Levonorgestrel-Releasing Intrauterine System vs. Oral Progestins for Treatment of Endometrial Hyperplasia

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Help Desk Answers provides answers to questions submitted by practicing family physicians to the Family Physicians Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review.

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Clinical Question

In women with endometrial hyperplasia without atypia, is the levonorgestrel-releasing intrauterine system (Mirena) or oral progestin therapy more effective in achieving complete resolution?

Evidence-Based Answer

The levonorgestrel-releasing intrauterine system achieves significantly higher resolution rates of endometrial hyperplasia without atypia compared with cyclic oral progestins (68% to 100% vs. 48% to 69%, respectively). (Strength of Recommendation [SOR]: A, based on consistent randomized controlled trials [RCTs].) Treatment with continuous oral progestins for six months is also more effective than cyclic progestins (96% vs. 69%) and is comparable to the levonorgestrel-releasing intrauterine system. (SOR: B, based on an RCT.)

Researchers randomized 120 premenopausal women with abnormal uterine bleeding and non-atypical simple or complex endometrial hyperplasia to receive a levonorgestrel-releasing intrauterine system (n = 59) or oral norethindrone (n = 61).[1] Endometrial hyperplasia was initially diagnosed by dilation and curettage; endometrial biopsy was performed for follow-up. Women in the norethindrone group received 5 mg three times per day, for three weeks per month, for three consecutive months. Treatment was continued for three or six additional months if patients did not have complete resolution. The levonorgestrel-releasing intrauterine system remained in place for the duration of the study (12 months). Compared with those in the norethindrone group, more women in the levonorgestrel group achieved complete resolution at three months (68% vs. 48%; relative risk [RR] = 1.4; 95% confidence interval [CI], 1.0 to 2.0), six months (80% vs. 61%; RR = 1.3; 95% CI, 1.0 to 1.7), and 12 months (88% vs. 55%; RR = 1.6; 95% CI, 1.2 to 2.0). This study was limited by lack of patient blinding. However, the pathologist who read the histologic surveillance was blinded to the treatment modality.

In another RCT, 104 pre- and postmenopausal women with abnormal uterine bleeding and non-atypical endometrial hyperplasia were randomized to treatment with the levonorgestrel-releasing intrauterine system for three months (n = 26), oral medroxyprogesterone (Provera) for three months (n = 26), the levonorgestrel-releasing intrauterine system for six months (n = 26), or oral medroxyprogesterone for six months (n = 26).[2] Those in the medroxyprogesterone groups received 10 mg daily for 10 days per month. Endometrial hyperplasia was diagnosed by biopsy. Follow-up was performed at two years. More patients in the levonorgestrel groups had complete resolution of endometrial hyperplasia compared with those in the medroxyprogesterone groups (84% vs. 50% at three months; $P = .001$; and 100% vs. 64% at six months; $P = .0001$). Patients were not blinded to therapy, and it was unclear whether the pathologist was.

In a multicenter RCT, 170 pre- and postmenopausal women (most with abnormal uterine bleeding) and simple, complex, or atypical complex endometrial hyperplasia were randomized to treatment with the levonorgestrel-releasing intrauterine system, oral cyclic medroxyprogesterone, or oral continuous medroxyprogesterone.[3] Endometrial hyperplasia was diagnosed by biopsy. Oral cyclic medroxyprogesterone was given

at a dosage of 10 mg daily for 10 days per month; continuous medroxyprogesterone was given at a dosage of 10 mg per day. All therapies were continued for six months. Complete resolution of endometrial hyperplasia was achieved by 100% of women in the levonorgestrel group, 96% in the continuous medroxyprogesterone group, and 69% in the cyclic medroxyprogesterone group. The levonorgestrel-releasing intrauterine system was significantly superior to oral cyclic medroxyprogesterone ($P = .01$); continuous medroxyprogesterone was superior to oral cyclic medroxyprogesterone ($P = .01$) and comparable with the levonorgestrel-releasing intrauterine system. Patients were not blinded to therapy, but the pathologist was.

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