Practice Guidelines

ACOG Updates Guideline on Diagnosis and Treatment of Endometriosis

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Endometriosis is a chronic gynecologic disorder that commonly manifests as chronic pain and infertility. It affects 6 to 10 percent of women of reproductive age, and it is present in approximately 38 percent of women with infertility and in up to 87 percent of women with chronic pelvic pain. It is thought to develop from attachment and implantation of endometrial glands and stroma on the peritoneum as a result of retrograde menstruation. Endometrial lesions result from overproduction of prostaglandins and estrogen, which leads to chronic inflammation.

The mechanism by which infertility occurs in women with early-stage endometriosis is not clear. Oxidative stress and higher concentration of inflammatory cytokines may affect sperm function in several ways, including causing sperm DNA damage. The abnormal peritoneal environment can also cause abnormalities in oocyte cytoskeleton function. In more advanced endometriosis with ovarian cysts and adhesions, the anatomic abnormalities can impair tubal function.

Diagnosis

Diagnostic evaluation of women with pelvic pain should include a thorough history and physical examination to rule out other gynecologic causes of pain. Nongynecologic causes (e.g., irritable bowel syndrome, interstitial cystitis, urinary tract disorders) can be ruled out with appropriate testing and referrals, if necessary.

Definitive diagnosis of endometriosis can be made only by histology of lesions that have been removed surgically. Imaging studies cannot be used to diagnose endometriosis, but they can be useful in patients with pelvic or adnexal masses. Ovarian endometriomas typically appear on ultrasonography as cysts that contain low-level homogeneous internal echoes consistent with old blood. Imaging alone seems to be highly predictive in differentiating ovarian endometriomas from other adnexal masses.

Transvaginal ultrasonography is the preferred imaging modality to determine the presence of endometriosis and deeply infiltrating endometriosis of the rectum or rectovaginal septum. Magnetic resonance imaging should be reserved for patients with equivocal ultrasound results and in whom rectovaginal or bladder endometriosis is suspected.

Treatment

Progestins, danazol, extended-cycle combined oral contraceptives, nonsteroidal anti-inflammatory drugs (NSAIDs), and gonadotropin-releasing hormone (GnRH) agonists can be used for initial treatment of pain in women with suspected endometriosis. However, recurrence rates are high after the medication is discontinued. If initial therapy is unsuccessful, diagnostic laparoscopy can be offered to confirm the diagnosis. Alternatively, empiric treatment with another suppressive medication is an option. Empiric therapy with a three-month course of a GnRH agonist is appropriate if initial treatment with oral contraceptives and NSAIDs is unsuccessful. It is important to explain to the patient that response to empiric therapy does not confirm the diagnosis of endometriosis.

TREATMENT OF RECURRENT ENDOMETRIOSIS

In women with a history of endometriosis who wish to preserve their fertility, NSAIDs or combined oral contraceptives can be used to treat recurrent pain. Oral or depot medroxyprogesterone acetate is also effective. If none of these therapies is successful, progestins, GnRH agonists, and androgens may be used. Use of the levonorgestrelreleasing intrauterine system (Mirena) reduces pelvic pain associated with endometriosis, but adverse effects (e.g., irregular bleeding, weight gain) are common.

ADD-BACK THERAPY

If treatment with a GnRH agonist is successful, the use of an add-back regimen can reduce or eliminate bone mineral loss and provide symptomatic relief without reducing pain relief. Add-back regimens have been used in women undergoing long-term therapy; they may include progestins alone, progestins plus bisphosphonates, lowdose progestins, or estrogens.

The U.S Food and Drug Administration (FDA) has approved the use of norethindrone (5 mg daily) as addback therapy in conjunction with a GnRH agonist. In women who cannot tolerate high-dose norethindrone, a daily combination of transdermal estradiol (25 mcg) and oral medroxyprogesterone acetate (2.5 mg) can be used. However, this regimen may not completely prevent bone mineral loss, and it has not been approved by the FDA. Calcium supplementation (1,000 mg daily) is recommended for women taking add-back therapy.

SURGERY

In women with endometriosis-related pain who wish to preserve their fertility, there is significant short-term improvement in pain after laparoscopy and surgical removal of lesions. However, as with medical management, pain recurrence is common.

Endometriomas are thought to result from progression of ovarian lesions that form cysts. These cysts can cause pain and infertility, and are associated with an increased risk of torsion and rupture. However, because they are attached to the ovary and the ovarian cortex where oocytes are embedded, removal of endometriomas carries a risk that normal tissue will also be removed. Endometriomas should be removed in women with no history of endometriosis. Simple drainage of an endometrioma is associated with a high recurrence rate; therefore, excision is recommended. Reoperation in women with recurrent endometriomas should be considered on a case-by-case basis, because it may result in reduced or total loss of ovarian function.

Definitive surgical management is appropriate in women who do not wish to preserve fertility and in whom conservative medical and surgical management have been unsuccessful. Hysterectomy with bilateral salpingo-oophorectomy is generally regarded as definitive therapy. However, in women with normal ovaries, a hysterectomy with ovarian conservation and removal of endometriotic lesions should be considered. In a study of 120 women who underwent excision of endometriomas and hysterectomy with or without oophorectomy, most patients did not require reoperation, even with ovarian conservation.

POSTOPERATIVE MEDICAL THERAPY

Hormone therapy with estrogen is not contraindicated after hysterectomy and bilateral salpingo-oophorectomy for endometriosis. Endometriosis will recur in up to 15 percent of women, regardless of whether they receive postoperative estrogen therapy. Hormone therapy may stimulate the growth of residual ovarian or endometrial tissue after total hysterectomy and bilateral salpingooophorectomy. There is also concern about the possibility of estrogen-induced malignant transformation in residual endometriosis; this has led some physicians to routinely recommend the addition of a progestin to the estrogen therapy. However, there is no evidence to support this recommendation.

TREATMENT OF INFERTILITY ASSOCIATED WITH ENDOMETRIOSIS

Medical suppressive therapy, such as oral contraceptives or GnRH agonists, is ineffective for treatment of infertility associated with endometriosis. Surgery improves pregnancy rates, but the magnitude of improvement is not clear. Excision of deeply infiltrating endometriomas may adversely affect fertility. After initial unsuccessful surgery for infertility associated with endometriosis, in vitro fertilization is preferred over repeat surgery unless pain is still present. Repeat ovarian surgery has a significant negative effect on in vitro fertilization outcomes.

Answers to This Issue's CME Quiz		
Q1. C	Q5. A, B	Q9. A, B, C
Q2. C	Q6. C, D	Q10. B
Q3. A, B, C	Q7. B	
Q4. C	Q8. A, B, C, D	