The Use of Levonorgestrel - IUD in the Treatment of Uterine Myoma in Thai Women

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Objective: *This study was designed to evaluate the potential usefulness of the levonorgestrel-releasing intrauterine device (LNG - IUD ; Mirena®) in treating women with uterine myomas.*
Design: *Prospective before-and-after (comparing) study.*
Setting: *Department of Obstetrics and Gynecology King Chulalongkorn Memorial Hospital.*
Subjects: *Sixteen women with uterine myomas who intended to receive treatment with the LNG IUD.*
Intervention(s): *Clinical and ultrasound examinations were performed prior to and at 1, 3 and 6 months after the LNG IUD insertion.*
Main Outcome Measures: *Myoma and Uterine volume, menstrual blood loss assessed with pictorial blood loss assessment charts and hematocrit.*
Results: *Use of the LNG IUD was associated with a statistically significant reduction in the total myoma volume, average uterine size and marked reduction in menstrual blood loss. After 6 months of use, the median total myoma volume decreased from 19.82 mL to 11.63 mL ($p < 0.05$), median pictorial blood loss assessment chart score declined from 89 to 3 ($p < 0.05$). Hematocrit level increased over 6 months of use. The most common side effects were bleeding disturbances (68.8%). No pregnancies occurred during the study.*
Conclusion: *The LNG IUD was associated with a profound reduction in myoma and uterine volume. For women with myomas of this size, the LNG IUD provides effective medical treatment of bleeding.*

Keywords: *Levonorgestrel, IUD, Uterine myoma, Menstrual bleeding*

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Uterine myomas are benign clonal tumors originating from the smooth muscle of the human uterus[1]. Most myomas are asymptomatic, but many women have significant symptoms warranting therapy. Symptoms attributable to myomas can generally be classified into three distinct categories: abnormal uterine bleeding, pelvic pressure, pain and reproductive dysfunction[1].

The most typical bleeding pattern of myoma is menorrhagia or hypermenorrhea[1], defined as menstrual blood loss of 80 mL or more per cycle[2]. Menorrhagia is the major reason for hysterectomy in these women. In the last few years, several medical and minimally invasive surgical procedures have been developed as an alternative to hysterectomy for women who want to preserve their uterus.

The use of the levonorgestrel-releasing intrauterine device (LNG-IUD) is currently undergoing extensive evaluation. This system consists of a T-shaped intrauterine device sheathed with a reservoir of levonorgestrel released at the rate of 20 µg daily from a total load of 52 mg[3].

In the recent studies that evaluated the effectiveness of a LNG IUD in the treatment of myoma - related menorrhagia, they reported significant reduction of menstrual blood loss[4,5]. Moreover, one study reported the decrease in total myoma volume by 6 months after the LNG IUD insertion[5].

The objectives of this study was to evaluate the potential usefulness of the levonorgestrel-releasing intrauterine device (LNG - IUD; Mirena®) in treating Thai women with uterine myomas.

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Material and Method

We performed a prospective study of 22 premenopausal female volunteers with uterine myomas who chose the LNG IUD as their method of treatment. The Inclusion and Exclusion criteria for all participants were as follows.

Inclusion criteria

- Age of 20- 45 years.
- Size of uterus estimated to be ≤ 12 weeks' gestational size by pelvic examination.
- Presence of at least one myoma by ultrasound examination.
- No contraindication for IUD use.
- Accept to use LNG IUD for at least 6 months.

Exclusion criteria

- History of pelvic inflammatory disease or ectopic pregnancy.
- Presence of sub-mucous myoma with distortion of the uterine cavity.
- Pregnancy.
- Malignancy of genital organ.
- Size of uterus estimated to be > 12 weeks' gestational size by pelvic examination.
- Acute or chronic liver disease.
- History of septic abortion within the last 3 months.
- Cervicitis or Cervical Intraepithelial Neoplasia

Demographic and baseline clinical data, including myomas volume, uterine size, menstrual blood loss, and hematocrit were obtained before the LNG IUD insertion (Table 1). The LNG IUD was inserted within the first 7 days of the menstrual cycle. Participants were followed-up three times thereafter (at the end of 1, 3, and 6 months) to repeat these measurements and compare them with the baseline values.

