Insertion of the Mirena Intrauterine System for Treatment of Adenomyosis-associated Menorrhagia: A Novel Method

Fu-Shaing Peng[1], Ming-Yih Wu[2], Jehn-Hsiahn Yang[2], Shee-Uan Chen[2], Hong-Nerng Ho[2], Yu-Shih Yang[2]*

[1]Department of Obstetrics and Gynecology, Far Eastern Memorial Hospital, and [2]Department of Obstetrics and Gynecology, College of Medicine and National Taiwan University Hospital, Taipei, Taiwan.

SUMMARY

Objective: Insertion of the levonorgestrel-releasing intrauterine system Mirena is difficult in women with adenomyosis, and the device is often subsequently expelled. We used a novel insertion technique (Yang's method) to overcome this problem.

Materials and Methods: This retrospective study enrolled 273 patients with adenomyosis who were receiving Mirena for treatment of menorrhagia and/or dysmenorrhea between 2001 and 2008. Clinical outcomes and expulsion rates were compared between patients treated using conventional insertion and those treated using Yang's insertion methods.

Results: Expulsion occurred in 25.3% of patients with the conventional method, compared with 10.2% of patients with Yang's method. Hemoglobin levels and dysmenorrhea improved greatly in both groups after Mirena insertion.

Conclusion: Yang's insertion method for levonorgestrel-releasing intrauterine system is more reliable in some difficult cases, such as patients with severe adenomyosis. This method ensures correct positioning, thus reducing the risks of uterine perforation and/or expulsion. [*Taiwan J Obstet Gynecol* 2010;49(2):160–164]

Key Words: adenomyosis, expulsion, levonorgestrel-releasing intrauterine system, menorrhagia, Mirena

Introduction

Adenomyosis is an important cause of menorrhagia and dysmenorrhea. It has an elusive etiology that is characterized by the presence of endometrial glands and stroma located deep within the myometrium [1]. Although the diagnosis is often made after hysterectomy, transvaginal sonography and magnetic resonance imaging have recently proven to be useful noninvasive techniques for the preoperative diagnosis of adenomyosis [2,3]. The effects of medical treatments are usually restricted to the duration of therapy, which are associated with obvious side-effects and poor compliance. Endometrial resection or ablation can improve the symptoms of menorrhagia but often fails to relieve dysmenorrhea. Hysterectomy is, therefore, usually the ultimate therapeutic procedure for these patients. However, it is unsuitable for women who desire to retain their fertility.

The levonorgestrel-releasing intrauterine system (IUS), Mirena, has been approved in Europe for contraception since 1990. Because of the suppressive effect of

Correspondence to: Dr Yu-Shih Yang, Department of Obstetrics and Gynecology, College of Medicine and National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei 100, Taiwan.
E-mail: yangys@ntu.edu.tw
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levonorgestrel on the endometrium, Mirena has also been proven to be effective for the management of menorrhagia and dysmenorrhea [4], and as a progestin component in postmenopausal hormone therapy [5]. It was introduced in Taiwan in 1995 as an alternative therapy for idiopathic menorrhagia [6]. Many cases of menorrhagia are caused by adenomyosis, and Mirena was, therefore, introduced for the treatment of adenomyosis in Taiwan in 2000. Although it has been shown to be effective in decreasing menstrual flow and relieving dysmenorrhea as reported in other studies [7,8], insertion problems and IUS expulsion were experienced more often among those with severe adenomyosis.

Because adenomyosis is usually associated with an enlarged uterus, uterine distortion or great retroflexed/anteflexed uterine curvature, Mirena is commonly positioned incorrectly in these patients and can be easily flushed out by the heavy menstrual flow [9]. In addition, low positioning or partial expulsion of Mirena may be related to a longer period of spotting and bleeding. We introduced a new insertion technique called Yang's method in 2001, to ensure accurate insertion and optimal positioning of Mirena in women with severe adenomyosis. This report provides a short description of this novel method and our experience of using this technique in women with adenomyosis.

