Compare and contrast laparoscopic surgery verses methotrexate in a woman with the diagnosis of ectopic pregnancy

Ectopic pregnancy is defined as the implantation of a conceptus outside of the uterine cavity. It occurs in 1:80 pregnancies (1). Of these, 95% implant into the fallopian tubes.

Management options for ectopic pregnancy (EP) include expectant, medical and surgical; laparoscopic or open. The treatment selected will be influenced by the history, examination and investigations performed in order to make the diagnosis. The choice of management strategy is an important decision, which needs to be made by the clinician and patient together. This essay will focus particularly on comparing and contrasting laparoscopic surgery with methotrexate.

The indications for laparoscopic surgery are haemodynamic instability, impending or ongoing rupture of the ectopic pregnancy, heterotopic pregnancy (especially if the intrauterine pregnancy is desired to continue), inability or unwillingness to comply with medical therapy and/or follow-up, medical contraindications to methotrexate, and failure of medical therapy (1). In contrast, methotrexate therapy, is only suitable women with a serum hCG <3000iu/l, minimal symptoms and normal blood test results (2). Suitable ectopics are small and can be tubal or non-tubal. In fact, methotrexate is particularly suited to the treatment of nontubal EPs where surgical access may be problematic.
The presence of fetal cardiac activity is a contraindication to methotrexate therapy because it is associated with a greatly reduced success rate \(^3\). Any signs or symptoms of rupture of the ectopic, such as excessive free fluid in the pouch of Douglas, are also contra-indications to medical management. Other contraindications to medical therapy as recommended by The American Congress of Obstetricians and Gynecologists include: breastfeeding, immunodeficiency (WCC \(<1.5 \times 10^9 /L\)), alcoholism or chronic liver disease, pre-existing blood dyscrasias, known sensitivity to methotrexate, active pulmonary disease, peptic ulcer disease, and hepatic, renal, or hematologic dysfunction \(^4\). Patient suitability is an important factor as compliance with long term follow-up is essential for patient safety. Once these contraindications have been applied, only 25-30% of women with ectopic pregnancy meet the safety criteria for medical management \(^5\). Therefore the majority are managed surgically.

Methotrexate therapy involves intramuscular methotrexate given as a single individualised dose calculated from the patient’s body surface area (50 mg/m\(^2\)). Methotrexate deactivates dihydrofolate reductase, which reduces tetrahydrofolate levels (a cofactor for deoxyribonucleic acid and ribonucleic acid synthesis), thereby disrupting rapidly-dividing trophoblastic cells \(^6\).

Methotrexate is administered on day 0 and serum hCG levels are checked on days 4 and 7 and a further dose is given if hCG levels have failed to fall by more than 15% between day 4 and day 7 \(^2\) \(^8\). Approximately 14% of women will require more than one dose of methotrexate, but less than 10% of women treated with this method will require surgical intervention \(^9\). Serial hCG measurements should be continued until \(<20\) I/mL to confirm ectopic resolution, due to the risk of persistent trophoblast. The average time to resolution is 3-7 weeks following a “single dose” regimen.

Multiple dose regimens have also been trialled \(^6\). However, given the greater simplicity and low complication rate of single-dose methotrexate, it is the preferred method in the UK even though multidose regimens might have slightly lower failure rates \(^7\).

If laparoscopic surgery is selected, further considerations need to be made to decide the exact procedure to be undertaken. In the presence of a healthy contralateral tube, salpingectomy is the method of choice \(^2\). This involves complete removal of the fallopian tube to prevent another EP from occurring in the tubal stump. However, if the contralateral tubal is diseased salpingostomy is preferentially performed if fertility is desired, as otherwise IVF will be required to conceive in the future. A salpingostomy involves the incising the tube on its antimesenteric border, removing the EP, ensuring haemostasis and leaving the tube to heal.

Follow-up is also important after laparoscopic surgery and is particularly important in bleeding ectopic pregnancies or when salpingostomy is performed, as there is a risk of
persistent trophoblast. Follow-up includes serial hCG measurements to ensure that they are declining appropriately, USS and administering methotrexate if levels fail to fall as expected (2). Common to both methods is the need to give anti-D if the patient is Rhesus D negative, the importance of follow-up to ensure resolution and counselling the patient about future pregnancy.

