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ПСИХОСОМАТИЧЕСКИЕ ОСЛОЖНЕНИЯ СНИЖЕНИЯ ИЛИ НАРУШЕНИЯ ГЕНЕРАТИВНОЙ ФУНКЦИИ У ПАЦИЕНТОК ОБЩЕСОМАТИЧЕСКОЙ СЕТИ (ОБЗОР ЛИТЕРАТУРЫ)

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Psychosomatic Complications of Decreased or Impaired Generative Function in General Medical Patients (Review)

Резюме

Помимо целого ряда соматических недугов у 49-100 % пациенток с бесплодием верифицируются психические расстройства: 35-56 % — депрессии разной степени тяжести, 25-76 % — тревожные и психосексуальные расстройства, 40 % — тревожно-депрессивные расстройства, 50 % — расстройства адаптации, к 9,5 % — суицидальные мысли и попытки. У 75 % женщин, обращающихся за медицинской помощью в период менопаузы, также выявляются расстройства тревожного, депрессивного, дисморфического и психотического спектров.

Психофармакотерапия у пациенток проводится с использованием современных антидепрессантов, анксиолитиков, антипсихотиков с акцентом на хорошую переносимость, совместимость с гормональной терапией, удобство дозирования.

Психотерапия, психологическое сопровождение и психокоррекционная работа позволяют уменьшить выраженность тревожно-депрессивной симптоматики и существенно повысить успешность лечебных процедур

Ключевые слова: *психические расстройства, бесплодие, менопауза, климакс, депрессия, тревога, дисморфическое расстройство, психоз, инволюция, лечение, терапия*

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Abstract

In 35-56 % of patients depression of varying severity was diagnosed, in 25-76 % — anxiety and psychosexual disorders, in 40 % — anxiety and depressive disorders, in in 50 % — adjustment disorders, to 9.5 % — suicidal thoughts and attempts. Anxiety, depressive, dysmorphic and psychotic spectrum disorders are identified in 75 % of women seeking medical care during the menopause.

Psychopharmacotherapy in female patients includes modern antidepressants, anxiolytics, and antipsychotics, with an emphasis on good tolerability, compatibility with hormone therapy, and easy dosing.

Psychotherapy, psychological support and psychocorrectional work can reduce the severity of anxiety and depressive symptoms and significantly increase the success of treatment procedures

Key words: *mental disorders, infertility, menopause, depression, anxiety, dysmorphic disorder, psychosis, involution, treatment, therapy*

Conflict of interests

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According to present-day literature, sharp and cyclic fluctuations of estrogens, changes in the level of estrogen receptors in brain structures (including amygdala, hippocampus, hypothalamus), as well as the suppression of the activity of GABAergic neurons by progesterone, decreased secretion of GnRH and melatonin, decreased stimulating effect of thyreoliberin on the secretion of TSH, corticoliberin on ACTH, and vasopressin on cortisol [1–2] lead not only to infertility or the early onset of the perimenopausal period, but also to a significant deterioration in the somatic and mental health of female patients seeking medical help in general healthcare facilities.

The objective of this review was to analyze the results of core studies on the psychosomatic complications of a decrease or impairment of the generative function in female patients of general healthcare facilities.

Search by keywords “mental disorders”, “infertility”, “menopause”, “climacteric”, “depression”, “anxiety”, “dysmorphic disorder”, “psychosis”, “involution”, “treatment”, “therapy” was conducted in the databases of articles published by domestic and foreign authors over last 25 years (PubMed, eLibrary, Scopus, and ResearchGate). The material obtained was of three types: reviews, books, and original research articles. For this analysis, domestic and foreign literature sources were selected, which revealed the nature of the studied population and were available to the authors of this publication.

The negative impact of impaired fertility (in cases of infertility) is accompanied by a deterioration in family and work adaptation, decreased regularity (50.4 %) and satisfaction (62.2 %) with sexual life, long duration and clinical severity of premenopausal symptoms [3]; female patients seek medical advice for these signs, primarily from general physicians.

It should be noted that heterogeneous causes of infertility[1] include such somatogenic factors as chronic immunological and endocrine disorders, urogenital infections, anomalies and pathologies of the uterus and fallopian tubes, substance abuse, and psychosexual disorders [6, 7].

