

Original research article

## Five years' experience with a small intracervical/intrauterine levonorgestrel-releasing device

Päivi Pakarinen<sup>a,b,\*</sup>, Tapani Luukkainen<sup>b</sup>

<sup>a</sup>Department of Obstetrics and Gynecology, Helsinki University Central Hospital, 00029 HUS Helsinki, Finland

<sup>b</sup>Steroid Research Laboratory, Institute of Biomedicine, University of Helsinki, 00029 HUS Helsinki, Finland

Received 23 February 2005; revised 25 April 2005; accepted 9 May 2005

---

### Abstract

**Objective:** A randomized study was performed to compare the efficacy, safety and acceptability of a new model of an intracervical/intrauterine contraceptive device (ICD) releasing 20 µg of levonorgestrel (LNG) per day.

**Methods:** The LNG-ICD was inserted in Group I into the cervical canal and in Group II into the uterine cavity. Group I included 151 women (age, 18–43 years) whereas Group II included 147 (age, 19–43 years). The number of nulliparous women was 145.

**Results:** The 5-year results are presented here. The results showed a total continuation rate of 50%; the continuation rate in the cervical group and that in the uterine group were 53.6% and 46.3%, respectively — the difference being statistically insignificant ( $p=.3593$ ). The main reason for termination was a wish for pregnancy, which is explained by the relatively young age and degree of nulliparity of the study population. During the first year, two pregnancies occurred in both groups. Two of these were ectopic, one in each group. The other two occurred after unnoticed expulsions. Thereafter, no pregnancies occurred. The cumulative gross rate for pregnancy was 1.3 and the Pearl index at 5 years was 0.425. The total expulsion rate was relatively high (11.1%). Expulsions occurring during the first few months of the first year were related to insertion. Removals because of bleeding and because of amenorrhea were low, the combined gross rate being 5.7 and the Pearl rate 1.8 at 5 years. Also, the gross rate of infection was low (0.7). The continuation was high in spite of a high rate of removals for planning pregnancy (15.4).

**Conclusions:** The method is safe and effective. There were only minor differences between the groups. There were no perforations and the incidence of infection was low. The device can also be used by young nulliparous women.

© 2005 Elsevier Inc. All rights reserved.

*Keywords:* Levonorgestrel-releasing intrauterine device; Intracervical device; Contraception

---

### 1. Introduction

A levonorgestrel-releasing intracervical contraceptive device (LNG-ICD) was designed so as to be easy to insert and to reduce the incidence of removals because of problems of bleeding and amenorrhea. A second frame modification, in a trial reported by Ratsula [1] with 198 users, was associated with no removals during the first 2 years due to amenorrhea.

The health benefits of the LNG-releasing intrauterine system (IUS), including a reduction in the duration of

bleeding and a significant increase in serum ferritin concentration, have also been observed during use of the ICD. The increase in hemoglobin concentration, however, was insignificant because values were already at non-anemic levels before insertion of the ICD [1].

A comparative study [2] revealed that the ICD is likely to be acceptable and could have a unique contraceptive role. However, in spite of these positive observations, the results also included disappointments. First, the high rate of expulsions, many of them unnoticed, resulted in accidental pregnancies. Second, the removal rate because of bleeding problems was not improved in comparison with earlier models [3].

In the present study, two approaches were taken. The side arms of the device were strengthened and the small device was inserted into either the cervical canal or the uterine cavity. Results after the first year have been

---

\* Corresponding author. Department of Obstetrics and Gynecology, Helsinki University Central Hospital, PO Box 140, 00029 HUS Helsinki, Finland. Tel.: +358 50 4271 531.

E-mail address: paivi.pakarinen@hus.fi (P. Pakarinen).

reported earlier [4]. The LNG concentrations in plasma were in the range of those associated with use of the LNG-IUS. Estradiol concentrations were not suppressed and serum progesterone concentrations were indicative of ovulation.

The contraceptive efficacy of this device is not based on ovulation suppression and the device is as effective in the cervical canal as it is in the uterine cavity. Initial results suggested that the frame of the device was not the reason for expulsions. Hence, follow-up was continued for another 4 years. The results at 5 years and annual accumulation of events are reported here.