The uterine and myoma volumes were measured by sonography. The same examiner performed the ultrasonographic evaluation in each participant with a real-time ultrasonography scanner using a 3.5-MHz transvaginal probe (TOSHIBA Sonolayer SSH 140A). The three diameters of the uterus and each myoma were measured to calculate uterine and individual myoma volumes using the formula for ellipsoid tumors: (4/3) x ¶ x (R1) x (R2) x (R3), where R1, R2, and R3 were the radii of each of the three uterine or myoma dimensions, respectively[6]. In case of multiple myomas, the volume of each tumor was calculated and added to estimate the total myoma volume. If more than three tumors were present, then the total volume of the three largest tumors was determined.

Menstrual blood loss was estimated using a pictorial blood loss assessment chart devised by Higham et al[7]. To minimize inter observer variation, all participants were provided the same sanitary protection product. The participants completed the charts for one menstrual cycle prior to the

LNG IUD insertion, and for the entire 1st, 3rd, and 6 th months afterward. We evaluated the completed charts according to the scoring system. The pictorial blood assessment chart score > 100 is equivalent to blood loss of > 80 mL, which defines menorrhagia[8]. Participants were asked not to use other hormonal contraceptive methods or other drug treatment for bleeding or anemia until the end of the study.

The statistical analysis was carried out by Wilcoxon Signed Ranks Test for the different variables with program SPSS version 12.0. A value of $p < 0.05$ was considered significant.

Results

Of the 22 participants fitted with the LNG IUD, 16 were eligible for analysis. One patient never returned for a study visit after the LNG IUD insertion. One patient could not insert a LNG IUD due to not being able to insert a uterine soundly. Four participants discontinued the study prematurely: one due to expulsion of the device, three for heavy menstrual bleeding; and they underwent hysterectomy. Data were obtained from 16 participants that completed the 6 months of observation.

The Characteristics of the participants were shown in Table 1. The mean age of the participants was 41 years. Menorrhagia (determined by the pictorial blood assessment chart score > 100) was diagnosed in

Table 1. Characteristics of subjects

Characteristics Median (range)	Number = 16
Age (year)	41 (33-45)
Height (cm)	157 (150-164)
Weight (kg)	58 (47-79)
Blood pressure (mm/Hg)	
Systilic	110 (100-130)
Diastolic	70 (70-80)
Uterine volume (mL)	139.4 (45.4-789.9)
Total leiomyoma volume (mL)	19.8 (1.0-546.6)
Menstrual blood loss (PBAC)	89 (5-438)
Hematocrit (%)	36.4 (27.8- 45.7)

Table 2. Myoma volume, uterine volume, PBAC score and hematocrit

Variable	At beginning Median (range)	6 months after insertion Median (range)
Total myoma volume (mL)	19.82 (1.01-546.65)	11.63 (0.35-377.43) p = 0.004
Uterine volume (mL)	139.42 (45.40-789.94)	109.09 (36.06-640.05) p = 0.002
PBAC	89 (5-438)	3 (0-460) p = 0.044
Hematocrit	36.40% (27.8-45.7)	38.40% (30.2-44.8) p = 0.163

44% of participants before the LNG IUD insertion. Anemia (hematocrit < 36.0%) was diagnosed in 38% of participants at the beginning.

No new formation of uterine myomas was observed in patients during the 6 months of the study. The median volume of the myoma at the beginning was 19.82 mL (range 1.01-546.65) and decreased to 11.63 mL (range 0.35-377.43) at the end of the study. The decreased volume was statistically significant compared with baseline value ($p < 0.05$). The details were shown in Table 2.

The median PBAC score at the beginning was 89 (range 5-438) and decreased to 3 (range 0-460) at the end of study. The decrease in PBAC score was significant ($p < 0.05$) (Fig. 1.) The median percentage of hematocrit increased from 36.4% to 38.4%.

The most common side effects were bleeding disturbances (68.8%), breast tenderness (31.3%) and pelvic pain (18.8%). The details were shown in Table 3.

