

The medical management of
ectopic pregnancy cannot be
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discuss

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Introduction

Ectopic pregnancy can be defined as the implantation and maturation of a conceptus outside of the uterine cavity and still accounts for approximately 11 in 1000 pregnancies in the UK today (1). The current Green-top 21 guidelines published by the Royal College of Obstetricians and Gynaecologists (RCOG) recommend three main approaches towards the management of tubal pregnancy; a surgical approach via laparotomy or laparoscopic salpingectomy or salpingostomy, medical treatment via systemic drug injection or occasionally by expectant management with careful observation alone (2).

A variety of medical interventions have been studied in the treatment of ectopic pregnancy, including the use of prostaglandins and hyperosmolar glucose (3). However, intramuscular methotrexate is the most widely used, a folate antagonist aimed at arresting development of the conceptus, resulting in subsequent termination of the pregnancy. Doses are based on the patient's body surface area, calculated at $50\text{mg}/\text{m}^2$ and follow-up involves close monitoring of serum β -hCG levels on days 4 and 7 post-injection (4).

Current guidelines for use of medical management in ectopic pregnancy

Many studies have demonstrated the successful use of single-dose methotrexate as a viable alternative to surgical intervention in the treatment of patients with ectopic pregnancy. Utilising transvaginal ultrasonography and serum β -hCG levels to make a confident clinical diagnosis, in properly selected patients, success rates equal that of surgery, at approximately 90% (3). Currently around 35% of patients are managed medically; however, importantly, this form of treatment is only appropriate for a certain subset of patients. The RCOG guidelines state that systemic methotrexate should be offered as first-line treatment to women who have; no significant pain, an unruptured ectopic pregnancy with an adnexal mass $<35\text{mm}$ with no fetal cardiac activity, a serum β -hCG $<1500\text{iu}/\text{L}$ and no intrauterine pregnancy as confirmed by USS (4).

It is also important to consider the contraindications to medical management, for example in patients who are haemodynamically unstable, or those with hepatic or renal impairment, immunodeficiency or active infection. Such patients should be managed surgically and therefore will not be discussed here.

Medical versus Surgical Management of Ectopic Pregnancy

Cochrane systematic review results

A systematic review published in 2009 evaluated the effectiveness and safety of the different management options for ectopic pregnancy, comparing treatment successes and other factors such as tubal preservation and future fertility (3). Direct comparison of systemic methotrexate treatment and laparoscopic salpingostomy revealed no significant difference in primary treatment outcomes with the use of a fixed multiple dose regimen or variable dose injection. However, single dose intramuscular injection was shown to have reduced efficacy compared to surgery, with a combined odds ratio of 0.38 in favour of a surgical approach, as shown in figure 1. This suggests that medical management does indeed have a role in the first-line management of ectopic pregnancy; however the dosage of methotrexate needs to be carefully considered. For example, some women may require a subsequent methotrexate injection if β -hCG levels do not fall by at least 15% between day 4 and 7 (2).

There was also no significant difference between the two interventions in terms of subsequent intrauterine pregnancy, recurrent ectopic pregnancy and tubal patency, suggesting that in patients whose concerns lie in these particular areas, there is no advantage in using medical management preferentially over a surgical approach, and vice versa. Therefore in patients meeting the RCOG criteria, medical management may certainly be appropriate for first-line treatment of ectopic pregnancy.

The role of medical management

First-line treatment with methotrexate in ectopic pregnancy holds many advantages, particularly in bypassing the need for surgery and its associated risks, such as those involving general anaesthesia. Medical management may also be the most optimal choice for patients with previous surgical adhesions, preventing the development of scar tissue, maintaining fallopian tubal patency and thus preserving fertility.

The loss in physical function occurring in individuals following a surgical procedure and hospital admission is also avoided in patients managed medically. Sowter et al. conducted a randomised controlled trial which identified significantly higher physical functioning at day 4 in patients treated with methotrexate versus those managed by laparoscopy, as measured by the Short Form-36 health survey (5).

