Medical: Woman not willing to wait
    - Vaginal prostaglandin (PG):
      1. Gemeprost 0.5 mg
      2. Gemeprost 1 mg
      3. Misoprostol 800 μg (4 × 200 μg)
  - Surgical: 1. Strong preference
    2. Heavy bleeding
    3. Infection — under antibiotic cover
    - Assess need for cervical priming

**INCOMPLETE**
- ET 15–50 mm
  - Continue as long as the woman is willing. If necessary, rescan at 1–2 week intervals until miscarriage complete
  - If heavy bleeding/infection changes mind

**SILENT/DELAYED/MISSSED/EARLY FETAL DEMISE**
- ET >50 mm
  - Rescan 1/52. If no change
  - Medical: Provided bleeding not heavy
  - Surgical: 1. Strong preference
    2. Heavy bleeding
    3. Infection — under antibiotic cover
    - Assess need for cervical priming

**Contraindications to medical management**
- Absolute
  - Adrenal insufficiency
  - Long-term glucocorticoid therapy
  - Haemoglobinopathies or anticoagulant therapy
  - Anaemia (haemoglobin <10 g/dl)
  - Porphyrria
  - Mitral stenosis
  - Glaucoma
  - NSAID ingestion in previous 48 hours
  - Hypertension
  - Severe asthma

- Relative

- Heavy bleeding/infection changes mind

*No one prostaglandin regimen is clearly superior
*Antiprogesterone may not be necessary (see text)
EPAU = early pregnancy assessment unit, ET = endometrial thickness, NSAID = non-steroidal anti-inflammatory drugs

All women attending EPAU should be offered chlamydia screening
prostaglandins only administered. Misoprostol by the vaginal route may be preferable, as the mean time to expulsion is longer by the oral route and the incidence of diarrhoea and fatigue higher with sublingual regimens.\textsuperscript{26,27} Single-dose vaginal misoprostol 800 µg was more effective than 400 µg (55.4% versus 40.2%, \( P < 0.05 \)) and more effective in delayed miscarriage compared with cases where there was an empty sac (50.3% versus 40.2%, \( P < 0.05 \)), which may require larger or repeat doses as they seem to respond less readily to medical treatment.\textsuperscript{28} One trial\textsuperscript{29} showed that an additional 1-week course of sublingual misoprostol did not improve either the success rate or the duration of bleeding, but increased the incidence of diarrhoea. Women receiving misoprostol experienced more pain and required more analgesia compared with a placebo.\textsuperscript{30} Higher success rates (85%) using 800 µg vaginal misoprostol were reported in one study, which demonstrated that bleeding for at least 2 weeks after vaginal misoprostol is common, although heavy bleeding is usually limited to a few days after treatment.\textsuperscript{31} Factors that seem to predict success include active bleeding, nulliparity\textsuperscript{32} and higher dosages of misoprostol.\textsuperscript{33}

Surgical evacuation

Surgical evacuation remains the treatment of choice if endometrial thickness is >50 mm, bleeding is excessive, vital signs are unstable or infected tissue is present in the uterine cavity (in which case surgery must be done under antibiotic cover). Fewer than 10% of women who miscarry fall into these categories.\textsuperscript{34} Certain women will still prefer to undergo surgical evacuation and their choice should be acknowledged. Rare surgical risks are: uterine perforation (1%), cervical tears, intra-abdominal trauma (0.1%), intrauterine adhesions, haemorrhage, infection and anaesthetic complications.

The Cochrane review\textsuperscript{35} on surgical procedures to evacuate incomplete miscarriage included two trials showing that vacuum aspiration is safe, quick to perform, has significantly decreased blood loss and is less painful than sharp curettage. Serious complications, such as uterine perforation, and other morbidity were rare. Analgesia and sedation should be provided as necessary for the procedure. In all women in whom surgery is being considered, the need for cervical priming should be assessed. While women with Chlamydia trachomatis, Neisseria gonorrhoea or bacterial vaginosis in the lower genital tract at the time of induced abortion are at increased risk of subsequent pelvic inflammatory disease,\textsuperscript{36} there is insufficient data to recommend routine antibiotic prophylaxis before surgical uterine evacuation for miscarriage. Screening for infection, including C. trachomatis, should be considered in all women. Antibiotic prophylaxis should be given based on individual clinical indications.\textsuperscript{37} An appropriate regimen would be 1 g rectal metronidazole at the time of surgery followed by 100 mg oral doxycycline twice daily for 7 days.\textsuperscript{38}

### Comparison of different methods of management

There are few robust randomised controlled studies with sufficient numbers of women to enable true comparison between expectant, medical and surgical management for incomplete miscarriage and early fetal demise (Table 2). The MIST trial\textsuperscript{39} revealed significantly more unplanned admissions and unplanned surgical curettage procedures after expectant management and medical management than after surgical management, although the risk of infection was low (2–3%), regardless of treatment modality. A recent meta-analysis\textsuperscript{40} to quantify the relative benefits and risks of different management options for first-trimester miscarriage reported that surgical treatment had the best success rate, followed by medical and expectant treatment, although many studies were of poor methodological quality.

