Clinical Practice Guideline

เรื่อง: Ectopic Pregnancy

ชื่อหน่วยงาน: กลุ่มงานสูตินรีเวชกรรม

ผู้ตรวจสอบ: ลงลายเซ็น (นายแพทย์ธีระ ศิ وعدุลย์)

ผู้อนุมัติ: ลงลายเซ็น (ระบุตำแหน่งงาน)

Symptoms/Sign suspected Ectopic pregnancy

- UPT +ve

Hemodynamic stable

Hemodynamic unstable

Surgical treatment for resumed ruptured ectopic

TVS

Ectopic pregnancy
*adnexal ring

IUP

No IUP

Symptoms/signs ruptured ectopic

Immediate Surgery

No symptoms/signs ruptured ectopic

- Plateau or rising β-hCG

- Serum β-hCG and TVS 24 h.

- Serum β-hCG ≥ 2000

- Serum β-hCG < 2000

- ≥ 15 % decline Serum β-hCG

TVS => Abortion
* Complete
* Incomplete

*No IUP

*Ultrasound consistent unruptured ectopic
เรื่อง: Ectopic Pregnancy

Serum β-hCG ≥ 2000

*No mass
*Mass ≤ 3.5 cm

MTX.

Serum β-hCG < 2000

Serum β-hCG and TVS 48 h.

IUP

Plateau or < 50% rise in β-hCG

Repeat Serum β-hCG and TVS when Serum β-hCG is expected ≥ 2000

No IUP

< 50% rise in β-hCG

Fail pregnancy (IUP or ectopic)

D&C
เรื่อง: Ectopic Pregnancy

D&C

Uterine curette content float in saline

Villi present

Await final histology

Villi present

Incomplete abortion

Villi absent

Serum β-hCG and TVS 24 h.

Serum β-hCG decrease

Follow Serum β-hCG in 48 h.

Serum β-hCG decrease

*Complete abortion

*Ectopic spontaneous resolution

Weekly serum β-hCG until negative
Approach to the Diagnosis

History
- The most common presenting symptoms
  - abdominal pain (98.6%)
  - amenorrhea (74.1%)
  - irregular vaginal bleeding (56.4%)

Physical Examination
- Unremarkable in a woman with a small, unruptured ectopic pregnancy.
- Hypotension and tachycardia along with rebound tenderness and guarding on abdominal examination should alert the clinician to a probable tubal rupture.

Laboratory Assessment
- The hCG enzyme immunoassay in urine (sensitivity of 25 mIU/mL)
  - Accurate screening test for detection of ectopic pregnancy (Positive in all documented ectopic pregnancies).

Transvaginal Ultrasonography
Characteristics of ectopic pregnancy by ultrasonographic.
- Adnexal rings => fluid sacs with thick echogenic rings that have a yolk sac or nonliving embryo.
  - Specific ultrasonographic signs of ectopic pregnancy
    - 22% of ectopic pregnancies using transabdominal ultrasonography
    - 38% using transvaginal ultrasonography.
- Complex or solid adnexal masses
  - Frequently associated with ectopic pregnancy
  - However, the mass may represent a corpus luteum, endometrioma, hydrosalpinx, ovarian neoplasm (e.g., dermoid cyst), or pedunculated myoma.

The presence of free cul-de-sac fluid
- Frequently associated with ectopic pregnancy and is no longer considered evidence of rupture.

- The presence of intra-abdominal free fluid should raise concern about tubal rupture.
- The pseudogestational sac => intrauterine fluid collection
  - ~8% - 29% of patients with ectopic pregnancy.
NATURAL HISTORY — If left untreated.

- **Rupture** — Tubal rupture is usually associated with profound hemorrhage, which can be fatal if surgery is not performed expeditiously to remove the ectopic gestation.
  - Salpingectomy is the most common surgical approach when the tube has ruptured.
- **Abortion** — Tubal abortion refers to expulsion of the products of conception through the fimbria.
  - This can be followed by resorption of the tissue or by reimplantation of the trophoblasts in the abdominal cavity (ie, abdominal pregnancy) or on the ovary (ie, ovarian pregnancy).
  - Tubal abortion may be accompanied by severe intraabdominal bleeding, necessitating surgical intervention, or by minimal bleeding, not requiring further treatment.
- **Spontaneous resolution** — It is difficult to predict which patients will experience uncomplicated spontaneous resolution.
  - Potential candidates are hemodynamically stable women with an initial hCG concentration < 2000 IU/L that is declining.

**Treatment**

**Surgery**

- **Laparotomy versus Laparoscopy**
  - Laparotomy
    - Hemodynamically unstable and an expedited abdominal entry is required.
    - Cornual or interstitial pregnancies.
    - Extensive abdominal or pelvic adhesive disease.
- **Salpingectomy versus Salpingostomy**
  - Salpingostomy
    - depends on the condition of the affected and contralateral fallopian tubes, history of a previous ectopic pregnancy in the affected tube, and the patient’s desire for future fertility.
    - patient has an unruptured ectopic pregnancy, wishes to retain her potential for future fertility, and the affected fallopian tube appears otherwise normal.
    - If the contralateral tube appears damaged, a salpingostomy should be considered.
  - Contraindications to a salpingostomy include
    - ruptured fallopian tube
    - use of extensive cautery to obtain hemostasis
    - severely damaged tube
    - recurrent ectopic pregnancy in the same tube
**Medical Treatment**

Methotrexate

- Methotrexate is a folic acid analogue that inhibits dehydrofolate reductase and thereby prevents synthesis of DNA and interrupts cell division.
  - Methotrexate affects actively growing cells including trophoblastic tissues, malignant cells, bone marrow, intestinal mucosa, and respiratory epithelium.
- According to American College of Obstetricians and Gynecologists (ACOG) guidelines, methotrexate therapy can be considered for those patients with confirmed, or high suspicion for, ectopic pregnancy who are hemodynamically stable with no evidence of rupture.

