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Experience of Differentiated Approach to Treatment of Various Forms of Premenstrual Syndrome

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Abstract. Today treatment of premenstrual syndrome (PMS) is still debatable and requires an individual differentiated approach.

The objective of research was to evaluate the effectiveness of differentiated treatment of PMS various forms.

Material and methods. The study involved 200 women of reproductive age with diagnosis of PMS. Combined estrogen-progestagen drugs with drospirenone, selective serotonin reuptake inhibitors, Vitex agnus castus extract or traditional treatment were prescribed according to the form and severity of disease.

Results of the research. Traditional therapy was quite effective for correction of psychological and somatic symptoms in patients with mild neuropsychic and edematous forms of PMS. However, it was not effective enough in the patients with severe PMS and persons with cephalgic and crisis forms. Differentiated treatment of neuropsychical and edematous forms with combined oral contraceptives containing drospirenone and the use of selective serotonin reuptake inhibitors in patients with cephalgic and crisis forms of PMS significantly helped to reduce the intensity and leveling of symptoms compared with traditional therapy. Herbal medicines with Vitex agnus castus were effective for correction of symptoms in women with mild neuropsychical form.

Conclusions. Treatment of patients with PMS should be individual and differentiated and depend on the clinical form and severity of the disease.

Keywords: premenstrual syndrome; treatment.

Problem statement and analysis of the recent research

Premenstrual syndrome is a functional disorder of the central nervous system under the influence of unfavorable exogenous or endogenous factors on the background of acquired or congenital lability of hypothalamic-pituitary-ovarian system [4]. Certainly, there is no one type of treatment for all women with PMS. Therefore, individually differentiated approach to the treatment of this disease is considered the most effective one [6, 8]. International Society for Premenstrual Disorders has proposed two main approaches of treatment. The first one is connected with medicines that affect the central nervous system including modulators of serotonin neurotransmitter. The second one is the therapy that suppresses ovulation [5]. Selective serotonin reuptake inhibitors are effective medicines that adjust the physical, functional and mental symptoms of PMS. However, treatment regimen still causes debates [3, 9]. Low-dose combined oral contraceptives decrease PMS clinical manifestations due to the ovulation inhibition. Particularly effective are drugs with drospirenone which has anti-aldosterone and antiandrogenic features in addition to the properties of progesterone [2, 7]. Herbal therapy as one of methods of PMS treatment has positive effect. One of the most common and effective drugs are medicines that contain Vitex agnus castus. Extract of this plant reduces symptoms of mastalgia, some mental and physical manifestations of the disease, normalizes dysbalance between estrogen and progesterone [1, 11].

The objective of the research was to estimate the effectiveness of individual differentiated approach to the treatment of PMS various forms.

Material and methods

The research included 200 women with diagnosis of PMS who formed basic group. The control group consisted of 50 women without PMS diagnosis. Verification of diagnosis was performed in accordance with Order # 676 of Ministry of Health of Ukraine [4]. The diagnosis of PMS was made by detection of cyclical manifestations of disease in luteal

phase of menstrual cycle on the basis of history taking and keeping patient's self-observation diary for 2-3 menstrual cycles (Menstrual Distress Questionnaire, R. Moos). R. Moos Menstrual Distress Questionnaire consists of 8 items which contain 47 symptoms. The intensity of each symptom was scored from "1" to "6" points on the 25th day of the menstrual cycle before and after treatment. PMS form (edematous, neuropsychical, cephalgic, crisis) was determined according to V. P. Smetnik's classification [10].

All patients with PMS were offered non-medical and pharmacological correction of diseases with duration of 6 months according to Order # 676 of Ministry of Health of Ukraine. Initially, we proposed lifestyle modifications: recommendations concerning the regime of work and rest, moderate exercises, sleep up to 8 hours a day, to keep fractional specific diet. According to the type of treatment patients of the main group were divided into two groups – I and II. Women of group I received differentiated therapy. Depending on the form and severity of the disease according to the treatment these patients were randomized into the following subgroups:

IA_1 (20 persons) included women with mild neuropsychical form of PMS who received herbal extract of Vitex agnus castus in a dose of 40 drops per day; IA_2 (15 persons) consisted of women with severe neuropsychical form, who took combined estrogen-progestagen medicines containing 20 mcg ethinylestradiol (EE) and 3 mg drospirenone in 24+4 regime; IB included patients with edematous form of PMS, including 20 persons with mild form (IB_1) and 15 persons with severe (IB_1) form who took estrogen-progestagen medicines containing 30 mcg EE and 3 mg drospirenone in 21+7 regime; IC (18 patients) consisted of women with cephalgic form and ID (13 patients) consisted of women with crisis form of PMS who received selective serotonin reuptake inhibitor fluoxetine 20 mg daily for two days from ovulation and in seven days after the first dose for two days.

