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Original Research

The Effect of the Levonorgestrel-Releasing Intrauterine Device on Hypoactive Sexual Desire Disorder in Women

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Abstract

This research focused on the evaluation of the relationship between the levonorgestrel-releasing intrauterine device and Hypoactive Sexual Desire Disorder in women. Sexual desire disorder is part of a group of sexual dysfunctions. A group of 60 women with a diagnosis of hypoactive sexual desire were tested in the period from July 2023 to July 2024 at the Institute of Sexology of the 1st Faculty of Medicine in Prague. These patients were examined for levels of prolactin, sex hormone binding globulin, total testosterone, and markers CA-125 and CA-19-9. All patients completed the Rosen Female Sexual Function Index questionnaire on sexual dysfunction, as well as two questionnaires; one for traumatic stress and the other for somatoform dissociation. The results show significant Spearman correlations of trauma and psychosocial stress symptoms with dissociative symptoms (R = 0.52), with sex hormone-

binding globulin (R = 0.80), and with sexual desire disorder score results (R = 0.65). The Spearman correlation of sex hormone-binding globulin with dissociative symptoms (R = 0.53) was also significant, as was the correlation between CA-125 and CA-19-9 (R = 0.45). The causal relationship regarding hypoactive sexual desire is not wholly resolved. We can assume that not only altered hormone levels, but also previous stressful experiences from sexual relationships and failure to fulfill sexual ideas and desires can play an important role. It is therefore necessary to pay close attention to the relationship between the levonorgestrel-releasing intrauterine device, sexual disorders, and social trauma and stress.

Keywords
Hypoactive sexual desire disorder; levonorgestrel-releasing intrauterine device; stress; sex hormone-binding globulin

1. Introduction

Hypoactive sexual desire disorder (HSDD) is a sexual dysfunction that affects about 10% of adult women [1]. Common symptoms of this disorder include a lack or loss of motivation for sexual activity due to decreased or absent spontaneous sexual desire for at least half a year.

Etiological factors include various diseases. The most common are gynecological and urological diseases, but also thyroid disorders, obesity, and diabetes mellitus. Hormones, as well as drugs such as the levonorgestrel-releasing intrauterine device (LNG-IUD), can adversely affect sexual desire [2, 3]. Also, medications such as antidepressants and antipsychotics, which reduce dopamine and oxytocin levels in the brain and increase prolactin and serotonin levels, can cause these sexual disorders [4]. A high percentage of women with these sexual problems do not inform any gynecologist or sexologist and therefore are often not treated at all.

CA-125 is a glycoprotein with a high carbohydrate component. CA-125 is produced during the fetal period by epithelial tissues and may occur in the normal epithelium of the fallopian tubes, cervix, or bronchi in adulthood. CA-125 is particularly important as a marker of various gynecological diseases, including cancer, especially of the ovary.

CA-19-9 is a penta-saccharide with a carbohydrate component containing fructose components and belongs to the group of oncofetal antigens. It can be produced in the glandular structures of the gallbladder, pancreas, and bronchus, and occurs in some gynecological diseases and tumors [5]. The relationship between sexual dysfunction and markers such as CA-125 and CA-19-9 has been monitored for a long time, because both markers are the most frequently used in diagnostics, namely, inflammatory diseases, oncological diseases, and, for example, endometriosis. On the other hand, these are non-specific markers, so they can be used to monitor sexual dysfunctions if we rule out organic diseases.

SHBG is a glycoprotein that plays an essential role in the regulation of steroids. It mainly binds estrogens and androgens. Its origin has been shown to exist in the brain, specifically in the hypothalamus and pituitary gland [6, 7]. The bioavailability of sex hormones is affected by SHBG levels. Some studies have already shown that SHBG is a reliable marker [8]. Many clinical institutions use it as an essential clinical marker [9]. In the context of HC in women, its values often change

significantly, which in turn previously led to the assumption that it can negatively affect women's sexual activity. In adult premenopausal women, SHBG values range between 40 and 120 nmol/l, and in our sample group, the mean value was 100.49 nmol/l.

