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Ease of insertion and clinical performance of the levonorgestrel-releasing intrauterine system in nulligravidas

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Abstract

Background: Despite the high contraceptive efficacy and the additional noncontraceptive benefits of the levonorgestrel-releasing intrauterine system (LNG-IUS), concerns persist with respect to its use in nulligravidas. The objective of this study was to evaluate the ease of insertion and clinical performance of the LNG-IUS in nulligravida women up to 1 year after insertion.

Methods: Two cohorts were formed after LNG-IUS insertion, one consisting of 159 nulligravidas and the other of 477 parous women. Each nulligravida women was paired with three parous women who had an LNG-IUS inserted on the same day. Insertion was classified as easy or difficult, and when classified as difficult, the use of Hegar dilators and/or misoprostol and insertion failure were additional factors recorded.

Results: In almost 80% of cases, no difficulty was encountered during insertion, and dilators and misoprostol were seldom required; however, when necessary, dilator use was almost threefold higher in nulligravida women. Insertion failed in one nulligravida women and in two parous women. Contraception was the most common reason for insertion, although some of the women received the LNG-IUS for both contraceptive and therapeutic purposes, including heavy menstrual bleeding, hematologic diseases, warfarin use, endometriosis-associated pain and following kidney or liver transplantation. The clinical performance of the device showed zero pregnancy rate, expulsion rates of ~4/100 women-year and 1-year continuation rate of over 90% in both groups.

Conclusions: The LNG-IUS is suitable for use by nulligravidas. It is simple to insert, and its clinical performance in nulligravidas is similar to that found in parous women.

Keywords: Levonorgestrel-releasing intrauterine system; Mirena; Insertion; Nulligravida women; Parous women

1. Introduction

Intrauterine contraceptives (IUC) constitute the most prevalent contraceptive method worldwide, the most common devices in use being the TCu380A intrauterine device (IUD) and the levonorgestrel-releasing intrauterine system (LNG-IUS) [1]. Despite the high contraceptive efficacy and low complication rate with both devices [2,3], many concerns persist regarding the use of copper IUDs, particularly in the United States [4].

One reason for the low rate of use in the United States and UK is a common belief among physicians that age [5] and parity constitute eligibility criteria for IUC. A recent survey conducted with 400 fellows of the American College of Obstetrics and Gynecology showed that 68% would not recommend copper-IUDs to nulliparous women, although 95% had a positive attitude toward the IUD and 95% acknowledged the efficacy and safety of the method [6]. In addition, another survey conducted in Australia with 701 fellows of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists showed that only 39.1% and 69.4% of respondents stated that the copper-IUD and the LNG-IUS, respectively, are suitable for nulliparous women [7].

Nevertheless, the copper-IUD and the LNG-IUS are excellent contraceptive methods and have been defined as "forgettable contraceptives" [8] since they provide contraception for at least 5 years following a single intervention. The TCu380A IUD was approved for 10 years' use, but 15

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and 20 years of use of the device have been reported [9,10]. The LNG-IUS is approved for up to 5 years of use [3] with a wide window of time for replacement [11].

Another reason for restricting use in nulligravidas may be the fact that when the TCu380A IUD was launched on the market in the United States in 1988, one of the recommendations regarding patient profile was that eligible woman should have a history of childbearing; however, this recommendation was removed in a new 2005 version, and use of the device by nulliparous women is no longer discouraged [12]. Nevertheless, the information contained in the LNG-IUS package insert still recommends use in parous women [13] despite the statement of the World Health Organization (WHO) that nulligravidas are classified as category 2 for the use of any IUC [14].

Furthermore, there is no consensus in the scientific literature regarding the evaluation of IUC, since in many studies, the term *nulliparous* was considered synonymous with *nulligravida women* [15,16] even when the women have a history of abortion. In view of the scarcity of information regarding use of the LNG-IUS in nulligravidas [17], the aim of the present study was to evaluate ease of insertion and performance of the LNG-IUS in nulligravidas compared to a cohort of parous women.

