Does the LNG-IUS treat endometrial hyperplasia as effectively as MPA?

Yes, according to this multicenter, randomized trial of 170 women from Norway. Women treated with the levonorgestrel-releasing intrauterine system (LNG-IUS) had histologically normal endometrium after 6 months of use, comparable to the therapeutic response in women taking continuous medroxyprogesterone acetate.

After 6 months, women in the LNG-IUS arm had a 100% response rate, compared with 96% for the continuous MPA group and 69% for cyclic MPA.

Histologic interpretation of hyperplasia is highly subjective
There are several problems inherent in a study like this. Although Orbo and colleagues address these problems tangentially, the problems affect the interpretation of results.

For example, the histologic interpretation of endometrial hyperplasia is known to be associated with low interobserver agreement.

WHAT THIS EVIDENCE MEANS FOR PRACTICE
In low-risk women with simple hyperplasia, the use of targeted low-dose progestins—oral or intrauterine—is appealing. While Orbo and colleagues present an interesting study, they do not definitively establish the optimal intervention.

As we enter a cost-conscious phase of medicine in the United States, we may discover that oral generic MPA (given continuously) may be the most cost-effective treatment despite the option of delivering a low-dose progestin via intrauterine device.
agreement. Clinical trials that use endometrial safety as an outcome require two primary pathologists to review the histology, with a third pathologist standing by in case of disagreement.

In the current study, two pathologists in the same department independently reviewed the histology. Orbo and colleagues used World Health Organization criteria for hyperplasia. However, as an adjunct, they also used a D-classification morphometric assessment. When I put in a casual call to local gynecologic pathologists, they told me that neither the D-classification nor the immunochemical-detected PTEN protein is used in routine clinical practice to determine the risk of progression.

Intermittent use of oral MPA is known to be ineffective

The cyclic use of MPA for only 10 days overlooks epidemiology from estrogen-progestin replacement regimens in postmenopausal women. Use of a progestin for fewer than 12 days during estrogen replacement increases the risk of endometrial cancer. Exogenous progestin must be given for more than 12 days to inhibit hyperplasia and neoplasia. The dose itself is not critical; the duration of administration is.

In the current study, both the LNG-IUS and continuous MPA met this criterion. Local delivery of the progestin with the LNG-IUS allows for a reduction of the delivered dose and mitigates side effects even as it uses a more potent progestin than MPA.

Assessment of outcomes was questionable

Although Orbo and colleagues suggest that there is no evidence of progression with the LNG-IUS and continuous MPA, they relied on a Pipelle biopsy of the endometrium performed after 6 months of treatment. The clinical settings that led to the hyperplasia in the first place are poorly characterized as either pre- or postmenopausal, and the cause of the hyperplasia is not identified. This approach overlooks such realities as the increased incidence of simple hyperplasia in many perimenopausal women, which appears to regress with further reduction in ovarian estrogen.

The final outcomes for women in the cyclic MPA arm are not provided. Hyperplasia without atypia progresses to carcinoma in 1.6% of cases, but when atypia is present, the progression rate is 23%.

References