The 2006 Cochrane review\textsuperscript{37} identified five trials comparing expectant with surgical management. Expectant care led to a higher risk of incomplete miscarriage, bleeding and need for surgical evacuation of the uterus, while surgery resulted in a significantly greater risk of infection (relative risk 0.29, CI 0.09–0.87, \( P = 0.03 \)). However, there was no strong medical argument for either approach and the individual woman’s preference was considered the major concern.

Filmy intrauterine adhesions are present in 7.7% of women examined hysteroscopically following surgical evacuation but not in those managed conservatively or medically. Long-term conception rates and pregnancy outcomes are no different following medical or surgical evacuation for miscarriage, the median time to pregnancy being 8 months in both groups.\textsuperscript{41,42}

### Table 2

<table>
<thead>
<tr>
<th>Comparison of management regimes\textsuperscript{10,11,21,23,24,26,28,36,38–40,42}</th>
<th>Expectant</th>
<th>Medical</th>
<th>Surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Success rates (%)</td>
<td>80–91</td>
<td>61–95 (prostaglandin)</td>
<td>95–100</td>
</tr>
<tr>
<td>2. Net societal cost per woman (£)</td>
<td>1086.20</td>
<td>1410.40</td>
<td>1585.30</td>
</tr>
<tr>
<td>3. Risk of infection (%)</td>
<td>2–3</td>
<td>2–3</td>
<td>2–3</td>
</tr>
<tr>
<td>5. Intrauterine adhesions (%)</td>
<td>0</td>
<td>0</td>
<td>7.7</td>
</tr>
<tr>
<td>6. Long-term conception rates and pregnancy outcomes</td>
<td>No differences between different treatment modalities</td>
<td>No differences between different treatment modalities</td>
<td>No differences between different treatment modalities</td>
</tr>
</tbody>
</table>
Cost analysis

Conflicting results have been reported on the cost effectiveness of different treatment strategies.44–47 Analysis of pooled data from 29 reports found misoprostol the least costly alternative ($1 000 [US dollars] per woman), followed by expectant care ($1 172) and surgical evacuation ($2 007).48 Misoprostol and expectant care groups were shown to be less costly than the surgical evacuation group 100% and 88% of the time, while the misoprostol group was less costly than the expectant group 100% of the time.

In an economic evaluation of the MIST trial,49 expectant management was shown to be cheaper (net societal cost per woman estimated at £1 086.20) than both medical (£1 410.40) and surgical management (£1 585.30). Overall, it was the most cost effective.

In a study by Rocconi et al.,50 expectant management ($915 [US dollars] cost per cure) was, similarly, more cost effective than both medical ($1 49) and conventional surgical management ($2 333), although manual vacuum aspiration, a technique little used in the UK, was the most cost effective ($793).

Women’s perspective about different choices

A survey51 of women attending a family planning clinic found a strong preference for expectant treatment in the event of a miscarriage, although physician recommendation would influence their decision. From a clinical viewpoint, the role of free choice is supported by the fact that health-related quality of life over time is best when women with miscarriage choose their own treatment.52 With no single ‘best way’ to treat miscarriage to suit all individuals, the largest qualitative study of women’s views on expectant, medical and surgical treatment concluded that informed choice was paramount.53 When surgical evacuation became necessary, women in the medical group resented having a second procedure, and a subsequent operation for failed expectant treatment was not perceived by women in the ‘wait and see’ group in such a negative way.54

Disposal of products of conception

Guidance from the Royal College of Obstetricians and Gynaecologists55 on early pregnancy loss recommends that tissue obtained at the time of a miscarriage should be submitted for histological examination to exclude trophoblastic disease and ectopic pregnancy. Each hospital trust should have a clear system and protocol for the sensitive disposal of fetal remains.56 A Scottish study57 to determine the extent to which health professionals have adopted these recommendations found that only 1% of records contained evidence of histological examination of tissue. Around 50% of women reported involvement with decisions about tissue disposal, although documentation was found in only 29% of records. It was concluded that the national guidance on these issues was contentious, implementation variable and that wide consultation with stakeholders was needed prior to publication of any revised guidance.

Conclusion

Modern treatment of miscarriage should provide a rapid, sympathetic diagnosis and adequate counselling. All women with early pregnancy problems should preferably have prompt access to a dedicated early pregnancy assessment unit that provides efficient management, counselling and access to appropriate information. At all times women should be supported in making informed choices about their care and management: ‘Given the lack of clear superiority of either approach, the woman’s preference should play a dominant role in decision making. Expectant and medical management of first-trimester miscarriage possess significant economic advantages over traditional surgical management.’58

References

Review


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