SHBG is a globulin that binds to sex hormones, especially testosterone and estradiol, and thus regulates their bioavailability. In connection with female sexual dysfunctions, we determine their level. In the event of a higher level, libido may be impaired, and sexual desire may be lost. If the SHBG level is reduced, sexual desire may, on the contrary, increase.

Testosterone is a steroid hormone that is considered a primary androgen. In men, it is synthesized by the Leydig cells of the testes; in women, it is produced by the adrenal cortex and the ovaries. Testosterone plays a vital role in promoting sexual characteristics such as sexual behavior. Testosterone is mainly bound to serum albumin and SHBG (approximately 54% & 44%, respectively). Only a small fraction, about 1-2%, is free, biologically active, and can enter a cell and activate a receptor. SHBG inhibits the function of these hormones. In adult premenopausal women, total testosterone (TT) values ranged from 0 to 2.6 nmol/l, and in our sample group, the mean value was 1.73 nmol/l (SD = 0.37).

The LNG-IUD can reduce androgens, estradiol, progesterone, and inhibit oxytocin – which can negatively affect the sexual behavior of both the woman and her partner.

2. Participants and Methods

In our prospective cohort study, we focused on 60 women (mean age 29.6, SD = 6.13, age range 19-42 years) who had been using an LNG-IUD as contraception for more than three years and reported a personal history of reduced or non-existent sexual desire. All women were regularly monitored gynecologically every six months from July 2023 to July 2024. Sonographic examination of the pelvis is part of every gynecological examination and helps to exclude possible organic diseases that could lead to sexual dysfunction. All gynecological and sonographic examinations were without pathological findings.

During the sexological examination, the levels of prolactin, SHBG, TT, and gynecological markers CA-125 and CA-19-9 were checked. Estradiol, progesterone, FSH, and LH were not monitored because they are affected by LNG-IUD. All patients completed the Rosen FSFI questionnaire, which focuses on women's sexual dysfunction. They also completed two questionnaires, TSC-40 for monitoring possible social traumas and the SDQ-20 for possible dissociative symptoms. Any patients with severe somatic or psychiatric illnesses were excluded from the study. Patients with thyroid disorders, obesity and diabetes mellitus were also excluded from the study.

2.1 Ethics Approval and Consent to Participate

All participants provided written informed consent, and the study was approved by the ethics committee of the University General Hospital. The Ethical Committee's (ec) decision No.142/23.

2.2 Measurement of Female Sexual Dysfunction

The Rosen Female Sexual Function Index (FSFI) questionnaire was used as a diagnostic tool to measure sexual function. The FSFI is a questionnaire with 19 questions that contain six subgroups - desire, excitement, lubrication, orgasm, satisfaction and pain. Patients' responses included their

sexual feelings over the last 4 weeks and were recorded on a five-point Likert scale; the total score is from 0 to 95. A lower score indicates higher sexual dysfunction [10]. The average value of the FSFI questionnaire in the group of examined women was 22 (SD = 3.71).

2.3 Psychometric Measures of Stress and Dissociative Symptoms Response

2.3.1 Trauma Symptoms Checklist (TSC-40)

Symptoms of stress and trauma were evaluated using the TSC-40 questionnaire. This is a questionnaire with 40 questions. These are listed on a 4-point scale, according to the Likert scale. The overall score is from 0 to 120. Questions include subgroups for sexual problems, depression, sleep disorders, anxiety, dissociation, and sexual abuse trauma (SATI) [11]. The average value of the TSC-40 questionnaire in the examined women was 46.17 (SD = 7.09).

