Research Article

Psychological hallmarks of endometriosis with emphasis on sexual dysfunction, stress, anxiety and depressive symptoms

Abstract

Endometriosis is associated with gynecological disorders and infertility. More than 50 % of women report that they suffer from sexual dysfunctions, the most significant of which is pain, which can subsequently be associated with stress, anxiety, depression and partner discomfort. In our study, we focused on evaluating these symptoms. A total of 92 patients with endometriosis were included in the study. Clinical examinations were focused on biochemical analysis of cortisol and prolactin, as important hormones that can respond to stress, anxiety and depressive symptoms. At the same time, sexual function, stress, anxiety and depressive symptoms were psychometrically evaluated in these patients. Positive correlations were found between psychosocial trauma/stress and results from the sexual function questionnaire (R=0.30). Furthermore, positive correlations were evaluated between the results of Beck's questionnaire for assessing depression and prolactin (R=0.39) and also between the results of Beck's questionnaire for assessing depression and the anxiety test (R=0.33). We also found a high correlation between prolactin and anxiety (R=0.86). All results were confirmed by the Mann-Whitney test. These results represent important findings regarding the relationship of certain stress hormones, with sexual dysfunction and symptoms related to stress, anxiety and depression in women with endometriosis, which are still receiving little attention within endometriosis.

Keywords: anxiety, depression, endometriosis, sexual function, psychology

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Abbreviations:

ADVIA, analyzer centaur bayer; BMI, body mass index; CA-125,ovarian cancer-related tumor marker, CA-19-9,Carbohydrate antigen 19-9, CLIA,Chemiluminescence immunoassay, DHEA- S, dehydroepiandrosterone sulfate; MRI, magnetic resonance imaging; PRL, prolactin

Introduction

Endometriosis is a serious gynecological disease that mainly affects patients of childbearing age.[1] Endometriosis has the character of an inflammatory, systemic and chronic disease, which can occur in up to 15 % of women. A characteristic feature is the presence of tissue resembling the endometrium outside the uterine cavity. The time from the first symptoms to a clear diagnosis often takes more than 10 years. This is because there are no specific markers for the diagnosis of endometriosis.[2] Nevertheless, some studies indicate that some non-specific markers may be used for testing, such as CA-125 or CA-19-9, or that certain hormone levels, such as DHEA-S values, can also be indicators.[3,4] Endometriosis is an estrogen-dependent disease that is associated with other disorders, such as fertility disorders (incidence up to 40 %) and sexual dysfunction (up to 50 % of patients). Some studies suggest that endocrine and immune changes may be associated with chronic stress, anxiety and even depression.[5] The results of some studies point out that patients with endometriosis, more than with other gynecological problems, suffer from psychopathological comorbidity - most often anxiety and depressive symptoms.[6] Other studies have even shown the possibility of an increased risk of developing not only symptoms, but even depressive and anxiety disorders.[7,8] In these cases, questionnaires such as the BDI or HAM-A were used, which we also used in our study, because the results of some current studies are often contradictory, partly due to the use of different and different methodologies.[9] Another difference is probably the possible occurrence of other psychiatric comorbidities, which have not yet been diagnosed in the patients, because the main diagnosis is precisely endometriosis and its complications.

The aim of our work in patients with endometriosis was to try to evaluate not only the relationship between sexual functions, stress, anxiety and depression, but also the results of the values of stress hormones such as cortisol and prolactin.

We also added to our research the TSC-40 questionnaire, which we have already used in our endometriosis research, which does not only focus on PTSD, but serves to assess other possible adverse situations, such as various stressful experiences or emotional and partner problems, which patients with endometriosis often mention. Using this questionnaire, we can evaluate wider psychological aspects, moreover, symptomatic reactions do not have to be tied only to a specific event.

Materials and methods

Study group and tissue specimens

A total of 92 patients with a mean age of 30.07 (SD=6.33), age range (24-46 years), were selected for our study from a total of 100 patients with a histologically confirmed diagnosis of endometriosis at the Department of Sexology of Charles University in Pilsen. The prospective study began in October 2018 and ended in September 2021. The average duration of endometriosis in our patients was 9.45 years (SD=2.13). The most common symptoms reported by patients were dysmenorrhea (73 patients), sex pain (66 patients), orgasmic disorders (45 patients), fear of sex (33 patients), mood swings (23 patients), partner discomfort (44 patients), depression (5 patients) and sleep disorders (18 patients). All 92 patients had one or more symptoms of endometriosis.[10]

