

MANAGEMENT OF EARLY PREGNANCY LOSS

Early pregnancy loss is a traumatic experience for any woman.

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A miscarriage is a pregnancy that ends spontaneously before the fetus has reached a viable gestational age. This definition equates both clinically and legally to a pregnancy that ends before 24 weeks of gestation (or a fetus of less than 500 g). An early pregnancy loss (EPL) refers to a miscarriage before 13 weeks' gestation (first-trimester miscarriage). It is the most common complication of human reproduction, affecting 50 - 70% of all conceptions, with the vast majority occurring early – before implantation and before the missed menstrual period. The incidence of clinically recognisable first-trimester miscarriage is about 15% and no more than 1 - 2% of pregnancies will miscarry spontaneously after the first trimester.

Pregnancy losses from ectopic pregnancy and gestational trophoblastic disease will not be dealt with in detail. Suffice it to say that they must be excluded in every clinical presentation of vaginal bleeding and pain after a period of amenorrhoea or a positive pregnancy test. Women suffering from recurrent EPL (3 or more consecutive first-trimester miscarriages) require referral for specialist care.

Although approximately 15% of all clinically recognised pregnancies end in spontaneous miscarriage worldwide, there are also an estimated 46 million induced abortions annually (WHO, 1997). The majority of these are performed illegally in unsafe conditions. They cause septicaemia and haemorrhage, resulting in approximately 78 000 deaths annually worldwide. Even though termination of pregnancy is legalised in South Africa, we must always be aware of the possibility of induced abortion. Not all women have access to state facilities or they might not use the service for fear of recrimination, either from society or the health service providers.

Miscarriage is one of the commonest gynaecological indications for admission to hospital and for emergency gynaecological surgery. This is costly for the health services as it has an impact on bed occupancy, surgical workload and theatre time.

Recognising the impact of miscarriage on the couple and the health service, all primary health care professionals must be able to manage, counsel and advise couples who have sustained a pregnancy loss.

AETIOLOGY

In the majority of women a chance occurrence due to random chromosomal abnormalities is responsible for EPL, and therefore it is not necessary to perform any investigations. Random chromosomal abnormalities are responsible for about two-thirds of all EPLs. The risk of recurrent miscarriage due to a chromosomal cause may occur where one of the parents has a balanced chromosomal translocation.

Poor implantation and placentation possibly also play an important role, but routine clinical tests to ascertain the cause are not currently available. Inadequate progesterone secretion to maintain the early pregnancy is related to a defective corpus luteum; however, progesterone replacement is probably of limited benefit apart from its established role in assisted conception cycles.

TERMINOLOGY AND TYPES OF EPL

The terms spontaneous abortion, pregnancy failure and abnormal pregnancy should not be used as they may contribute to the development of negative self-perceptions

in women already feeling a sense of failure, guilt and perhaps shame. In 1997 the Royal College of Obstetricians and Gynaecologists recommended that the term miscarriage replace spontaneous abortion, and incomplete miscarriage replace incomplete abortion.

The introduction of transvaginal ultrasonography (TVS) has given insight into the different types of EPL. Previously used terminology such as blighted ovum and missed miscarriage are inappropriate. There is no such entity as a blighted ovum, and a missed miscarriage was a diagnosis made before the advent of ultrasonography when there was at least an 8-week difference in clinical palpation of gestational age versus the patient's menstrual dates. What was previously called a blighted ovum is really an anembryonic pregnancy. A missed miscarriage is seen on ultrasound as the presence of an embryo or a fetus without cardiac pulsations and is now referred to as embryonic or fetal demise. Both anembryonic pregnancy and embryonic/fetal demise are seen at different stages of the same clinical process and the recommended alternative terminology of early fetal demise should be used for both. Table I lists the classification of miscarriage.