2.3.2 Somatoform Dissociation Questionnaire (SDQ-20)

Somatoform dissociative symptoms were measured using the SDQ-20 questionnaire. It contains 20 questions that assess the feelings of pain, changes in perception, loss of control, gastrointestinal symptoms, and other related symptoms. The subjects record their feelings on a 5-point Likert scale. A significant incidence of somatoform dissociative symptoms is a score greater than 30 [12]. The average value of the SDQ-20 questionnaire in the examined women was 38.20 (SD = 6.77).

2.4 Neuroendocrinological Markers

For biochemical evaluation of all mentioned hormones and markers (PRL, SHBG, CA-125, and CA-19-9), 2 ml of blood serum was collected in a special vacuum gel separation tube according to routine procedures at the Institute of Sexology, Charles University in Prague.

The sample transport time was 20 minutes. Blood samples were transported in a refrigerator at 4°C to the Central Laboratory of the Institute of Medical Biochemistry and Laboratory Diagnostics, Faculty of Medicine in Prague. Blood samples were evaluated using routine laboratory tests to determine serum PRL, SHBG, CA-125, and CA-19-9 levels.

2.5 PRL Measurement

Blood for PRL testing was routinely collected and transported to the faculty laboratory under standard conditions. The collection took place two hours after the patients were awakened. PRL levels in individual samples were measured by the technique of chemiluminiscent immunoassay (CLIA). Depending on the type of laboratory method, the normal PRL level values ranged from 3 to 25 µg/L. The average value of the PRL in the examined women was 18.3 g/l (SD = 2.4).

2.6 CA-125 and CA-19-9 Measurement

Blood for CA-125 and CA-19-9 was routinely collected and transported to the faculty laboratory under standard conditions. The collection took place two hours after the patients were awakened. The levels of both markers were measured by reacting the antigen with a monoclonal antibody. Normal CA-125 levels range from 0 to 35 kU/l, and CA-19-9 values range from 0 to 37 kU/l. The

average value of the CA-125 in the examined women was 17.23 kU/l (SD = 9.34), and that of the CA-19-9 was 15.57 kU/l (SD = 8.72).

2.7 SHBG Measurement

Blood for testing SHBG level was measured by a chemiluminescent immunoassay (Alinity/Abbott Laboratories). In adult premenopausal women, SHBG values range between 40 and 120 nmol/l, and in our patients, the mean value was 100.49 nmol/l (SD = 19.58).

2.8 Total Testosterone Measurement

For Total testosterone (TT) examination, blood is best taken in the morning and examined by chemiluminescence immunoassay (Beckman Coulter). In adult premenopausal women, TT values range between 0 and 2.6 nmol/l, and in our patients, the mean value was 1.3 nmol/l to 1.73 nmol/l (SD = 0.37).

2.9 Statistical Methods

The statistical evaluation of all our psychometric measurements included descriptive statistics and Spearman's correlation coefficients. Statistical methods were evaluated using Statistica software, version 12.

3. Results

3.1 Study Group

The results show that stress-related symptoms (TSC-40, SDQ-20) are closely related to the Rosen FSFI score, which confirms possible sexual dysfunction, as well as the results of the SHBG values. These results are confirmed by significant Spearman correlations of TSC-40 with SDQ-20 (R = 0.55), with FSFI (R = 0.65), and with SHBG (R = 0.80) (Figure 1). The significant Spearman correlations are confirmed between SDQ-20 and SHBG (R = 0.53) (Figure 2) and also between CA-125 and CA-19-9 (R = 0.45) (Figure 3). We did not find any significant associations with PRL and TT.