<table>
<thead>
<tr>
<th>Contraindications for Medical Therapy</th>
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<tbody>
<tr>
<td><strong>Absolute Contraindications</strong></td>
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<tr>
<td>● Hemodynamically unstable</td>
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<tr>
<td>● Ruptured ectopic pregnancy</td>
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<tr>
<td>● Unstable to comply with medical management follow-up</td>
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<tr>
<td>● Breastfeeding</td>
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<tr>
<td>● Immunodeficiency</td>
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<tr>
<td>● Alcoholism, alcoholic liver disease or chronic liver disease</td>
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<tr>
<td>● Preexisting blood dyscrasias</td>
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<tr>
<td>● Known sensitivity to methotrexate</td>
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<td>● Active pulmonary disease</td>
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<tr>
<td>● Peptic ulcer disease</td>
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<tr>
<td>● Hepatic, renal, or hematologic disorder</td>
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<tr>
<td><strong>Relative Contraindications</strong></td>
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<tr>
<td>● Gestational sac &gt; 3.5 cm</td>
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<td>● Embryonic cardiac motion</td>
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Prefer an initial approach with single dose therapy => easier for patient compliance.

- ~ 15 - 20 % of women will require a second dose of MTX and patients should be made aware of this before starting the protocol
- Fewer than 1 % of patients need > 2 doses.
- Maximum of three doses of MTX.
  - If the hCG falls <15 % between weekly measurements after a 3\textsuperscript{rd} dose => perform a laparoscopic salpingostomy or salpingectomy.
- The $\beta$-hCG concentration usually declines to < 15 mIU/mL by 35 days post-injection, but may take as long as 109 days

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<th>Methotrexate Treatment Regimen</th>
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<td><strong>Single dose regimen</strong></td>
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<tr>
<td>- Administer MTX $50 \text{ mg/m}^2$ on day 0</td>
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<tr>
<td>- Measure $\beta$-hCG level on days 4 and 7</td>
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<tr>
<td>- If levels drop by 15%, monitor $\beta$-hCG weekly until non-pregnant level</td>
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<tr>
<td>- If level do not drop by 15% between Days 4 and 7, repeat dose of MTX</td>
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<tr>
<td>- On Day 14, if there is a &lt;15 % hCG decline from Days 7 to 14, a third dose of MTX $50 \text{ mg/m}^2$ IM is given.</td>
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<tr>
<td><strong>Multiple dose regimen</strong></td>
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<td>- Administer MTX $1 \text{ mg/kg}$ IM days 1,3,5,7</td>
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<tr>
<td>- Administer leucovorin $0.1 \text{ mg/kg}$ days 2,4,6,8</td>
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<tr>
<td>- Measure $\beta$-hCG levels on days 1,3,5,7 until 15 % decrease between 2 measurements</td>
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<tr>
<td>- Once $\beta$-hCG levels drop 15%, stop MTX and monitor $\beta$-hCG weekly until non-pregnant level</td>
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Prior to the administration of methotrexate, a patient should have a complete blood count, blood type, liver function tests, electrolyte panel including creatinine, and a chest x-ray if there is any history of pulmonary disease.

- These studies are usually repeated 1 week after administration of methotrexate to evaluate for any potential complications from the therapy.

### Initiation of methotrexate: Physician Checklist and Patient Instructions

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<th>Physician checklist</th>
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<tr>
<td>Obtain hCG level</td>
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<tr>
<td>Check CBC, liver function tests, creatinine, and blood type</td>
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<tr>
<td>Administer RhoGAM if patient is Rh-negative</td>
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<td>Identify unruptured ectopic pregnancy smaller than 3.5 cm (relative contraindication)</td>
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<td>Obtain informed content</td>
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<tr>
<td>Prescribe FeSO$_4$ 325 mg PO bid if Hct &lt; 30%</td>
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<tr>
<td>Schedule follow-up appointment on days 4 and 7</td>
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<th>Patient Instructions</th>
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<tr>
<td>Refrain from alcohol use, multivitamins containing folic acid, NSAID use and sexual intercourse until hCG level is negative</td>
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<tr>
<td>Call your physician if:</td>
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<td>Prolonged or heavy bleeding</td>
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<td>The pain is prolonged or severe (lower abdomen and pelvic pain is normal during the first 10-14 days of treatment)</td>
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<td>Use oral contraception or barrier contraceptive methods</td>
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Posttreatment management

Ultrasound follow-up
- Ultrasound evaluation for peritoneal fluid is indicated for women with severe abdominal pain.

Side effects and complications
- Nausea, vomiting, diarrhea, gastric distress, dizziness, and stomatitis.

Pain after treatment
- Occasionally pain may be severe, but women with severe pain who are hemodynamically stable often do not need surgical intervention.

EXPECTANT MANAGEMENT

Selection criteria
1. Transvaginal ultrasound does not show a gestational sac or demonstrate an extrauterine mass suspicious for an ectopic pregnancy
2. β-hCG concentration is low (≤200 mIU/mL) and declining

เอกสารอ้างอิง
2. Beckmann CR., Ling FW. ECTOPIC PREGNANCY and Abortion in Obstetrics and Gynecology 6TH 2010: 141-150
3. UpToDate; 2013