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Uterine perforation in women using a levonorgestrel-releasing intrauterine system

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Abstract

Objective: To determine an estimated incidence of uterine perforations related to the insertion of a levonorgestrel-releasing intrauterine system (LNG IUS) and to identify possible risk factors.
Design: Retrospective, case report study.
Setting: Hospitals in Limburg, the Netherlands.
Methods: Gynecologists in hospitals in Limburg were asked about uterine perforations related to the insertion of a LNG IUS between 1999 and 2002. The charts of the reported perforations were studied. Data on the patient, doctor, insertion, diagnosis and removal were collected for every reported uterine perforation.
Results: In Limburg, the estimated incidence of uterine perforations related to the insertion of a LNG IUS is 2.6 per 1000 insertions. Insertion in lactating women, even beyond 6 weeks after delivery, was shown to be an important risk factor.
Conclusions: Complete registration of complications provides a greater insight into the actual incidence of LNG IUS-related uterine perforations and their possible consequences. This may eventually lead to a decrease in complications.

Keywords: Contraception; Intrauterine device; Levonorgestrel; Uterine perforation; Pharmacovigilance

1. Introduction

An intrauterine device (IUD) is considered to be a very reliable, long-term, reversible, contraceptive method requiring a single application. The IUD is one of the most commonly used forms of contraception, with an estimated 110 million users worldwide, almost half of these being in China [1]. In the Netherlands, approximately 2% of women using contraception rely on an IUD. The levonorgestrel-releasing intrauterine system (LNG IUS), marketed as Mirena® (Schering, Germany), was introduced in the Netherlands in 1996. In large, comparative multicenter trials, the first-year gross pregnancy rate has been estimated to be 0–0.2%, and the cumulative pregnancy rate over 5 years 0.5–1.1% [2–4]. The 5-year ectopic pregnancy rate of the LNG IUS is 0.02 per 100 women-years. Approximately 20% of conceptions with the LNG IUS are ectopic. A few case reports of ectopic pregnancies associated with the LNG IUS have been published [5–8]. The contraceptive and therapeutic effects of the LNG IUS are based on the local effects of LNG in the uterine cavity, i.e., prevention of endometrial proliferation, inhibition of sperm motility and function, and thickening of the cervical mucus. The LNG IUS is known to markedly reduce menstrual blood flow, which is of particular value in women with menorrhagia [9], and it alleviates dysmenorrhoea [10]. The LNG IUS is also registered for prevention of endometrial hyperplasia during estrogen replacement therapy in peri- and postmenopausal women [11].

A potentially serious complication associated with the insertion of an IUD is uterine perforation, with an estimated risk of 0–1.3 per 1000 insertions [12]. Only a few cases of

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LNG IUS-related uterine perforation have been reported [8,13–16]. Recently, a report of 14 extrauterine IUDs of which nine were LNG IUSs was published. It was concluded by the authors that lost LNG IUSs are associated with a higher rate of localization errors by clinical evaluation than copper-bearing IUDs [17].

2. Methods

A retrospective, case report study was conducted. Gynecologists in hospitals in Limburg, the Netherlands, were asked about uterine perforations related to the insertion of a LNG IUS between 1999 and 2002. The charts of the reported perforations were studied. Data on the patient, doctor, insertion, diagnosis and removal were collected for every reported uterine perforation.

3. Results

Relevant data from the 21 reported cases of uterine perforation with a LNG IUS follow below.

3.1. Insertor and insertor's experience with LNG IUS

In 10 cases, the LNG IUS was inserted by a consultant gynecologist; in five cases, by a registrar in obstetrics and gynaecology; in five cases, by a general practitioner (GP); and in one case, by a doctor attached to an abortion clinic.

All doctors claimed to insert at least 10 LNG IUSs per year.

3.2. Patient age and parity

The median age of the patients was 30 years (range 21–47 years). All except for one patient, who had the LNG IUS inserted after a first trimester termination of pregnancy, were parous. For the parous patients, 10 patients had delivered once, nine patients twice and one patient five times.

