АКУШЕРСТВО И ГИНЕКОЛОГИЯ

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PSYCHOSOMATIC ASPECTS OF THE INFERTILITY TREATMENT WITH THE IN VITRO FERTLIZATION METHOD

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On the example of 114 patients aged 20 to 37 years, from which 84 patients suffered tubal-peritoneal infertility were included in the treatment methods of assisted reproductive technologies. Control group consisted of fertile women. Women with infertility revealed a significant incidence of comorbid psychiatric disorders associated with the stressful effects of IVF treatment, characterized by comorbidity of anxiety and depression with the prevalence of anxiety disorders. The high level of personal anxious and mental maladjustment are risk factors for negative outcome of IVF. Correction of the mental state improves the effectiveness of treatment for women with infertility. Refs 30. Tables 10. Fugs 8.

Keywords: mental illness, infertility, in vitro fertilization.

ПСИХОСОМАТИЧЕСКИЕ АСПЕКТЫ ЛЕЧЕНИЯ БЕСПЛОДИЯ МЕТОДОМ ЭКСТРАКОРПОРАЛЬНОГО ОПЛОДОТВОРЕНИЯ

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Обследовано 114 женщин в возрасте от 20 до 37 лет, из которых 84 пациентки страдали трубно-перитонеальным бесплодием и были включены в программу лечения методами вспомогательных репродуктивных технологий. Контрольную группу составили фертильные женщины. У женщин с бесплодием выявляется значительная частота сопутствующих психических расстройств, ассоциированных со стрессогенным воздействием лечения экстракорпоральным оплодотворением, характеризующихся коморбидностью тревоги и депрессии с преобладанием расстройств тревожного спектра. Высокий уровень личностной тревожности и психической дезадаптации является фактором риска отрицательного результата экстракорпорального оплодотворения. Коррекция психического состояния способствует повышению эффективности лечения женщин с бесплодием. Библиогр. 30 назв. Табл. 10. Ил. 8.

Ключевые слова: психические расстройства, бесплодие, экстракорпоральное оплодотворение.

Introduction

Infertility is characterized by complex psychosomatic interconnections. On the one hand, the hormones of stress such as catecholamines — epinephrine, norepinephrine and dopamine interact with LH and FSH and disturb the ovulation process by affecting the ce-

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rebral cortex, hypothalamus, pituitary and genital glands activation of hypothalamus-pituitary-adrenal cortex system [11; 23]. In the stressful situation the level of serotonin rises, forwarding in increased concentrations of prolactin, which in its turn suppresses normal folliculosteroidogenesis in the ovaries [11; 12]. Under the influence of stress the contractility of the ovary rises by the activation of symphatoadrenal system. This affects the size of the follicle, its blood supply and the ovulation. Stress hormones rise the contractility of the uterine tubes with an impact on the delivery of the gametes and the fertilization of an egg [19; 26].

Up to 80 % of females with infertility have psychiatric disorders [1, 10, 14, 15, 17], that can be considered as a link of infertility pathogenesis. Also the psychiatric state is often considered a result of psychosomatic interaction of a variety of factors [21; 22, 27].

Studies of interrelation between the levels of epinephrine, norepinephrine and cortisol, anxiety and depression and the results of in vitro fertilization (IVF) have shown a positive correlation between the urine concentration of epinephrine in the beginning of the treatment, before embryo implantation and the severity of depression [16; 24].

Reproductive anamnesis (the duration of the diagnostic procedures and the treatment of infertility), specifics of partner relations, together with the number of IVF procedures are also considered to be the determinants of the psychiatric condition [3, 4]. Women with unsuccessful experience of IVF procedures are noted to have depression [25]. The psychiatric disorders are corrected with the positive IVF results [2, 7, 8].

The cyclic psychosomatic dependence is characteristic for infertility. psychiatric disorders are risk factors for infertility and its unsuccessful treatment. Infertility at the same time worsens the psychiatric condition in females by the stresses of diagnostic procedures and treatment [28–30].

Some authors point on the necessity of psychological help to females with infertility as well as to females undergoing IVF treatment [5, 6, 18, 22]. Human Fertilization and Embriology Authority (HFEA) recommend sociopsychological consultation for patients undergoing IVF. However, the system of psychological help to females involved in IVF is still underdeveloped [9, 13].