Group II of women received traditional therapy at the second phase of menstrual cycle – vitamin E in a dose of 200 mg 1 time per day, vitamin B (Neurovitan 1 table 1 per day), verospiron in a dose of 25 mg 2 times a day, indomethacin suppository in a dose of 0.05g rectally once a day. In order to compare the effectiveness of treatment between persons of group I and II we divided women of group II into subgroups: IIA_1 (22 women) and IIA_2 (15 women) – persons with neuropsychical form of PMS with mild and severe course respectively; IIB_1 (22 women) and IIB_2 (15 women) – patients with edematous form with mild and severe course respectively; IIC (15 women) – persons with cephalgic form and IID (12 patients) – women with crisis form of PMS.

For statistical analysis we used Statistica 6.0 program. We calculated arithmetic mean value (M), standard error of the mean (m), probability of differences of research results (p). Nonparametric Mann-Whitney test was used to compare two independent groups by one feature, Wilcoxon test was applied to compare two dependent groups. The difference between the compared values was considered reliable at $p<0.05$.

Results of research and their discussion

Items "pain", "behavior change", "autonomic reaction" and "arousal" were the most significant in patients with cephalgic and crisis forms of PMS (Tables 1-3). Such items as "impaired concentration" and "negative affect" were typical for women with neuropsychical form of diseases, "water retention" was characteristic of women with edematous form.

Analysis of the clinical manifestations intensity convincingly indicated the positive effects of differentiated treatment in patients with neuropsychical form of PMS (Table 1). The components "impaired concentration", "behavior change" decreased from "moderate" to "subtle" manifestations and component "negative affect" decreased from "expression" demonstrations to "subtle" symptoms in women with mild course of this form of IA_1 subgroup after the proposed therapy. Dynamics of reduction of these components was respectively 50.65 % ($p<0.001$), 54.05 % ($p<0.001$) and 53.85 % ($p=0.008$). In women of IIA_1 subgroup after the treatment indices of these components were "weak", and their reductions were respectively 18.02 % ($p<0.001$), 19.44 % ($p=0.002$) and 28.45 % ($p<0.001$).

Table 1

Dynamics of R. Moos scale components in patients with neuropsychical form of PMS after treatment, M±m, points

Scale components	Stage of treatment	Mild form, subgroups		Severe form, subgroups		Control group, n=50
		IA_1, n=20	IIA_1, n=22	IA_2, n=15	IIA_2, n=15	
Pain	before	1.80±0.20°	1.86±0.21°	2.73±0.27°°	2.40±0.27°°	1.22±0.08
	after	1.25±0.12	1.27±0.12*	1.47±0.19*	160±0.21	
Impaired concentration	before	3.85±0.18°°	4.05±0.15°°	4.40±0.13°°	4.27±0.18°°	1.40±0.10
	after	1.90±0.19**°	3.32±0.18**°^	2.07±0.21**°	3.80±0.20*°^	

Impaired concentration	before	3.70±0.16°°	3.55±0.23°°	4.13±0.24°°	4.00±0.22°°	1.44±0.10
	after	1.70±0.15**	2.86±0.20**°^	1.87±0.13**°	3.40±0.24**°^	
Autonomic reaction	before	1.95±0.28°	2.00±0.25°	2.40±0.34°	2.47±0.34°°	1.18±0.07
	after	1.25±0.10*	1.41±0.11*	1.47±0.13*°	1.93±0.23*°	
Water retention	before	2.00±0.26°	1.64±0.19	2.93±0.23°°	2.80±0.22°°	1.26±0.06
	after	1.20±0.09*	1.23±0.09**	1.33±0.13*	1.53±0.17**	
Negative affect	before	4.55±0.17°°	4.64±0.15°°	5.20±0.20°°	5.00±0.20°°	1.58±0.10
	after	2.10±0.14**°	3.32±0.14**°^	2.47±0.17**°	3.93±0.12*°^	
Arousal	before	3.35±0.20°°	3.45±0.18°°	4.33±0.16°°	4.13±0.17°°	1.14±0.05
	after	1.70±0.13**°	2.45±0.17**°^	2.07±0.18**°	3.20±0.17*°^	
Control	before	1.20±0.12	1.27±0.13	1.40±0.19	1.47±0.22	1.00±0.00
	after	1.05±0.05	1.09±0.06	1.07±0.07	1.33±0.16	