A single injection of methotrexate administered in the outpatient setting also holds substantial financial benefit, something which is particularly relevant in the current economic climate. Data suggests that in patients meeting the aforementioned criteria for medical management, costs for systemic methotrexate treatment are below half that of laparoscopic surgery (6). Costs may be reduced both directly, due to lack of hospitalisation and removing the cost associated with the surgical procedure itself, and indirectly due to reducing time spent off work.

Disadvantages of medical management and the role of surgery

A major flaw in the use of methotrexate in the treatment of ectopic pregnancy is the risk of tubal rupture, a life-threatening medical emergency which occurs in an estimated 7% of patients following medical management, according to pooled data from uncontrolled studies (7). Although this risk, however small, is present in all patients diagnosed with ectopic pregnancy, the use of surgery as first-line treatment eliminates the possibility of tubal rupture and reduces the risk of maternal mortality associated with it. Figures from a large analysis of 315 ectopic pregnancies found that 7% of patients went on to require surgery despite initial methotrexate therapy, favouring the argument that surgery is the better option for first-line management (8). With this method, patients' and health professionals' time is saved, along with trust funds and the potential complications of requiring a longer treatment course are avoided.

The significant side effect profile associated with the use of methotrexate also makes it a less attractive option in the management of ectopic pregnancy. Up to 75% of patients will experience abdominal pain following treatment (8) which may prompt surgical intervention to avoid suspected tubal rupture. Other rarer adverse effects include conjunctivitis, gastrointestinal upset and bone marrow suppression (8). Some patients may not be able to tolerate such adverse effects, particularly those with pre-

existing disease and another option might be more appropriate such as expectant management, if the criteria are fulfilled.

The current NICE guidelines state that any woman with a β -hCG level between 1500iu/L and 5000iu/L, meeting the additional criteria detailed previously, may choose between surgical and medical management (4). However, there is clear evidence that at higher β -hCG levels, the success of methotrexate therapy declines, risk of tubal rupture increases and the need for surgical intervention is greater (9). Any financial benefit of medical therapy is also lost due to the increased follow up required and subsequent treatment delivered. In these circumstances, it is important to clearly inform patients of the risks and benefits of both treatments, involve them in the decision making process and take in to account any other factors which may influence their decision.

Psychological considerations

A pregnancy outside of the uterine cavity is incompatible with foetal survival, hence the diagnosis of an ectopic pregnancy presents a variety of emotional and psychological issues which need to be addressed in terms of patient management. This is a difficult time for both the patient and her family, as they experience a range of emotions; on the one hand grieving for the loss of a baby, but also wanting the 'problem' to be resolved and health to return to normal (10). The diagnosis may also lead to complications such as post-traumatic stress disorder, lengthening the recovery process and decreasing quality of life.

The process of methotrexate therapy can also cause additional worry for women; the week-long course to monitor a fall in β -hCG levels and uncertainty of the success of treatment causes anxiety in an already emotionally stressful situation. In some patients it may be more appropriate to opt for a surgical approach if they are unable to cope with the added anxiety, in the knowledge that the procedure will be curative.

It is therefore vital that each patient is treated individually; the clinician should address all factors when considering patient management, offering support and ensuring that treatment is tailored to their needs to facilitate their emotional recovery.

There are very few studies comparing the psychological and emotional effects of medical and surgical management, and those that do have shown no significant difference in psychological functioning between patients treated with methotrexate or laparoscopic salpingostomy (5). However the authors suggest the need for more sensitive techniques or perhaps the effect of early pregnancy loss overbears any differences between management techniques. Hence, as stated in the current NICE guidelines, there is a need for this type of research to provide another level of evidence and guidance to aid the clinician in the best approach for treatment.

Conclusion

There are many advantages to the use of methotrexate as first-line treatment of ectopic pregnancy, particularly in the avoidance of surgery, however it is important to realise that each intervention has its limitations. The clinician's role is to take a holistic approach to patient care, evaluating the risks and benefits of each management option, involving and considering the patient's needs and taking a patient-centred approach to management.

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