

# Risk Factors for Levonorgestrel-releasing Intrauterine System (LNG-IUS) Expulsion among Chinese Women Treated for Menstrual Disorders: Retrospective Cohort Study in a Regional Hospital

**FYL KUNG** MBChB

Department of Obstetrics and Gynaecology, Princess Margaret Hospital, Hong Kong

## *Objective:*

To investigate the risk factors for levonorgestrel-releasing intrauterine system (LNG-IUS) expulsion among Chinese women treated for menstrual disorders.

## *Methods:*

This was a retrospective cohort study in patients who had had LNG-IUS insertion, and involved comparison of characteristics in women in whom the system had or had not been expelled. The patients who were reviewed had LNG-IUS insertions carried out between 1 January 2001 and 31 December 2009 at the Princess Margaret Hospital, Hong Kong. The parameters studied were: age at insertion, number of previous vaginal births, number of previous Caesarean sections, the lowest haemoglobin level recorded in the last 2 years, previous pelvic sonographic examination, presence of fibroids, presence of adenomyosis, and the sounded uterine length at insertion.

## *Results:*

Expulsion of LNG-IUS was noted in 29% (23/80) of cases, in 52% (12/23) of whom expulsion had occurred within the first 6 months. We observed that pre-insertion sonographic pelvic examination ( $p < 0.05$ ) was associated with a higher LNG-IUS expulsion rate. For all other factors, there was no statistically significant association with expulsion.

## *Conclusion:*

No significant isolated risk factors were encountered for LNG-IUS expulsion. Pre-insertion sonographic pelvic examination probably implied presence of significant uterine pathologies. A low haemoglobin level reflecting menorrhagia correlated with the expulsion rate. In view of treatment effectiveness, LNG-IUS should be offered for the treatment of menstrual disorders when indicated. The unexpectedly high LNG-IUS expulsion rate noted in this study reinforces the need for patient counselling regarding this possibility.

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## Introduction

The levonorgestrel-releasing intrauterine system (LNG-IUS) has been available in Europe since 1990 and in the United States since 2000<sup>1</sup>. Apart from being an effective contraceptive, it is also used for the treatment for a variety of gynaecological disorders, including menorrhagia, dysmenorrhoea, and pain associated with endometriosis. It can also be used as an adjunct

to oestrogen replacement therapy<sup>1-3</sup>. Moreover, there is growing evidence for using LNG-IUS as a fertility-preserving conservative treatment for endometrial hyperplasia or even early endometrial cancer<sup>4-6</sup>. An in-utero LNG-IUS is a prerequisite to allow controlled release of levonorgestrel so as to facilitate effective

*Correspondence to:* Dr FYL Kung

*Email:* kyl769@ha.org.hk

treatment, and its expulsion is a recognised reason for treatment failure. The risk of LNG-IUS expulsion is approximately 1 in 20, and in general there is no difference in the rate of expulsion between this system and copper-bearing intrauterine devices (IUDs)<sup>3</sup>. Knowing the risk factors for LNG-IUS expulsion can theoretically facilitate patient selection for treatment and possibly facilitate more appropriate counselling. In this study, we set out to evaluate the patient characteristics who had had in-situ LNG-IUS insertions, in whom the system had or had not been expelled, and in so doing determine possible risk factors for expulsion.

## Methods

A retrospective study was carried out in the Department of Obstetrics and Gynaecology, Princess Margaret Hospital, Hong Kong. Its outpatient-based minor operation database of the involved institution covering a 9-year period (1 January 2001 to 31 December 2009) was reviewed. Some patients had their LNG-IUS inserted in the operating theatre under general anaesthesia, for which the operation record list was used to retrieve details via the hospital's computerised management system. "IUCD insertion" was used as the keyword for the search. Outpatient and inpatient medical records were reviewed for data collection. The parameters retrieved were age at insertion, number of previous vaginal births, number of previous Caesarean sections, lowest haemoglobin level recorded in previous 2 years, previous pelvic sonographic examinations, presence of fibroids, presence of adenomyosis, and the sounded uterine length at insertion.

Statistical analysis was undertaken using the Statistical Package for the Social Sciences (Windows version 16.0; SPSS Inc, Chicago [IL], US). The Chi-square association test was used for categorical variables. The Mann-Whitney *U* test was used for continuous variables as they were not normally distributed. The level of significance was set at a *p* value of less than 0.05.

## Results

The records of 95 cases were retrieved, of which 87 patients had had their LNG-IUS inserted in an outpatient setting and the remaining 8 underwent insertion under general anaesthesia in the operating theatre. Approximately 16% of the cases (15/95) were excluded, as the patients had defaulted follow-up and

the treatment response could not be evaluated. The remaining 80 patients (all Chinese) constituted the study sample.