Table 3. Side effects

Side effect	Percentage (%) (n)
Bleeding disturbance	68.8% (11)
Amenorrhea	37.5% (6)
Irregular bleeding	31.3% (5)
Breast tenderness	31.3% (5)
Headache	6.3% (1)
Abnormal discharge	6.3% (1)
Dizziness	6.3% (1)

Three women discontinued the study because of the LNG IUD induced side effects. No cases of pelvic inflammatory disease occurred. No pregnancies occurred during the study.

There were no significant differences in blood pressure and body weight between the time of insertion and the 6 months follow up.

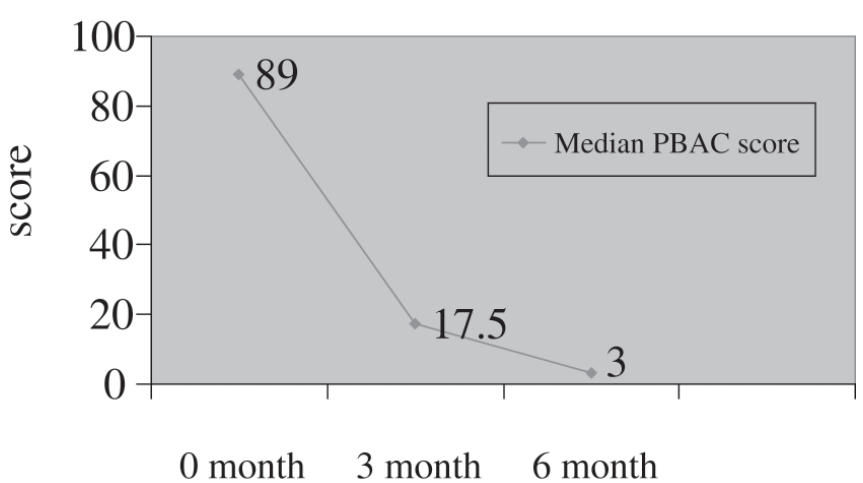

Fig. 1 PBAC score after LNG IUD insertion

Discussion

Myoma uteri were the common tumor of women in reproductive age[1]. Excessive uterine size, myoma volume, and menorrhagia are the causes of surgical intervention[1]. However, there are presently many non-surgical treatments for myoma uteri. LNG-IUD is an alternative treatment in women with uterine myoma, who want to preserve their uterus[4,5]. The recent studies demonstrated the effectiveness of a LNG IUD in the treatment of myoma - related menorrhagia[4,5]. Mercorio et al and Grigorieva et al reported that LNG-IUD was significant reduction of menstrual blood loss in women with uterine myoma[4,5]. Grigorieva also reported the decrease of total myoma volume within 6 months after the LNG IUD insertion[5]. Stewart et al reviewed the used of LNG IUD and found that it could reduce menorrhagia and increase hematocrit level[8].

However, the use of LNG IUD had limitation with large myoma, patient who had contraindication for IUD insertion and patient who had myoma that distorted uterine cavity. Nevertheless, there is limited knowledge about the types of uterine myoma which response to LNG - IUD treatment.

The use of LNG IUD produces some side effects. The most common side effect was spotting, amenorrhea, breast tenderness, and pelvic pain[9,10]. The limitations of this study were the small sample size, short period of time of follow up and no control group. However, the results of this study demonstrated that LNG-IUD should be able to reduce myoma volume and menstrual blood loss. LNG-IUD may be an alternative treatment of myoma uteri in women who need to preserve their uterus and avoid hysterectomy.

