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PRACTICE

GUIDELINES

Ectopic pregnancy and miscarriage: summary of NICE guidance

Emma Newbatt *research associate*[1], Zosia Beckles *information scientist*[1], Roz Ullman *senior research fellow and clinical lead (midwifery)*[1], Mary Ann Lumsden *professor of gynaecology and medical education and honorary consultant gynaecologist*[2], on behalf of the Guideline Development Group

[1]National Collaborating Centre for Women's and Children's Health, London W1T 2QA, UK; [2]University of Glasgow, Glasgow G4 0SF, UK

This is one of a series of *BMJ* summaries of new guidelines based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists.

Many women will experience complications in early pregnancy. The loss of a pregnancy can cause considerable emotional distress for women and their families, as well as physical morbidity that results in over 50 000 inpatient admissions in the UK annually.[1] The mortality associated with ectopic pregnancy is decreasing but remains at an estimated 0.2 per 1000 ectopic pregnancies. Of the women who died during 2006–08, half were from minority ethnic groups—and so may have accessed care later or experienced difficulty in communication—and most deaths were associated with substandard care due to failure to consider ectopic pregnancy when presentation was atypical.[2] Therefore, it is vital that healthcare professionals in all specialties are alert to the possibility of ectopic pregnancy in order to avoid missed opportunities for diagnosis. This article summarises the most recent recommendations from the National Institute for Health and Clinical Excellence (NICE) on the care for women with ectopic pregnancy and miscarriage.[3]

Recommendations

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in italics in square brackets.

Support and information giving

- Throughout a woman's care, give her and (with agreement) her partner, specific evidence based information in a variety of formats. This should include (as appropriate):

  -When and how to seek help if existing symptoms worsen or new symptoms develop, including a 24 hour contact telephone number.

  -What to expect during the time she is waiting for an ultrasound scan (for example, whether new symptoms might develop and what these are likely to be).

  -What to expect during the course of her care (including expectant management), such as the potential length and extent of pain or bleeding, and possible side effects. This information should be tailored to the care she receives.

  -Information about postoperative care (for women undergoing surgery).

  -What to expect during the recovery period (for example, when it is possible to resume sexual activity or try to conceive again, and what to do if she becomes pregnant again). This information should be tailored to the care she receives.

  -The likely impact of her treatment on future fertility.

  -Where to access support and counselling services, including leaflets, web addresses, and helpline numbers for support organisations.

Ensure that sufficient time is available to discuss these issues with women during the course of their care and arrange an additional appointment if more time is needed.

[*Based on high to very low quality evidence from randomised controlled trials, observational studies and qualitative studies*

Correspondence to: R Ullman rullman@ncc-wch.org.uk

and the experience and opinion of the Guideline Development Group (GDG)]

Initial assessment

- All healthcare professionals involved in the care of women of reproductive age should have access to pregnancy tests.

[*Based on the experience and opinion of the GDG*]

- During clinical assessment of women of reproductive age be aware that they may be pregnant. Consider offering a pregnancy test even when symptoms are non-specific, because the symptoms and signs of ectopic pregnancy can resemble those of other conditions (such as gastrointestinal conditions or urinary tract infection). Ectopic pregnancy can present with a variety of symptoms, and even if a symptom is less common it may still be important.
  Symptoms of ectopic pregnancy include
  -Common symptoms:
  Abdominal or pelvic pain

  Amenorrhoea or missed period

  Vaginal bleeding with or without clots

  -Other reported symptoms:
  Dizziness, fainting, or syncope

  Breast tenderness

  Gastrointestinal symptoms such as vomiting and diarrhoea

  Shoulder tip pain

  Urinary symptoms

  Passage of tissue

  Rectal pressure or pain on defecation.

[*Based on moderate to low quality evidence from observational studies and case series of women with ectopic pregnancy and the experience and opinion of the GDG*]

- Refer women immediately to an early pregnancy assessment service (or out of hours gynaecology service if this is not available) if they have a positive pregnancy test and any of the following:
  -Pain and abdominal tenderness

  -Pelvic tenderness

  -Cervical motion tenderness.

[*Based on the experience and opinion of the GDG*]

- Refer women to an early pregnancy assessment service (or out of hours gynaecology service if this is not available) if they have bleeding or other symptoms and signs of early pregnancy complications and any of the following:
  -Pain

  -A pregnancy of ≥6 weeks' gestation

  -A pregnancy of uncertain gestation.

The urgency of this referral depends on the clinical situation.

[*Based on the experience and opinion of the GDG*]

Early pregnancy assessment services

- Regional services should be organised so that an early pregnancy assessment service (see box 1) is available seven days a week for women with early pregnancy complications, where scanning can be carried out and decisions about management made.

[*Based on low to very low quality evidence from observational studies and the experience and opinion of the GDG*]

- Early pregnancy assessment services should accept self referrals from women who have had recurrent miscarriage or a previous ectopic or molar pregnancy. All other women with pain or bleeding should be assessed by a healthcare professional (such as a general practitioner, accident and emergency doctor, midwife, or nurse) before referral to an early pregnancy assessment service.