The majority of patients had LNG-IUS inserted for menorrhagia, which accounted for 85% (68/80) of all cases, whilst 13% (10/80) were for dysmenorrhoea, and 4% (3/80) for dysfunctional uterine bleeding. In essence, all the patients had undergone LNG-IUS insertion to treat menstrual disorders, none having had them shortly postpartum or post-abortion, or for contraception purposes.

Approximately 93% (74/80) of the patients had had endometrial sampling in the previous 3 years, most of whom were confirmed to have a normal endometrium. In two cases, histological examination of the endometrial specimens yielded simple hyperplasia without cellular atypia. Subsequent re-sampling after LNG-IUS insertion confirmed regression of the endometrium in the patients. 80% (64/80) of the patients had undergone pelvic ultrasound examination in the preceding 3 years. Uterine fibroids were found in 28% (22/80) of patients; their mean diameter being 3.3 cm (range, 1.4-6 cm). Regarding the latter 22 patients, none had documented distortion of the uterine cavity. Ultrasonic features suggestive of adenomyosis were noted in 15% (12/80) of the patients.

Expulsion of the LNG-IUS had occurred in 23 patients, accounting for 29% of all cases. The mean time to expulsion was 6.3 months (range, 0.3-21 months) post-insertion. Table 1 shows a comparison of LNG-IUS expulsion rates in patients with or without specified categorical variables. Table 2 summarises the analysis of different patient characteristics belonging to those in whom the system remained in-situ and those who experienced its expulsion. Most of the variables did not yield any statistically significant differences. A preceding sonographic examination of the pelvis was associated with a statistically significant difference ( $p < 0.05$ ). Lower preceding haemoglobin levels appeared to favour LNG-IUS expulsion, though the difference did not reach statistical significance ( $p = 0.06$ ).

## Discussion

The LNG-IUS expulsion rate encountered in this study was 29%, which was much higher than rates

**Table 1. Comparison of expulsion rates among patients with or without the specific categorical variables (Chi-square association test was used)**

	Yes	No	p Value
Previous vaginal birth	32% (19/60)	20% (5/20)	0.4
Previous Caesarean section	35% (6/17)	29% (18/63)	0.18
Previous pelvic ultrasound	36% (23/64)	6% (1/16)	0.02
Uterine fibroid	36% (8/22)	28% (16/58)	0.31
Adenomyosis	25% (3/12)	31% (21/68)	0.49

**Table 2. Comparison of patient characteristics in in-situ levonorgestrel-releasing intrauterine system patients and those who had experienced expulsion\***

	Median (range)		p Value
	In-situ group (n=56)	Expulsion group (n=24)	
Age at insertion (years)	45 (32-52)	44 (38-53)	0.5
No. of vaginal births	2 (0-4)	2 (0-6)	0.23
No. of Caesarean sections	0 (0-2)	0 (0-2)	0.67
Lowest haemoglobin level (g/l)	95.5 (58-144)	84 (49-127)	0.06
Sounded uterine length (cm)	8 (6-12)	8 (7-12)	0.35

\* Analysis entailed the Mann-Whitney *U* test

reported in the literature. Previous studies were mainly concerned with the efficacy of LNG-IUS or other IUDs as contraceptive devices, which very likely entailed women without menstrual problems and having normal size, non-pathological uteruses. In our series, the selected patients had menstrual disorders and some also had uterine pathologies. Though the high expulsion rate might be related to the small sample size, differences in clinician competence or other factors suggested that the chance of expulsion may be somewhat higher in women with gynaecological disorders. This finding may be of value when it comes to counselling of patients having LNG-IUS insertion for menstrual disorders.

Merki-Feld et al<sup>7</sup> observed that more than 50% of the IUD dislocations occurred within 6 months of insertion; only 20% occurred more than a year later. In our study, 57% (13/23) of expulsion cases ensued within the first 6 months of insertion, while only 9% (2/23) occurred after 12 months. The competence of the clinicians performing LNG-IUS insertion was not evaluated, as it was not feasible to retrieve the individual number of IUD insertions by each clinician from the medical records. The Faculty of Sexual and Reproductive Healthcare requires a log of at least 12 insertions in 12 months or six in 6 months using at least two different types of device in unanaesthetised patients

for clinicians to be revalidated<sup>3</sup>.

Previous studies suggested that expulsion of IUD, young age, hypermenorrhoea, nulliparity, and uterus sounding more than 9.0 cm were associated with higher rates of IUD dislocations<sup>8-11</sup>. Diaz et al<sup>12</sup> observed an expulsion rate of up to 31% at 12 months after insertion if there was a prior history of IUD expulsion. Regrettably, this information was not well-documented in most of the medical records, for which reason such analysis was not feasible. In all probability, patients with a history of IUD expulsion would have already been counselled to use other treatment modalities.