The exclusion criteria were: pregnancy, cancer, hormonal or metabolic disorders such as obesity, diabetes mellitus, as well as psychiatric disorders - psychosis, schizophrenia, bipolar disorder and psychiatrist-diagnosed anxiety and depressive disorder, as well as diagnosed PTSD, which could affect the results of psychometric measurements. The revised American Society for Reproductive Medicine (rASRM) score was used to classify endometriosis.[11] Endometriosis was diagnosed by histological examination. Histological diagnosis of endometriosis was based on the presence of endometriotic glands and stroma.[12]

All patients underwent an initial gynecological examination, following up on previous gynecological findings, as well as basic biochemical tests to rule out other diseases. On the second to fourth day of the cycle, prolactin (PRL) and cortisol were obtained from peripheral blood. The gynecological examination was supplemented by a detailed ultrasound examination. Laparoscopic examination was performed in 89 patients with subsequent confirmation of histological findings, laparotomy examination was performed in 3 patients. MRI of the gynecological area of the small pelvis was performed in 6 patients.[13]

Neuroendocrinological markers

To evaluate the correlations, we primarily focused on the results of cortisol and prolactin as the stress hormones. For their evaluation, 2 ml of blood serum were collected in a special vacuum gel separation tube according to routine procedures at the Institute of Biochemistry at Charles University in Pilsen. The sample transport time was 20 minutes. Blood samples were transported in a refrigerator at 4°C to the Central Laboratory in Pilsen and were evaluated using routine laboratory laboratory tests.

PRL measurement

Blood for PRL testing was routinely collected and transported to the faculty laboratory under standard conditions. Collection took place two hours after awakening of patients and samples were measured by chemiluminescence immunoassay (CLIA). Normal PRL levels ranged from 3 to 25g/l. The average PRL value in the examined women was 23.48g/l (SD=13.01).

Cortisol

Cortisol samples were taken in the morning, preferably between 07:00 and 09:00 hours and then between 13:00 and 15:00hours, to minimize daily cortisol fluctuations. Subsequently, the serum cortisol level was determined in a biochemical laboratory according to normal analytical procedures.[14] Serum cortisol levels were identified by chemiluminescent immunoassay (CLIA) using an ADVIA analyzer (Centaur Bayer). The intra- and interassay scattering coefficients were 2.9 and 12.2 %, respectively. The cortisol value normally ranges from 118-618nmol/l. Our patients had mean values of 289.87nmol/l (SD=182.91).

Psychometric measurements

The female sexual distress scale-revised (FSDS-R)

The FSDS-R questionnaire is used in connection with the examination of sexual function. It was revised in 2005 and evaluates the issues over the last 30 days on a scale of: never 0, rare 1, sometimes 2, frequently 3, always 4. It contains 13 questions. A score ≥11 indicates FSD (Female Sexual Dysfunction).[15] The average values of the questionnaire in the examined group were 28.68 (SD=5.90).

Trauma symptoms checklist (TSC-40)

The TSC-40 uses 40 questions, which are evaluated on a Likert four-point scale. The total score is from 0 to 120. Using the questionnaire, the symptoms of stress associated with traumatic experiences are evaluated in the examined patients. This is a highly reliable test.[16] For a total of 92 patients, TSC-40 values were statistically processed with a mean value of 24.42 (SD=12.54).

Beck depression inventory-II (BDI-II)

This is a questionnaire that contains a self-assessment scale of the severity of depression. It consists of 21 items (these are also individual symptoms and negative thoughts occurring to varying degrees in depressed individuals).[17] The mean value of this questionnaire was 7.5 in patients (SD=3.36).

Hamilton rating scale for anxiety- HAM-A

HAM-A is one of the important assessment scales that can be used to measure the severity of anxiety symptoms in research conditions. The scale consists of 14 items and each is defined by a series of symptoms and measures mental and somatic anxiety. Each item is rated on a scale from 0 (not present) to 4 (severe), with a total score range of 0-56.[18]

HAM-A had a mean value of 20.00 in patients (SD=11.01). The completion of the FSDS-R, TSC-40 and BDI-II questionnaires was supervised by a sexologist, and the HAM-A questionnaire was administered by a psychologist with the patients.

Statistical analysis

Statistical evaluation of all psychometric measurements included descriptive statistics and Spearman's correlation coefficients. The statistical results were subsequently confirmed by the Mann-Whitney test. This test is also called the Mann-Whitney-Wilcoxon test (MWW rank-sum test). It is a non-parametric test of the null hypothesis for randomly selected values of x and y from two sets.[19] Statistical methods were evaluated using Statistica software version 12.