2. Subjects and methods

This retrospective study was conducted at the Human Reproduction Unit, Department of Obstetrics and Gynecology, School of Medicine, University of Campinas, Campinas, Brazil. The Institutional Review Board of the School of Medicine approved the study protocol and authorized the review of the medical records. Informed consent was not required because the data were retrospectively collected from the medical records, and all insertions and follow-up visits were performed during routine clinical practice. Two cohorts were formed, consisting of women requesting insertion of an LNG-IUS (Mirena®; Bayer Oy, Turku, Finland) between 2007 and 2009, the first composed of all nulligravidas and the second of parous women. Each nulligravida was paired with the first three parous women who had an LNG-IUS inserted on the same day as the nulligravida or on the next working day (in cases in which three women were not available on the same day) to avoid selection bias. The exclusion criteria followed the recommendations of the WHO: a malformed or distorted uterine cavity, current purulent cervicitis and cervical or breast cancer [14].

All the LNG-IUS were inserted within the first 5 days of the menstrual cycle, by trained gynecologists, residents in Obstetrics and Gynecology or Family Medicine, medical students (interns) and trained nurses. Follow-up visits were conducted at 45±7 days and 1 year ±30 days after insertion according to the routine at our clinic. The information about insertion was recorded in the medical chart as routine in the clinic. The uterus position was evaluated based on clinical judgment and uterine sounding. Insertion was classified as easy or difficult. Difficult was recorded at four levels: (1) only difficult when the professional described any difficulty at insertion; however, those insertions were successful only with the use of uterine sound; (2) difficult, with the use of Hegar dilators (4–6 mm in diameter); (3) difficult even with the use of dilators and insertion performed at 1-day delay to allow misoprostol to be used (200 mcg intravaginally 12 and 4 h before insertion (Prostokos, Hebron, Caruaru, Pernambuco, Brazil) and (4) insertion failure when the professional failed to insert the device even after these two procedures.

Calculation of the sample size was estimated based on a hypothesis that nulligravida women presented more failed insertions than parous women with a type I (alpha) error of 5% and a type II error of 20%, resulting in a sample size of 137 women in each group. The study was retrospective, and women were not prospectively enrolled. To estimate the sample size, it was used the Proc Power procedure from the SAS software, version 9.1.3 (SAS Institute Inc., Cary, NC, USA, 2002-2003).

The sociodemographic and anthropometric variables and ease of insertion were compared between the groups using Pearson χ^2 test. Life table analysis [18] was used to evaluate clinical performance and included only those women in whom the device was actually inserted. The statistical significance of the differences between groups was tested using the Wilcoxon–Gehan test. Significance was established at $p<.05$. The cutoff date for analysis was September 30, 2010.

3. Results

A total of 159 nulligravidas and 477 parous women were included in the study. The nulligravidas were significantly younger than the parous women (mean 29.9 vs 33.3 years), had a lower body mass index (kg/m^2) and were more likely to report previous hormonal contraceptive use. The group of parous women had had a mean of just under two previous pregnancies and deliveries, and 310 (64.9%) of 477 parous women had a history of one or more cesarean sections. The majority of women in both groups had an anteverted uterus, and the mean total uterine length of the participants of the study as a whole was ~7 cm (Table 1).

There was no difficulty in inserting the LNG-IUS in 80.8% and 82.2% of the nulligravidas and parous women, respectively, without significance. Nevertheless, in the difficult cases, the use of dilators was 7.7% in nulligravidas and 3.1% in parous women, while the use of misoprostol for priming the cervix was 0.6% in nulligravidas and 2.5% in parous women. In one nulligravida (0.6%) and two parous women (0.4%), insertion proved impossible even after the use of dilators and misoprostol due to the narrow internal os of the cervix. No anesthetic of any kind was used (Table 2). In 60 (73%) of the 82 parous women in whom insertion was difficult, the patient had an obstetrical history of one or more