Subjects and methods

114 females with the minimum age of 20 and maximum of 37 years (mean age — 29,4$\pm$2,2 years) were evaluated. 84 patients of them with infertility were treated by IVF.

The control group consisted of fertile women of the reproductive age (mean age — 29,6$\pm$0,6 years) with 1–2 children. These females were planning a new pregnancy and were not using hormonal methods of contraception.

The evaluation was handled with the use of sociological, catamnestical, clinical and psychometric methods in combination with laboratory studies. The levels of FSH, LH, estradiol in blood serum on the 2–4 days of the menstrual cycle and the levels of prolactin and progesterone on the 20–23 days of the menstrual cycle were measured. The Spielberger State-Trait Inventory and the Beck Depression Inventory were used in the study, The Index of Life Style was used for evaluating mechanisms of psychological defense while The Semantic Differential of Time — was applied to evaluate the time perception as a symptom of depressive disorders.

Statistical methods for data analyses.included Students t-criterion for means comparison and Pearson correlation for correlation studies.

Results

The study showed that 48 of 84 females had primary infertility (57,1 %). In 36 cases secondary infertility was diagnosed (42,8 %).

The gynecological anamnesis in patients with infertility was overburdened with cervix disorders (32,1 %), ovarian masses (17,8 %), STD (genital herpes, chlamydiosis, CMV, ureaplasmosis) (69 %). 42,8 % of the females had previous pregnancies in their anamneses, however only 3,5 % had resulted in labor. 28,5 % females experienced induced abortions, 9,5 % — miscarriages and 20,2 % — ectopic pregnancies.

In the control group the pregnancies more often resulted in successful labor (20 %), induced abortions performed only by 10 % of females and the miscarriage occurred only in one case.

Among extragenital pathology chronic infectious diseases, which were more common in women with infertility, should be especially notified chronic bronchitis (23 %), pneumonia (13,3 %), chronic sinusitis and tonsillitis (42,8 % and 26,6 %); chronic pyelonephritis, cystitis (30,9 % and 20 % of all cases). The frequency of Hepatitis A in the infertility group was twice higher (14,2 % and 6,6 %, respectively).

Every third female with infertility has experienced pelvic surgery in the past, while in the control group the surgery has been previously performed only in 6,6 % .

Hormonal evaluation of the patients with tubal infertility factor showed no difference for basal secretions of LH and FSH from normal levels. The LH level in the follicular phase was 7,2 ME/L, FSH — 5,1 ME/L. Prolactin level in the luteal phase was 454 ME/L, that is significantly ($p<0,05$) higher in comparison with the control group data.

In patients with infertility higher education was predominant, especially in women with primary infertility. Among women with secondary infertility and in the control group the secondary education was more common ($p<0,01$) (Table 1).

Table 1. **The educational characteristics of evaluated patients**

Education	Main group, n=84				Control group, n=30	
	Primary infertility, n=48		Secondary infertility, n=36			
	Number of women		Number of women		Number of women	
	Abs.	%	Abs.	%	Abs.	%
Secondary	3	6,2	3	8	—	—
Secondary professional	10	20	13	36	21	70
Higher	35	**72**	20	55	9	30

It was found, that most of the patients were employed (76,1 % of cases), whereas the number of unemployed was quite low (3,2 % of cases).

The study showed, that compared to the control group in the treated group the professional activity was significantly ($p<0,05$) more connected with emotional and intellectual tension, and supposed much more time spent on computer operating (Table 2).

It was noted, that the professional activity in patients with endometriosis (29 patients of the main group — 34,5 %) were significantly more often connected with intellectual tension and unlimited working day than the activity of the patients with tubular-peritoneal infertility (Table 3).

Table 2. **The characteristics of professional activities in the evaluated women**

The characteristics of the professional activities	Main group n=84				Control group, n=30	
	Primary infertility, n=48		Secondary infertility, n=36			
	Abs.	%	Abs.	%	Abs.	%
Activity with the physical tension	9	18,7	8	22,2	12	40
Activity with the emotional tension	19	39,5	18	50	19	63
Long computer working hours	27	56,2	20	55	5	16
Unlimited working day	32	66	24	66	18	60

Table 3. **The characteristics of the professional activities in different types of infertility etiology**

The characteristics of the professional activities	Number of women, n=84			
	Tubular-peritoneal factor, n=55		Endometriosis, n=29	
	Абс.	%	Абс.	%
Activity with the physical tension	15	27	2	6,8
Activity with the emotional tension	19	34,5	18	62
Long working hours with the computer	26	47,2	21	72,4
Unlimited working day	31	56	25	86,2

It was found, that 82,1 % of the patients were experiencing chronic psychotraumatic situation because of troublesome family relations. According to the interview, in 32 % cases patients have chosen the IVF treatment method being pressurized by theirclose relatives.