[*Based on the experience and opinion of the GDG*]

Ultrasonography for diagnosis

- Offer women who attend an early pregnancy assessment service (or out of hours gynaecology service if this is not available) a transvaginal ultrasound scan to identify the location of the pregnancy and whether there is a fetal pole and heartbeat.

[*Based on moderate to very low quality evidence from observational studies and the experience and opinion of the GDG*]

- Consider a transabdominal scan for women with an enlarged uterus or other pelvic pathology, such as fibroids or an ovarian cyst.

[*Based on the experience and opinion of the GDG*]

- If a transvaginal ultrasound scan is unacceptable to the woman, offer a transabdominal ultrasound scan and explain the limitations of this method of scanning.

[*Based on the experience and opinion of the GDG*]

Serum human chorionic gonadotrophin (hCG) measurements in women with pregnancy of unknown location

- Be aware that women with a pregnancy of unknown location could have an ectopic pregnancy until the location is determined.

[*Based on the experience and opinion of the GDG*]

- For a woman with a change in serum hCG concentration between a 50% decline and a 63% rise inclusive over 48 hours, refer for clinical review in the early pregnancy assessment service within 24 hours.

[*Based on low to very low quality evidence from observational studies*]

Management of miscarriage

Expectant management

- For women with a confirmed diagnosis of miscarriage (see box 2), use expectant management (waiting to see if the miscarriage will resolve naturally without intervention) for 7–14 days as the initial management strategy.
- Explore other management options if
  -The woman is at increased risk of haemorrhage (for example, she is in the late first trimester)

  -The woman has had previous adverse or traumatic experience associated with pregnancy (such as stillbirth, miscarriage, or antepartum haemorrhage)

  -The woman is at increased risk from the effects of haemorrhage (for example, if she has coagulopathies or is unable to have a blood transfusion)

  -There is evidence of infection.

[*Based on high to very low quality evidence from randomised controlled trials, a high quality economic evaluation, and the experience and opinion of the GDG*]

Box 1: Early pregnancy assessment service

An early pregnancy assessment service is a dedicated service provided by healthcare professionals competent to diagnose and care for women with complications in early pregnancy. It should offer ultrasound scanning and assessment of serum human chorionic gonadotrophin (hCG) levels and be staffed by healthcare professionals with training in sensitive communication and breaking bad news

Medical management

- Do not offer mifepristone as a treatment for missed or incomplete miscarriage (see box 2).

[*Based on moderate quality evidence from a randomised controlled trial*]

- Offer vaginal misoprostol for the medical treatment of missed or incomplete miscarriage. Oral administration is an acceptable alternative if this is the woman's preference.

[*Based on high to very low quality evidence from randomised controlled trials*]

Surgical management

- Where clinically appropriate, offer women undergoing a miscarriage a choice of

  -Manual vacuum aspiration under local anaesthetic in an outpatient or clinic setting

  -Surgical management in a theatre under general anaesthetic.

[*Based on moderate to very low quality evidence from one randomised controlled trial and observational studies*]

Management of ectopic pregnancy

Surgical and medical management

- Offer systemic methotrexate as a first line treatment to women who are able to return for follow-up and who have all of the following:

  -No significant pain

  -Unruptured ectopic pregnancy with an adnexal mass <35 mm with no visible heartbeat

  -Serum hCG concentration <1500 IU/L

  -No intrauterine pregnancy (confirmed on an ultrasound scan).

Offer surgery if treatment with methotrexate is not acceptable to the woman.

[*Based on high to low quality evidence from randomised controlled trials, a health economic model developed for the guideline and the experience and opinion of the GDG*]

- Offer surgery as a first line treatment to women with an ectopic pregnancy who are unable to return for follow-up after methotrexate treatment or who have any of the following:

  -Significant pain

  -Adnexal mass of ≥35 mm

  -Fetal heartbeat visible on ultrasound scan

  -Serum hCG level ≥5000 IU/L.

[*Based on high to low quality evidence from randomised controlled trials and the experience and opinion of the GDG*]

- Offer the choice of either methotrexate or surgical management to women with an ectopic pregnancy who have a serum hCG level of ≥1500 IU/L and <5000 IU/L, who are able to return for follow-up, and who meet all of the following criteria:

  -No significant pain

  -Unruptured ectopic pregnancy with an adnexal mass <35 mm with no visible heartbeat

  -No intrauterine pregnancy (confirmed on an ultrasound scan).

Advise women who choose methotrexate that their chance of needing further intervention is increased and they may need to be urgently admitted if their condition deteriorates.

[*Based on high to low quality evidence from randomised controlled trials, a health economic model developed for the guideline and the experience and opinion of the GDG*]

Performing laparoscopy

- When surgical treatment is indicated for women with an ectopic pregnancy, it should be performed laparoscopically whenever possible, taking into account the condition of the woman and the complexity of the surgical procedure.

[*Based on moderate to very low quality evidence from randomised controlled trials and observational studies*]

Salpingectomy and salpingotomy

- Offer a salpingectomy to women undergoing surgery for an ectopic pregnancy unless they have other risk factors for infertility, in which case consider salpingotomy.

