Causes of chronic pelvic pain
Endometriosis

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Common non-malignant conditions associated with chronic pelvic pain in women

- **Endometriosis**: most common gynecologic cause
- **Leiomyoma**
- **Adenomyosis**
- Recurrent ovarian cysts
- **Hydrosalpinx**
- **Ovarian remnant syndrome**
- **PID**
- Pelvic adhesive disease
- Post-tubal ligation pain syndrome
Endometriosis and pain

• The presence and severity of endometriosis do not correlate with symptom severity except in the case of posterior cul-de-sac disease and severity of dyspareunia.

• Treat endometriosis when identified in symptomatic women as well as diligently identify and treat all other possible sources of pain regardless of the presence of endometriosis.

• The coexistence of other pain syndromes in women and adolescents with endometriosis is higher than in the general population.
introduction

**Endometriosis requires a lifelong management plan**

Treatment decisions are individualized and consider:

- Clinical presentation
- Symptom severity
- Disease extent and location
- Reproductive desires
- Patient age
- Medication side effects
- Surgical complication rates
- Cost
ASRM

- endometriosis is a chronic disease that requires a lifelong management plan

With the goal of

- Maximizing the use of medical treatment
- Avoiding repeated surgical procedures
Treatment

• Mild to moderate pain and no ultrasound evidence of an endometrioma:
  - NSAIDs: first line, women desire conception can use NSAID alone
  
  For women attempting conception we avoid celecoxib and other selective COX-2 inhibitors (prevent or delay ovulation)
  
  - continuous hormonal contraceptives

  **NSAIDs are commonly combined with a contraceptive hormonal therapy**
<table>
<thead>
<tr>
<th>drug</th>
<th>Initial dose</th>
<th>Subsequent dose, as needed</th>
<th>Maximum does per day in short term use (≤ 3 days)</th>
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<tbody>
<tr>
<td>ibuprofen</td>
<td>400 to 600 mg</td>
<td>400 to 600 mg Q 4-6 hours</td>
<td>2400 mg</td>
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<tr>
<td></td>
<td>800 mg</td>
<td>800 mg Q 8 hours</td>
<td>2400 mg</td>
</tr>
<tr>
<td>Naproxen base</td>
<td>500 mg</td>
<td>250 mg Q 6-8 hours</td>
<td>1250 mg</td>
</tr>
<tr>
<td>Mefenamic acid</td>
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<td>250 mg Q 6 hours</td>
<td>1000 mg</td>
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<tr>
<td>indomethacin</td>
<td>25 mg</td>
<td>25 mg Q 8 hours</td>
<td>150 mg</td>
</tr>
<tr>
<td>diclofenac</td>
<td>75 to 100 mg</td>
<td>50 mg Q 8 hours</td>
<td>150 mg</td>
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<tr>
<td>piroxicam</td>
<td>20 mg</td>
<td>10 to 20 mg daily</td>
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Treatment
Estrogen-progestin contraceptives

• First line treatment
• Can be used long term
• Well tolerated
• Inexpensive
• Easy to use
• Provide contraception, decreasing risk of ovarian and endometrial cancers
• Include combined OCPs, transdermal patches, and vaginal rings
Treatment

Estrogen-progestin contraceptives

• Typically begin a COC containing 20 mcg of ethinyl estradiol, continuous dose fashion

• Both cyclic and continuous dose regimens are effective

• Continuous regimens are most effective

• Mechanism: decidualization and subsequently atrophy of endometrial tissue- may slow progression of disease
Treatment progestins

• Unable to take or prefer to avoid COCs
• MPA, dienogest (Visanne), norethindrone acetate

• Depot MPA: 150 mg IM Q 3 months or 104 mg SC Q 3 months
• Dienogest: 2 mg oral pill daily or OCP (Natazia)
• Norethindrone acetate: 5 mg by mouth daily, can be increased to 15 mg daily depending on side effects including breakthrough bleeding
Endorin-IH Dienogest
Each Tablet Contains: Dienogest 2 mg
Manufactured by Iran Khodro Pharmaceutical Co., Tehran, Iran, since 1994

