GENERAL GYNECOLOGY

Clinical effects of the levonorgestrel-releasing intrauterine device in patients with adenomyosis

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OBJECTIVE: The aim of this study was to evaluate the long-term clinical effects of a levonorgestrel-releasing intrauterine device (LNG-IUD) on adenomyosis.

STUDY DESIGN: A LNG-IUD was inserted into 47 patients who were diagnosed with adenomyosis. Uterine volume, uterine artery blood flow, pictorial blood loss assessment chart (PBAC) scores, and the degree of dysmenorrhea were evaluated before and 36 months after insertion of the LNG-IUD.

RESULTS: Pain scores and PBAC scores dropped dramatically in 6 months and showed significant decrease after 36 months. A significant decrease in mean uterine volume was noted 12 months (156.85 ± 49.79 mL to 118.64 ± 41.36 mL; $P < .001$) and 24 months (128.84 ± 48.70 mL; $P < .001$) after LNG-IUD insertion, but no significant differences were noted at 36 months. The mean pulsatility indices of both uterine arteries increased significantly 12 months after insertion ($P = .002$ for right; $P = .011$ for left) and decreased after 24 months without significance. Uterine volume and uterine blood flow were negatively correlated (Pearson's correlation, $P < .05$). Significant increase of uterine volume, pain scores, and PBAC scores were noted at 36 months compared with 12 months after insertion($P = .034$, .021, and .001, respectively).

CONCLUSION: For patients with clinical diagnosis of adenomyosis, the LNG-IUD is effective for the reduction of uterine volume with improvement of vascularity and relief of symptoms. However, the efficacy of LNG-IUD on uterine volume may begin to decrease 2 years after insertion.

Key words: adenomyosis, Doppler color flow, levonorgestrel intrauterine system, uterine artery, uterine volume

Cite this article as: Cho S, Nam A, Kim H, et al. Clinical effects of the levonorgestrel-releasing intrauterine device in patients with adenomyosis. Am J Obstet Gynecol 2008;198:373.e1-373.e7.

Adenomyosis remains an important cause of menorrhagia and dysmenorrhea, which can result in great stress for the woman involved.[1] Traditionally, adenomyosis has been diagnosed based on clinical findings and histopathologic confirmation after surgery. Until recently, hysterectomy was advocated as the definitive treatment. However, noninvasive diagnosis is now possible with transvaginal ultrasonography (TVS) and magnetic resonance imaging.[2] Such advances had led gynecologists to seek treatment alternatives to hysterectomy for the management of this frustrating disorder, which includes endometrial ablations, danazol, hormonal suppression with gonadotrophin-releasing hormone agonists, or levonorgestrel-releasing intrauterine system.[3-7] The levonorgestrel-releasing intrauterine system is an intrauterine device that releases synthetic progesterone into the endometrial cavity at a rate of 20 μg/d over a 5-year period.[8] Although it was developed primarily as a contraceptive device, it is now used widely for the purpose of noncontraceptive effects for conditions such as menorrhagia and dysmenorrhea. Recently, the device has been reported to be effective for the management of adenomyosis and appears to decrease uterine volume and effectively reduce adenomyosis-related symptoms, which include dysmenorrhea and menorrhagia.[9,10] However, no data have been published on the efficacy of long-term use of the levonorgestrel-releasing intrauterine system on adenomyosis. In this study, we evaluated the efficacy of a levonorgestrel-releasing intrauterine device (LNG-IUD) in women with adenomyosis over a period of 3 years by measuring changes in uterine volume and uterine artery blood flow with color Doppler transvaginal ultrasound.

Materials and Methods

From July 2003 to March 2007, 47 women, who were 31-45 years old, participated in this study with their informed consent. The study was approved by the institutional review board at Yongdong Severance Hospital. All patients had complaints of menorrhagia and dysmenorrhea for at least 6 months. Each woman underwent a TVS examination with an Ultramark HDI 5000 unit (Advanced Technology Laboratories, Bothell, WA) with a wide-band 5- to 9-MHz transducer. All transvaginal ul-

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Received May 11, 2007; accepted Oct. 12, 2007.