References

1. Stewart EA. Uterine fibroids. Lancet 2001; 357: 293-8.
2. Hallberg L, Hogdhal A-M, Nilsson L, Rybo G.. Menstrual blood loss: a population. Acta Obstet Gynecol Scand 1966; 45: 320-51.
3. Xiao BL, Zhou LY, Zhang XL, Jia MC, Luukkainen T, Allonen H. Pharmacokinetic and pharmacodynamic studies of levonorgestrel releasing intrauterine device. Contraception 1990; 41: 353-62.
4. Mercorio F, De Simone R, Di Spiezio Sardo A. The effect of a levonorgestrel - releasing intrauterine device in the treatment of myoma - related menorrhagia. Contraception 2003; 67: 277-280.
5. Grigorieva V,Chen-Mok M,Tarasova M. Use of a levonorgestrel-releasing intrauterine system to treat bleeding related to uterine leiomyomas. Fertil Steril 2003; 79: 1194-8.
6. Shawker TH. Monitoring response in therapy. In: Brascho DJ, Shawker TH, editors. Abdominal ultrasound in the cancer patient. New York: John Wiley and Sons; 1980: 113-34.
7. Higham JM, O'Brien PMS, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. Br J Obstet Gynaecol 1990; 97: 734-9.
8. Stewart A, Cummins C, Gold L, Jordan R, Phillips W. The effectiveness of the levonorgestrel-releasing intrauterine system in menorrhagia: a systematic review. BJOG 2001; 108: 74-86.
9. Sivin I, Stern J. Health during prolonged use of levonorgestrel 20 µg/d and the copper TCu 380Ag intrauterine contraceptive devices: a multicenter study. Fertil Steril 1994; 61: 70-7.
10. Sukonthaman K, Taneepanichskul. Menstrual patterns and side effects during the use of Mirena in Thai women 18-35 years old. Thai J Obstet Gynaecol 2003; 15: 231-5.

การศึกษาผลการใช้ห่วงอนามัยชนิดที่มีฮอร์โมน Levonorgestrel ในการรักษาเนื้องอกมดลูกในหญิงไทย

กนก จินดาบรรเจิด, สุรศักดิ์ ฐานีพานิชสกุล

วัตถุประสงค์: *เพื่อศึกษาผลการรักษาเนื้องอกมดลูกด้วยห่วงอนามัยชนิด ที่มีฮอร์โมน Levonorgestrel ในหญิงไทย*
รูปแบบการวิจัย: *การศึกษาไปข้างหน้า แบบเปรียบเทียบ ก่อน-หลัง*
สถานที่: *ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย*
ผู้ป่วยที่ได้ทำการรักษา: *ผู้ป่วยหญิงไทยที่มีเนื้องอกมดลูก ที่ต้องการรักษาด้วยห่วงอนามัยชนิด ที่มีฮอร์โมน Levonorgestrel*
วัสดุและวิธีการ: *ทำการเก็บข้อมูลของขนาดเนื้องอกมดลูก, ขนาดของมดลูก โดยใช้เครื่องอัลตราซาวด์เปรียบเทียบก่อนและหลังใส่ห่วงอนามัยที่มีฮอร์โมน Levonorgestrel ครบ 6 เดือน, เก็บข้อมูลของปริมาณประจำเดือนโดยใช้แผ่นภาพประเมินปริมาณประจำเดือน (PBAC) และตรวจความเข้มข้นของเลือด ก่อนและหลังใส่ห่วงอนามัย ครบ 6 เดือน*
ผลการศึกษา: *ห่วงอนามัยที่มีฮอร์โมน Levonorgestrel มีผลช่วยลดขนาดของเนื้องอกมดลูก และขนาดของมดลูก โดยขนาดของเนื้องอกมดลูกลดลงจากค่ามัธยฐาน 19.82 มล. เหลือ 11.63 มล. หลังจากใส่ห่วงอย่างน้อย 6 เดือน อย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) และสามารถลดปริมาณของประจำเดือนได้ด้วย จากค่า PBAC 89 เหลือ 3 ($p < 0.05$) โดยพบว่าความเข้มข้นของเลือดเพิ่มขึ้นด้วย ไม่พบการตั้งครรภ์เกิดขึ้นขณะทำการวิจัย*
สรุป: *การใช้ห่วงอนามัยที่มีฮอร์โมน Levonorgestrel สัมพันธ์กับการลดลงของเนื้องอกมดลูก และขนาดของมดลูกในผู้ป่วยเนื้องอกมดลูกที่ทำการวิจัย โดยสามารถใช้ลดปริมาณประจำเดือนลงได้ด้วย*