In turn, the complications of infertility, along with an increased incidence of diseases of internal organs (endocrine, cardiovascular, reproductive systems), include psychogenic mental disorders [3, 6, 8, 9], all falling under the concept of “biopsychosocial crisis” [10].

In general medical practice, typical signs of a “biopsychosocial crisis” for women in connection with infertility are behavioral disorders, such as proneness to conflict, accusing physicians of incompetence, dedicating life to the fixed (up to obsession) idea of getting pregnant with a radical change in lifestyle, refusal to eat certain products, exhausting physical exercises, diets, developing a special sleep schedule, etc. [11], as well as the dissimulation of bodily health problems in order to appear “healthier than they really are” [12].

Emotionally, patients are characterized by mood swings, anxiety, infantilism, dependence, loss of control over ongoing events, unstable or low self-esteem, negative attitude towards themselves, a sense of shame that impedes their empathy with others, absence of a holistic cognitive concept of the disease, and the dominance of mystical ideas about the unfulfillment of the maternal role [13–14].

[1] Infertility is the inability of a sexually active couple to achieve pregnancy after one year of unprotected sex [4]. In clinical studies and medical practice, infertility is a disease of the reproductive system that is manifested in the absence of a clinical pregnancy after 12 or more months of regular unprotected sex [5].

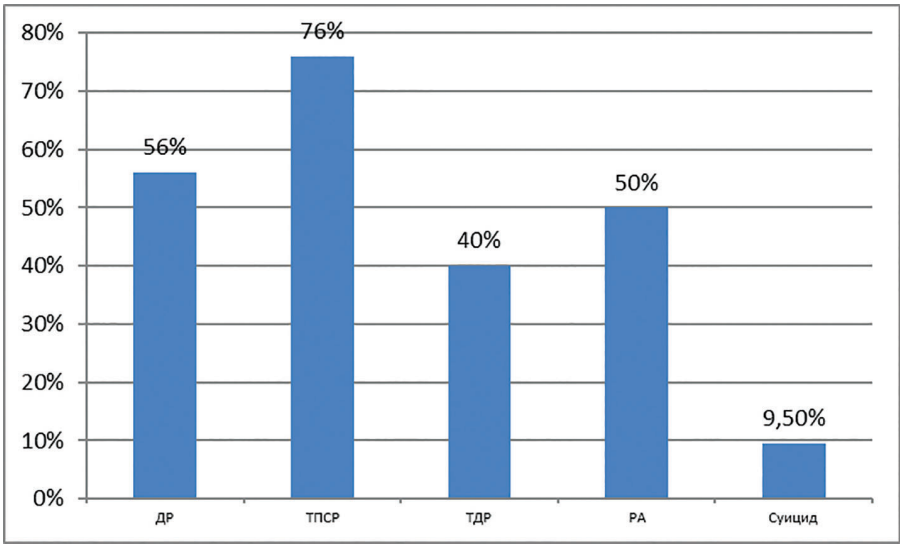

Figure 1. *Frequency of mental disorders in infertility*
Note: ДР — Depression, ПТСР — Posttraumatic Stress Disorder, ТДР — Anxiety & Depression Disorders, Suicide

The development of clinically defined forms of mental disorders with an underlying "biopsychosocial crisis" is confirmed in 49–100 % of female patients [1, 8, 15, 16]: 35–56 % develop depression of varying severity (VD) [17, 18], 25–76 % — anxiety and psychosexual disorders (APSD) [16, 18], 40 % — anxiety-depressive disorders (ADD), 50 % — adjustment disorders (AD) [18]. 9.5 % of patients have suicidal thoughts and attempts [6, 19] (Figure 1).

It should be emphasized that in case of depression due to infertility, patients often have complaints of hypersomnia, hyperphagia, and somatization (hysteralgia) disorders that become the reason for seeing a general physician and require differential diagnosis with laboratory tests and instrumental examinations.

In order to facilitate and accelerate the correct diagnosis, physicians can perform an additional examination of patients, including psychometric scales that allow establishing increased levels of asthenic and apathetic, anxiety and phobic symptoms, dysphoria, lethargy, and mood lability.

