Management of Endometriosis

Clinical specialty: Obstetrics and Gynecology
Intended users: Physicians and students
Source of Evidence: The Cochrane Library and DARE

JC Objective
To discuss the evidence for the effectiveness of interventions for women with endometriosis

Recommendations

Diagnosis

A. History:
   a. a significant proportion of affected women are asymptomatic
   b. symptoms include
      i. infertility
      ii. severe dysmenorrhea, deep dyspareunia, chronic pelvic pain, ovulation pain
      iii. cyclical or perimenstrual symptoms, such as bowel or bladder, with or without abnormal spotting or pain
      iv. dyschezia
   c. each of these symptoms can have other causes (there is often a delay of up to 12 years between symptom onset and a definitive diagnosis)

B. Examination:
   a. May be NORMAL
   b. pelvic tenderness, a fixed, retroverted uterus, tender uterosacral ligaments or ovarian cyst
   c. deeply infiltrating nodules on the uterosacral ligaments or in the Douglas pouch

C. investigations
   a. Laparoscopy is the gold standard diagnostic test.
      i. Typical appearance: superficial ‘powder-burn’ or ‘gunshot’ lesions on the ovaries, serosal surfaces and peritoneum: black, dark-brown or bluish puckered lesions, nodules or small cysts containing old hemorrhage surrounded by a variable extent of fibrosis
      ii. Endometriomas usually contain thick fluid, like chocolate. Such cysts are often densely adherent to the peritoneum of the ovarian fossa and the surrounding fibrosis may involve the tubes and bowel.
iii. Deeply infiltrating endometriotic nodules extend more than 5 mm beneath the peritoneum and may involve the uterosacral ligaments, vagina, bowel, bladder or ureters. The depth of infiltration is related to the type and severity of symptoms.

iv. A meta-analysis of its value against a histological diagnosis showed (assuming a 10% pre-test probability of endometriosis) that
   1. a positive laparoscopy increases the likelihood to 32% (95% CI 21–46%)
   2. a negative laparoscopy decreases the likelihood to 0.7% (95% CI 0.1–5.0%).

v. Visual inspection is usually adequate but histological confirmation of at least one lesion is ideal.

vi. In cases of ovarian endometrioma (> 3 cm in diameter) and in deeply infiltrating disease, histology should be obtained to identify endometriosis and to exclude rare instances of malignancy.

   b. Compared with laparoscopy, measuring serum CA125 levels (may be elevated in endometriosis) has no value in diagnosing endometriosis.

   c. Compared with laparoscopy, TVUS has no value in diagnosing peritoneal endometriosis.

      i. TVUS is useful for the diagnosis of an ovarian endometrioma.

   d. There is insufficient evidence to indicate that MRI is a useful test compared to laparoscopy.

D. Classification:

   a. All classification systems for endometriosis correlate poorly with pain symptoms, but may be of value in infertility prognosis and management.

Intervention

Pharmacologic Interventions

A. NSAID: Comparing NSAIDs to placebo, no evidence regarding

   a. Effect on pain relief
   b. additional analgesia
   c. side effects

B. Ovarian suppression

   a. for pain

      i. COCP, progestogens, gestrinone, danazol, GnRHa

      ii. Suppression of ovarian function for 6 months reduces endometriosis-associated pain. Symptom recurrence is common after stopping treatment.
iii. Women receiving GnRHa became amenorrheic during the treatment period of 6 months, women taking COCP reported a decrease in dysmenorrhea.
   1. No evidence of a difference between the two groups regarding dysmenorrhea at 6 months follow up after stopping treatment
   2. For endometriosis-associated dysmenorrhea, COCP and oral norethindrone or DMPA are effective and are equivalent to other more costly regimens.

iv. Evidence for a decrease in dyspareunia was found at the end of treatment in women in the GnRHα group, although no evidence of a significant difference in dyspareunia was observed at the end of the six months follow up.
   a. When relief of pain from treatment with a GnRHα supports continued therapy, the addition of add-back therapy prevents GnRHα-induced bone mineral loss without reducing the efficacy of pain relief.
   b. For subfertility:
      i. Suppression of ovarian function to improve fertility is not effective and should not be offered for this indication alone.
      ii. OR for pregnancy
         1. Ovulation suppression versus placebo or no treatment: no difference
         2. All agents versus danazol
            a. 1.38 (95% CI 1.05 to 1.82) for all women
            b. 1.37 (95% CI 0.94 to 1.99) for subfertile couples only.
         3. GnRHα versus COCP: no difference
         4. GnRHα versus danazol
            a. 1.45 (95% CI 1.08 to 1.95) for all women
            b. 1.63 (95% CI 1.12 to 2.37) for subfertile couples only.
   c. Duration of therapy is determined by response to treatment and adverse events.

C. LNG-IUS appears to reduce endometriosis-associated pain

D. Anti-TNF-α: (One trial, 21 participants): infliximab versus placebo
   a. No evidence of an effect of infliximab, on pain reduction, endometriotic lesions, dysmenorrhea, dyspareunia or pelvic tenderness.
   b. No evidence of an increase in adverse events

E. Pentoxifylline (immunomodulator): (4 trials, 334 participants)
   a. For reduction in pain (MD -1.60, 95% CI -3.32 to 0.12).
   b. For recurrence of endometriosis: OR of 0.88 (95% CI 0.27 to 2.84).
   c. No evidence of an increase in clinical pregnancy rate
   d. No trials reported the effects on the odds of live birth rate or adverse events.
Conservative Surgery:

A. Laparoscopic surgery (Ablation of endometriotic lesions and adhesiolysis) versus diagnostic laparoscopy only
   a. for pain:
      i. pain relief: OR 5.7 95% CI 3.1 to 10.6
      ii. There is a significant rate of pain recurrence.
      iii. LUNA by itself does not reduce endometriosis-associated pain
   b. for subfertility:
      i. clinical pregnancy rates: OR 1.66 (95% CI 1.09 to 2.51) (*note the SIZE of the effect*).
      ii. fetal losses: no difference.
   c. For ovarian endometriomas
      i. Laparoscopic ovarian cystectomy is better than drainage and coagulation
      ii. Laparoscopic ovarian cystectomy is recommended before ART for endometriomas >3 cm

B. Hormonal suppression before or after surgery
   a. no evidence of benefit compared to surgery alone for the outcomes of pain, disease recurrence, pregnancy rates
   b. pre-surgical hormonal suppression versus post-surgical hormonal suppression: One trial found no evidence of a difference for reduction of pain.
   c. post-surgical hormonal suppression versus both pre and post-surgery: One trial found no evidence of a difference in the outcomes of AFS scores and pregnancy rate.
   d. NO trials compared hormonal suppression before and after surgery with surgery alone.

Assisted reproduction in endometriosis

A. Treatment with IUI improves fertility in minimal to mild endometriosis
B. IVF is appropriate treatment, especially
   a. if tubal function is compromised,
   b. if there is also male factor infertility,
   c. if other treatments have failed

Hysterectomy

A. If a hysterectomy is performed, all visible endometriotic tissue should be removed
B. BSO may result in improved pain relief and a reduced chance of future surgery.
C. HRT is not contraindicated after hysterectomy and BSO for endometriosis.