

Effect of Levonorgestrel-Releasing Intrauterine System on Sexual and Urinary Functions

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Abstract

Aim: The effects of the levonorgestrel-intrauterine system (LNG-IUS) on urinary and sexual functions of women with idiopathic menorrhagia were evaluated using two internationally validated questionnaire forms.

Methods: This prospective study included (30-49) year-old women with idiopathic menorrhagia (n=91), who visited the Gynecology and Obstetrics Clinic of the hospital. The index of female sexual function (IFSF) questionnaire and the international consultation on incontinence modular questionnaire short form (ICIQ-UI) were used to evaluate sexual and urinary system functions, respectively, pre-, and 6 and 12 months post-LNG-IUS insertion.

Results: The IFSF scores were (mean \pm SD) 27.1 ± 6.9 , 30.0 ± 7.2 , and 32.7 ± 7.5 at pre-, and 6 and 12 months post-LNG-IUS insertion, respectively ($p < 0.001$). Compared with pre-LNG-IUS use among 91 patients, the IFSF score (symptoms improved) was increased in 47 and 60 patients and decreased (worsening symptoms) in 10 and 8 patients at 6 and 12 months post-LNG-IUS use, respectively. The ICIQ-UI scores were 4.9 ± 4.4 , 3.7 ± 4.0 , 2.8 ± 3.0 in pre-, 6, and 12 months post-LNG-IUS insertion, respectively ($p < 0.001$). Compared with pre-LNG-IUS use, the ICIQ-UI score decreased (symptoms improved) in 33 women either in 6 or 12 months post-LNG-IUS use and increased (symptoms worsened) in 11 and 4 patients at 6 and 12 months post-LNG-IUS insertion, respectively.

Conclusion: A significant increase in the IFSF score and a marked decrease in the ICIQ-SF score because of LNG-IUS use in women with idiopathic menorrhagia indicate a noteworthy improvement in urinary and sexual functions.

Keywords: Levonorgestrel-Releasing Intrauterine System; Menorrhagia; Urinary Function; Sexual Function

Introduction

The levonorgestrel-intrauterine system (LNG-IUS; Mirena® Leiras Oy, Turku, Finland) has been used worldwide for various clinical indications, such as menorrhagia and dysmenorrhea, in addition to its common use as a contraceptive since it was first commercially introduced in 1990 [1]. Initially, 20- μ g levonorgestrel is released within 24 hours, while levonorgestrel release has been demonstrated to continue in a dose of higher than 14 μ g at the end of 5 years [2]. The efficacy of treatment is continuous by means of this regular release [3].

Menorrhagia and chronic pelvic pain negatively affect the quality of life as well as sexual and urinary functions of women [4-9]. In cases of unresponsiveness to medical treatment, radical elimination of abnormal uterine bleeding by hysterectomy may worsen sexual and urinary functions. In addition to an increased risk of morbidity and mortality, damage to the innervation of the pelvic region may cause further health issues [10]. The LNG-IUS is an effective, reliable, reversible and relatively less invasive low cost therapy to treat menorrhagia, endometrial hyperplasia, and dysmenorrhea [11].

By evaluating the effects of abnormal uterine bleeding, pelvic pain, and pressure on sexual functions, Mathias *et al.* [12] established menorrhagia and pelvic organ prolapse [13] as one of the most important underlying factors affecting sexual functions. Similarly, abnormal uterine bleeding was similarly proven to negatively affect the quality of life of women [14,15].

The literature contains a few studies that have evaluated the effect of LNG-IUS use on either urinary or sexual functions in patients with menorrhagia [16-19]. However, this is the first study to evaluate both urinary functions and sexual life by using two internationally validated standard questionnaires to objectively establish the effects of LNG-IUS use on urinary and sexual functions of women with menorrhagia.