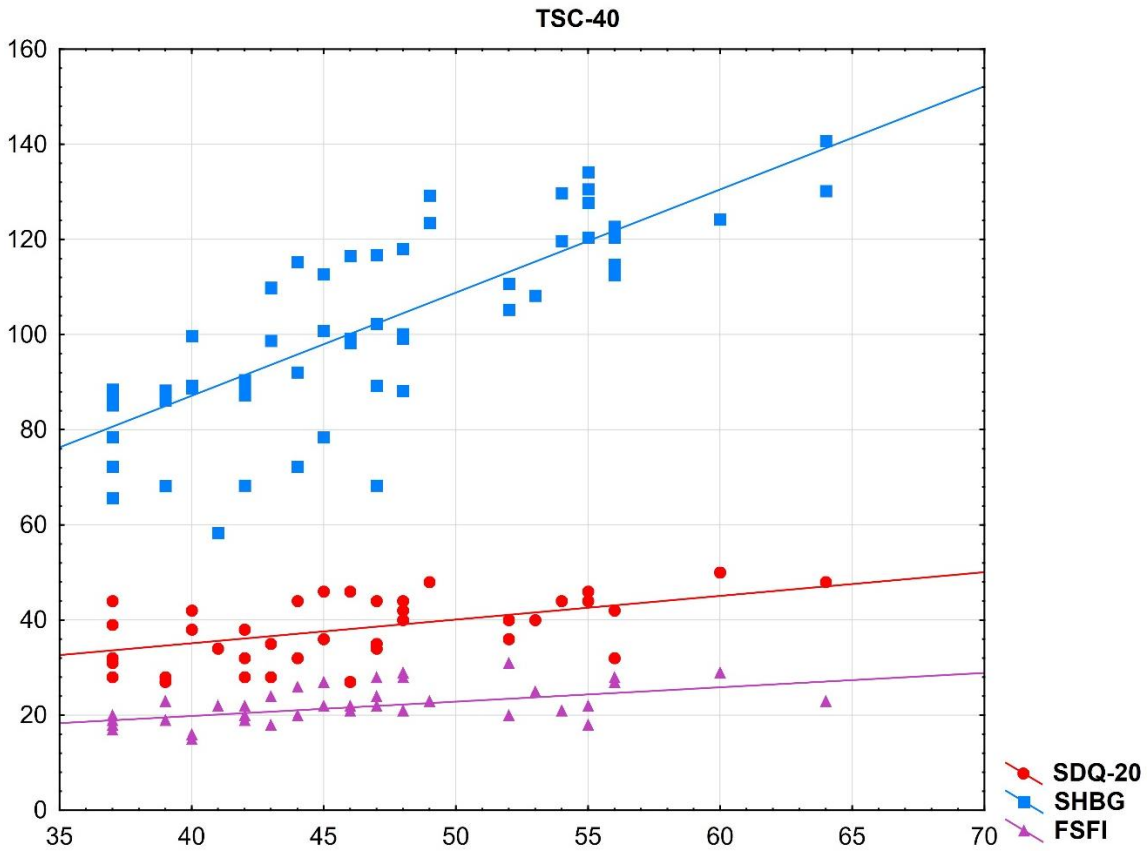

Figure 1 Relationship of TSC-40 score with SDQ-20 score, with SHBG levels, and FSFI score in the study group.