Compliance with the follow-up is essential for successful and safe medical treatment of ectopic pregnancy. Women who have difficulty communicating with health professionals because of a language barrier and those who live far from acute hospital units, alone or unsupported, are less likely to attend for follow-up visits and they should not be routinely offered medical treatment (5). Methotrexate management can be quite burdensome for the patient due to the need for extensive follow up and commitment to abstain from intercourse during treatment and use contraception for 3 months, because of a possible teratogenic risk posed by methotrexate. They are also advised to avoid alcohol and exposure to sunlight, and to maintain ample fluid intake. Therefore, some women may prefer to opt for the less burdensome surgical option.

Both of these management options have potential complications. The main complication of laparoscopic and methotrexate is persistent trophoblast, which may persist and cause delayed haemorrhage (2). With laparoscopic management this is more common following salpingostomy than salpingectomy (2) (3). Factors which may increase the risk of developing persistent trophoblast include higher preoperative serum hCG levels (>3000 iu/l), a rapid preoperative rise in serum hCG and the presence of active tubal bleeding (2). The use of prophylactic methotrexate at the time of laparoscopic salpingotomy/ salpingostomy has been reported in one randomised trial. When compared with simple salpingotomy alone there was a significant reduction in the rate of persistent trophoblast (1.9% versus 14%, RR 0.12, 95% CI 0.02–0.97) (10). Other complications of laparoscopic surgery include repeat ectopic, adhesions, pelvic pain, bleeding, infection and other complications of surgery and general anaesthesia.

The advantage of methotrexate is that it avoids surgical risks, but its other complications and side effects include abdominal pain(75%), tubal rupture(7%), conjunctivitis, stomatitis, haematoma formation, bone marrow suppression, elevated liver enzymes, rash, alopecia, nausea, and diarrhoea pulmonary fibrosis, non-specific pneumonitis, liver cirrhosis, renal failure, and gastric ulceration (2) (7). Recurrent ectopic rates following methotrexate are 15% at 1year and 24% at 2years. Most women do not experience any serious complications or side effects. The most common complaint during methotrexate therapy is excessive bloating and flatulence. One trial showed that women experienced more pain, had less energy, and had worse health perception during the first few weeks after methotrexate treatment, but they had the same quality of life after 16 weeks as those who had surgical treatment (11). However other studies have shown conflicting evidence, or no significant difference in psychological or physical variables (8). Overall the Cochrane 2007 review
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(CD000324) showed that outcomes after methotrexate were equivalent to laparoscopic salpingostomy (12).

One of the main concerns for the women undergoing treatment for ectopic pregnancy is its effect on their future fertility potential. In a recent online survey conducted by the Ectopic Pregnancy Trust, a UK charity, 90% of women ranked the preservation of their future fertility as their primary concern (5). With this in mind, health care professionals must be able to provide information and support to help patients with their choices about treatment of ectopic pregnancy (5). Laparoscopy has similar tubal patency and future fertility rates (90% and 50-65% respectively) as medical treatment (12).

Laparoscopic procedures also have diagnostic value, which could be of great benefit if the diagnosis or possibility of complications was uncertain. (5) However, in many women a confident diagnosis of ectopic pregnancy can now be made without needing a laparoscopy (8).

Methotrexate can be given as outpatient management which has cost benefits and may also be preferred by patients. Economic evaluations undertaken alongside randomised trials comparing methotrexate and laparoscopic surgery have shown direct and indirect costs for medical therapy to be less than half of those associated with laparoscopy, if used in patients with serum hCG levels above 1500 iu/l (2).

As laparoscopy has more evidence supporting its safety, with salpingectomy being the gold standard; the numerous possible adverse outcomes from methotrexate might be unacceptable. However, as more ectopic pregnancies are diagnosed at an earlier stage due to patient awareness, the increased sensitivity of home pregnancy kits and high resolution transvaginal USS, and the provision of out of hours service by dedicated emergency gynaecology teams it is likely that there are more frequent indications for the use of methotrexate therapy.

Overall, in terms of the best outcome for the patient, actually making the diagnosis and initiating management is more significant than choosing which type of management to use and any management is better than the diagnosis being missed. When we come to making management decisions it is important to weigh up the advantages and disadvantages based on the best evidence, but also taking into account patient choice.

Bibliography