Materials and Methods

Sample selection

A total of 273 women aged 24–52 years who attended the National Taiwan University Hospital between January 2001 and June 2008 with symptoms of adenomyosis-associated menorrhagia and/or dysmenorrhea were included in the study. They underwent either transvaginal sonography or magnetic resonance imaging for the diagnosis of adenomyosis, and were then fitted with Mirena (Bayer Schering Pharma, Berlin, Germany) after signing an informed consent form. Patients with adenomyosis in combination with submucosal myoma or suspected endometrial disorders, such as endometrial polyps, endometrial hyperplasia or malignancies detected in the imaging study, were excluded. Mirena was inserted after menstruation had ended or the menstrual flow had decreased. All the procedures were performed at our outpatient clinics by experienced clinical staff. The use of Mirena to treat hypermenorrhea was approved by the institutional review board of National Taiwan University Hospital.

The cases were divided into two groups, according to the insertion method and the physician: Yang's method, performed by M.Y.W. and Y.S.Y., and the conventional method using the standard insertion technique, performed by other physicians.

Symptoms of hypermenorrhea and dysmenorrhea

Hypermenorrhea was reported by the patients themselves as the passage of blood clots or episodes of heavy bleeding during their menstruation. The severity of dysmenorrhea was determined using the visual analog scale which was calibrated from 0 to 10, with 0 representing no pain and 10 representing the highest possible level of pain [10]. Higher scores reflected a greater severity of menstrual cramps. Other demographic data (age, parity, mode of delivery) were also collected. Yang's insertion procedure is shown schematically in the Figure and is described below.

Insertion technique

Physicians wore sterile gloves and maintained sterile conditions throughout the insertion procedure. After opening the package of the device, both threads were pulled and fixed tightly in the cleft at the end of the handle. The outer plastic tube was disconnected from the handle by firmly pulling and rotating it, and separating it from the whole insertion kit. The remaining plunger attached to the Mirena was placed in the sterile package. The sounding probe was placed into the lumen of the plastic tube and inserted into the fundus (Figure A). The outer plastic insertion tube was then slid forward to the fundus, and the inner sounding probe was withdrawn, with care being taken to keep the outer tube in the correct position within the uterine cavity (Figure B). The arms of the Mirena were then pinched off (again being careful to keep the outer tube in the correct position within the uterine cavity), and it was reinserted into the outer tube, followed by the plunger (Figure C). Care was taken to align the loop holding the strings with the cup-like receptacle at the top of the plunger, when reinserting the plunger. Finally, the plunger was pushed forward until the handle reached the outer tube, and slight pressure was exerted to reconnect them. Lastly, the Mirena was released while holding the inserter firmly in position and pulling the slider all the way down, as per the instructions (Figure D).

Follow-up

The bleeding pattern, intensity of dysmenorrhea and hemoglobin level were recorded before and 3–5 months after insertion. If the insertion time was close to the next period, the contraceptive pill, Diane-35 (Bayer Schering Pharma), was administered to postpone menstruation in both groups by at least 2 weeks. This aimed to prevent heavy blood flow from flushing out the Mirena before the endometrium had completely atrophied. Patients who