Results

In the mutual statistical assessment, positive correlations were found between the results of the Beck scale questionnaire for assessing the severity of depression (BDI-II) and PRL (R=0.39), then confirmed by Mann-Whitney test (z-score is 5.98019, P value is <0.00001, result is significant at $P<0.05$). Furthermore, the correlation between BDI-II and HAM-A (R=0.33), confirmed by the Mann-Whitney test (z-score is -8.55827, P value is <0.00001, the result is significant at $P<0.05$) (Figure 1). Positive correlations were found between TSC-40 and FSDS-R (R=0.30), confirmed by Mann-Whitney test (z-score is 3.89503, the value of P is 0.0001, the result is significant at $P <0.05$). We also found a high correlation between PRL and HAM-A (R=0.86).

Discussion

Endometriosis is one of the most common causes of female pelvic pain, which can manifest as dyspareunia, but also as dysmenorrhea, ovulation pain or dysuria and dyschezia. According to research, it seems that the level of pain may not depend on the size of the extent of endometriosis. This suggests that psychological factors may be involved in the nature of the pain, which may have significant negative effects on their mental health, quality of life, women may be limited in social activities, and it also affects their partner relationship and sex life.
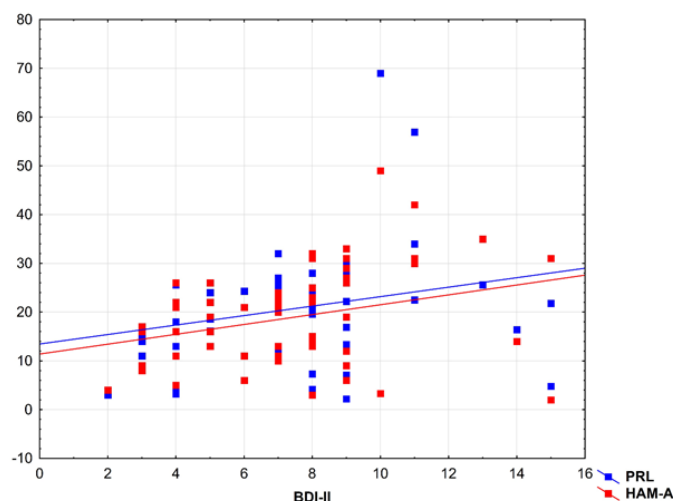
Figure 1 Relationship of BDI-II score with HAM-A score and PRL level.

Significant Spearman correlations between depression (BDI-II) and PRL level (R=0.39) and between depression (BDI-II) and anxiety (HAM-A) (R=0.33) observed in patients with endometriosis are illustrated.

In addition to pain, individual patients may experience other types of symptoms, such as anxiety, fear, and depression, as well as signs of sexual dysfunction, such as reduced desire, satisfaction, or orgasmic symptoms. Sexual dysfunction usually accompanies up to 50 % of patients with endometriosis.[20]

These symptoms subsequently negatively affect the nature of pain experienced by women with endometriosis. In addition, the subsequent development of sexual dysfunction can also occur in the partners of women with endometriosis, especially those who are intensely aware of their problems.

Therefore, it is necessary to focus not only on the treatment of endometriosis foci, but also on the psychogenic part of this serious disease. A better knowledge of understanding these relationships can help to positively influence these symptoms subsequently.

The results of this study are consistent with the hypothesis of possible relationships between stress, anxiety, depression and neuroendocrine markers in patients with endometriosis.[21] We found significant relationships confirmed by the Spearman correlation between the results of the FSDS-R score, which indicates sexual dysfunction, and the TSC-40 questionnaire, which describes psychosocial trauma and stress, as well as positive study results between the BECK-II, which describes depressive symptoms, and the results of the HAM- questionnaire A, which captures different states of anxiety and levels of PRL. Cortisol levels did not show any positive correlation. One of the possible reasons why there was a correlation only with prolatin and not also with cortisol is the fact that the possible influence of fat mass in patients (BMI) is mentioned in the professional literature, which leads to different results. However, no one has studied this effect in detail. BMI was not determined for the patients in our study.[22]

Conclusion

In conclusion, limited research suggests that women with endometriosis are at risk of psychosocial or psychiatric disorders.[23] It remains to be determined whether these problems are caused by endometriosis associated with chronic gynecological pain or also by other factors.[24] Women diagnosed with the symptoms of endometriosis should also be examined for psychosocial and psychiatric disorders at the same time. In this regard, it is important not to underestimate the psychological assessment of those patients who are at risk of developing symptoms of anxiety and depression and to provide them with appropriate psychological support.[25] It is necessary to emphasize the importance of a multidisciplinary approach not only in the diagnosis, but subsequently in the treatment of women with endometriosis.

Conflicts of interest

The authors state that there are no conflicts of interest regarding the publication of this article.