Table I. **Classification of miscarriage**

Spontaneous
• Threatened
• Inevitable
• Incomplete
• Complete
• Early fetal demise
Induced
• Therapeutic termination of pregnancy
• Unsafe/illegal termination of pregnancy

DIAGNOSIS

Both the clinical presentation and TVS are used in making the appropriate diagnosis in women presenting with vaginal bleeding and/or pain after

a period of amenorrhoea. In less obvious cases, such as women with irregular menses and an adnexal mass, a urine or serum β hCG, in addition to ultrasonography, will be of value in excluding ectopic pregnancy.

Threatened miscarriage

The patient presents with a history of painless vaginal bleeding after a period of amenorrhoea. She has not passed any tissue or leaked any amniotic fluid. Clinical examination will reveal a haemodynamically stable patient with no evidence of pelvic tenderness, and the cervical os is closed on gynaecological examination. Bleeding through the cervical canal may be noted or old blood may be seen in the posterior fornix of the vagina. Bleeding from another source, such as a lesion on the cervix, or urethral or rectal bleeding, must be excluded. TVS will reveal an intrauterine gestational sac containing an embryo with cardiac pulsations.

Management includes reassurance and counselling. The chance of a successful pregnancy is in the order of 98 - 99%. No medical therapy is indicated unless the conception had resulted from *in vitro* fertilisation where luteal support is usually prescribed. Avoidance of sexual intercourse may be of psychological benefit to the patient, but she may continue with her normal daily activities. If the bleeding or pain intensifies, or if any tissue is passed, she should return for immediate re-evaluation. There is no need for anti-D immune globulin in an Rh-negative mother with threatened miscarriage under 12 weeks' gestation.

Inevitable miscarriage

The prognosis for the pregnancy is poor if there is a worsening of the pain and bleeding. Blood clots are often passed per vagina, but not any tissue. Examination will reveal suprapubic and uterine tenderness and the cervix will be dilated. The process is now irreversible, and the uterine contractions will ultimately cause the patient to miscarry.

Management depends on the patient's general condition and the duration of the pregnancy. She may require resuscitation and blood transfusion if she is haemodynamically unstable. In first-trimester miscarriage, pain relief will suffice and the patient may miscarry completely. In the second trimester, oxytocin in addition to pain relief is administered until the fetus is passed, and then the patient is assessed as to whether the miscarriage is complete (placenta expelled completely) or incomplete.

Incomplete miscarriage

The history is one of passage of blood with clots and tissue (the products of conception). Examination may reveal a stable patient or one who is bleeding profusely, is pale and may or may not be in haemodynamic shock. Abdominal palpation may reveal an enlarged uterus that may also be tender. On pelvic examination the cervical os will be open and products of conception may be palpated either in the vagina or within the dilated cervix. In this situation the diagnosis is a clinical one without the need for pelvic ultrasound. It is prudent to remove products which may be at the external cervical os as this will help to relieve the pain experienced by the patient and also to reduce the amount of bleeding. In some situations there may be bleeding in the presence of an open cervical os or an os that admits the tip of the finger, without any palpable products of conception. TVS in this situation may help to confirm whether the miscarriage is complete or incomplete. Many studies have used the presence of heterogeneous echogenic material in the uterine cavity with an endometrial thickness of greater than 15 mm to designate retained products of conception or incomplete miscarriage necessitating surgical evacuation.

Complete miscarriage

The patient passes the entire product of conception intact after significant cramping, bleeding and the passage of clots. In early miscarriage (less than 6 weeks) there may be less cramping and the bleeding may subside within 48 hours. In cases of second-trimester

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miscarriage, the diagnosis may be confirmed if the fetus and entire placenta are delivered. If the products were passed unnoticed, for instance in a toilet, clinical examination will confirm a normal-sized uterus with a closed cervical os. TVS may also confirm an empty uterine cavity and an endometrial thickness of less than 15 mm. The bleeding will have subsided, and there is no need for further medical or surgical intervention. If there is uncertainty, the patient is managed as a pregnancy of unknown location with serial β hCG and TVS. This will confirm or exclude a complete miscarriage, early intrauterine gestation or an ectopic pregnancy. The β hCG falls and should return to negative within 3 weeks after a complete miscarriage.