Diaz et al<sup>12</sup> also found an increased risk for dislocations in parous adolescents. The expulsion rate for the LNG-IUS was reported to be slightly increased in women younger than 25 years<sup>9</sup>. However, as the majority of our patients were of more advanced age, the effect of age on LNG-IUS expulsion rate may not have been demonstrated.

Birth history (vaginal or abdominal delivery) did not appear to influence the expulsion rate in the current study. Diaz et al<sup>12</sup> suggested that nulliparity to be a risk factor for IUD expulsions. However, among our 80 patients, only three were nulliparous, none of whom

experienced an expulsion. In our locality, acceptance of LNG-IUS by nulliparous patients was low, and thus insertion was seldom practised and could not reflect the effect of parity on expulsions.

A previous study suggested that a longer sounded uterine length favoured LNG-IUS expulsion<sup>10</sup>. It is reasonable to hypothesise that increased length of the endometrial cavity is associated with a larger uterine cavity, which may allow easier LNG-IUS dislocation or displacement. A larger uterine cavity may also be a reason for heavy menstrual flow, thus leading to flushing out of the LNG-IUS. However, our study revealed no difference in the sounded uterine length in the in-situ group and expulsion groups.

A lower haemoglobin level before insertion was also associated with a higher expulsion rate. For this purpose we used the lowest documented haemoglobin level in the preceding 2 years before insertion, which served as a surrogate marker of underlying menorrhagia. To a certain extent, this provided an objective assessment of severity, as it would have been difficult to review clinical records without standardisation in menstrual flow descriptions. In theory, heavier menstrual flows might flush out LNG-IUS more easily, which was consistent with hypermenorrhoea being reported a risk factor for expulsion.

Notably, any patient who had had ultrasonography before insertion was more likely than the rest to experience LNG-IUS expulsion, of which the difference was statistically significant. In general, pelvic ultrasound was not routinely performed if bimanual examination confirmed a normal-size uterus without any suspicion of intracavitary lesion. Thus, the expulsion group probably included more patients with an enlarged uterus, fibroids and adenomyosis, and resulted in a selection bias.

There is little evidence demonstrating a causal relationship between uterine fibroids and LNG-IUS expulsion. According to the UK medical eligibility criteria for contraception use, uterine fibroids without distortion of the uterine cavity is classified as category 1 (unrestricted use), and category 4 (unacceptable risk) if the uterine cavity is distorted. Nor does fibroid size appear important. Tasci et al<sup>13</sup> observed a reduction in the size of uterine fibroids 1 year after LNG-IUS insertion.

In our study, uterine fibroids were not associated with an increased risk of the LNG-IUS expulsion. Regarding patients with ultrasound-confirmed uterine fibroids, none showed distortion of the uterine cavity. Patients with known fibroids need not be restricted from using LNG-IUS. However, they should be properly counselled that the primary aim was largely to control menstrual blood loss.

Whilst this study aimed at investigating the LNG-IUS expulsion rate specifically in treating menstrual disorder patients of Chinese ethnicity, it had a few limitations. Firstly, it was limited by the small sample size. On reviewing the records over the past 10 years, there were only 95 cases. Moreover, a significant portion of patients defaulted and were lost to follow-up. The latter might represent patients who responded satisfactorily to treatment. Regrettably, we failed to incorporate patient demographics into the current study. Secondly, our study was retrospective, so data retrieval was based on review of medical records. Since the consultation notes were not standardised, interpretation could be difficult. Also, as our patients were of more advanced age and parous, the effects of age and nulliparity were not demonstrable. In addition, in our clinical records, information about prior IUD expulsion and prior postpartum or post-abortion status was limited.

Consistent with the literature, in our patients lower haemoglobin levels reflected a degree of menorrhagia, and though not statistically significant such patients were more likely to suffer from LNG-IUS expulsion. No other specific factors (age, parity, presence of uterine fibroids or sounded uterine length) showed any association with expulsion. According to the National Institute for Health and Clinical Excellence clinical guideline published in 2007 for heavy menstrual bleeding, LNG-IUS was a first-line treatment<sup>14</sup>. Since LNG-IUS is an effective treatment for various menstrual problems, women should be offered this treatment option when indicated and provided there are no contraindications. Our study in women with menstrual disorders and other uterine pathologies demonstrated a relatively high LNG-IUS expulsion rate. This information should be used to counselling such patients, to provide realistic expectations and enhance satisfaction. A prospective study with a larger sample size is required to study the expulsion rate of LNG-IUS for treating menstrual

disorders and delineate further putative risk factors.

## Declaration

This study was approved by the Kowloon West

Cluster Clinical Research Ethics Committed (KWC-CREC), with KWC-CREC reference: KW/EX/10-055(30-31). No conflicts of interest in this work were declared by the author.

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