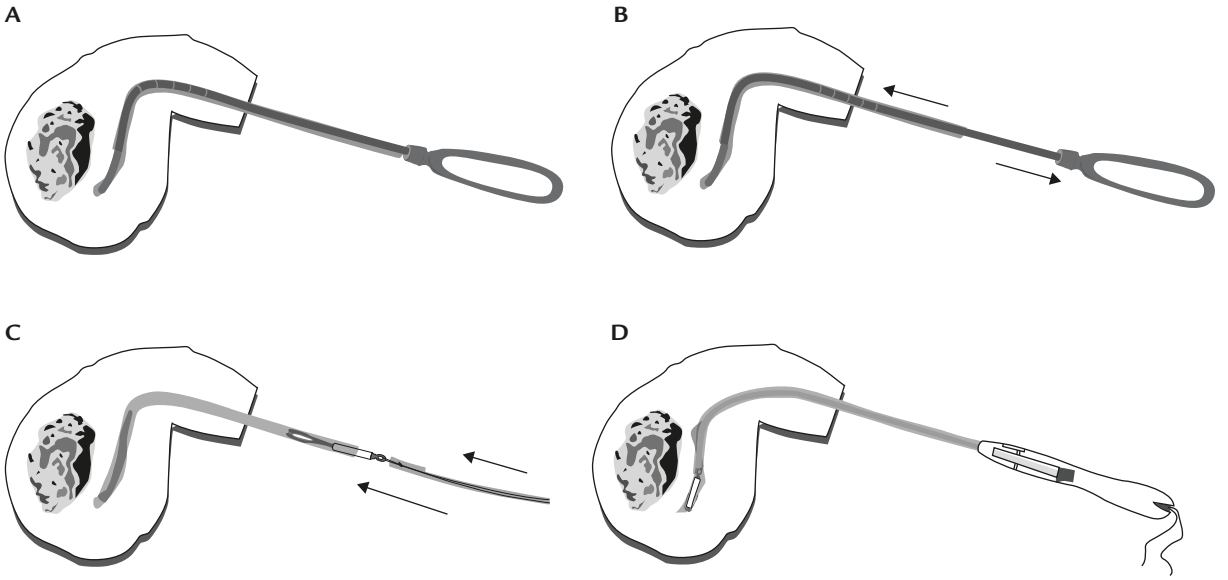

Figure. Yang's method of Mirena insertion. (A) The sounding probe is put into the lumen of the plastic tube and inserted into the fundus. (B) The outer plastic insertion tube is slid forward, and the inner sounding probe is withdrawn, leaving the outer tube in the correct position in the uterine cavity. (C) The Mirena arms are picked up and put it into the tunnel of the outer tube, followed by insertion of the plunger. (D) The plunger is pushed forward until the handle reaches the outer tube, then slight pressure is exerted to reconnect them. With the inserter held firmly in position, the Mirena is released by pulling down the slider all the way, as shown in the instructions.

Table 1. Baseline characteristics of 273 patients with adenomyosis*

Characteristic	Group 1 (Standard method; $n=146$)	Group 2 (Yang's method; $n=127$)	p
Age, mean ± SD (yr)	40.5 ± 6.9	41.1 ± 7.0	0.46
Parity, mean ± SD			
NSD	1.1 ± 1.1	1.1 ± 1.0	0.81
C/S	0.5 ± 0.8	0.4 ± 0.8	0.63
Pre-insertion condition, mean ± SD			
Dysmenorrhea (VAS)†	6.7 ± 2.1	7.0 ± 1.8	0.23
Hb (g/dL)	10.0 ± 2.5	10.5 ± 2.1	0.08
Post-insertion‡, *n* (%)			
IUS expulsions	37 (25.3)	13 (10.2)	0.001
IUS removals§	12 (8.2)	9 (7.1)	0.73

**Statistical analysis was performed using t tests for all items except intrauterine system loss; †visual analog scale was used to grade the severity of dysmenorrhea, as described in the Methods; ‡Pearson χ^2 test was used to compare intrauterine system loss ratios; §patients requested premature Mirena removal because of complications (e.g. vaginal spotting, back pain, watery discharge), critical conditions (e.g. severe anemia) or for other reasons (e.g. wish for pregnancy). SD = standard deviation; NSD = normal spontaneous delivery; C/S = cesarean section ; VAS = visual analog scale; Hb = hemoglobin; IUS = intrauterine system.*

experienced prolonged spotting (> 14 days) were given Diane-35 (once or twice a day) for the first 6 months. Bleeding control is important in Asian women, because prolonged spotting is associated with poor compliance. Any suspicion of expulsion, including abrupt increases in menstrual flow or missing the IUS tail in a pelvic examination, was confirmed by ultrasound.

Statistical analysis

Values of qualitative variables, such as pain and hemoglobin, were compared before and after Mirena treatment using paired *t* tests. IUS loss was defined as complete expulsion or partial expulsion into the cervix. Pearson χ^2 test was performed to compare the IUS loss rates between these two groups. Values of $p < 0.05$ were considered statistically significant.