3.3. Relevant obstetric details

Four patients had a cesarean section in the past, of which in one patient the LNG IUS was inserted in the postpartum period (7 weeks postpartum).

3.4. Number of weeks after delivery and lactation

In nine women, the LNG IUS was inserted during the postpartum period with a median of 8 weeks after delivery (range 4–24 weeks). Five patients were breastfeeding at the time of insertion (4, 7, 8, 9 and 24 weeks after delivery). Insertion in lactating women, even beyond 6 weeks after delivery, was shown to be an important risk factor.

3.5. Measured length of uterine cavity

The median measured length of the uterine cavity was 8 cm (range 7–10 cm); in nine cases, the length was not recorded.

3.6. Ultrasound findings at routine check-up

In 16 cases, a transvaginal scan (TVS) was performed at the routine check-up around 6 weeks after insertion of a LNG IUS. In seven cases, the LNG IUS was reported as being located inside the uterine cavity. In three cases, as part of the routine check-up, an abdominal ultrasound scan was performed by the radiology department to confirm the position of the LNG IUS. In two of these cases, the LNG IUS was reported as being located in the uterine cavity. In two cases, no ultrasound scan was performed as part of the routine check-up.

3.7. Signs, symptoms and occasions leading to diagnosis of uterine perforation

Four patients had reported the insertion of the LNG IUD as being very painful. In these patients, this did not alert the physician to the possibility of a perforation.

In nine cases, uterine perforation was initially suspected at the routine check-up; in six cases, after the patient presented with abdominal complaints; in two cases, because of the occurrence of a pregnancy (one spontaneous abortion and one ectopic pregnancy); and in four cases, on other occasions.

3.8. Type and timing of treatment

In 14 cases, it was possible to remove the LNG IUS during a laparoscopy. In one case, a hysteroscopy and, in three cases, both a hysteroscopy and laparoscopy were performed. In one case, a laparotomy was performed because of acute peritonitis with massive adhesion formation, while the LNG IUS was found to be partially embedded in the uterine fundus. In one case, the partially perforated LNG IUS was removed under general anesthesia through the uterus by firmly pulling the threads that were still in the uterine cavity. In one patient, the LNG IUS remains located intra-abdominally. In 10 cases, the perforated LNG IUS was retrieved from the omentum, and in four cases, the LNG IUS was partially embedded in the uterine fundus. The median time at which the perforated LNG IUS was removed was 30 weeks after insertion (range 1–177 weeks).

4. Discussion

Uterine perforation with IUD is a rare but potentially serious complication. The incidence of uterine perforations related to the insertion of an IUD (other than the LNG IUS) is 0–1.3 per 1000 insertions [12]. Zakin et al. [18,19] analyzed 356 reported cases of uterine perforations over a 15-year period. Some cases of LNG IUS-related uterine perforation have been reported [8,13–16]. Recently, a report of 14 extrauterine IUDs of which nine were LNG IUSs was published. It was concluded by the authors that lost LNG IUSs are associated with a higher rate of localization errors by clinical evaluation than copper-bearing IUDs [7].

According to the Netherlands Pharmacovigilance Centre Lareb, which registers and evaluates adverse side effects and complications with drugs, at least 24 LNG IUS-related uterine perforations were reported in the Netherlands (LNG IUSs inserted before 2003) since registration of the LNG IUS in February 1996. None of the 21 uterine perforations reported in the present study had been reported to the Lareb. This indicates a considerable underreporting of this complication. Apparently, a perforation with an IUD is not considered to be an event that has to be reported to the Lareb. After consent was obtained from the doctors who performed the insertion of the LNG IUS, the 21 uterine perforations discussed here were reported to the Lareb by the authors.