Note.
1. * – probability of the difference of indicator before and after treatment ($p<0.05$);
2. ** – probability of the difference of indicator before and after treatment ($p\leq0.001$);
3. ° – probability of the difference of indicator relative to control group ($p<0/05$);
4. °° – probability of the difference of indicator relative to control group ($p\leq0.001$);
5. ^ - probability of the difference of indicator after treatment between I and II groups of certain form ($p<0.05$).

In persons with severe course of neuropsychical form who received traditional treatment components "impaired concentration", "behavior change" and "arousal" decreased from "moderate" to "weak" manifestations by 11.01 % (p=0.018), 15.00 % (p=0.008), 22.52 % (p=0.002) respectively, and the component "negative affect" decreased from "expressed" to "moderate" manifestations by 21.40 % (p=0.002). In subgroup IA_2 dynamics of these components reduced after proposed therapy by 52.95% ($p<0.001$), 54.72 % ($p<0.001$), 52.19 % ($p<0.001$) and 52.50 % ($p<0.001$), respectively and reached values of IA_1 subgroups.

Both types of therapy resulted in almost identical correction of scales in women with mild edematous form (Table 2). Thus, according to our study "water retention" in patients with edematous form of PMS was the most significant component and after treatment it returned to normal indices in all subgroups of women. In persons of IB_1, IIB_1 and IB_2 subgroups the intensity of this component reduced from "expressed" to "subtle" symptoms and in women of IIB_2 subgroup – to "weak" manifestations. Dynamics of component reduction was more significant in patients with severe course. The proposed therapy led to its decline by 65.31 % ($p<0.001$), traditional therapy – by 47.93 % ($p<0.001$).

Table 2

Dynamics of R. Moos scale components in patients with edematous form of PMS after treatment, M±m, points

Scale components	Stage of treatment	Mild form, subgroups		Severe form, subgroups		Control group, n=50
		IB_1, n=20	IIB_1, n=22	IB_2, n=14	IIB_2, n=14	
Pain	before	3.10±0.27°°	3.00±0.25°°	3.64±0.32°°	3.79±0.21°°	1.22±0.08
	after	1.30±0.15**	1.41±0.16**	1.43±0.20*	2.29±0.22*°^	
Impaired concentration	before	2.15±0.23°	2.14±0.22°	3.00±0.26°°	3.14±0.14°°	1.40±0.10
	after	1.30±0.13*	1.50±0.14*	1.50±0.23**	1.86±0.18*°	
Impaired concentration	before	1.75±0.18	1.64±0.17	3.29±0.19°°	3.21±0.19°°	1.44±0.10
	after	1.30±0.11*	1.45±0.11	1.64±0.20**	2.43±0.20*°^	
Autonomic reaction	before	1.50±0.15	1.45±0.18	2.43±0.34°°	2.14±0.33°	1.18±0.07
	after	1.20±0.09*	1.32±0.14	1.29±0.13*	1.36±0.13*	
Water retention	before	4.65±0.17°°	4.55±0.16°°	4.93±0.16°°	5.07±0.13°°	1.26±0.06
	after	1.80±0.09**°	2.05±0.12**°	1.71±0.13**°	2.64±0.13**°^	
Negative affect	before	2.25±0.24°	1.95±0.25	3.21±0.35°°	3.43±0.31°°	1.58±0.10
	after	1.40±0.11**	1.55±0.17*	1.71±0.22*	2.29±0.27*°	
Arousal	before	1.35±0.13	1.27±0.10	3.36±0.17°°	3.21±0.19°°	1.14±0.05
	after	1.15±0.08	1.18±0.08	1.43±0.20*	2.71±0.24°*^	
Control	before	1.00±0.00	1.00±0.00	1.14±0.10	1.07±0.07	1.00±0.00
	after	1.00±0.00	1.00±0.00	1.00±0.00	1.07±0.07	

Notes:
1. * – probability of the difference of indicator before and after treatment ($p<0.05$);
2. ** – probability of the difference of indicator before and after treatment ($p\leq0.001$);
3. ° – probability of the difference of indicator relative to control group ($p<0.05$);

4. °° – probability of the difference of indicator relative to control group (p≤0.001);
5. ^ - probability of the difference of indicator after treatment between I and II groups of certain form (p<0.05).