Results

There were no significant differences in the demographic data between the two groups (Table 1). The insertion of Mirena was smooth in all cases, with no need for anesthesia. Thirty-seven of 146 cases (25.3%) who received

Table 2. Comparison of symptoms pre- and post-Mirena insertion*

	Pre-insertion, mean ± SD	Post-insertion, mean ± SD	*p*
Dysmenorrhea (VAS)†	6.9 ± 2.0	1.7 ± 1.6	< 0.001
Group 1 (Standard method)	6.7 ± 2.1	1.7 ± 1.6	< 0.001
Group 2 (Yang's method)	7.0 ± 1.8	1.6 ± 1.5	< 0.001
Hb (g/dL)†‡	10.1 ± 2.1	11.2 ± 2.3	< 0.001
Group 1 (Standard method)	10.0 ± 2.5	11.1 ± 2.2	0.001
Group 2 (Yang's method)	10.5 ± 2.1	11.6 ± 2.3	0.003

**Data are shown as mean ± standard deviation; †statistical analysis was performed using paired t tests for comparing values before and after Mirena treatment; ‡some cases lacked paired hemoglobin data for comparison (58 cases left in Group 1; 59 cases left in Group 2). SD = standard deviation; VAS = visual analog scale; Hb = hemoglobin.*

the standard insertion method (Group 1) experienced IUS expulsion at 1 month to 2 years, compared with only 13 of 127 cases (10.2%) who received Yang's method (Group 2) ($p = 0.001$ by χ^2 test; Table 1). In addition, 12 patients in Group 1 (8.2%) and nine in Group 2 (7.1%; $p = 0.73$) requested premature removal of Mirena prematurely because of complications (e.g. vaginal spotting, back pain, watery discharge), critical conditions (e.g. severe anemia), or other reasons (e.g. wish for pregnancy).

Dysmenorrhea symptoms were greatly improved in both groups after Mirena insertion (visual analog scale: Group 1, 6.7 *vs.* 1.7, $p < 0.001$; Group 2, 7.0 *vs.* 1.6, $p < 0.001$; by paired *t* tests; Table 2). Although some cases lacked adequate hemoglobin data for comparison, both groups demonstrated significant improvements in anemia after Mirena insertion (Group 1, 10.0 *vs.* 11.1 g/dL, $p = 0.001$; Group 2, 10.5 *vs.* 11.6 g/dL, $p = 0.003$; by paired *t* tests; Table 2).

Discussion

Although Mirena has been reported to be highly effective for the treatment of menorrhagia and reducing menstrual blood loss [4,11], its efficacy in treating adenomyosis has seldom been reported. A previous observational study noted that Mirena significantly improved the symptoms of adenomyosis and increased hemoglobin and serum ferritin levels [7]. A recent Korean study demonstrated that Mirena was effective in reducing uterine volume and uterine blood flow, and in relieving the symptoms of adenomyosis for 2 years [12]. Most patients in both groups in the current study experienced pain relief and significantly increased hemoglobin levels.

Problems with Mirena insertion are often encountered in routine clinical practice among patients with adenomyosis; Mirena insertion was reported to be more difficult and painful than insertion of the copper device [13], possibly because of its more rigid and broader insertion tube [14]. The uterine cavity of women with adenomyosis is sometimes large and distorted by anteflexion or retroflexion. This abnormal anatomy may lead to IUS placement in the lower uterine cavity. These factors may further hinder the insertion of Mirena and lead to incorrect positioning, which is a risk factor for expulsion [15]. This could partially explain why Mirena has a higher expulsion rate than copper devices (about 4–9%) in therapy for menorrhagia [16].

We have reported a novel method for Mirena insertion in patients with a uterus distorted by adenomyosis. The technique differs from the conventional method in the use of a sounding probe as a guide wire to introduce the outer rigid plastic tube. The metal sounding probe can be easily bent to fit various uterine shapes, and provides an accurate route for reaching the fundus. The guidance provided by this sounding probe allows the outer tube to be easily slid forward along the sounding probe and Mirena to be located in the correct fundal position. This is particularly important, because the correct fundal position can ensure uniform exposure of the endometrium to levonorgestrel, maximize the efficacy of the device, and prevent expulsion. A significantly higher expulsion rate and prolonged vaginal spotting were noted with a levonorgestrel-releasing intracervical device situated in the cervical canal, compared with an IUS in the uterine cavity [17].

Moreover, using the standard insertion method, the insertion of the outer tube into the uterine cavity depends on blind attempts, which increases the risk of uterine perforation, especially in patients with a distorted uterus. Furthermore, a difficult insertion may be time consuming and cause significant pain, which may, in turn, create a need for anesthesia and so reduce the acceptability of the treatment. We believe that this novel technique makes Mirena insertion easier and safer, irrespective of the uterine shape.