According to sales figures of the LNG IUS in the region where the study was performed (regional wholesale figures; IMS View), 1189, 2492 and 2941 LNG IUSs were provided in the second half of 2000, 2001 and 2002, respectively. Data on the number of LNG IUSs provided in 1999 and the first half of 2000 could not be retrieved. Assuming that all provided LNG IUSs were inserted, that insertion took place in the region and year of provision, and that no expulsions occurred nor devices removed because of side effects, the estimated incidence of uterine perforations in the studied region is at least 2.6 per 1000 insertions. The actual incidence of LNG IUS-related uterine perforations cannot be calculated because of incomplete data of the provided numbers of LNG IUSs in 1999 and the first half of 2000, failure to recollect all cases and possible negligence in reporting cases.

The supposed mechanism for uterine perforation during or prior to the insertion of an IUD is immediate traumatic perforation of the myometrium by the sound, the inserter tube or the IUD itself. Another mechanism might be partial perforation at the time of insertion, resulting in uterine contractions causing complete perforation [12].

Risk factors can be insertor-, patient- and/or IUD-related. All the insertors in this study performed more than 10 insertions of a LNG IUS per year. It has been shown that the incidence of uterine perforation is related to the experience of the doctor who is performing the procedure [20].

Reports disagree whether uterine perforation is more common in lactating women. In this report, in nine women the IUD was inserted in the postpartum period; five women were lactating. Insertion in lactating women, even beyond 6 weeks after delivery, was shown to be an important risk factor. An accelerated rate of uterine involution and prolonged uterine contractility may affect the risk of uterine perforation. Insertion of an IUD in lactating women seems to be associated with less pain than interval insertions, and uterine perforation may therefore easily pass unnoticed [21]. According to the guidelines for intrauterine contraceptive devices from the Dutch Society for Obstetrics and Gynaecology, insertion of an IUD before the recommended postpartum visit 6 weeks after delivery is considered a contraindication [22]. The manufacturer of the LNG IUS currently recommends that postpartum insertions should be postponed until 8 weeks after delivery. Insertion of an IUD immediately after a first-trimester abortion seems to be both safe and practical [23].

Another risk factor could be the technique used for insertion of the IUD. Uterine perforation at insertion seems less likely to occur if a withdrawal rather than a push-out technique — the recommended technique for a LNG-IUS — is used [24].

It is well known that an IUD-related uterine perforation can go undetected at the time of insertion. In the present study, in only four cases had the patients reported the insertion of the LNG IUS to be very painful.

A routine check-up 6 weeks after insertion of a LNG IUS is recommended, including a TVS to determine the location of the IUD [20]. One might consider performing a TVS immediately after insertion, especially if the insertion is not easily accomplished or if the insertion is reported by the patient as very painful. The LNG IUS has a typical sonographic appearance [25]; however, correct fundal positioning of the IUS appears not always easy to recognize.

As shown in this report, women can remain asymptomatic for months or even years before the diagnosis of a uterine perforation is made. One patient in this study became amenorrheic (no previous history of amenorrhea apart from pregnancy) despite the LNG IUS being located intra-abdominally. It can be assumed that the blood supply of the omentum in which the IUD was buried allowed the systemic levonorgestrel to reach a higher level than is usually found with the LNG IUD [13].

In general, there seems to be a consensus for removal of a perforated IUD mainly because of the potential for adhesion formation [16]. Except for one case, all perforated LNG IUSs in this study were removed. At this stage, we would recommend removal of a perforated LNG IUS.

5. Conclusion

Studies on uterine perforations related to the insertion of copper-bearing IUDs report an estimated incidence of 0–1.3 per 1000 insertions. The present study, performed in Limburg, the Netherlands, focused on uterine perforations with a LNG IUS and reports an estimated incidence of at least 2.6 per 1000 insertions.

Complete registration of complications provides a greater insight into the actual incidence of LNG IUS-related uterine perforations and their possible consequences. This may eventually lead to a decrease in complications. Therefore, it is highly desirable to report adverse side effects not only of drugs but also of IUDs to a national pharmacovigilance center.

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