The patients with infertility were characterized by significantly higher anxiety levels as a stable personality trait. The mean trait anxiety score according to the STAI in the main group was $34,9 \pm 2,53$, whereas in the control group the score was $23,3 \pm 1,1$ ($p<0,05$).

The state anxiety mean score was moderate, but in the same time it was significantly higher than in the control group ($43,6 \pm 5,29$ and $23,00 \pm 0,81$, respectively, $p<0,05$).

The data in the table 4 show that patients with endometriosis differ from the patients with tubular-peritoneal infertility by higher levels of the trait anxiety and significantly higher levels of the state anxiety.

Table 4. **The levels of anxiety in different types of infertility**

Anxiety, STAI scores	Tubular-peritoneal factor	Endometriosis	Significance, p
Trait anxiety	$39,5 \pm 2,53$	$42,4 \pm 2,52$	—
State anxiety	$40,2 \pm 2,89$	$44,5 \pm 2,73$	<0,05

From the data in the table 5 it is seen, that the tension of the most defense mechanisms in the group with infertility was significantly higher than in the control fertile group. That means the presence of the psychological desadaptation.

Clinical psychiatric disorders were diagnosed in 45 % of the patients treated with the artificial reproductive technologies.

15,4 % of women were diagnosed with Generalized Anxiety Disorder (F41.1 according to ICD-10). The conative (volition) part of the anxiety included elements of disorga-

Table 5. **The system of psychological defense in the patients**

Mechanisms of psychological defense	Main group	Control group	Significance
	Mean scores (M±m)	Mean scores (M±m)	P
Denial	67,0±2,2	63,9±4,2	—
Suppression	45,1±2,6	41,7±2,4	—
Regression	66,9±2,3	39,4±2,1	p<0,05
Compensation	69,4±4,6	43,7±3,2	p<0,05
Projection	46,5±3,2	23,6±1,3	p<0,05
Displacement	55,8±3,5	41,5±2,6	p<0,05
Intellectualization	48,3±3,6	31,4±4,1	p<0,05
Reaction formation	55,6±0,9	39,1±3,2	p<0,05

nization and inconsecutive behavior. These were represented by ideational manifestations such as fixed ideas of low self-esteem based on infertility. The disorders of cognitive functioning were represented by difficulties in prompt functioning such as lower concentration of attention, inequality in the pace of intellectual functioning. Vegetosomatic and motor components of anxiety (tense gestures, predominance of the SNS) succumbed to psychiatric manifestations such as emotional tense feelings, and feelings of uneasiness.

In cases when patients underwent the IVF procedure for the first time, they were often preoccupied with anxious doubts about the righteousness of their choice: «Should I receive treatment, if the nature is against». Females included in the IVF program were excessively fixed on the development and growth of the follicles in the ovaries and on the control of the size and numbers of the eggs. After the puncture of the ovaries patients circumstantially asked about the «destiny» of all eggs and were constantly returning to that question. The excessive attention to the size of the abdomen was also noted. In number of cases the patients experienced fear of the physiological body changes and the loss of their prettiness because of the possible pregnancy.

Along with the unspecified anxiety for the future, specific isolated phobias were discovered — the phobias of multiple pregnancy, failed pregnancy. They can be classified as Phobic Anxiety Disorders F40 (7 % of cases).

Somatisation Disorder (F45.0) (12 % of cases) was presented by polymorphic symphtoms, especially with the migratory pain phenomena in the areas of the abdomen, the back and the head. These painful sensations appeared in the first days of superovulation stimulation and became stronger after the implantation of the embryo into the uterine cavity. Most cases matched the criteria for Hypochondriacal Disorder F45.2, less often for Other Neurotic (Conversion) Disorders F45.8.

In cases of the masked hypochondrias the patients developed “partnership” with the infertility problem. On the one hand, they participated in the regular diagnostic and treatment procedures with the realization of the infertility problem and with the fears about its prognosis. Constant fixation on the gynecological sphere and different body sensations associated with the possible pregnancy were common for them. On the other hand, the overcoming and active style of behavior was common. As a life credo they took ideas of high social functioning and success, despite the problem of childbearing.