References

1. Králíčková M, Fiala L, Losan P, et al. Altered immunity in endometriosis: what came first? *Immunol Invest*. 2018;47:569–582.

2. Moradi M, Parker M, Sneddon A, et al. Impact of endometriosis on women's lives: a qualitative study. *BMC Womens Health*. 2014;14:123.

3. Fiala L, Bob P, Raboch J. Oncological markers CA-125, CA 19-9 and endometriosis. *Medicine*. 2018;97:e13759.

4. Simitsidellis I, Saunders PTK, Gibson DA. Androgens and endometrium: New insights and new targets. *Mol Cell Endocrinol*. 2018;465:48–60.

5. Králíčková M, Vetvicka V, Fiala L, et al. The search for biomarkers in endometriosis: a long and windy road. *Reprod Sci*. 2022;29:1667–1673.

6. Pope CJ, Sharma V, Sharma S, et al. A systematic review of the association between psychiatric disturbances and endometriosis. *J Obstet Gynaecol Can*. 2015;37:1006–1015.

7. Gambadauro P, Carli V, Hadlaczky G. Depressive symptoms among women with endometriosis: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2019;220:230–241.

8. Sepulcri Rde P, do Amaral VF. Depressive symptoms, anxiety, and quality of life in women with pelvic endometriosis. *Eur J Obstet Gynecol Reprod Biol*. 2009;142:53–56.

9. Friedl F, Riedl D, Fessler S, et al. Impact of endometriosis on quality of life, anxiety, and depression: an Austrian perspective. *Arch Gynecol Obstet*. 2015;292:1393–1399.

10. Taylor HS, Kotlyar AM, Flores VA. Endometriosis is a chronic systemic disease: clinical challenges and novel innovations. *Lancet*. 2021;397:839–852.

11. Lee SY, Koo YJ, Lee DH. Classification of endometriosis. *Yeungnam Univ J Med*. 2021;38:10–18.

12. Lenz J, Chvatal R, Fiala L, et al. Comparative immunohistochemical study of deep infiltrating endometriosis, lymph node endometriosis and atypical ovarian endometriosis including description of a perineural invasion. *Biomed Pap Med Fac Univ Palacky Olomouc*. 2021;165:69–79.

13. Ito TE, Abi Khalil ED, Taffel M, et al. Magnetic resonance imaging correlation to intraoperative findings of deeply infiltrative endometriosis. *Fertil Steril*. 2017;107:e11–e12.

14. Hannibal KE, Bishop MD. Chronic stress, cortisol dysfunction, and pain: a psychoneuroendocrine rationale for stress management in pain rehabilitation. *Phys Ther*. 2014;94:1816–1825.

15. Derogatis L, Clayton A, Lewis-D'Agostino D, et al. Validation of the female sexual distress scale-revised for assessing distress in women with hypoactive sexual desire disorder. *J Sex Med*. 2008;5:357–364.

16. Briere J. Dissociative symptoms and trauma exposure: specificity, affect dysregulation, and posttraumatic stress. *J Nervous Mental Dis*. 2006;194:78–82.

17. Beck AT, Steer RA, Ball R, et al. Comparison of beck depression inventories -IA and -II in psychiatric outpatients. *J Pers Assess*. 1996;67:588–597.

18. Thompson E. Hamilton rating scale for anxiety (HAM-A). *Occup Med (Lond)*. 2015;65:601.

19. Perme MP, Manevski D. Confidence intervals for the Mann-Whitney test. *Stat Methods Med Res*. 2019;28:3755–3768.

20. Fiala L, Lenz J, Bob P. Effect of psychosocial trauma and stress on sexual dysfunction in women with endo metriosis. *Medicine (Baltimore)*. 2021;100:e26836.

21. Laganà AS, La Rosa VL, Rapisarda AMC, et al. Anxiety and depression in patients with endometriosis: impact and management challenges. *Int J Womens Health*. 2017;9:323–330.

22. Roelfsema F, Pijl H. Phase difference between serum prolactin and cortisol rhythms is related to body mass index in humans. *J Clin Endocrinol Metab*. 2012;97:E2293–E2296.

23. Brasil DL, Montagna E, Trevisan CM, et al. Psychological stress levels in women with endometriosis: systematic review and meta-analysis of observational studies. *Minerva Med*. 2020;111:90–102.

24. Ruoff GE. Depression in the patient with chronic pain. *J Fam Pract*. 1996;43(6 Suppl):S25–33; discussion S34.

25. Basson R, Gilks T. Women's sexual dysfunction associated with psychiatric disorders and their treatment. *Womens Health (Lond)*. 2018;14:1745506518762664.