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0002-9378/$34.00

doi: 10.1016/j.ajog.2007.10.798

trasound examinations were performed by the same examiner, and each examination was interpreted in real time. We used sonographic diagnostic criteria for adenomyosis that had been reported in previous studies: myometrial cyst, distorted and heterogeneous myometrial echotexture, poorly defined focus of abnormal myometrial echotexture, and a globular and/or asymmetric uterus. Myometrial cyst was defined as a round anechoic area of 1-7 mm diameter. Heterogeneous myometrium was defined by the presence of an indistinctly marginated myometrial area with decreased or increased echogenicity.[11-13] Globular and/or asymmetric uterus was defined as a regular enlarged uterus with possible myometrial asymmetry that was unrelated to leiomyoma. Once the diagnosis was made, the volume of the uterus was measured. The uterine length was first measured from fundus to internal os, with the vaginal probe in a sagittal plane. The probe was turned through 90 degrees to a transverse plane and adjusted to give the maximum anteroposterior diameter. The anteroposterior and transverse diameters were then measured. The uterine volume was calculated with use of the formula for a prolate ellipsoid (volume = 0.52 × length × anteroposterior diameter × transverse diameter). Doppler blood flow assessment of the uterine arteries was performed by the identification of both uterine arteries on a transverse scan at the level of the internal os of the cervix. The Doppler gate was positioned when a vessel with a good color signal was identified on the screen. The pulsatility index (PI; systole − diastole/mean), the resistance index (RI; systole − diastole/systole), and the ratio of time averaged maximal systolic and diastolic blood flow velocities (S/D ratio) of both uterine arteries were calculated from the mean of 3 similar consecutive waveforms of good quality. Menstrual blood loss was quantified with a pictorial blood loss assessment chart (PBAC).[14] The patients were instructed carefully on how to fill in the charts. PBACs were completed by all patients during the course of 2 menstrual cycles before their enrollment and during all episodes of bleeding during the first 12 months after entry. PBACs for the 24- and 36-month visits were completed for the last episode of bleeding before the visit. The scoring was based on the number of sanitary pads and tampons used each day and their degree of soiling. The number and size of any clots that were passed were also taken into account. The PBACs were read by 1 of the authors. A score of 75 on the PBAC, which corresponds to a blood loss of ≥60 mL, was regarded as excessive bleeding.

The degree of dysmenorrhea was evaluated with a visual analogue scale that consisted of a 10 cm-linear analogue scale marked from 0-10, in which 0 represented no pain at all and 10 represented the most severe pain.[15] The score was recorded by marking a point somewhere along the 10-cm line.

An LNG-IUD (Schering, Oy, Turku, Finland) was inserted into 47 patients. The uterine volume, RI, PI, and S/D ratio of the uterine arteries, the pain score, the PBAC scores, and the serum CA-125, serum ferritin, and serum hemoglobin levels were evaluated for each patient before the device was inserted. The serum CA-125, ferritin, and hemoglobin levels were compared for statistical significance after 12 months, and the uterine artery blood flow analysis were made after 12, 24, and 36 months. The uterine volume, PBAC scores, and pain scores were measured at 6, 12, 24, and 36 months after the insertion of the IUD; the differences were evaluated for statistical significance.

The statistical analysis was done with the SPSS statistical software (version 13.0; SPSS Inc, Chicago, IL). Comparisons were made with the use of paired sample *t*-test and the nonparametric Friedman test for multiple comparisons. Significant results were further analyzed with the use of the Wilcoxon signed rank test. The correlation between changes in uterine volume and uterine artery blood flows was evaluated with the use of Pearson's correlation coefficient. Probability values of $<.05$ were considered statistically significant

RESULTS

Insertion of the LNG-IUD was performed without anesthesia in all cases, and no particular patient discomfort was noted. The mean age of the patients was 39.89 ± 3.91 years old, and the mean parity was 1.70 ± 0.79. There were 2 spontaneous expulsions of the LNG-IUD at 2 and 13 months after insertion, respectively. In 1 patient, the LNG-IUD was removed after the first month because of abdominal pain and irregular bleeding. These women were excluded from the postinsertion analysis. As a result, 44 patients were included in the analysis. Among these, 32 patients were followed for >36 months (Figure 1). Two patients had the original device removed, and a new LNG-IUD was reinserted at 30 months and 32 months because of increasing dysmenorrhea and vaginal bleeding.

The laboratory findings before and after insertion of the LNG-IUD are shown in Table 1. Serum hemoglobin, ferritin, and CA-125 levels were evaluated before and 12 months after insertion of the LNG-IUD. They all showed significant improvement at 12 months after insertion. The serum hemoglobin and serum ferritin levels increased from 11.22 ± 1.59 g/dL to 12.53 ± 2.21 g/dL ($P < .001$) and from 29.5 ± 23.95 ng/mL to 41.18 ± 36.11 ng/mL ($P = .026$), respectively; the serum CA-125 levels decreased from 44.45 ± 31.63 U/mL to 25.32 ± 16.58 U/mL ($P = .009$).

Figure 2 shows changes of the uterine volume before and after insertion of the LNG-IUD. The initial mean uterine volume was 156.85 ± 49.79 mL. After 6 months, the mean volume of the uterus significantly decreased to 127.17 ± 46.85 mL ($P < .001$). After 12 months, the mean volume had decreased further to 118.64 ± 41.35 mL ($P < .001$). Twenty-four months after insertion of the LNG-IUD, the mean volume was still significantly lower than the initial uterine volume (128.84 ± 48.70 mL; $P < .001$). However, the uterine volume began to increase after 12 months and was significantly higher after 36 months than after 12 months (118.64 ± 41.35 mL to 139.87 ± 29.93 mL; $P = .034$). The volume after 36 months was still less than the initial volume, but the difference was statisti-