An alternative to surgery in treating ectopic pregnancy

**AUTHOR** Linda Scott, BSc, RGN, is nursing sister, pregnancy support centre, Edinburgh Royal Infirmary.


In an ectopic pregnancy the fertilised egg becomes implanted outside the uterus. It affects around one in every hundred pregnancies. Traditionally the condition has been managed surgically. However, in recent years many women have been treated with methotrexate therapy.

Ectopic pregnancy affects 11.5 per 1,000 pregnancies annually in the UK. It is potentially fatal and is responsible for approximately five maternal deaths in the UK each year (RCOG, 2004). A diagnosis of ectopic pregnancy should be considered when:

- A fertilised egg is seen outside the uterus on ultrasound scan;
- An empty uterus is seen with a suboptimal rise in human chorionic gonadotropin (hCG) <66% in 48 hours;
- An empty uterus is seen with an undefined adnexal mass and/or small free fluid;
- An empty uterus is seen with no chorionic villi on endometrial sample and is unlikely to signal an early pregnancy failure.

The most common site for ectopic pregnancy is the ampullary end of the fallopian tube. However, there are several sites where ectopic pregnancy may develop (Box 1) (Sepilian, 2005).

**Causes**

One of the main causes of ectopic pregnancy is pelvic inflammatory disease, which is principally due to *Chlamydia trachomatis* (Sepilian, 2005). Pelvic inflammatory disease leads to deciliation of the lining of the fallopian tubes. The cilia transport the fertilised egg into the uterus where it should implant and develop. If the cilia are damaged and unable to move the egg to the correct place it may implant and begin to grow.

Other causes of ectopic pregnancy include:

- Tubal pathology as a result of infection or previous pelvic surgery, which can lead to the formation of adhesions. This causes problems with patency due to narrowing or scarring, or with function, which can delay the passage of the egg (Sepilian, 2005);
- Of patients who conceive following sterilisation, 35–50% experience ectopic pregnancy (Sepilian, 2005);
- Ectopic pregnancy is most common in women aged 35 to 44. This rate is four times higher than in women aged 15 to 24, which is probably due to progressive loss of myoelectrical activity along the fallopian tube (Sepilian, 2005);
- Use of an intrauterine contraceptive device (IUCD) is responsible for 3–4% of ectopic pregnancies. The IUCD does not actually cause ectopic pregnancy but prevents intrauterine pregnancy so pregnancies that result are more likely to be ectopic (Sepilian, 2005).

Ectopic pregnancy becomes life-threatening due to the high risk of haemorrhage as the trophoblast invades the surrounding tissue. The risk of haemorrhage is increased in cervical, abdominal and cornual ectopic pregnancies (Sepilian, 2005).

**Treatment**

Historically ectopic pregnancy was treated with surgery, either a laparotomy with a salpingectomy or salpingostomy. Advances in laparoscopic techniques have led to most ectopic pregnancies being removed by this technique, which carries lower morbidity than major surgery. However, some units now offer medical management with the use of single dose intramuscular methotrexate.

The first recorded use of methotrexate to treat ectopic pregnancy was in 1982 (Tanaka, 1982). It works by interfering with the way the body processes folate, which is a vitamin necessary in the development of the rapidly growing pregnancy cells. This stops the pregnancy from developing any further and it is then reabsorbed by the body.

However, it is important to be aware that methotrexate is not appropriate for all women with ectopic pregnancy (Box 2, p26). It is therefore important that units that offer this form of...
management have a policy to determine whether methotrexate is suitable for the patient.

The Royal College of Obstetricians and Gynaecologists produced a guideline in May 2004 that can be used to structure such local policies. It is advised that methotrexate is appropriate if the patient has minimal symptoms and an hCG level below 3,000iu/L (RCOG, 2004). This treatment is contraindicated if a mass is seen on ultrasound scan that is larger than 4cm and there is moderate or significant free fluid (RCOG, 2004).

It can be useful to create a checklist that staff can complete if they are considering using methotrexate. This ensures that errors of omission are eliminated as all aspects of the treatment must be considered before administration of the treatment.

Nurse role

The role of the nurse in methotrexate therapy will depend on the unit in which she or he works. In nurse-led units where the patient is initially seen by a nurse, she or he will be responsible for informing the patient of the diagnosis and discussing treatment options with them. The nurse will then support the patient during the decision-making process. When the patient feels they have made their choice the medical staff will be informed and will also become involved in the care.

In other units patients are seen by a doctor who will provide them with this information and help them to decide which treatment option would be the most appropriate. In these situations nurses are usually also present and contribute to the psychological support of patients during this difficult time. However, in all units the ultimate decision on whether the patient is given methotrexate is made by the consultant in charge of the case.

It can take several days to establish the diagnosis and confirm whether the patient meets the criteria to allow treatment with methotrexate. During this time the patient must be kept fully informed of the possible diagnosis and therapies that are available. It is important that they are told that it is not advisable to become pregnant for three months following treatment with methotrexate as it could cause teratogenic damage to a developing foetus (RCOG, 2004).