During the screening depression of different severity was diagnosed in 20,2 % of women with the mean score of 15,6±3,2 according to BDI, while no depression was de-

tected in the control group (2,82±0,82, p<0,05). The specific anhedonia was detected, when all interests were centered on the infertility treatment and the problem of childbearing. It was common for the patients with depression to have feelings of insecurity. The specific fixed depressive ideas of self-accusation for the inability to become a mother and the feeling of guilt for the previous mistakes (for example, first abortion) were specific for these patients. 14 % females thought that the IVF program was considered antisocial and they were doing «something bad». Despite the obvious decrease in the levels of energy and motivation, the initiative and the workability were preserved with the small decrease in productivity and the ability to handle daily activities. The increase in irritability and the appearance of the asthenia component were noted along with the hormonal treatment. The depression did not overpass the neurotic level and was classified into two ICD-10 categories: Mood (Affective) Disorders F30–39 and Neurotic, Stress-related and Somatoform Disorders F40–9. Adjustment Disorders F 43.2 (including Mixed Adjustment Disorder With Anxiety F43.22 and Adjustment Disorder With Depressed Mood F43.21) were presented in 10 % of patients with the psychiatric disorders.

In 7 % of cases Dysthymia (F34.1) with the prolonged, more than two years, period of chronic depressed mood of the neurotic level was detected.

8,3 % of the females showed clinical signs of Neurasthenia (F48.0), which were presented by irritability, anxiety, hypothymia, emotional liability, different sleep disorders and fatigue. The asthenia symptoms were characterized by the dominance of irritability, fatigue and signs of hyperesthesia.

The study results gave the opportunity to establish some psychosomatic interconnections. The positive correlations between the severity of anxiety and depressive disorders and the levels of prolactin were detected (r=0,45; p<0,01). The correlation analyses proved that endometriosis promoted increase in personal anxiety (r=0,42; p<0,01) and raised risks of depression and anxiety disorders development (r=0,44; p<0,01) (r=0,46; p<0,01). With the increase of the infertility duration as well as the duration of its diagnostics and treatment the personality ? changes of anxious type (r=0,36; p<0,05) and the severity of anxiety (r=0,42; p<0,01) were increasing.

The study results gave the opportunity to establish specific patterns of changes in depression severity depending on the duration of infertility. The depression was more severe in the beginning period of infertility at terms from 1 year to 3 years (r=0,45; p<0,01). However with the increase of infertility duration (up to 6 years) the level of depressive symptoms was decreasing (r=0,35; p<0,05), and the anxiety symptoms became predominant.

Ectopic pregnancy with the following tubectomy, which gave women the only chance to become pregnant by the IVF procedure, significantly increased the risk of future depression (r=0,36; p<0,05). Previous pregnancies regardless of its results (spontaneous abortion, induced abortion or labor) significantly decreased the possibility of the depressive disorders in women with the infertility in the future (p<0,05). The severity of depression was higher in women with the experience of failed IVF, moreover there was a linear correlation between the level of depression and the number of IVF procedures (r=0,44; p<0,01).

Two subgroups of patients with positive (34,5 %) and negative (65,5 %) IVF results were formed on the base of the IVF outcome. It was shown that the psychiatric disorders were significantly more common in the group of women with the negative IVF result (Table 6).

Table 6. **Psychiatric disorders in women with different IVF results**

Diagnosis according to ICD-10	Number of women		Significance p
	Positive IVF result	Negative IVF result	
Generalized Anxiety Disorder (F41.1)	4,7 %	10,7 %	<0,05
Dysthymia (F34.1)	3,0 %	6,5 %	<0,05
Adjustment Disorders (F43.2)	2,3 %	9,7 %	<0,05
Neurasthenia (F48.0)	3,5 %	6 %	<0,05
Somatoform Disorders (F45.0)	5 %	7 %	<0,05
Phobic Anxiety Disorders (F40)	3 %	4 %	<0,05
Total	21,5 %	43,9 %	

The clinical data matched the results of the scales scores. In the group of women with negative IVF results the levels of trait (38,0±3,3) and state (45,03±3,4) anxiety were higher than in the group with resulted pregnancy (28,72±3,1 and 31,72±4,3, respectively; p<0,05 in both cases) (fig. 1).