## 2. Methods

The characteristics of the women selected by means of randomization into those who underwent intracervical insertion of the device and those who underwent intrauterine insertion in this study performed in two clinics in Helsinki have been reported earlier [4]. Women were assigned to the cervical or the fundal insertion group using a random-number table with group allocation predetermined and placed in consecutively numbered, opaque and sealed envelopes. As the women entered the study, they received a randomized envelope that was opened just before the LNG-ICD was inserted. The study was carried out according to the ethical principles set forth in the Helsinki Declaration and was approved by the ethical committees of the clinics. Age, weight, height, parity and number of abortions were comparable in the two groups. The degree of nulliparity was 48% in the women participating in the present study.

Ultrasonography was used for measurement of endometrial thickness before insertion, three times during the first year after insertion and thereafter at every visit. There was a planned visit once a year and the possibility of an extra visit if necessary. The measurements did not show any significant difference in endometrial thickness in the two groups at examinations carried out at 3, 6 and 12 months after insertion [5]. In some cases, the devices did not remain in the fundal part of the uterine cavity but migrated to a lower position; in addition, many devices placed in the cervical canal migrated to the uterine cavity. Hence, the two groups of women are labeled intracervical (Group I) and intrauterine (Group II) according to the sonographically determined location of the devices.

### 2.1. Statistical analyses

Differences in gross rates between the two groups (intracervical/intrauterine) were studied by survival analysis produced by the Kaplan–Meier method. Cox's proportional hazards models with hazard ratios and 95% confidence intervals were used to analyze the prognostic factors of expulsions. Computations were done using the SAS System for Windows (release 8.2/2001) [6].

## 3. Results

### 3.1. Pregnancies

There were four pregnancies during the early months of use. Two of these were tubal pregnancies, verified by histological examination. Two other early pregnancies were after unnoticed expulsions. The effectiveness of these small devices after the first few months of use was excellent. During the following period of observation, there was no single pregnancy, with nearly 950 women-years of exposure. Table 1 gives the number of events in the two groups at 1, 3 and 5 years according to the different reasons for discontinuation.

### 3.2. Expulsions

Expulsions were largely related to the immediate post-insertion period and mostly to one of the two clinics involved. The insertion technique differed from that in earlier studies [1]. In Group I, the device was pushed within the insertion tube, horizontal arms bending outside along the insertion tube, to the uterine cavity. The tube was removed and the device was gently pulled by its strings to the cervical canal such that the horizontal arms were resting in the inner mouth of the uterus. In Group II, the device was pushed identically within the tube up to the fundal part of the uterine cavity; the device was released rotating the tube and the tube was removed and the device was left in the fundal part of the uterine cavity. This was not always successful because often the device was still in the tube when it was withdrawn. In these cases, the tube was pushed in again and the device was released by means of repeated rotations. The plunger was eliminated to reduce the cost of the method.

### 3.3. Bleeding problems

Because amenorrhea was the reason for removal in only two women during 5 years of use, bleeding problems and

Table 1  
Accumulation of events at 1, 3 and 5 years

Event	Year 1		Year 3		Year 5	
	Group I	Group II	Group I	Group II	Group I	Group II
Pregnancy	2	2	2	2	2	2
Ectopic	1	1	1	1	1	1
Intrauterine	1	1	1	1	1	1
Expulsions	17	10	19	12	19	14
Removals	8	10	38	47	49	63
Pain	2	0	6	4	6	5
Bleeding	1	3	5	7	10	7
Infection	0	1	0	1	0	2
Hormonal	2	1	5	7	7	8
Planning pregnancy	3	3	18	19	21	25
Other personal	0	0	1	5	1	9
Other reason	0	2	3	4	4	7
Any termination	27	22	59	61	70	79

Table 2  
Five-year life table analysis

	Total (N=298)		Intracervical (n=151)		Intrauterine (n=147)		Log rank p	Hazard ratio	95% Hazard ratio confidence interval
	Gross rate	n	Gross rate	n	Gross rate	n			
Pregnancy	1.3	4	1.3	2	1.4	2	.9905	1.01	0.14–7.18
Expulsions	11.1	33	12.6	19	9.5	14	.4132	0.75	0.38–1.50
Pain	3.7	11	4.0	6	3.4	5	.7604	0.83	0.25–2.73
Bleeding	5.7	17	6.6	10	4.8	7	.5673	0.76	0.29–1.99
Infection	0.7	2	0	0	1.4	2	.1493	*	*
Hormonal	5.0	15	4.6	7	5.4	8	.7667	1.17	0.42–3.22
Planning pregnancy	15.4	46	13.9	21	17.0	25	.5123	1.21	0.68–2.17
Other personal	3.4	10	0.7	1	6.1	9	.0081	9.70	1.23–76.60
Any termination	50.0	149	46.4	70	53.7	79	.3593	1.16	0.84–1.60