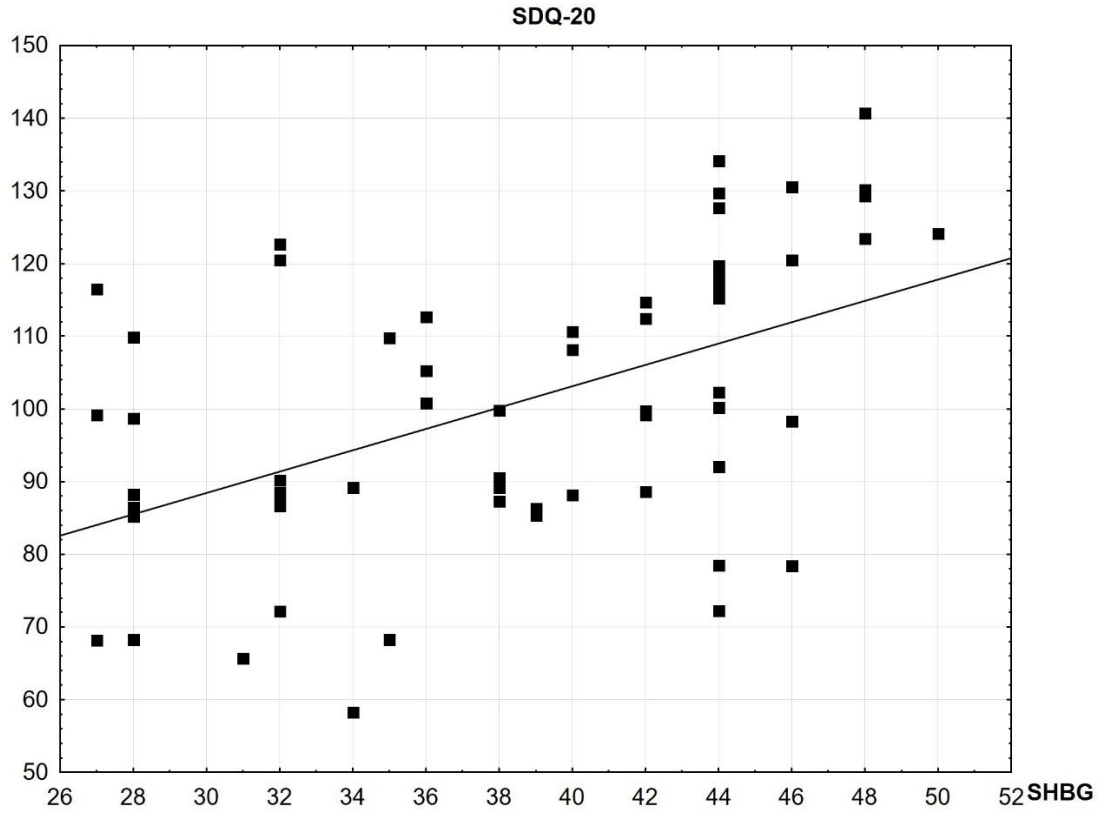

Figure 2 Relationship of SHBG with SDQ-20 score and FSFI score in the study group.