Materials and Methods

This prospective study was performed on patients who presented with menorrhagia between June 1, 2014 and October 1, 2015 at the Department of the Gynecology and Obstetrics Clinic of the Health University Adana Numune Education and Training Hospital in Turkey; the hospital's ethics board approved this study. A detailed explanation of the study and information about the application of LNG-IUS were provided to each participant, and both written and verbal consent was obtained. Initially, endometrial biopsy was performed on the patients to evaluate the etiology of menorrhagia. Following the evaluation of the pathology reports, LNG-IUS was applied to patients with abnormal uterine bleeding. This study included 91 women in the age range 30–49 years who were experiencing idiopathic menorrhagia according to clinical and pathological findings. A total of 94 patients were excluded from the study, including those planning to become pregnant (26 patients) or those with space-occupying lesions in the uterine cavity, such as endometrial polyp (12 patients), leiomyoma (9 patients), endometritis (7 patients), a malignant pathology (4 patients), simple atypical hyperplasia (3 patients) or complex atypical hyperplasia (2 patients) as detected by endometrial biopsy, or sexually transmitted diseases (8 patients), such as chlamydia or gonorrhea related pelvic inflammatory disease (PID), or abnormal PAP smear result (6 patients) or cases with pelvic organ prolapses (4 patients) or a history of either thromboembolism (1 patient) or stroke or coronary heart disease (1 patient), or cardiac valve replacement and chronic use of thrombolytic drugs (2 patients) or any type of cancer (2 patients) or migraines (4 patients).

Patients in the study groups were questioned about age, duration of marriage, level of education, number of births, and status of menstruation and the results were recorded. Body mass index (BMI) was calculated by measuring the patients' height and weight. The index of female sexual function (IFSF) form was used to evaluate sexual functions prior to the application. All women included in the study were asked to read and answer the IFSF questions, which included nine items, on their own. A female resident physician assisted illiterate women. This domestically and internationally validated form was used to evaluate sexual function with a minimum of five and a maximum of 45 points. IFSF was used to assess sexual function of the patient. Linguistic validation of this questionnaire was conducted in Turkey [20]. The specific questions analyzed in the IFSF included quality of sexual intercourse (questions 1 and 2; possible total score, 0 to 10), desire (questions 4 and 5; possible total score, 2 to 10), overall satisfaction with sexual function (questions 6 and 7; possible total score, 2 to 10), ability to achieve orgasm (question 8; possible total score, 1 to 5), the degree of lubrication (question 2; possible total score, 0 to 5), and the degree of clitoral sensation (question 9; possible total score, 1 to 5). The responses were graded on a scale of 1 (almost never or never) to 5 (almost always or always). A score of 0 indicated no attempt at intercourse. The total scores range from 5 to 45 with lower scores representing poorer sexual function. Urinary problems were evaluated with the standard international consultation on incontinence modular questionnaire short form (ICIQ-UI), which was previously validated both domestically and internationally with a minimum of 0 and a maximum of 20 points [21]. This form questions the frequency and amount of urinary incontinence; the effects of this problem on daily life; and whether the urinary incontinence is stress, urge, mixed or not.

General systemic and gynecological examinations of all patients included in the study were performed. Bimanual genital examination and transvaginal-ultrasonography (TV-USG; Mindray, DC-7 Nanshan Shenzhen P.R. China 5-7 MHz vaginal probe) was applied to all patients prior to LNG-IUS application. A vaginal speculum was inserted prior to the application of LNG-IUS, the cervix and vagina were cleaned, and the anterior cervix was held by a single-tooth tenaculum. The LNG-IUS was placed into the endometrial cavity using the standard method without anesthesia. After the application, TV-USG was used to determine if the device was placed correctly. At the end of both 6 and 12 months, the status of bleeding, any side effects, or any additional problems observed were recorded. The urinary and sexual functions of the patients were re-evaluated 6 and 12 months after the LNG-IUS application. The total IFSF and ICIQ-UI short form scores of women were calculated and compared for both time periods.

Student's t-test was used to analyze parametric data to determine the difference between the two independent groups, and a paired t-test was used to determine differences between two dependent groups. ANOVA was used to compare differences between more than two independent groups followed by a Tukey post-hoc test. Repeated measures ANOVA were used to compare differences between more than two dependent groups. The Friedman test was used to compare the ranks of more than two dependent groups for the analysis of nonparametric data. Frequency and percentage were used to describe categorical data. A p value < 0.05 was accepted as significant. MedCalc and SPSS software were used in the analyses.

Results

The LNG-IUS was applied to 91 patients appropriate the study inclusion criteria and with benign pathology results. The mean age of the patients was 42.6 years (range from 30 to 49). The mean number of births and BMI was 3.4 (range from 0 to 8) and 27.6 kg/m² (range from 21.3 to 40.1), respectively. No complications occurred in any patient during the LNG-IUS insertion (Table 1).

The level of education among the subjects was low (79% at the level of middle school or under). More than 92% of the patients were unemployed with the majority being housewives (Table 2).