[*Based on very low quality evidence from observational studies*]

Overcoming barriers

The guideline recommends transvaginal rather than transabdominal ultrasound scanning for most women with suspected complications in early pregnancy. This may require a shift in practice in some units, and may have implications for training of healthcare professionals: for example, junior doctors in the UK currently receive routine core training in transabdominal scanning for early pregnancy care, with transvaginal scanning taught only to interested trainees at a later stage of training. However, a shift towards transvaginal scanning in early pregnancy is likely to result in more accurate diagnoses and consequently in fewer scans being performed.

Recommending 7–14 days of expectant management as first line treatment for most women with miscarriage may be perceived by healthcare professionals and women as a barrier to women's choice. However, the explicit recommendations about the information and support that women should receive may resolve many of these concerns. Where expectant management is not acceptable to women, the guideline recommends offering medical management.

Recommendations for a dedicated early pregnancy assessment service available seven days a week may cause concern about substantial expenditure; however, rotating weekend cover between several units could achieve the recommended accessibility without overburdening individual facilities. Similarly, the guideline does not recommend that the services be available 24 hours a day, so it is anticipated that minimal reconfiguration of the system could provide suitable cover without increasing the operating budget. The guideline recommends that most women be triaged by another healthcare professional before referral to an early pregnancy assessment

Box 2: Terms used to describe miscarriage in the first trimester

Complete miscarriage—The term used after an intrauterine pregnancy when all pregnancy tissue has left the uterus

Confirmed miscarriage—A non-viable intrauterine pregnancy, as diagnosed on one or more ultrasound scans

Incomplete miscarriage—A diagnosed non-viable pregnancy in which the process of miscarriage (such as bleeding and pain) has begun, but pregnancy tissue remains in the uterus

Missed miscarriage—A non-viable pregnancy identified on ultrasound scan, without associated bleeding and pain (also known as early fetal demise, delayed miscarriage, or silent miscarriage)

Threatened miscarriage—Vaginal bleeding in the presence of a viable pregnancy

service, with guidance on when to refer, to ensure optimal care and appropriate use of this service.

The members of the Guideline Development Group were Lauren Bardisa-Ezcurra (until April 2011), Zosia Beckles, Liz Bickerdike, Fiona Blake, Nicola Davies, Karen Easton, Roy Farquharson, Joanne Fletcher, Rupert Franklin, Maryam Gholitabar, Paul Jacklin, David James, Liz Jones (until July 2011), Mary Ann Lumsden (chair), Emma Newbatt, Julie Orford (from July 2011), Caroline Overton, Shammi Ramlakhan, Roz Ullman, and Helen Wilkinson.

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Further information on the guidance

This guideline was prompted by concern about the mortality that continues to be associated with ectopic pregnancy, and, in particular, the deaths that occurred as a result of missed opportunities for diagnosis. During the period of 2006–08, two thirds of the women who died as a result of an ectopic pregnancy in the first trimester presented with diarrhoea, dizziness, or vomiting, but in each case the attending healthcare professional did not consider the possibility of an ectopic pregnancy. The subsequent rupture of the ectopic pregnancy caused deaths that could have been prevented if the diagnosis had been made earlier.[2] There is also variation in practice and availability of services for women with complications in early pregnancy. For example, it is widely believed that care in a dedicated early pregnancy assessment service results in improved outcomes for women, but such facilities are not available everywhere, and where they do exist the organisation and accessibility of the service vary considerably.[4]

Methods

This guidance was developed by the National Collaborating Centre for Women's and Children's Health in accordance with NICE guideline development methods (www.nice.org.uk/guidelinesmanual). A Guideline Development Group (GDG) was established by the National Collaborating Centre for Women's and Children's Health, which incorporated healthcare professionals (gynaecologists, nurses, a general practitioner, a psychiatrist, and a consultant in emergency medicine), women with experience of miscarriage or ectopic pregnancy, and experts in guideline methodology. The GDG identified relevant clinical questions, collected and appraised clinical evidence, and evaluated the cost effectiveness of proposed interventions where possible. The draft guideline underwent a public consultation in which stakeholder organisations were invited to comment; the GDG then took all comments into consideration when producing the final version of the guideline.

Four different versions of this guideline have been produced: a full version containing all the evidence, the process undertaken to develop the recommendations, and all the recommendations; a care pathway; a version containing a list of all the recommendations, known as the "NICE guideline"; and a version for patients and the public. All of these versions are available from the NICE website (www.nice.org.uk/CG154).

Future research

The GDG identified five key areas for future research:

- A national evaluation of service provision of early pregnancy assessment units should be carried out to identify factors affecting outcomes
- How does the timing and frequency of ultrasound examination affect diagnosis and outcomes of early pregnancy complications, including women's experience and cost effectiveness?
- Are progesterone or progestogens effective in treating threatened miscarriage?
- In women with confirmed miscarriage, does the type of management strategy (expectant, medical, or surgical) affect women's experiences, including psychological and emotional outcomes?
- In women with ectopic pregnancy, does the type of intervention (laparoscopy or medical management) affect women's experiences, including psychological and emotional outcomes?