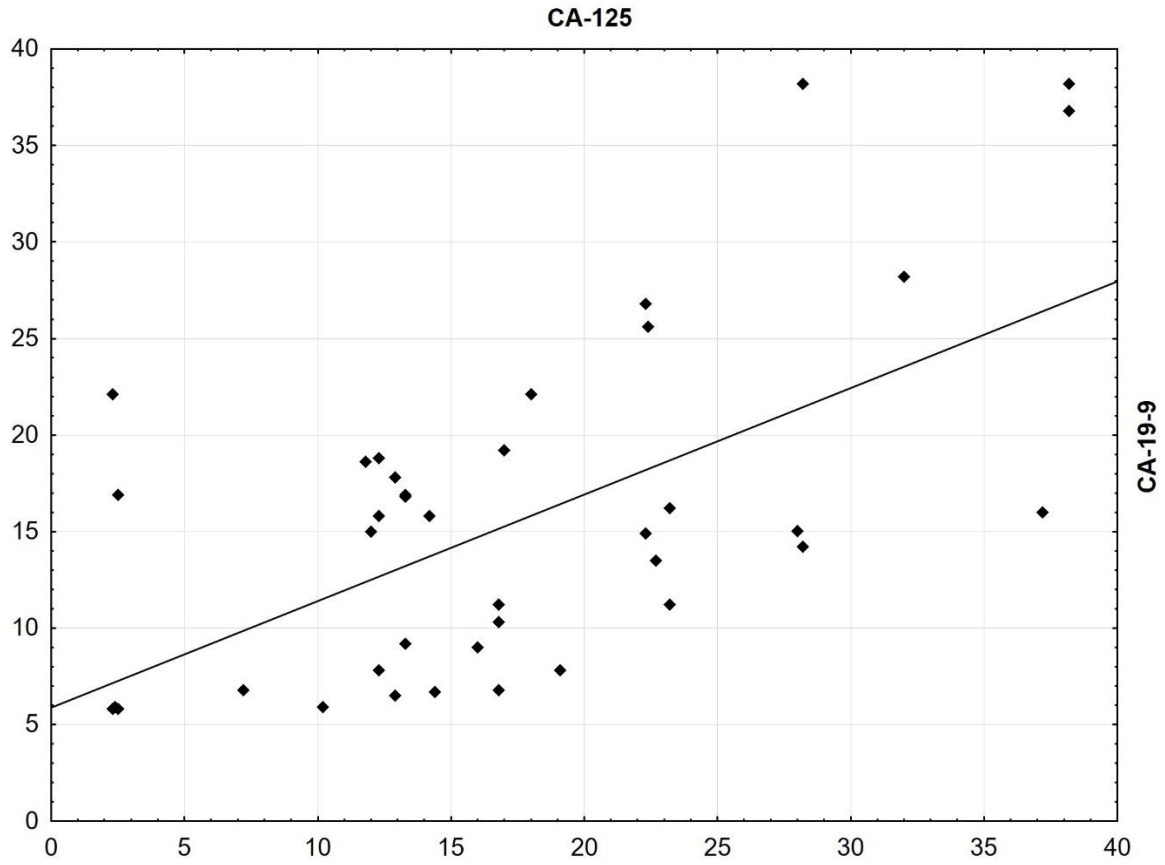

Figure 3 Relationship of CA-125 and CA-19-9 in the study group.

When the individual FSFI subscales were evaluated according to Rosen, the following values were found: desire (3.64; SD = 1.21); excitement (4.38; SD = 0.75); lubrication (3.87; SD = 0.59); orgasm (3.67; SD = 0.64); satisfaction (5.04; SD = 0.66); pain (4.47; SD = 0.73). The investigated patients in our study reported that the most intense sexual disorder was a decrease or complete disappearance of sexual desire, followed by perceptions of problems with orgasm, lubrication, arousal, and the least intense perception was of pain and satisfaction (Figure 4).

