Editorial

J Gynecol Oncol Vol. 24, No. 2:103-104
http://dx.doi.org/10.3802/jgo.2013.24.2.103

pISSN 2005-0380
eISSN 2005-0399

Journal of Gynecologic Oncology
jgo

LNG-IUS treatment of non-atypical endometrial hyperplasia: Can Pipelle endometrial sampling be an accurate method of follow-up evaluation?

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See accompanying article on page 128.

Endometrial hyperplasia (EH) is a common disease affecting women of all ages [1]. It is clinically important because it can cause abnormal uterine bleeding, and can precede, or occur concurrently, with endometrial carcinoma.

There are many progestin therapy regimens available for treatment of EH. The main progestational agents are oral progestogens such as norethisterone acetate, megestrol acetate, and medroxyprogesterone 17-acetate. More recently, the levonorgestrel-releasing intrauterine system (LNG-IUS; Mirena, Bayer Schering Pharma Oy, Turku, Finland) also has been used successfully to treat EH [2,3]. Several observational studies have shown higher regression rates for LNG-IUS than for the oral progestogens [4-6]. However, systematic examination of the literature indicates that the quality of the published data, derived from small sample sizes and short-term follow-up, is relatively poor [5].

In this issue of the *Journal of Gynecologic Oncology*, Abu Hashim et al. [6] reports a prospective randomized controlled trial (RCT) that compared the efficacy of LNG-IUS with norethisterone acetate (NET) for treatment of non-atypical EH in perimenopausal women. As noted above, there are many reports on the best way to treat this condition, but only observational studies are available to inform clinical practice. Therefore, many gynecologists consider an RCT on the use of oral progestogens versus LNG-IUS in the management of EH to be required [7]. In this sense, the present study carries clinical significance.

The authors of the present report found a significantly higher regression rate in the LNG-IUS group than in the NET group at the 3rd-, 6th- and 12th-month follow-up visits (67.8% vs. 47.5%; 79.7% vs. 60.7%; 88.1 vs. 55.7%). These findings match those of a recent meta-analysis of 190 observational studies including 1,001 women. This analysis showed that a significantly higher regression rate was achieved with LNG-IUS than with oral progestins in treatment of non-atypical complex EH (92% vs. 66%). The authors also reported that the LNG-IUS regression time ranged from 3 to 12 months (median, 3 months), a significant proportion of the patients (67.8%) having achieved regression by the 3rd month. This success rate accords with data reported by Lee et al. [8] for a prospective observational study of 12 Korean women diagnosed with EH and treated with LNG-IUS. In that study, complete regression of EH was achieved in all cases (100%, 12/12), most of the patients (66%, 8/12) having attained it within three months. In light of these results, the authors concluded that LNG-IUS is superior to high-dose oral NET therapy for non-atypical EH and should therefore be considered a valuable treatment option in such cases.

Whereas these results are certainly encouraging, there is yet an important concern with respect to the accuracy of the follow-up evaluation method employed by the authors. Specifically, Pipelle endometrial sampling was utilized. But can Pipelle endometrial sampling be an accurate method for follow-up evaluation? The authors note that a recent trial reported almost equal EH-diagnostic success rates between Pipelle biopsy and dilatation & curettage (D&C) [9]; however, these results were obtained for cases where the LNG-IUS was not in the uterus and where there were no progestin effects on the endometrium. According to the reported literature,

Received Mar 9, 2013, **Accepted** Mar 9, 2013

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in cases of EH treatment using LNG-IUS, the endometrial response has been evaluated by endometrial aspiration biopsy while the LNG-IUS is in the uterus or by D&C after LNG-IUS removal [2-6,8]. Nevertheless, there has been no report comparing the accuracy of these methods.

In our recent study comparing the diagnostic accuracy of endometrial aspiration biopsy with the LNG-IUS in the uterus with that of D&C after LNG-IUS removal, the diagnostic concordance between examinations was assessed for nine of 28 cases examined (32.1%). In our results, the diagnostic accuracy of endometrial aspiration biopsy with LNG-IUS in place was shown to be very poor [9]. Furthermore, a high prevalence of insufficient tissue for pathologic evaluation (17 of 28 cases, 60.7%) was noted with endometrial aspiration biopsy [10]. Significantly, when using oral progestin and LNG-IUS, the number of cases where there is insufficient tissue for pathologic evaluation can be increased due to endometrial atrophy, and in these instances, we must pay more attention, because non-diagnostic endometrial tissue does not rule out endometrial pathology. All in all, therefore, endometrial aspiration biopsy with LNG-IUS in place is less accurate than D&C after removal of LNG-IUS; in fact, it might not be reliable for follow-up evaluation where patients have been treated with LNG-IUS for EH. To confirm our findings, a Korean prospective multicenter study is currently underway [11], and will provide more reliable data on this issue.

The study of Abu Hashim et al. [6] is meaningful for being the first RCT to date that has evaluated the efficacy of LNG-IUS for treatment of non-atypical EH. However, the accuracy and reliability of any such results on the effectiveness of hormonal treatment depend on a precise follow-up method of endometrial evaluation. Therefore, until which method is confirmed to be more accurate, differences between the results for oral progestogens and LNG-IUS in the treatment of non-atypical EH, even if they appear to be significant, should be interpreted with caution.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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