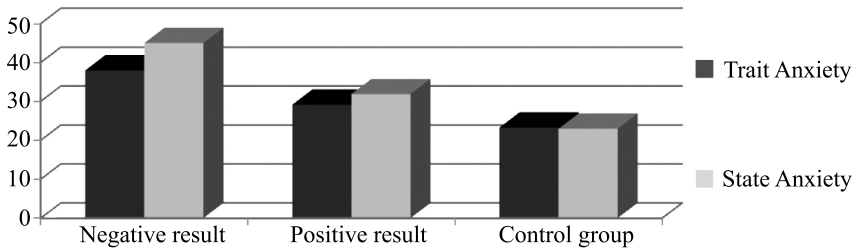

Fig. 1. The levels of anxiety in women with negative (n=55) and positive (n=29) results of IVF cycle after the embryo implantation ? (scores of the STAI)

The level of depression was higher in the group with negative IVF results in comparison with the group with positive outcome (16,19±2,2 and 15,44±1,3 according to the BDI, respectively). The symptoms in women with negative IVF results were experiencing a series of changes with formation of the sense of «grudge on fate», despair and the increasing pessimistic views of the future.

It was determined in the study that in women with negative IVF results the levels of state (43,69±3,48) and trait (37,11±3,32, according to the STAI) anxiety before the embryo implantation were higher than in women with successful IVF cycle results (31,72±2,75 and 28,72±1,72 respectively, p<0,05) (fig. 2).

The discovered pattern was maintained during the analysis of the level of anxiety depending on the persistence of endometriosis: the trait and state anxiety in women with endometriosis with negative results of IVF was higher than in women with tubular-peritoneal infertility (Table 7).

In the group with positive IVF results the level of anxiety among women with endometriosis was higher than among women with tubular-peritoneal infertility (Table 8).

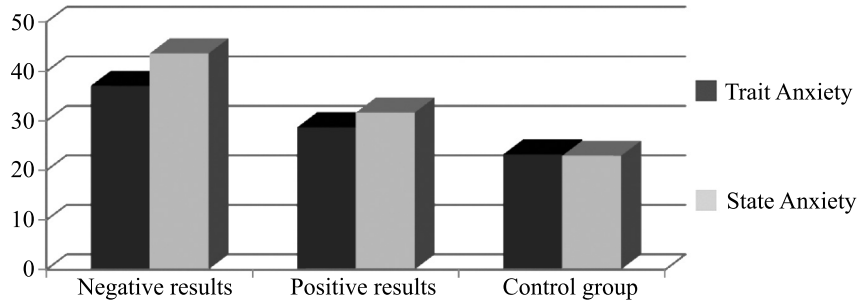

Fig. 2. The levels of anxiety in women with negative (n=55) and positive (n=29) results of IVF cycle before the embryo implantation (scores of the Spilberger Scale)

Table 7. **The levels of anxiety in women with negative results of IVF before embryo implantation of the?**

Anxiety, scores according to Spielberger Scale	Tubular-peritoneal infertility n=34 (62 %)	Endometriosis n=21 (38 %)	Significance P
Trait Anxiety	40,5±5,75	44,6±7,01	<0,05
State Anxiety	41,4±6,32	46,4±7,87	<0,05

Table 8. **The anxiety in women with positive IVF results depending on the etiology of infertility**

Anxiety, scores according to Spielberger Scale	Tubular-peritoneal infertility n=21 (72 %)	Endometriosis n=8 (27 %)	Significance P
Trait Anxiety	29,6±2,75	39,2±3,89	<0,05
State Anxiety	32,8±3,12	40,1±4,07	<0,05

The data on the fig. 3 demonstrates absence of significant differences between the severity of depression before the embryo implantation in women with the different IVF results: 16,39±2,0 with negative result and 16,94±1,4 with positive result.