Visanne 2 mg tablets
Dienogest 2 mg
Bayer Pharma AG for Pyravan

Verogest Dienogest 2 mg
20 tablets
Each tablet contains: Dienogest 2 mg

Norethisterone Tablets
For oral use
30 tablets
Each tablet contains 5 mg norethisterone

OVIRO
OviroBeauty
Treatment progestins, mechanisms

• Inhibit endometrial tissue growth causing initial decidualization and then atrophy
• Suppression of matrix metalloproteinases which is important in growth and implantation of ectopic endometrium
• Inhibition of angiogenesis
Treatment progestins, advantages

• Avoids the estrogen related thromboembolic risk
• Compared with GnRH analogs, is not associated with bone loss and is less expensive
• Compared with danazol, are better tolerated, have no androgenic side effects, and less impact on lipids
Treatment progestins, side effects

• irregular uterine bleeding/spotting, amenorrhea
• weight gain
• mood changes eg depression
• bone loss (specific to long term use of depot MPA)
• reduction of HDL, increases in LDL and TG(specific to long term use norethindrone acetate)
Treatment
alternate progestin treatment options
limited data

• Etonogestrel implant
• Levonorgestrel IUD
Treatment
GnRH agonists/antagonists agonist analogs

• Nafarelin, leuprolide, buserelin, goserelin, triptorelin
• More effective than placebo
• As effective as danazol, levonorgestrel, COC for relieving pain
• To minimize the hypoestrogenic side effects, begin add back therapy with oral norethindrone acetate 5 mg daily or OCP
• When used with add back therapy side effects are often better tolerated compared with a progestin only or danazol treatment
• Mechanism: induction of amenorrhea and progressive endometrial atrophy
Treatment
GnRH agonists/antagonists
agonist analogs - adverse effects

- Hot flashes
- Vaginal dryness
- Decreased libido
- Mood swings
- Headache
- Decreased bone density
Treatment
GnRH agonists/antagonists
antagonist analogs: Elagolix

• Suppress pituitary gonadotropin hormone production and create a hypoestrogenic state to inhibit endometriotic cell proliferation
• Effective immediately
• Do not cause an initial surge in LH and FSH
• Do not require 7 to 14 days for GnRH suppression
• Oral and injectable forms
• A treatment option for women who do not respond to NSAIDs, OCP, or progestins
Danazol

- Not commonly used because of androgenic side effects
- Orally in dividing dose from 400 to 800 mg daily for 6 months
- Mechanisms:
  - inhibition of pituitary gonadotropin secretion
  - direct inhibition of ovarian enzymes responsible for estrogen production
  - inhibition of endometriotic implant growth
Aromatase inhibitors

• Reserve AI treatment for women with severe, refractory endometriosis related pain
• often used in combination with progestins, COC, or GnRH analog
• Oral anastrozole 1 mg once daily – letrozole 2.5 mg once daily
• Mechanisms:
  ➢ regulate local estrogen formation within endometriotic lesions
  ➢ inhibiting estrogen production in ovary, brain, and adipose tissue
Neuropathic pain treatments

• For women who continue to have pain despite medical treatment options for endometriosis-related pain listed before

• Initial treatment: either selective antidepressants {ie. Tricyclic antidepressants (eg, nortriptyline & Amitriptyline) or serotonin-norepinephrine reuptake inhibitors (eg, Duloxetine) or antileptic drugs (ie, gabapentin or pregabalin)}

• Second line: adjunctive topical therapy (eg, topical lidocaine) when pain is localized, tramadol

• Third line: Botulinum toxin, strong opioid
Neuropathic pain treatments

- **Gabapentin**: IR 300 to 1200 mg orally TDS (کپسول 100 و 300 و 400 میلی گرم)  
  ER: 600-1800 mg orally BD
- **Duloxetine**: IR 60-120 mg orally once daily (کپسول 20 و 30 و 60 میلی گرمی)
- **Nortriptyline**: 25-75 mg orally once daily (قرص 10 و 25 و 50 میلی گرم)
- **Amitriptyline**: 25-125 mg orally once daily (قرص 10 و 25 و 50)
- **Lidocaine patch**: 1 to 3 patches to painful area for \(\leq 12\) hours in 24 hour period
- **Tramadol**: IR 100-200mg orally TDS (50 و 100 میلی گرم)  
  ER 100-200 mg orally BD
- **Botulinum toxin**: 50-200 units SC to painful area Q 3 months
- **Strong opioids**
Surgery: consider surgery in women with