Eighty-two patients (90.1%) preferred to continue the system 6 months after insertion and 77 patients (84.6%) preferred to continue using the system 12 months after insertion. Hypomenorrhea, hypermenorrhea, spotting, and amenorrhea were observed in 50 (64.8%), 6 (6.6%), 9 (9.9%) and 17 (18.7%) patients at 6 months and 48 (52.7%), 0 (0%), 13 (14.3%), and 20 (22.0%) at 12 months after insertion, respectively (Table 3).

	N	Min.	Max.	Mean	SD
Age (year)	91	30	49	42.6	4.7
Parity	91	0	8	3.6	1.6
Duration after the last birth (year)	87	1	26	12.1	5.9
BMI	91	20.7	40.1	26.9	3.6

Min: Minimum; **Max:** Maximum; **SD:** Standard Deviation; **BMI:** Body Mass Index

Table 1: Distribution of patients according to age, number of births, duration after the last delivery, and BMI

		Frequency	Percentage
Status of Employment	Employed	7	7.7
	Unemployed	84	92.3
Level of education	Illiterate	5	5.5
	Literate	12	13.2
	Primary school graduate	55	60.4
	High school graduate	14	15.4
	University graduate	5	5.5
Systemic disease	DM	10	11.0
	Hypertension	12	13.2
	Thyroid disease	13	14.3
	None	56	61.5

DM: Diabetes Mellitus

Table 2: Classification of patients according to the level of education, type of employment, and presence of systemic diseases

Pain	Pre-LNG-IUS N (%)	6 months later N (%)	12 months later N (%)
Yes	44 (48.3)		
No	47 (51.7)	49 (53.8)	55 (60.4)
Pain increase		8 (8.7)	6 (6.5)
Pain decrease		15 (16.4)	13 (14.2)
No change		10 (10.9)	7 (7.6)
Discontinuation		9 (9.8)	10 (10.9)
Bleeding pattern			
Hypomenorrhea	0	50 (64.8)	48 (52.7)
Hypermenorrhea	91	6 (6.6)	0 (0)
Spotting	0	9 (9.9)	13 (14.3)
Amenorrhea	0	17 (18.7)	20 (22.0)
Discontinuation	0	9 (9.9)	10 (11.0)
Incontinence status			
No incontinence	35	31	27
Urge incontinence	3	3	4
Stress incontinence	21	36	33
Mix incontinence	32	14	13
Discontinuation	0	9	10

Table 3: Clinical features before, and 6 months and 12 months after LNG-IUS therapy

The sexual questionnaire score increased in 47 patients (74.6%), decreased in ten patients (12.7%), and was unchanged in 10 patients (12.7%). Eight patients did not answer the sexual questionnaire score at the time of pre-LNG-IUS insertion due to taboo status or cultural reasons. An additional 4 and 7 subjects were not included in the sexual questionnaire score because the LNG-IUS slipped out of the uterine cavity or voluntary termination of LNG-IUS use as well as undergoing surgical procedures at the end of 6 months and 12 months after insertion, respectively. In addition, 64 patients (70.3%) and 65 patients (71.4%) reported that both

urinary and sexual symptoms improved according to the questionnaire score at the end of 6 months and 12 months after insertion, respectively. In contrast, 7 patients (8.5%) reported worsening in both urinary and sexual symptoms at the end of 6 and 12 months. The mean ICIQ-UI short form score at baseline (pre-LNG-IUS insertion) was 4.9 ± 4.4 (mean \pm SD) which significantly reduced to 3.7 ± 4.0 at the end of 6 months ($p < 0.005$) and reduced further to 2.8 ± 3.0 at the end of 12 months after insertion ($p < 0.005$). Mean IFSF score prior to the LNG-IUS application was 27.1 ± 6.9 . Mean sexual function score was lowest (23.0 ± 4.3) in women with heavy uterine bleeding and mixed urinary incontinence ($p < 0.005$) and increased to 30.0 ± 7.2 , and to 32.7 ± 7.5 , 6 months and 12 months post-LNG-IUS insertion, respectively ($p < 0.005$). A further 2.7 increase in mean IFSF score was significant at 12 months post-LNG-IUS insertion vs. 6 months post-LNG-IUS insertion ($p < 0.005$; Table 4a and b).