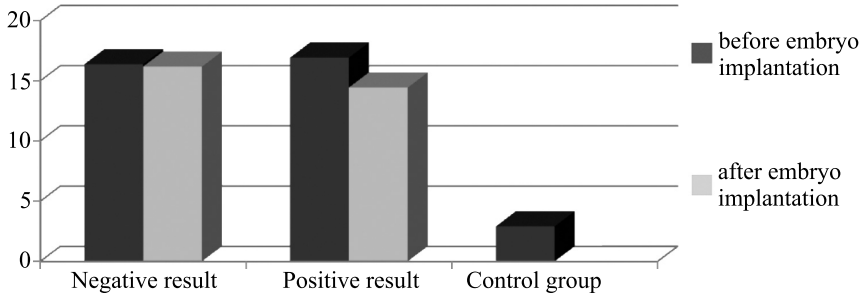

Fig. 3. The levels of depression in women with negative (n=55) and positive (n=29) results of IVF cycle before the embryo implantation (scores of the BDI)

While the depression in women with negative IVF results after the embryo implantation was nearly the same as before it (bench mark 16,19±2,2 in whole group according to the BDI), in women with the successful IVF cycle after the embryo implantation the depression became lower and scored 15,44±1,33.

It was discovered that women, who experienced negative IVF results, had a depressive view of future perspectives (Table 9). In the group of women with positive IVF results there were no depressive evaluations neither of the future, nor of the past and present.

Table 9. **The characteristic of time perception as a depressive symptom depending on the IVF results**

Factors	Negative IVF result	Positive IVF result
Present time		
Activity of time	–4,2	0,1
Emotional tinge of time	–3,03	0,8
Size of time	–1,4	1,8
Structure of time	–0,8	0,6
Sense of time	–0,6	1,09
Future time		
Activity of time	–2,1	6,07
Emotional tinge of time	–1,2	9,02
Size of time	0,6	7,08
Structure of time	0,3	4,64
Sense of time	0,1	4,60
Past time		
Activity of time	–2,8	5,06
Emotional tinge of time	–1,8	7,04
Size of time	–0,8	6,04
Structure of time	–0,6	3,06
Sense of time	–0,5	2,6

As it can be seen from the table 10, the structure of psychological defense was significantly different depending on the IVF results. Women with negative IVF results had significantly higher expression of the "Denial" defense mechanism ($p<0,05$). The expression of "reaction formation" and the "regression" showed the predominance of immature defense mechanisms, which were connected both with the removal of subjective unpleasant emotions and the refuse of dealing with significant problems. On the opposite side, for women with positive IVF results more mature defense mechanisms such as "intellectualization" and "projection" were more common. In these defense mechanisms the traumatic information was allowed to enter the consciences area but was interpreted in the "safest" way.

Table 10. **The mechanisms of the psychological defense in women with tubular-peritoneal infertility depending on IVF results**

Mechanisms of Psychological Defense	Women with negative IVF results, (n=55)		Women with positive IVF results, (n=29)	
	Mean scores (M±m)	Rank	Mean scores (M±m)	Rank
Denial	84,0±2,2	1	43,9±4,2	4
Suppression	45,1±2,6	8	41,7±2,4	6
Regression	70,9±2,3	3	39,4±2,1	8
Compensation	69,4±4,6	4	43,7±3,2	5
Projection	46,5±3,2	7	72,6±1,3	2
Substitution	65,8±3,5	5	65,5±2,6	3
Intellectualization	48,3±3,6	6	87,4±4,1	1
Reaction formation	76,6±0,9	2	39,1±3,2	7

In our study we also analyzed the influence of psychological correction of psychiatric disorders on the results of the IVF in the sample of 30 women with secondary tubular-peritoneal infertility.

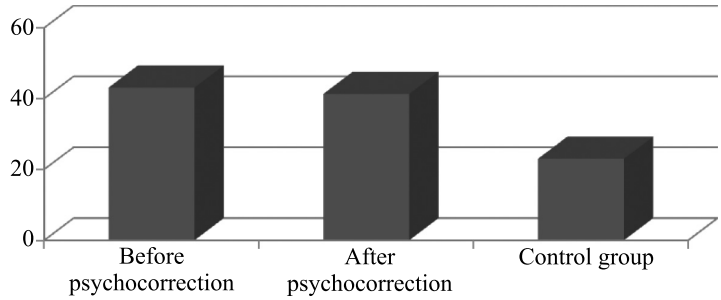

Fig. 4. Reactive anxiety in the group of women received psychological correction before IVF (scores according to the STAI)

As it can be seen from the image 4, there was a tendency of anxiety levels decrease during the process of psychological training for the IVF procedure, and the decrease from the high to moderate level was most significant in women with positive IVF cycle (fig. 5 and 6).