The period of decline and end of fertility (premenopausal period, menopause, climacteric) is characterized by other endocrinological changes. Physiologically, the whole menopausal period is characterized by a decrease in reproductive function with a gradual increase in the threshold of sensitivity of the hypothalamic-pituitary complex to homeostatic regulation of estrogens by feedback type, as well as a decreased level of receptors for peptide and steroid hormones in the hypothalamus, increased concentration of pituitary FSH, and impaired melatonin production [21, 22].

The duration of premenopause varies from 2 to 15 years. Menopause starts with the last spontaneous period. Menopausal age is determined retrospectively, after 12 months of the absence of periods. Early menopause happens when a woman's periods stop before the age of 45; late menopause — after the age of 55. The perimenopausal period includes premenopause and two years after the last spontaneous menstruation. Postmenopausal period lasts from menopause to almost complete end of ovarian function [20].

From a therapeutic point of view, it is significant that 35–80 % of women have climacteric syndrome (N95.1 according to ICD-10, pathological "climacteric comorbidity" [23]), with the combination of menopausal signs (vasomotor: hot flashes, night sweats; urogenital and metabolic, somatized, cognitive and, finally, anxiety and depressive signs (Table 1) [1, 21, 24, 25].

A specific feature of the clinical presentation of such women during their appointment is the verbalization of statements indicating the presence of one or more pathopsychological symptom complexes: "midlife crisis", "pension bankruptcy", "loneliness phenomenon" [26],

Table 1. *Symptoms of pathological «menopausal comorbidity»*

Symptom group	Symptom
Urogenital	Vaginal dryness, dyspareunia, decreased sexual activity
Metabolic	Slower metabolism and lower energy level
Somatized	Pain symptoms of various localizations, distress, breathing difficulties
Cognitive	Impaired attention and memory
Anxiety-depressive	Depression, irritability, sleep disturbances

"downhill of life", "empty nest syndrome" [27], "loss of female attractiveness" syndrome (body image, physical self-concept, self -image [28]), "generation gap" and "sandwich syndrome" (the need to solve a dilemma between the supporting different generations of the family: children with their problems (enrollment into university, marriage) and somatically aging parents [29]), etc.

Also, the main complaints in 75 % of women seeking medical care during menopause are low mood and sleep disturbances [50, 56–62]. Depression is diagnosed in 15.8–20 % of women [24].

Predictors of depression in the perimenopausal period include the manifestation of somatic diseases, low physical activity, early onset of menopause, changes in family roles, social functioning, financial status, stressful situations, mental disorders that developed in the postpartum period [2].

The identification by a general physician of any specialization of depressive states in female patients in involution has a critical prognostic and social significance.

Firstly, involutional depressions are characterized by a high level of irritability, anxiety, fears ("imminent old age", loneliness, financial insecurity, loss of external attractiveness), multiple asthenic and somatovegetative signs (conversion, somatization, vegetative: hot flashes or chills, increased sweating, intolerance to stuffiness, sense of not getting enough air, sense of "burning" in the body, palpitations, algia, dyspepsia, "squeezing" sensation in the heart, trembling, pseudosyncope, dizziness, "spasms" in throat) and hypochondriacal phobias (hysterophobia, obsessive fears of a serious disease) with active seeking of medical advice from general physicians, "extortion of care", ostentation, dramatic "grieving", suicidal threat. All these symptoms greatly complicate the diagnosis of actual somatic disorders and delay the choice of adequate pharmacotherapy and referral of the patient to a psychiatrist or psychotherapist.

Secondly, the late involvement of a mental health specialist in the joint management of patients in menopause can often lead to a sharp aggravation of the mental (Table 2) and somatic condition of the patients.

Involutional melancholy is observed in 82 % of women and 10–46 % of patients of a general practitioner [24]. Its causes can be somatogenic (genetic predisposition, hypertension, coronary heart disease, cardiac arrhythmias), endocrine (hypoestrogenia, hormonal disorders in the reproductive system due to uterine fibroids, endometriosis, hystero- or oophorectomy) and psychogenic (chronic or subjectively severe conflicts, death in the family, loss or change of job, place of residence, financial difficulties, etc.) [30–31].