\* Cannot be calculated because there were no infections in the intracervical group.

amenorrhea were combined in the analysis. During the first year, only four women requested removal of the device for these reasons.

Table 2 gives the 5-year life table gross rates for the two groups, individually and combined. In Table 3, the reasons for termination are expressed as Pearl rates. During 5 years of use, there was no significant between-group difference in the rates of removal because of bleeding. The low annual rate of bleeding problems led to a low cumulative rate of removal at 5 years in all women participating in the study and to a high continuation rate in spite of a high percentage of nulliparous women.

#### 3.4. Pain, infection, hormonal reasons and personal reasons

Rates of removal because of pain, infection or hormonal reasons were all low and there were no significant differences according to the location of the device. The infection gross rate was 0.7 and no infection occurred in the intracervical group. The only real difference between the groups was in the removal rate for other personal reasons. The gross rate because of personal reasons was 0.7 in the intracervical group, which is significantly lower than that in the intrauterine group (6.1) ( $p=.0081$ ). There was no common reason for these removals and none of them were associated with the device.

Table 3  
Pearl rate for reasons for terminations at 5 years

Termination	Cases	Women-years	Per 100 women-years
Pregnancy	4	941.8	0.425
Ectopic	2	941.8	0.212
Intrauterine	2	941.8	0.212
Expulsions	33	941.8	3.504
Removals	101	941.8	10.724
Pain	11	941.8	1.168
Bleeding	17	941.8	1.805
Infection	2	941.8	0.212
Hormonal	15	941.8	1.593
Planning pregnancy	46	941.8	4.884
Other personal	10	941.8	1.062
Other reason	11	941.8	1.168
Any termination	149	941.8	15.821

#### 3.5. Planning pregnancy

A high removal rate was found for planning pregnancy, the total gross rate being 15.4. It reflects the high percentage (48%) of nulliparous women in the study. Their personal situations changed during this long-term study.

#### 4. Discussion

There were only four pregnancies during the 5 years (nearly 950 women-years). These pregnancies were during the first few months of the first year. The cumulative gross pregnancy rate in the combined material was 1.3 at 5 years and the Pearl rate was 0.425. The gross pregnancy rate in this study is comparable with the cumulative gross pregnancy rate of 1.1 at 5 years reported by Sivin et al. [7] in 1990 for Mirena<sup>®</sup>, with a larger population, but higher than the gross rate at 5 years in a European study reported by Andersson et al. [8] in 1994. In this study, we found that women do not recognize mild symptoms of pregnancy such as mild breast tenderness and nausea without vomiting. We propose that a sensitive pregnancy test should be performed before insertion if menstrual bleeding is late.

The effectiveness of the LNG-IUS (Mirena<sup>®</sup>) is higher than that of any other contraceptive method. The LNG-IUS is associated with the same low failure rate irrespective of the age of the user [9]. All other methods, including sterilization, are associated with a higher failure rate in younger women and a decreasing rate with increasing age. Young nulliparous women using Mirena<sup>®</sup> are therefore as well protected against unwanted pregnancy as older women.

The high contraceptive efficacy of the present method is not surprising because the device has the same steroid reservoir releasing 20 µg of LNG daily as the LNG-IUS (Mirena<sup>®</sup>). The present study shows that the new device is also equally effective in the lower part of the uterine cavity. A positive aspect of this small device is that it cannot easily penetrate the myometrium and perforations are unlikely to occur because of its design. There has been no single perforation in our three long-term studies and in other developmental studies [1,10].

The main problem in developmental work has been early expulsion. Two unnoticed expulsions in this study resulted in pregnancies. During the early years of development, it was thought that the problem of expulsion was related to the small frame. However, earlier alterations of the frame did not prevent expulsions. In the present study, the expulsions were mainly associated with one clinic, possibly because of a deviation in the insertion technique. A similar device inserted with a plunger in a trial among perimenopausal women was not associated with problems of expulsion [11].