Early fetal demise

Some intrauterine pregnancies may undergo spontaneous embryonic/fetal death. These patients may be asymptomatic or may present with vaginal bleeding after a period of amenorrhoea and a positive pregnancy test. The diagnosis is made on ultrasonography when no cardiac motion is observed in the embryo or fetus. The role of ultrasound in the diagnosis of early pregnancy and its complications cannot be overstated, and it is of vital importance in the diagnosis of early 'fetal' demise. TVS is preferred, given that embryonic structures are seen 1 week earlier when compared with transabdominal ultrasound. The normal gestational sac may first be seen 29 - 32 days after the last menstrual period. The

yolk sac is the first structure to become visible within the gestational sac. It is about 8 mm in diameter at about 5 weeks (day 35), and should always be seen when the mean gestational sac diameter is greater than 11 mm. The embryo may be visible as early as 5 weeks; however, the heartbeat will not be detected in all embryos with a crown-rump length (CRL) of 3 mm. At 6 weeks the gestational sac diameter is greater than 14 mm, the CRL is 5 mm, and there is a visible heartbeat.

Early embryonic demise is defined as an intact gestational sac of greater than 20 mm mean diameter with no other internal structures, and early fetal demise as a 'fetus' of over 6 mm CRL with no heart activity on TVS.

MANAGEMENT

For more than 60 years the standard management of EPL (first-trimester miscarriage) has been surgical evacuation of the products of conception by dilatation and curettage (D&C). Although commonly performed, a D&C is not an entirely innocuous procedure. Aside from the small anaesthetic risk, it has been associated with a 4 - 10% rate of early complications, including infection, bleeding and, less frequently, injuries to the cervix and uterine perforation. This may predispose patients to secondary infertility, pelvic pain and an increased risk of ectopic pregnancy. The advent and widespread use of antibiotics, improved general health of women, easy access to health services, early diagnosis of miscarriage by ultrasound and legalisation of termination of pregnancy have resulted in the evaluation of non-surgical methods for the treatment of EPL.

Alternative treatment options for EPL include outpatient manual vacuum aspiration, medical management using prostaglandin analogues, or expectant management. The MIST trial by Trinder *et al.* (2006) found a low incidence of gynaecological infection (2 - 3%) after surgical, expectant and medical management of first-trimester miscarriage, and no

evidence of a difference resulting from the method of management. Clinicians may offer women one of three options and, depending on individual circumstances, will be able to recommend one option or the other. Women are now able to make an informed choice regarding their options for treatment of their miscarriage. Certain criteria, however, need to be fulfilled before embarking on medical or expectant management of miscarriage.

Surgical: dilatation and curettage and manual vacuum aspiration

This option of management remains standard treatment for the evacuation of the retained products of conception. The other modalities of medical and expectant management have to be complemented by surgical intervention in cases of incomplete medical or spontaneous evacuation of the products of conception.

Women may now choose either surgical, medical or expectant management. Surgical management has several advantages, including that it is a quick procedure which may be performed at the first visit as a day case, giving early resolution of the pregnancy loss. The patient may also have other responsibilities around family and domestic issues or work-related deadlines that may preclude frequent outpatient visits for medical or expectant management. She may be emotionally upset and may not want to carry an abnormal pregnancy while undergoing expectant management. It is imperative in all situations that the patient is appropriately counselled before she accepts one of the modalities of management.

Suction curettage is favoured over sharp curettage as it is associated with less pain and intraoperative bleeding, lower risk of uterine perforation and shorter theatre time. It may be performed in an outpatient setting using manual vacuum aspiration in cases of incomplete miscarriage. Women with early fetal loss (cervix closed) will require dilatation of the cervix under general anaesthesia in

theatre before suction curettage. To reduce the risk of cervical trauma the cervix may be primed with a prostaglandin analogue such as misoprostol 200 µg 2 - 4 hours preoperatively.

