Menstrual disturbances in perimenopausal women: What’s best?

**Evidence-based answer**

It’s best to start with nonsteroidal anti-inflammatory drugs (NSAIDs), which effectively reduce heavy menstrual bleeding (strength of recommendation [SOR]: B, systematic review of randomized clinical trials [RCTs]).

Perimenopausal women with heavy bleeding not controlled by NSAIDs, or other forms of dysfunctional uterine bleeding, can benefit from continuous, combined hormonal therapy with estrogen and progestin; hormonal therapy with estrogen and a cyclical progestin; or a cyclical progestin alone (SOR: B, RCTs and a systematic review of RCTs). Intrauterine devices (IUDs) containing levonorgestrel also effectively reduce bleeding and may avoid surgical intervention (SOR: B, systematic review of RCTs).

If medical management fails, endometrial ablation offers an effective, minimally invasive alternative to hysterectomy (SOR: B, systematic review of RCTs and 1 RCT). Hysterectomy should be considered when medical management or endometrial ablation fails (SOR: B, systematic review of RCTs and 1 RCT).

**Evidence summary**

Perimenopause encompasses the period of irregular menstrual cycles and flow that precedes menopause (absence of menstrual bleeding for 1 year). Menopause generally occurs between 45 and 55 years of age; the average is 51 years. A review of 500 perimenopausal women seen sequentially by a gynecology service found that 18% had menorrhagia (heavy bleeding), metrorrhagia (intermenstrual bleeding), or hypermenorrhea (frequent periods).1

Because few studies have examined the treatment of abnormal menstrual bleeding specifically during perimenopause, therapeutic approaches are based primarily on studies of women before and shortly after this stage. Once malignancy and other causes of abnormal uterine bleeding (pregnancy, bleeding disorders, infection, thyroid disorders, uterine fibroids, or polyps) have been excluded, treatment of perimenopausal dysfunctional uterine bleeding should address the goals of:

- stopping acute bleeding
- avoiding future irregular or heavy bleeding
- considering future family planning needs
- preventing complications (anemia, unnecessary therapeutic procedures).

**NSAIDs reduce heavy bleeding**

A Cochrane review of 16 small RCTs that examined the use of NSAIDs for menor-
rhagia found NSAIDs to be superior to placebo and comparable to other medical treatments such as luteal progestin, oral contraceptive pills, and progestin-releasing intrauterine systems.\textsuperscript{2}

**Hormone therapy is also effective**

An RCT of 132 perimenopausal women compared 24 weeks of combination hormonal therapy (20 mcg ethinyl estradiol/1 mg norethindrone acetate) with placebo for treating climacteric symptoms, including abnormal uterine bleeding.\textsuperscript{3} The combination therapy shortened the menstrual cycle (27.7 vs 30.4 days), decreased its variability (17.5-46.7 days vs 22.4-66 days), and lowered bleeding severity scores (6.9 vs 10.2).

Hormonal therapy didn’t shorten bleeding episodes, however, and was associated with a higher incidence of intermenstrual bleeding during the first 3 months of treatment.

**Continuous, combined estrogen/progestogen therapy**

An RCT of 120 perimenopausal women with irregular menstrual cycles compared low-dose (1 mg) continuous estradiol and cyclical progestogens (10 mg dydrogesterone) with cyclical progestogens alone.\textsuperscript{4} In the combined treatment group, the incidence of cyclical menstrual bleeding was 86\%, and 76\% of all cycles were rated normal in amount and duration of bleeding. In the cyclical progestogen group, the incidence of cyclical menstrual bleeding during treatment was 76\%, and 70\% of all cycles were rated normal.

A systematic review, comprised primarily of RCTs, examined uterine bleeding patterns in 3000 postmenopausal women taking combined continuous hormones (various regimens of estrogen and progestin).\textsuperscript{5} In 22 of 23 studies that included data past 6 months, 75\% or more of participants became amenorrheic while on therapy. Irregular uterine bleeding before 6 months of therapy was common, however, and was presumed to lower patient compliance.

**Combined therapy avoids risk of endometrial hyperplasia**

A more recent Cochrane review of 30 RCTs examined hormone replacement therapy for irregular bleeding and endometrial hyperplasia in postmenopausal women who had been amenorrheic for at least 6 months (a more liberal criterion for inclusion).\textsuperscript{6} The review concluded that many of the women treated with continuous estrogen and progestin became amenorrheic after 1 year of therapy. It also reiterated that unopposed estrogen increased the risk of endometrial hyperplasia, whereas continuous combined estrogen and progestogen treatment didn’t.

**Continuous progestogen regimen has blood loss benefit**

No randomized trials have compared oral progestogens with placebo. A Cochrane review examined the use of cyclical progestogens (given from 10 to 20 days per cycle) for heavy menstrual bleeding.\textsuperscript{7} Cyclical progestogens appeared comparable in efficacy to NSAIDs for their effect on duration of menstruation; no statistically significant difference in menstrual blood loss was noted. Progestogens given in more continuous regimens offered greater benefit in terms of blood loss.

**IUDs help avoid surgery, but can have side effects**

A Cochrane review found that progestogen-releasing IUDs significantly reduce heavy menstrual bleeding and are more effective than cyclical norethisterone (21 days). Patients did, however, report greater progestogenic side effects (breast tenderness and intermenstrual bleeding) than cyclical therapy.\textsuperscript{8} One unblinded RCT that randomized women scheduled for hysterectomy for heavy bleeding to the levonorgestrel intrauterine device (LNG-IUD) or their existing medical therapy (not further described) found that women in the LNG-IUD group were more likely to cancel surgery.

Another RCT comparing hysterecto-
Among patients followed for more than 5 years after endometrial ablation, 20% to 40% required repeat treatment or hysterectomy.