	IFSF score			ICIQ-UI score		
	Pre-LNG-IUS	Post-LNG-IUS		Pre-LNG-IUS	Post-LNG-IUS	
		6 mo.	12 mo.		6 mo.	12 mo.
N	83	79	72	91	82	77
Min.	5	5	5	0	0	0
Max.	43	44	44	14	14	12
Mean	27.1	30.0*	32.7 ^ψ	4.9	3.7*	2.8*
SD	6.9	7.2	7.5	4.4	4.0	3.0

Min.: Minimum; Max.: Maximum; SD: Standard Deviation; Mo.: Months

* $p < 0.005$ vs. pre-LNG-IUS. ^ψ $p < 0.005$ vs. 6 months post-LNG-IUS

Table 4a: IFSF and ICIQ-UI scores before (pre-) and 6 or 12 months after (post-) LNG-IUS insertion

		N	Correlation	P
Pair 1	IFSF score 0 & IFSF score 6	79	0.795	0.005
Pair 2	IFSF score 0 & IFSF score 12	72	0.734	0.005
Pair 3	IFSF score 6 & IFSF score 12	72	0.937	0.005
Pair 4	ICIQ-UI score 0 & ICIQ-UI score 6	82	0.718	0.005
Pair 5	ICIQ-UI score 0 & ICIQ-UI score 12	77	0.677	0.005
Pair 6	ICIQ-UI score 6 & ICIQ-UI score 12	77	0.889	0.005

Table 4b: Paired Samples Correlations

Discussion

Menorrhagia is a commonly encountered problem affecting the quality of life of women of reproductive age and especially during the premenopausal period [22,23] with negative physical, social, and emotional consequences resulting in withdrawal from daily life [6,24] and the sexual life of women [15,22,24]. LNG-IUS is a widely preferred application with proven efficacy and reliability in contraception and in the treatment of menorrhagia in 120 countries worldwide [25,26]. In a study in which mean satisfaction was evaluated in women using LNG-IUS, 95% women were satisfied with this system and 99% women selected the same method at the end of 5 years [27]. Several other studies also reported improvement in sexual functions in women using LNG-IUS [8,28,29]. In addition to this beneficial effect, additional positive effects of LNG-IUS use on patient satisfaction and quality of life have been reported because it decreases the amount of bleeding and the pelvic sensation of pain [30-33] and also helps to reduce dysmenorrhea and provide relief from premenstrual stress symptoms due to the progestogenic effect of levonorgestrel [4,7,34,35]. Moreover, LNG-IUS has positive effects on urinary functions [19,36,37].

Positive correlation between these two scorers was observed at both 6 and 12 months.

LNG-IUS delivers low plasma levonorgestrel and results in minimal side effects. The occurrence of a systemic disease, such as DM or HT, suggests the use of LNG-IUS [38,39]. This study population experienced a higher rate of DM, HT, and thyroid diseases.

The socio-cultural context is the most important factor when determining the method to be applied to women and the type of treatment method that should be performed [40]. The choice of LNG-IUS is influenced by larger social factors, economic status, education level, and both individual and interpersonal experience [41-43]. Previous studies have also indicated that the socio-cultural context influences the experience of menorrhagia, particularly with regard to sexuality and LNG-IUS preferences [41-43]. The current study population had low socio-economic and low education levels. Working status was also associated with some aspects of LNG-IUS use; the current study population was generally midwives. Women working outside the home or those in formal employment also used modern contraception methods more than those in self-employment or the unemployed [44]. Low-

income women preferred LNG-IUD, which provides LNG-IUS through general health insurance. Our results show that women who reported abnormal uterine bleeding preferred to use LNG-IUS among unemployed housewives and women with a low level of education.

A previous study has reported that in 58.6% women using LNG-IUS, no serious complications were noted at the end of 12 months [45]. However, spotting was observed in 17.1% patients, heavy bleeding in 1.4%, and amenorrhea in 22.9% which increased to 27.5% at the end of 18 months [45]. However, at the end of 12 months, the rates of amenorrhea (22%) and spotting (14.3%) observed in the current study were much lower than those reported in previous studies.

Following application, the LNG-IUS may drop from the uterine cavity or some patients may request the removal of the system due to dissatisfaction for various reasons [46]. In the present study, the rate of continuation of LNG-IUS use was 90.2% at the end of 6 months and 84.6% at the end of 12 months. This rate was reported as 74% at the end of an 18-month follow-up by a previous study assessing the efficacy of LNG-IUS to prevent heavy menstrual bleeding [45], and 93% at the end of a follow-up of 12 months in another study assessing LNG-IUS-related contraceptive experience and levels of satisfaction [47]. Moreover, in a recent contraceptive-related study, satisfaction (85.2 %) and continuation (78.6%) of LNG-IUS use was reported at the end of a follow-up of 6 months, including expulsions (3 patients, 2.7%) and removals (20 patients, 18.75%) [48]. These results suggest that the medical reasons for LNG-IUS use may significantly affect continuation and satisfaction rates.