Yang's insertion method provides a more reliable technique to ensure the correct placement of Mirena in

patients with conditions such as severe adenomyosis. This affords homogenous release of hormone, prevents expulsion, and diminishes the risk of unpleasant complications. Although the cases in this study were not randomized, the results, nevertheless, suggest that this insertion method was suitable for overcoming the problems of device insertion in patients with severe adenomyosis and a distorted uterus. A randomized study with longer follow-up is needed to allow more definite conclusions to be drawn. Consideration should also be given to the difference in size between Mirena and that of some uterine cavities in patients with adenomyosis; a standard-sized Mirena IUS may not be optimal in patients with heavy menstrual bleeding. It is possible that a variety of sizes of IUS may be required in the future.

References

1. Ferenczy A. Pathophysiology of adenomyosis. *Hum Reprod Update* 1998;4:312–22.
2. Andreotti RF, Fleischer AC. The sonographic diagnosis of adenomyosis. *Ultrasound Q* 2005;21:167–70.
3. Arnold LL, Ascher SM, Schruefer JJ, Simon JA. The nonsurgical diagnosis of adenomyosis. *Obstet Gynecol* 1995;86: 461–5.
4. Irvine GA, Campbell-Brown MB, Lumsden MA, Heikkila A, Walker JJ, Cameron IT. Randomised comparative trial of the levonorgestrel intrauterine system and norethisterone for treatment of idiopathic menorrhagia. *Br J Obstet Gynaecol* 1998;105:592–8.
5. Suvanto-Luukkonen E, Kauppila A. The levonorgestrel intrauterine system in menopausal hormone replacement therapy: five-year experience. *Fertil Steril* 1999;72:161–3.
6. Wu MY, Ho HN, Chao KH, Chen CD, Yang YS, Lee TY. Clinical performance of the levonorgestrel intrauterine device (Mirena) in Taiwanese women as a contraceptive and its effect on menorrhagia. *Taiwan J Obstet Gynecol* 1999;38:131–9.
7. Fedele L, Bianchi S, Raffaelli R, Portuese A, Dorta M. Treatment of adenomyosis-associated menorrhagia with a levonorgestrel-releasing intrauterine device. *Fertil Steril* 1997; 68:426–9.
8. Fong YF, Singh K. Medical treatment of a grossly enlarged adenomyotic uterus with the levonorgestrel-releasing intrauterine system. *Contraception* 1999;60:173–5.
9. Hidalgo M, Bahamondes L, Perrotti M, Diaz J, Dantas-Monteiro C, Petta C. Bleeding patterns and clinical performance of the levonorgestrel-releasing intrauterine system (Mirena) up to two years. *Contraception* 2002;65:129–32.
10. Han SH, Hur MH, Buckle J, Choi J, Lee MS. Effect of aromatherapy on symptoms of dysmenorrhea in college students: a randomized placebo-controlled clinical trial. *J Altern Complement Med* 2006;12:535–41.
11. Milsom I, Andersson K, Andersch B, Rybo G. A comparison of flurbiprofen, tranexamic acid, and a levonorgestrel-releasing intrauterine contraceptive device in the treatment of idiopathic menorrhagia. *Am J Obstet Gynecol* 1991;164: 879–83.
12. 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;198:373–7.
13. Sivin I, el Mahgoub S, McCarthy T, et al. Long-term contraception with the levonorgestrel 20 mcg/day (LNg 20) and the copper T 380Ag intrauterine devices: a five-year randomized study. *Contraception* 1990;42:361–78.
14. Chi IC. An evaluation of the levonorgestrel-releasing IUD: its advantages and disadvantages when compared to the copper-releasing IUDs. *Contraception* 1991;44:573–88.
15. Van Kets H, Wildemeersch D, Van der Pas H, et al. IUD expulsion solved with implant technology. *Contraception* 1995; 51:87–92.
16. Diaz J, Bahamondes L, Monteiro I, Petta C, Hildalgo MM, Arce XE. Acceptability and performance of the levonorgestrel-releasing intrauterine system (Mirena) in Campinas, Brazil. *Contraception* 2000;62:59–61.
17. Pakarinen P, Luukkainen T, Elomaa K, et al. A 12-month comparative clinical investigation of a levonorgestrel-releasing intracervical device situated in the uterine cavity or cervical canal. *Contraception* 1996;54:187–92.