• Persistent pain despite medical therapy
• Contraindications to or refusal of medical therapy
• Need for tissue diagnosis of endometriosis
• Exclusion of malignancy in adnexal mass
• Obstruction of the bowel or urinary tract
Surgical resection of endometriosis

• Provides a histologic diagnosis and reduces pain by destroying the endometriotic implants

1. conservative: ablation or resection of lesions with the intent of preserving the uterus and as much ovarian tissue as possible

2. Definitive: hysterectomy with or without oophorectomy in addition to resection of endometriosis
Nerve transection

• Laparoscopic uterosacral nerve ablation
• Presacral neurectomy: treatment of midline pain associated with menses
Complementary therapies

• Acupuncture: In a systematic review of acupuncture for treatment of endometriosis related pain, only one randomized trial met the inclusion criteria- significantly more effective than Chinese herbal medicine.

• Diet: No dietary recommendations for treatment of endometriosis.
Treatment of special populations infertility

• Infertility: combination of surgery and ART
• Pain: NSAIDs
Treatment of special populations endometrioma

• Goals of endometrioma treatment
  ➢ relive pain or mass
  ➢ prevent rupture or torsion
  ➢ Exclude malignancy
  ➢ Improve subfertility
  ➢ Preserve ovarian function
✓ medical therapy does not resolve endometriomas
✓ symptomatic or expanding endometriomas removed laparoscopically
✓ to protect ovarian reserve asymptomatic and small (≤ 5 cm) can be left in place
Treatment of special populations presumed endometriosis

• NSAIDs
• Hormonal treatments

• Surgically confirming the diagnosis is preferred before initiating medication with significant side effects such as GnRH analogs
Treatment of special populations adolescents: pain

• Trial of cyclic HT and / or NSAIDs

Pain improves: diagnosis_ primary dysmenorrhea, continue cyclic HT and / or NSAIDs

Pain persists: diagnosis: secondary dysmenorrhea, endometriosis is considered as the most likely underlying cause, offer trial of medical therapy for menstrual suppression with

• Continuous COC or vaginal ring or
  continuous progestin- only pill, implant, or injection

➢ symptoms improve: continue medical therapy for menstrual suppression
Treatment of special populations adolescents: pain-symptoms persist, > 18 years

offer trial of empiric GnRH agonist or antagonist

Desire: GnRH therapy, stop drugs used for menstrual suppression – if symptoms persist: offer laparoscopy

Not desire: laparoscopy for diagnosis and treatment

Laparoscopy

Endometriosis: excision of deep lesions or ablation of superficial disease

No visible endometriosis: evaluation for other sources
Treatment of special populations adolescents: pain-symptoms persist, ≥ 16 years

Offer laparoscopy for diagnosis and treatment

Laparoscopy

Endometriosis: excision of deep lesions or ablation of superficial disease

No visible endometriosis: evaluation for other sources
Postoperative medical treatment

• No procedure or medical therapy results in a cure for endometriosis

• Surgery alone is not adequate treatment for endometriosis, microscopic residual disease, must be suppressed with medical therapy
Postoperative medical treatment: until they have completed child bearing

Combination hormonal therapy or GnRH agonists with add-back (first line)
<16: only continuous combination hormonal therapy

Progestins: norethindrone (0.35 mg daily), norethindrone acetate (5-15 mg daily), MPA (30-50 mg daily), DMPA (150 mg q 1-3 months IM)

GnRH antagonists:------ , Danazol: poorly tolerated

If symptoms persist: continue medical therapy, add therapies focused on pain reduction including

• pelvic floor physical therapy
• pain management consultation
• behavioral therapies
• evaluate for issues that could worsen pain including anxiety / depression and history of ongoing abuse
Add back therapy

• Norethindrone acetate (5 mg daily) alone
• Conjugated estrogen (0.625 mg) plus Norethindrone acetate (2.5 to 5 mg daily)
• Conjugated estrogen (0.625 mg) plus MPA (5 mg daily)