Heliövaara *et al.* [49] compared two groups of patients (117 who underwent hysterectomy and 119 who received LNG-IUS) and found that urinary tract infections, dysuria, decrease in the daily frequency of urination, and lower urinary tract symptoms significantly improved in the group with LNG-IUS application at the end of 6 months. On the other hand, the mean ICIQ-UI short form score was higher in the current study compared with previously published results [50]. Although the purpose of using LNG-IUS was different in the current study, the evaluation of 160 patients in the age range 20–35 years using LNG-IUS versus a copper IUD revealed significantly increased scores for the SF36 questionnaire at the end of 6 months with regard to physical function, general health, social function, emotional role, life energy, and mental health [51]. Studies performed to establish both the effects and treatment of abnormal uterine bleeding on the quality of life showed that women preferred the use of LNG-IUS to hysterectomy and found that the use of LNG-IUS improved the quality of life of women [27,52]. In addition, studies of premenstrual syndrome (PMS) also showed that LNG-IUS use improved sexual functions in this patient population [4,8,28].

Similar to the findings in prior studies [10,27,53], the use of the IFSF score in the present study detected improved sexual functions of patients with idiopathic menstrual bleeding 6 and 12 months post-LNG-IUS insertion vs pre-LNG-IUS insertion. In a previous study performed in Italy [4], the mean IFSF score in patients using LNG-IUS was 30.1 at baseline and 32.0 at the end of 12 months with no statistically significant difference in the sexual function score. These scores stated above were higher than the scores in the present study. However, they reported a significant improvement in sexual desire and a decreased sensation of pain during sexual intercourse at the end of 12 months.

The patients were evaluated using a visual analog scale (VAS) in one study performed on 66 premenopausal women with an age range of 26–55 years. This questionnaire included questions related to pelvic pain, sexual life (libido), and a general feeling of health. The baseline score of pelvic pain (4.32) decreased significantly to 3.55 at the end of 6 months. Scores of libido and a general feeling of health were 4.27–4.95 and 3.47–6.87 at baseline and at the end of 6 months, respectively. The general quality of life score was significantly increased from 3.47 to 6.87 before and after the insertion of LNG-IUS, respectively. In that study, the level of libido, sensation of pain, and general well-being of women notably improved at the end of 6 months after LNG-IUS application [34]. In a previous study that compared LNG-IUS versus other copper-containing IUDs, quality of life scales such as energetic self-sensation, emotional well-being, and sexual desire and libido scores were significantly higher in individuals using LNG-IUS [29]. In contrast, other studies have reported unchanged or slightly decreased scores (2%) of Brief Index of Sexual Functioning for Women (BISF-W) and Arizona Sexual Experiences Scale (ASEX) that were used to evaluate sexual desire [54]. Additionally, parallel to that study, another study reported that LNG-IUS application resulted in a decrease in sexual functions and sexual desire (35.1% of patients) [55].

LNG-IUS use effectively decreases pain and improves quality of life in women experiencing heavy menstrual bleeding and dysmenorrhea [30,32,56,57]. In several clinical conditions, chronic pelvic pain may occur in the form of dysmenorrhea, dyspareunia, continuous or intermittent pelvic pain, and pain on micturition. During reproductive life, particularly premenopausal period 40% to 95% of all women encounter such problems [52,57]. Following LNG-IUS insertion, LNG release elicits local effects on the endometrium and other layers of the uterus. However, minimal passage of LNG to the systemic circulation decreases the sensation of pain and discomfort on genital and other pelvic organs, lessens endometrial bleeding [58] and reduces blood flow to the uterus and endometrium and thus, decreases pelvic congestion, bleeding, and pelvic pain [59,60]. Our results further support the beneficial effects of LNG-IUS on urinary functions. The result may be a markedly greater beneficial effect for those using LNG-IUS with baseline low IFSF scores

Conclusion

In conclusion, in the present study, LNG-IUS use in women with menorrhagia had positive effects on urinary and sexual functions compared to baseline, showed a significant increase in IFSF score, and a significant decrease in the ICIQ-SF score compared to

pre-LNG-IUS insertion. In addition, changes in urinary and sexual symptoms compared to pre-LNG-IUS use showed a positive correlation and urge incontinence symptoms in patients with mixed urinary incontinence was significantly reduced. The LNG-IUS may be used in women with idiopathic menorrhagia and may have good acceptance and tolerance.

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