Typical features of ***involutional psychosis*** [32] are an illusory perception of the world around, agitation, Charpentier symptom of impaired adaptation (when the anxiety of patients increases when changing location or being transferred to another ward or hospital), Cotard's syndrome (patients cry, wring their hands, are sure that their "body has died, decomposed", or that their "children, relatives have died"; sometimes with the ideas of the death of the world), Kleist's symptom (a woman whines for a long time, asks for help; if the physician tries to talk to her, she immediately stops talking, refuses to talk, as soon as the physician leaves, she starts whining again), autoaggressive and suicidal tendencies (Table 2) [33–36].

Patients with ***hypochondriacal delusion*** try to normalize/restore functions of internal organs (respiratory, digestive, cardiovascular systems) that are lost from their point of view. The absurdity of the substance of such a delusion (a deviated septum "affects the supply of oxygen to different lungs", the shape of cheekbones has an effect on the development of obstipation, etc.) is combined with a high degree of systematization, detailed elaboration based on data obtained from specialized literature sources. Patients interpret the lack of results expected from treatment as a sign of "undertreatment" and the need to continue that or another type of treatment until full recovery (Table 2) [37–40].

Involutional paranoid disorder starts gradually with the development of persistent delusional ideas. Patients are convinced that their neighbors or relatives enter their apartment at night or in their absence, using specially made keys, steal things, poison food, release toxic gas, pour poisonous powder (small delusions), meet at night, arrange gatherings of suspicious people with "loud voices that can be heard behind the wall". The behavior of patients is characterized by suspicion, distrust, tendency to various quarrels and squabbles. They file complaints with various authorities (police, community courts, prosecutor's office), demand punishment for people who have caused material damage, and they lock everything that can be locked — boxes, cupboards and even pots. The condition is accompanied by verbal and olfactory hallucinations. Change of residence does not help eliminate such painful experiences (Table 2) [33–36].

Involutional catatonia is characterized by staged development of symptoms in the form of depression, hypochondriacal phobias, unmotivated anxiety coupled with delusional ideas of persecution, self-accusation, development of Cotard's syndrome, and a stuporous state with complete immobility and mutism. Psychosis ends with the development of presenile dementia.

With a malignant form of involutional catatonia, i.e., ***presenile psychosis***, anxiety and depressive state, incoherent speech, confusion with massive psychomotor agitation are replaced by inhibition with clouded consciousness of the oneiroid type and illusory delusions, Cotard's syndrome. Patients think they are attending their own funeral or the funeral of relatives or acquaintances, that they see various events and regard them as "the death of the Earth, the catastrophe of the Universe". Patients refuse to eat, cachexia is registered. Death in such cases can occur from an associated/exacerbated somatic disease (Table 2) [33–36].

Patients with ***dysmorphic delusions*** (dysmorphomania regarding "beauty", "ugliness", "nose", "weight", "appearance", etc.) have dominating erroneous uncorrectable and behavior-determining ideas about "ugliness", "abnormal structure" or "deformities" of certain

parts of their body. Overestimation and enthusiastic admiration of the appearance of others are combined with categorical, multiple and inconsistent complaints against one's own appearance, active and annoying visits to several specialists at once in order to correct a "physical defect", requirements of ever new methods of examination and therapy with inability to comply with medical recommendations and to wait for the effect, as well as litigious reactions on dissatisfaction with the results of surgeries, demands for material compensation (paranoia of struggle, 24.1 %) [41, 42]. The behavior of patients is also characterized by the use of protective camouflage of imaginary defects with the help of special hairstyles or make-up, wearing of extravagant clothes or eye-catching jewelry, darkened glasses, hats, clothes of a special cut that cover the "ugly" parts of the body.

A typical sign is auto-aggression with a desire to remove (sometimes with a razor, knife, hot objects) "pigmented spots" and other "ugly" skin areas or correct a "defect" (shaving and pulling out hair, cutting nose, filing teeth) on their own, with subsequent visit to a cosmetologist or plastic surgeon to correct the results of such interventions (Table 2) [37–42].

Patients with involutional ***erotomanic delusions*** constantly visit specialists in aesthetic medicine in order to correct their appearance to achieve sexual attractiveness for a partner. The requests do not fit the patient's age and/or somatic condition: physical abilities are overestimated, the difference in age and social status is not considered. Patients are convinced that after cosmetic or surgical treatment, they will "certainly" acquire an appearance that is "irresistible" for the object of their ecstatic affection, achieve mutual feelings, and enter into marriage or intimate relationships. Having failed to achieve what they were looking for, patients return to aesthetic medicine specialists with complaints of poorly performed treatment and ask for repeated and additional interventions. In 6.9 % of female patients, the physician becomes involved in the system of erotic delusions and persecuted by the patient (Table 2) [37–42].