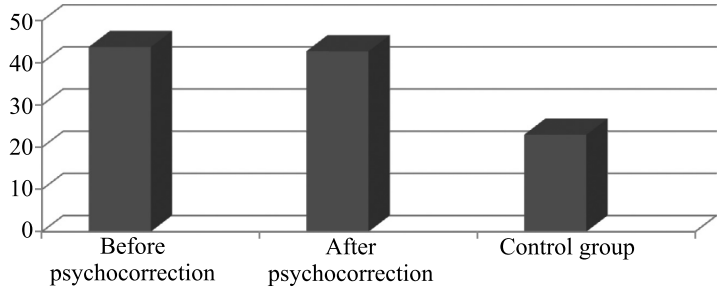

Fig. 5. State anxiety in the group of women with negative IVF result (n=19)

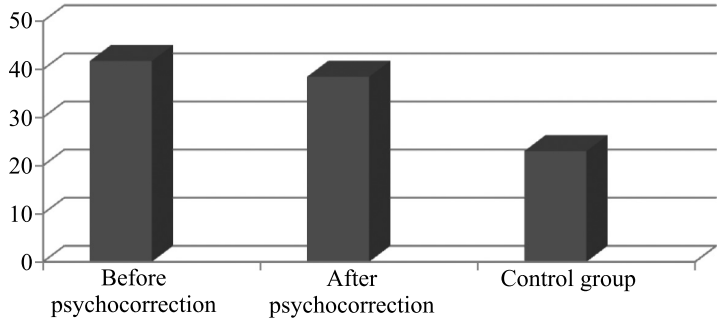

Fig. 6. State anxiety in the group of women with positive IVF result (n=11)

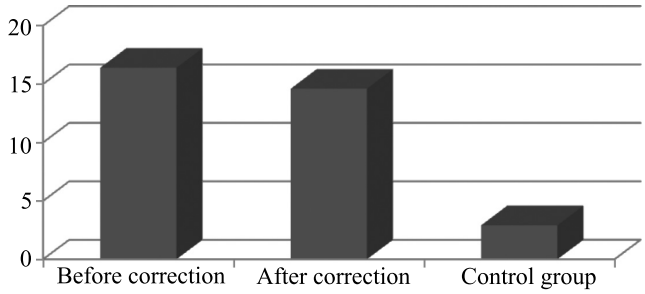

Fig. 7. Depression in women, participated in psychological correction before the IVF procedure (n=30)

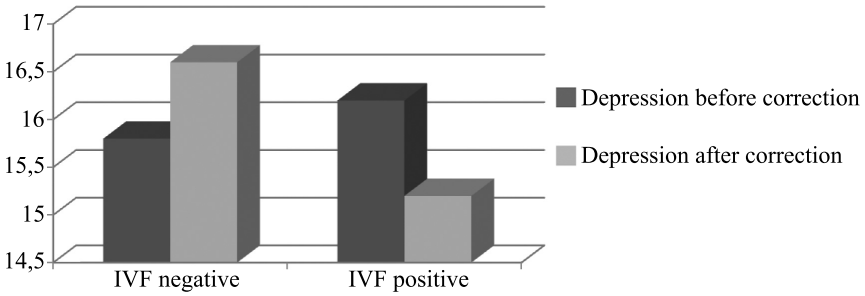

Fig. 8. The levels of depression in women after psychological correction with positive and negative IVF results

During the depression level evaluation, its decrease was also noted throughout the process of psychological correction (fig. 7). It was more significant in women with the following pregnancy (fig. 8).

Conclusions

Women with infertility, who were included in the program of IVF treatment, showed a significant number of psychiatric disorders of neurotic spectrum. These disorders were developed by interaction of different psychological and somatic (gynecological) factors and were presented by anxiety and depressive disorders with changing ratios of anxiety and depression during the therapy of infertility. The clinical presentation of nosogenic disorders showed a stressful influence of the infertility and its treatment. The continuous primary infertility with unsuccessful efforts of treatment is a chronic psychotraumatic situation, which leads to the formation of anxious personality traits and specific system of psychological defense. The high levels of anxiety, the presence of the anxiety disorders and psychological disadaptation are negative predictors for IVF results. Correction of the psychological state in women with infertility supports IVF efficacy increase. The results of the study point to the necessity of organizing a special psychological help service in the IVF centers, as well as realization of interdisciplinary, polyprofessional evaluation of these

patients with participation of a psychiatrist, psychotherapist, reproductologist-embryologist, obstetrician and gynecologist. It will encourage efficacy increase of the infertility treatment in IVF programs.

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