The aim of studies on intracervical/small intrauterine devices is not to develop a method to replace the LNG-IUS, which is more for specialists able to place it in a fundal position for therapeutic applications. This ICD has been developed for easy and safe insertion, to meet the demands of less well-trained providers such that they could insert it safely and correctly. It is a common misconception that one can learn a complicated insertion technique without high-quality training by doing it many times by oneself. This approach leads to expulsions, pregnancies and bleeding problems, which can be misinterpreted as problems of the method and not as results of poor insertion [12].

The devices in the present study are easy to insert and less well-trained providers can therefore achieve good results in the prevention of pregnancy with low rates of bleeding and pain. Young women and women in many societies are worried about amenorrhea and request removal of the device. There were only two removals because of amenorrhea in the present study. The study by Ratsula [1] also showed that this reason for discontinuation is minimal with this small device.

In the present study, 48% of the women were nulliparous. The method can be considered as a safe long-term contraceptive because the removal rate because of infection was low. The women with intracervical insertion experienced no removals because of infection. Many of them used the “mini-IUS” for spacing with success. The high continuation rate compared with other methods of family planning supports the conclusions of the acceptance study reported by Shain et al. [2].

The long-term nature and reversibility of the contraceptive action of the present method meet the needs of young women. This method could protect women from unplanned pregnancies during the years they complete their professional education until they are ready for motherhood. For them, it is important that the method be safely distributed by providers everywhere.

## Acknowledgments

We are grateful for the strong support of Dr. Allan Barns and Dr. Ted King during the early part of this developmental work. We also express our gratitude to Professor David Grimes and Dr. Laneta Dorflinger of Family Health International and Dr. James Shelton of USAID for constructive advice and help. The study would not have been possible without Marjatta Tevilin, Eeva Harju, Marja Tikka, Drs. Henri Kurunmäki, Kari Ratsula, Juhani Toivonen, Pekka Venesmaa and Pekka Lähteenmäki of the Steroid Research Laboratory and Family Planning Clinics of the City Maternal Hospital, Helsinki, Finland, and the Sexual Health Clinic, The Family Federation of Finland, Helsinki, Finland. We are also grateful to Anne Kaljonen for statistical analyses and Dr. Nick Bolton for reviewing the language of this article.

## References

- [1] Ratsula K. Clinical performance of a levonorgestrel-releasing intracervical contraceptive device during the first two years of use. *Contraception* 1989;39:187–93.
- [2] Shain RN, Ratsula K, Toivonen J, et al. Acceptability of an experimental intracervical device: results of a study controlling for selection bias. *Contraception* 1989;39:73–84.
- [3] Ratsula K. Clinical performance of a levonorgestrel-releasing intracervical contraceptive device during the first year of use. *Contraception* 1987;36:659–66.
- [4] 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.
- [5] Pakarinen P, Luukkainen T, Laine H, Lähteenmäki P. The effect of local intrauterine levonorgestrel administration on endometrial thickness and uterine blood circulation. *Hum Reprod* 1995;10:2390–4.
- [6] Collett D. *Modelling binary data*. London: Chapman & Hall; 1991.
- [7] 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.
- [8] Andersson K, Odland V, Rybo G. Levonorgestrel-releasing and copper-releasing (Nova T) IUDs during five years of use: a randomized comparative trial. *Contraception* 1994;49:56–72.
- [9] Luukkainen T. Levonorgestrel-releasing intrauterine device. *Ann N Y Acad Sci* 1991;626:43–9.
- [10] Kurunmäki H, Toivonen J, Lähteenmäki P, Luukkainen T. Intracervical release of levonorgestrel for contraception. *Contraception* 1981;23:473–85.
- [11] Wollter-Svensson LO, Stadberg E, Andersson K, Mattson LA, Odland V, Persson I. Intrauterine administration of levonorgestrel 5 and 10 ug/24 hours in perimenopausal hormone replacement therapy. *Acta Obstet Gynecol Scand* 1997;76:449–54.
- [12] Faundes A, Alvarez F, Diaz J. A Latin American experience with levonorgestrel IUD. *Ann Med* 1993;25:149–53.