REVIEW ARTICLE

Recent Trends in the Management of Ectopic Pregnancy

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Ectopic pregnancy is a life threatening condition that every obstetrician and gynecologist encounters in his or her practice; therefore it is imperative to be familiar with latest methods of treatment. Improved technology has resulted in the diagnosis of ectopic pregnancy in unruptured stage thereby making less invasive treatment and even medical management possible. This article reviews the recent trends in the management of ectopic pregnancy.

Various Treatment Options

Surgical : Salpingectomy or salpingotomy through laparoscopy or laparotomy.

Medical : Administration of cytotoxic drugs.

Surgical Treatment

Lawson Tait first described the life saving procedure of salpingectomy in 1884 (1). It was not until 70 years later that less radical operations with conservation of involved tube were performed (2-4). Laparoscopic methods were first used for the management of ectopic pregnancy in 1980s (5,6). More conservative and less invasive management is now feasible as a result of developments in endoscopy (7).

Laparotomy versus Laparoscopy

The classical approach for ectopic pregnancy is by open laparotomy. The laparoscopic treatment of ectopic pregnancy will depend on patients' physical condition, location, size and state of ectopic pregnancy, experience of surgeon and availability of equipment. The advantages of laparoscopic surgery are short hospital stay, quick return to normal routine, few post operative analgesic requirement and reduced cost (8-11). Murphy et al (12) reported no significant difference in the operation time between laparoscopy and laparotomy. However, the patients treated by laparoscopy had reduction in intraoperative blood loss and post-operative hospital stay. A prospective study by Yao and Tulandi (11) showed that intrauterine pregnancy rate was 70% after laparoscopic surgery compared to 55% after laparotomy. The recurrent ectopic pregnancy rate was also lower after laparoscopy (5%) than after laparotomy (16.6%). However there was higher rate of persistent trophoblastic tissue following laparoscopic approach (12.2%) as compared to laparotomy(1.7%). Therefore weekly HCG levels should be done following conservative surgery(13). Persistent or rising levels of HCG require surgical or medical treatment. Haemodynamic instability is an absolute contraindication to laparscopy. The other contraindications include extensive pelvic adhesions, extensive haemoperitoneum and obesity, which are dependent on operator skill and experience (13,14).

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In a follow up study, development of adhesions was significantly less following laparoscopy than laparotomy ($p>0.0001$) (15).

Salpingectomy versus salpingotomy

All tubal pregnancies can be treated by salpingectomy. However, in patients who wish to conserve fertility and who are haemodynamically stable with unruptured, pregnancy (size of 5cm), and absent or damaged contralateral tube, conservative surgery in the form of salpingotomy may be more suitable. Studies on fertility after radical or conservative surgery have shown no difference in intrauterine pregnancy or ectopic pregnancy rates (11,16). Incidence of persistent ectopic was more after salpingotomy (4.8-11%) in contrast to no case following salpingectomy (17-20)

A persistent trophoblast does not necessarily require further surgery and in some cases may be managed by medical treatment (21-24).

A single randomized trial investigated the effect of suturing the salpingotomy incision (25) Intrauterine pregnancy rate at 12 months was higher in those without surgical repair but by 24 months the rates with or without suture were similar. Therefore it has been observed that suturing the tube after salpingotomy provides no benefit.

Medical Treatment

Early diagnosis has made medical treatment possible for women with unruptured ectopic pregnancy (13,14) thus avoiding surgery altogether. It is particularly indicated in a haemodynamically stable reliable and complaint patient with ectopic pregnancy definitely within tube measuring <3.5 cms with no evidence of rupture (14,26). HCG greater than 10,000 IU/l and fetal cardiac activity are relative contraindications.

Methotrexate has been used successfully in Japan and USA. Methotrexate is an anti-folate which prevents the growth of rapidly dividing cells by interfering with DNA synthesis. It has also been successfully used in the treatment of gestational trophoblastic disease for nearly four decades. It has also been used to promote early resorption of placental tissues in abdominal ectopic pregnancy. The successful resolution of a tubal pregnancy with methotrexate was first described in 1982 by Tanka et al (27). Methotrexate can be administrated locally by laparoscopy or under ultrasound guidance or systemically. The two most commonly used regimens are :

(a) Multidose administration

The multidose regimen was described in 1991. Methotrexate is administered intramuscularly at the dose of 1mg/kg followed by leucovorin 0.1mg/kg 24 hrs later. One injection is given daily. This regimen is continued until HCG levels decrease by 15%. On two consecutive days, upto four doses can be given, but not all patients require four doses.

(b) Single dose administration

The other commonly used regimen is single dose methotrexate. Dose of 50mg/m^2 of body surface area is used without folinic acid rescue. Stovell and Ling (28) reported that in a prospective study of 120 women with ectopic pregnancy, <3.5 cm in greatest dimension, 113 women had successful resolution of pregnancy. The dose of methotrexate was repeated if the serum HCG levels failed to fall below 15% between day 4 and 7. A repeat injection of methotrexate was required in 4 (3.3%) cases. Tubal patency was demonstrated on ipsilateral side in 51 of 62 (82.3%) patients. The subsequent fertility experience after different regimens is difficult to summate because of gross discrepancies between collection methods used in individual trials. In Yao and Tulandi's reviews, 54% of those attempting pregnancy

achieved an intrauterine pregnancy (IUP) and 7% had future ectopic pregnancy. A slightly lower IUP rate of 48% were noted after local injection under USG guidance as compared to 58% under laparoscopic control. The overall success rate is 88% with single dose whereas it is 93% with multidose.

Methotrexate is contraindicated if there is evidence of immunocompromise, hepatic, renal or haematological dysfunction, peptic ulcer disease. Women should be screened with complete blood count, liver function tests and renal function tests. If women have pulmonary disease they should be screened with chest radiography. Cases of fatal interstitial pneumonitis have been reported after methotrexate administration in patients with underlying pulmonary disease.

Side Effects

The incidence is related to both dose and mode of administration. The side effects include stomatitis, alopecia, haematosalpinx, elevation of liver enzymes. Multiple ovarian cysts are reported in 14.3% cases by Ben-Scholomo et at (29). Late complications like haematosalpinx and haematoceles presented with abdominal pain, abnormal bleeding and pelvic mass 3-5 months after treatment (30). Failure of therapy is more likely to occur if HCG levels are high (32% if levels > 10,000 IU compared to 3% if <10,000IU), with large tubal diameters (24% failure when ectopic pregnancy is < 2 cms and 48% when diameter is > 2 cms) (31,32). Side effects must be distinguished from treatment effects which include abdominal pain, an initial rise in HCG levels and vaginal bleeding.

Methotrexate has been used to treat persistent ectopic pregnancy, cervical interstitial ovarian or abdominal pregnancy. The chances of successful management can be improved with adjuvant use of local injection of KCL with or without uterine artery embolisation.

Feto-maternal haemorrhage may occur in Rh-negative women with Rh-positive fetus. It is therefore recommended that anti-D should be given in non-sensitized mothers.

Conclusion

Ecotpic pregnancy is a life threatening condition. Though the incidence is showing increasing trend, mortality is decreasing due to prompt diagnosis and management. Traditional treatment is laparotomy followed by salpingectomy or salpingotomy. Laparoscopic treatment is less invasive but needs expertise. Unruptured ectopic pregnancy can be managed by medical treatment. While newer treatment options offer several benefits to patients and health care providers, patients with ectopic pregnancy should be counselled properly and monitored carefully. The patients should understand the possible risk and should have 24 hour access to emergency.

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