Medical management

Medical treatment using misoprostol, a prostaglandin E₁ analogue, has been increasingly used over the past decade in women with EPL. It has been shown to be 80 - 100% effective in the evacuation of incomplete miscarriage. In cases of early fetal demise it is associated with a success rate of 60 - 90%. The varying success rates are attributed to the various dosing regimens used, different routes of administration (oral or vaginal) and different definitions of success (the time allowed until surgical evacuation is performed).

Exclusion criteria for medical management include the following:

- unable to attend for outpatient visits
- haemodynamically unstable
- anaemia (haemoglobin below 10.0 mg/dl)
- a history of a clotting disorder or use of anticoagulants
- allergy to prostaglandins or non-steroidal anti-inflammatory drugs
- severe asthma
- mitral stenosis
- signs of severe infection (temperature > 37.5 °C) or
- any suspicion of an ectopic pregnancy.

The side-effects of misoprostol are mainly gastrointestinal and include nausea, vomiting and diarrhoea. Misoprostol 600 - 800 µg used vaginally and repeated if necessary after 48 - 72 hours has been found to be effective and acceptable. About one-third of women may have successful evacuation of the uterus after one dose and the higher rate of success is dependent on the period of time used to assess success, with 7 - 10 days being better than 3 - 5 days. Women find medical management acceptable when they are informed that if the miscarriage is not complete within a specific time frame (e.g. 1

week), surgical evacuation will be performed. The latter may be required in 10% of women who have embarked on medical treatment.

It is imperative to ensure adequate follow-up to ascertain resolution of the pregnancy loss with a negative urine βhCG. This also helps to exclude trophoblastic disease (hydatidiform mole). Rhesus-negative women must receive anti-D immunoprophylaxis if subjected to medical or surgical management of a first-trimester miscarriage.

Expectant management

Some women may choose expectant management of their miscarriage. Expectant management of incomplete miscarriage results in a cumulative success rate after 1, 2, 3, and 4 weeks of follow-up of 54%, 83%, 89% and 91% respectively. Expectant management may, however, not be an attractive option in women experiencing early fetal demise without vaginal bleeding, as a success rate as low as 25% has been reported after 6 weeks of follow-up.

It is therefore important that women are counselled appropriately regarding the need for prolonged follow-up and ready access to the health facility. There is no need to administer anti-D to rhesus-negative women undergoing expectant management of EPL.

CONCLUSION

EPL is the commonest complication of pregnancy (20%), which has traditionally been managed by surgical curettage. Research over the past two decades has supported the options of medical and expectant management. With appropriate counselling women are now able to make an informed choice regarding the various treatment options. All three modes of therapy have advantages and disadvantages, which need to be considered according to the individual needs of each patient. The MIST trial by Trinder and colleagues puts to rest the perceived increased risk of infection if immediate surgical treatment of miscarriage is not offered.

Further reading

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IN A NUTSHELL

Miscarriage is the commonest complication of pregnancy.

Historically, surgical evacuation was the treatment of choice to prevent death from haemorrhage and sepsis.

Access to medical care, progress in ultrasonography and legalisation of abortion have allowed the use of conservative treatment such as medical and expectant management.

Transvaginal ultrasound is essential in making a diagnosis of early fetal demise.

Surgical evacuation after resuscitation remains the gold standard for treatment of women who are haemodynamically unstable or who have concurrent sepsis.

Appropriate counselling, availability of transport and access to the health care facility are prerequisites to conservative treatment of miscarriage.

Clinicians must know the exclusion criteria before embarking on medical treatment with misoprostol.

All rhesus-negative women receiving surgical and medical management of first-trimester miscarriage must receive anti-D immunoprophylaxis.