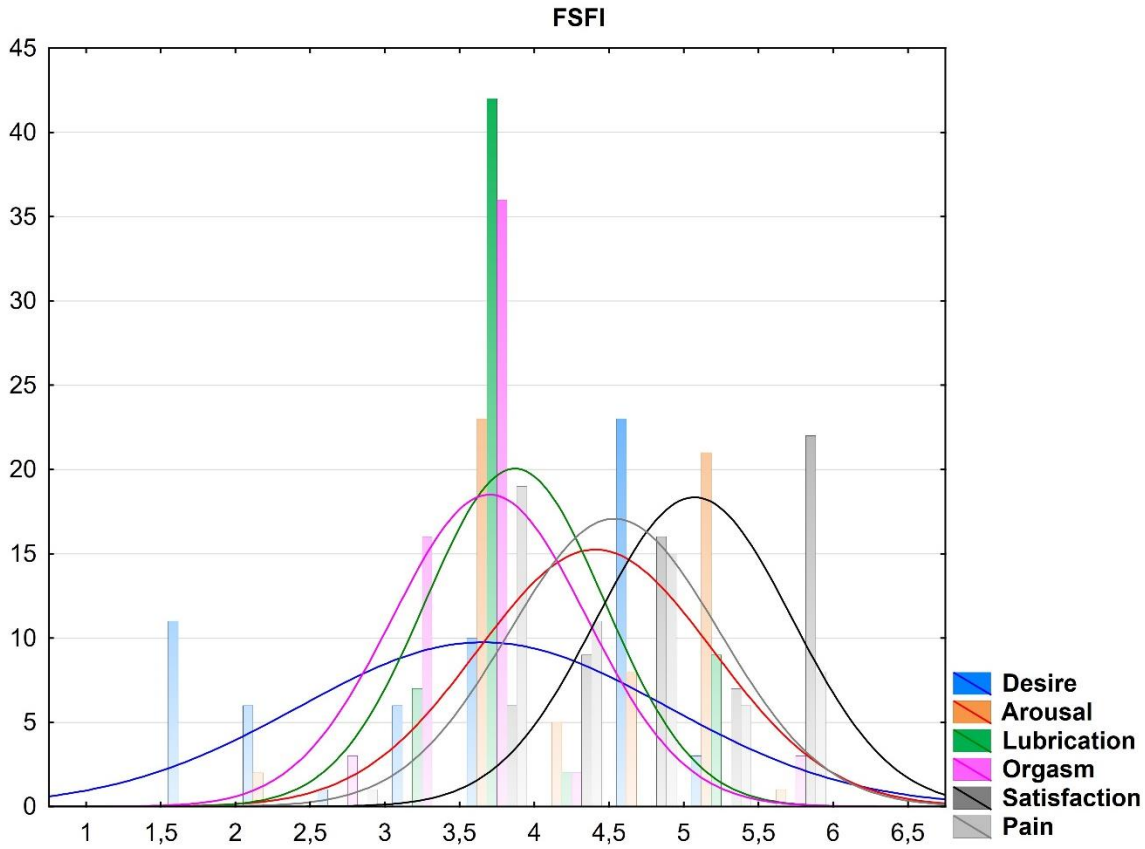

Figure 4 Relationship of individual parts of the FSFI questionnaire (desire, arousal, lubrication, orgasm, satisfaction, and pain).

4. Discussion

HSDD has a high prevalence that appears to be relatively constant throughout women's lives [13]. Official statistics indicate a 10% rate, but many women do not discuss these issues [14]. This sexual disorder significantly affects women's health. It can be part of many organic diseases, such as endometriosis, pelvic inflammatory processes, urinary tract infections, vertebrogenic disorders, and many others. However, the problem can also be psychogenic or a combination of organic and psychogenic causes. HSDD can occur in patients with mental disorders treated with antidepressants or antipsychotics [4], which often lead to changes in PRL levels [15]. Hyperprolactinemia is associated with low sexual desire [16]. It is also thought that the use of HC can lead to sexual dysfunction [3].

This study confirms significant correlations between psychosocial stress (TSC-40 score), sexual dysfunction (FSFI score) (R = 0.52) and with SHBG values (R = 0.80), as well as significant correlation between dissociative symptoms (SDQ-20 score) and SHBG values (R = 0.53) and also between CA-125 and CA-19-9 (R = 0.45). We did not find any significant associations with PRL and TT.

The correlations we found do not imply that one factor causes the other; we merely state that they are related, and it is therefore necessary to seek more detailed information about these correlations.

LNG-IUD appears to lead to decreased levels of androgens, estradiol, and progesterone and possibly to the inhibition of oxytocin [17]. As a result, LNG-IUD can adversely affect the sexual behavior of women and, consequently, their partners [8]. A few studies have looked at the link

between hormonal contraceptives and sexual dysfunction in women, but the results are not convincing. It can be said that further extensive research is needed in this area [18]. In conclusion, the data obtained from this study point to a possible etiological relationship between psychosocial stress, dissociative symptoms, SHBG levels, and hypoactive sexual desire disorder in women using the levonorgestrel-releasing intrauterine device, but further research in this area is needed. Our study is unique in that it examines the relationship between possible female sexual dysfunctions and the levonorgestrel IUD. Other studies, for example, in Turkey or Brazil, only compare the effects of different IUDs with each other [19].

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Author Contributions

Dr. Ludek Fiala data collection, research and manuscript. Dr. Jiri Lenz data control and manuscript control. Dr. Sarka Papadaki statistics.

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Competing Interests

Authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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