Therefore, mental disorders that develop with underlying impairment, decline and loss of fertility are heterogeneous. Their effect on the somatic state of patients, as well as clinical and dynamic diversity requires timely diagnosis, as early as the stage of contacting general physicians and joint management with psychiatrists.

Dealing with the management of psychosomatic complications and reducing the generative cycle in women in general healthcare facilities require emphasizing the obligatory joint management of patients with psychotic conditions with a psychiatrist and optional consultation for anxiety and depressive disorders, due to the likelihood of the manifestation/exacerbation of these disorders that are both independent of the somatic status of the patient, and caused by changes in her somatic and endocrinological state.

Table 2. *Main clinical symptoms of involutional psychoses*

Involutional psychosis [32-36]	Illusory perception Agitation Charpentier's symptom Cotard syndrome Kleist symptom Autoagressive and suicidal tendencies
Involutional paranoid [33-36]	Suspiciousness, mistrustfulness Delusion of detriment Verbal and olfactory hallucinations Querulousness Suffocation
Hypochondriacal delusion [37-40]	Absurd systematized delusion Uncorrected desire to normalize/restore «lost» internal organ functions
Involutional catatonia	Depression Unmotivated anxiety Delusion of persecution, self-blame Cotard syndrome Stupor Mutism Presenile dementia
Presenile psychosis [33-36]	Involutionary catatonia Oneiroid Manichean delirium Eating disorders
Dysmorphic delusion [37-42]	Uncorrected and behavior-defining ideas of «ugliness», «structural abnormalities», or «deformities» of certain body parts Protective camouflage Autoaggression The demands of ever-new examination and therapy methods Sutile reactions
Erotomania [37-42].	Inconsistent with somatic and social status demand for correction of appearance to achieve erotic attractiveness for a partner

Psychopharmacotherapy in female patients with infertility is carried out using advanced antidepressants, anxiolytics, antipsychotics with an emphasis on good tolerance, compatibility with hormonal therapy, and easy dosing. When choosing agents, in addition to following the standard recommendations, one should consider risk factors (heredity, comorbid disorders, sex, age, etc.) for the development of adverse events (AEs), the range of somatotropic and endocrine side effects typical for each drug, the balance of efficacy and safety, the possibility of drug-drug interactions with therapeutic medications.

Psychotherapy, psychological support, and psychocorrection work can also reduce the severity of anxiety and depressive symptoms and increase the success of treatment procedures (for example, in cases of IVF, from 29.8 % to 42.1 %) [43].

In our opinion, the effectiveness of hormone replacement therapy (HRT, including those with "general tonic" drugs, vitamins, dietary supplements, physiotherapy) is not obvious in cases of mental disorders in the pre- and menopausal periods. Some studies indicate that estrogen replacement therapy is moderately effective in preventing and managing menopausal depression [44]. Others suggest that women receiving HRT in the perimenopausal period have a higher level of depression than those who do not receive such agents [45]; that using hormonal agents is ineffective, and can even trigger an exacerbation of psychopathological symptoms and worsening of patient's condition [46].

The use of estrogen and melatonin to augment psychopharmacotherapy has been discussed in recent years [40].

SSRIs (fluvoxamine, citalopram), SNRIs (duloxetine) and agomelatine are among the preferred antidepressants [47].

Long-term use of any antidepressants can result in decreased bone mineral density, increased body weight, and metabolic syndrome [21].

According to post-marketing studies, non-benzodiazepine agents, such as fabomatizole [48], 4,6,8-tetramethyl-2,4,6,8-tetraazabicyclo-(3,3,0)-octanedione-3,7 (mebicarum, adaptol) [49] and nootroph D-,L-hopantenic acid, are recommended as drugs with an anxiolytic effect for use in the perimenopausal period [50].

Psychotherapy is aimed at building a constructive psychological defense (in particular, self-control and responsibility) and adaptive behavioral coping strategies (reattribution with a decreased threatening meaning of somatized symptoms, creating the conviction that there is no life-threatening physical disease, proper assessment of the actual situation, and desisting from manipulations) [30].

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