Patients should also be given written information to help them to understand and reach a decision about whether they would prefer methotrexate rather than surgery if they are clinically suitable (RCOG, 2004).

Administration

Once it has been confirmed that the patient is to have methotrexate there are a few procedures that are required prior to administration of the therapy. Blood should be taken to determine the patient’s blood group. In addition a full blood count, urea and electrolytes, and liver function tests should be undertaken. They should also be screened for C. trachomatis (RCOG, 2004).

On the day the methotrexate is given the patient must have their hCG level measured to ensure it remains at an acceptable level. They should also have an ultrasound scan to ensure that the size of the mass and level of free fluid remain within appropriate limits. The patient should have their height and weight recorded as the dose of methotrexate is calculated according to the patient’s body surface area (50mg/m²).

Patients must sign a consent form before they are given methotrexate. It is also good practice to ask them to read through and then sign an information checklist on methotrexate. The patient should be given a copy of this form to take home.

Before the medication is given two nurses should complete a checklist to ensure that the correct procedures prior to administration of methotrexate have been adhered to and that follow-up arrangements have been made.

Methotrexate is administered by intramuscular injection. The most usual site for this is the gluteus maximus. However, it is important that the drug reaches muscle so if there is doubt of this due to a covering of fat it should be given into the deltoid muscle instead.

Nurses must be aware that methotrexate is a cytotoxic drug and therefore appropriate precautions should be followed during administration.

The efficacy of the treatment is measured by tracking the level of hCG. The patient should return for follow-up measurement of this after the methotrexate treatment.

The day on which they attend may vary between units but one example of a regimen is for attendance on days four, seven and eleven (RCOG, 2004). If their hCG level fails to fall more than 15% between days four and seven a repeat dose may be necessary (RCOG, 2004).

Patients should also have their full blood count,
urea and electrolytes, and liver function tests repeated on days four and eleven (RCOG, 2004). If the blood test results are satisfactory the patient should then attend the hospital or clinic weekly until the hCG is less than 5iu/L (the non-pregnant level may vary between units) (RCOG, 2004).

### Side-effects

It is important that the patient is aware of the side-effects of methotrexate as 75% of patients will experience pain (RCOG, 2004). Other side-effects include gastrointestinal upset, stomatitis, conjunctivitis and transient elevation in liver enzymes (Sepilian, 2005).

While 15% of women require more than one dose of methotrexate, 10% of women will require surgical intervention and 7% of patients will rupture their tube during follow-up (RCOG, 2004). Therefore, the patient must have emergency contact details and be instructed to get in touch with the hospital if they have any concerns.

There are variations in the reports of success following the administration of methotrexate, which range from 88% to 94% (Sepilian, 2005). An important predictor of success is the level of hCG prior to treatment.

Lipscomb (1999) noted that ‘among women with tubal ectopic pregnancy a high hCG is the most important factor associated with failure of treatment with a single dose methotrexate protocol’.

Potter (2003) reported the following outcomes:
- hCG <1,000iu/L – 98% success;
- hCG 1,000 – 5,000iu/L – 80% success;
- hCG > 5,000iu/L – 38% success.

Other studies have shown that progesterone levels affect success. Lipscomb et al (2004) found that success was most likely in women with mean levels of 6.7ng/ml. Failure was most likely for women with mean levels of 10.7ng/ml. Bixby (2005) found that 88% of patients in whom a yolk sac was present had treatment failure.

Those with a history of ectopic pregnancy showed an increase in failure rates (Lipscomb et al, 2004), which may be due to poor blood supply to a damaged tube (Gallagher, 2003).

The presence of a foetal heart is also a predictor of failure (Lipscomb et al, 2004; RCOG, 2004) but studies into the effect of age and parity showed no differences in the effect of methotrexate (Lipscomb et al, 2004).

### Discharge

When the patient’s hCG levels have reached the level of a woman who is not pregnant they can then be discharged. Prior to discharge the patient should be reminded to avoid pregnancy for three months (RCOG, 2004). She should also be informed that although she has an increased risk of developing a further ectopic pregnancy, the chance is less than one in ten (Sepilian, 2005). She should be advised to contact her local early pregnancy unit if she becomes pregnant so that she can access early ultrasound scanning and professional support.

The success rates for future pregnancies following administration of methotrexate are comparable with those subsequent to surgical procedures for treatment of ectopic pregnancy (Sepilian, 2005).

### Conclusion

Methotrexate is an excellent alternative therapy to surgery for certain patients with ectopic pregnancy and should therefore be considered for all patients who meet the eligibility criteria. Methotrexate has particular advantages in ectopic pregnancies that carry the greatest risk of haemorrhage such as cervical, abdominal and cornual ectopic pregnancies (Sepilian, 2005).
REFERENCES

Reference name. (1999) 'Reference title' of the source document follows the authors name. Publishers name follows in 'Ref. body' text style. Note all right hand side-text columns containing reference information always have the copy range left.

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