What is the best diagnostic approach to postmenopausal vaginal bleeding in women taking hormonal replacement therapy (HRT)?

Evidence-Based Answer

Independent of hormonal therapy, the workup for a postmenopausal woman with vaginal bleeding should be either an endometrial biopsy or transvaginal ultrasound (TVUS) followed by endometrial biopsy or hysteroscopy as indicated (SOR: C, consensus opinion guideline). The incidence of endometrial carcinoma is lower in women with postmenopausal bleeding on HRT compared with those not on HRT (SOR: B, cross-sectional study and a retrospective study).

Vaginal bleeding is the presenting sign in more than 90% of postmenopausal patients with endometrial carcinoma. Bleeding in postmenopausal HRT users can be due to the irregular use of the hormones or to underlying causes such as polyps, leiomyoma, atrophy, or carcinoma.¹

A retrospective medical record review of 326 women with postmenopausal bleeding was conducted from 2005 to 2009.² Of these women, 24% were on topical or systemic HRT and 76% were not on HRT. The diagnostic workup of postmenopausal bleeding independent of the presence or absence of HRT started with TVUS. If endometrial thickness was between 5 and 10 mm, then endometrial biopsy was done. If endometrial thickness was more than 10 mm, then women underwent hysteroscopy with endometrial biopsy or curettage followed by histopathological analysis.

Six percent of the 326 women in this study were diagnosed with endometrial cancer; none were taking HRT. There was a significantly lower risk of endometrial cancer in the HRT group compared with the non-HRT group (OR 0.08; 95% CI, 0.04–0.13).²

A cross-sectional study published in 2012 compared 4,847 postmenopausal women who presented to a gynecology oncology center with postmenopausal bleeding; 15% were on HRT and the remaining 85% were not.³ The diagnostic workup was similar to the protocol in the study above. The HRT group had a significantly thicker endometrium (median 5.2 vs 4.6 mm, respectively; P=.0024).

Endometrial carcinoma was diagnosed in 6.1% of all women with postmenopausal bleeding. Women in the HRT group were less likely to be diagnosed with both type I (estrogen-dependent, low-grade) and type II endometrial cancer (non-estrogen–dependent, high-grade) (OR 0.23; 95% CI, 0.12–0.45) compared with the non-HRT group.³

The American College of Obstetricians and Gynecologists published consensus opinion guidelines for the management of postmenopausal bleeding.⁴ Any episode of vaginal bleeding in postmenopausal women should be investigated to exclude malignancy. They recommend performing either immediate endometrial biopsy or TVUS. If endometrial thickness is more than 4 mm on TVUS, then endometrial biopsy is required. When postmenopausal bleeding persists despite negative or suboptimal evaluation, then additional evaluation with hysteroscopy, sonohysterography, and endometrial biopsy should be pursued.

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What prophylactic treatments are effective for patients with recurrent bacterial vaginosis?

Evidence-Based Answer

In patients with recurrent bacterial vaginosis (BV) who have just completed therapy for active disease, intravaginal probiotics for 14 additional days or intravaginal metronidazole gel 0.75% twice a week for 16 weeks decreases the recurrence rate (SOR: B, small RCTs). A 5-day course of intravaginal probiotic followed by a 5-day course of intravaginal metronidazole gel 0.75% after each menses may also lower the recurrence rate (SOR: C, low-quality cohort study).

A 2010 double-blind RCT assessed the efficacy of repopulating the vaginal flora with vaginal probiotic capsules in 120 healthy women of Asian descent with history of recurrent BV (≥2 BV episodes in the previous year).¹ Patients were randomly assigned to receive either daily Probaclovag® vaginal probiotic (n=58, or placebo capsule n=62) for two 7-day periods with a 7-day break.
between. The primary endpoint was diagnosis of BV by Amsel criteria at any time during the 2-month follow-up.

The probiotic group had a lower BV recurrence rate through 2 months (16% vs 45%; OR 0.23; 95% CI, 0.10–0.55). At an 11-month follow-up telephone interview, patient-reported BV symptoms remained lower in the intervention group (11% vs 28%; OR 0.31; 95% CI, 0.11–0.93).

A 2006 multicenter, prospective, open-label RCT studied the use of suppressive vaginal metronidazole for the prevention of recurrent BV in 157 women with active BV and a history of at least 2 episodes of BV in the previous year. Patients received treatment with 0.75% metronidazole gel intravaginally at bedtime for 10 days. Ninety-five women who had been successfully treated for BV at 3 to 5 days after completion of the initial therapy were randomly assigned to receive suppressive metronidazole vaginal gel (n=51) or placebo (n=44) twice per week for 16 weeks. The women were evaluated every 4 weeks for recurrence of BV by Amsel criteria. Those who were without recurrence after 16 weeks were followed for an additional 12 weeks without any intervention.

At 16 weeks, fewer women in the metronidazole group had recurrence compared with the placebo group (26% vs 59%; RR 0.43; 95% CI, 0.25–0.73). Recurrences were also lower in the metronidazole group at 28 weeks (51% vs 75%; RR 0.68; 95% CI, 0.49–0.93).

Another prospective study evaluated the efficacy of extended antibiotic treatment with adjuvant lactobacilli in reducing the rate of relapse in 63 women with active BV diagnosed by Amsel criteria and no history of recurrent BV. Patients were treated initially with 2% vaginal clindamycin cream and 300 mg oral clindamycin twice a day for 7 days. After treatment with clindamycin, the women were treated with a 5-day course of intravaginal capsules containing lactobacilli and then 5 more days of metronidazole vaginal gel. This cycle of lactobacillus and metronidazole was repeated after each menstrual cycle for a total of 6 menstrual cycles. The patients sent vaginal samples by mail after each cycle. Follow-up was at 6, 12, and 24 months, unless relapse occurred sooner.

Cure rate (by Amsel criteria) was 75%, 65%, and 56% after 6, 12, and 24 months, respectively. An important weakness on this study was the lack of a comparison with a control group and the possibility of enrollment bias due to the lack of blinding.

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