Table 3

Dynamics of R. Moos scale components in patients with cephalgic and crisis forms of PMS after treatment, M±m, points

Scale components	Stage of treatment	Cephalgic form, subgroups		Crisis form, subgroups		Control group, n=50
		IC, n=18	IIC, n=15	ID, n=13	IID, n=12	
Pain	before	4.94±0.17°°	4.93±0.18°°	5.00±0.23°°	5.00±0.21°°	1.22±0.08
	after	2.50±0.22**°	3.53±0.26*°^	2.92±0.24**°	4.17±0.17*°^	
Impaired concentration	before	3.33±0.16°°	3.20±0.24°°	3.46±0.18°°	3.33±0.19°°	1.40±0.10
	after	1.78±0.17**	2.87±0.22°^	2.00±0.23**°	3.00±0.21°^	
Impaired concentration	before	4.83±0.17°°	4.67±0.25°°	4.92±0.14°°	4.58±0.19°°	1.44±0.10
	after	2.39±0.12**°	4.00±0.22*°^	2.54±0.14**°	4.00±0.21*°^	
Autonomic reaction	before	4.11±0.29°°	3.93±0.30°°	5.08±0.18°°	5.00±0.21°°	1.18±0.07
	after	2.06±0.17**°	3.47±0.24*°^	2.54±0.18**°	4.33±0.19*°^	
Water retention	before	2.00±0.30	1.87±0.29	2.00±0.28°	1.92±0.23°	1.26±0.06
	after	1.39±0.14*	1.33±0.13*	1.31±0.13*	1.33±0.14*	
Negative affect	before	3.17±0.31°°	3.00±0.38°°	4.08±0.18°°	3.92±0.29°°	1.58±0.10
	after	1.83±0.17**	2.60±0.34*°	2.08±0.14**°	3.25±0.28*°^	
Arousal	before	4.61±0.20°°	4.27±0.33°°	4.62±0.21°°	4.42±0.19°°	1.14±0.05
	after	2.33±0.16**°	3.53±0.26*°^	2.92±0.21**°	3.67±0.14*°^	
Control	before	1.22±0.15	1.27±0.18	4.77±0.20°°	4.92±0.26°°	1.00±0.00
	after	1.00±0.00	1.20±0.14	2.23±0.12**°	4.25±0.22*°^	

Notes:
1. * – probability of the difference of indicator before and after treatment (p<0.05);
2. ** – probability of the difference of indicator before and after treatment (p≤0.001);
3. ° – probability of the difference of indicator relative to control group (p<0.05);
4. °° – probability of the difference of indicator relative to control group (p≤0.001);
5. ^ - probability of the difference of indicator after treatment between IC and IIC subgroups and between ID and IID subgroups (p<0.05).

Such component as “pain” was marked as “subtle” and its reduction constituted 39.58 % (p=0.002) in women of IIB_2 subgroup after therapy. In patients of IB_2 subgroup this index was “absent” and decreased by 60.71 % after treatment compared to the level before treatment (p=0.005), corresponding to control rate and was significantly lower than the index of IIB_2 subgroup (p=0.017). Such components as “impaired concentration”, “behavior change” and “negative affect” decreased in both IB_2 and IIB_2 subgroups from “weak” to “subtle” indicators. Decrease in “impaired concentration” was by 50.00 % (p=0.001) and 40.76 % (p=0.003) respectively, “behavior change” – by 50.15 % (p=0.001) and 24.30 % (p=0.003). Most dynamic reduction of “negative affect” was also observed in subgroups IB_2 and IIB_2 –by 46.73 % (p=0.003) and 33.24 % (p=0.002) respectively, component “arousal” – by 57.44 % (p=0.003) and 15.58 % (p=0.018).

Component “pain” which was the most intensive among other parameters of R. Moos Menstrual Distress Questionnaire in patients with cephalgic form of PMS was successfully corrected after proposed therapy (Table 3). In patients of IC subgroup it decreased from “expressed” to “subtle” manifestations by 49.39 % (p<0.001), in patients of IIC subgroup it reached level of “moderate” manifestations and reduced by 28.40 % (p=0.003). A similar trend was observed in relation to the component “behavior change”. In IC subgroup it decreased from “significant” manifestations to “subtle” level reducing by 50.52 % (p<0.001), in patients of IIC subgroup it decreased only by 14.35 % (p=0.008). More intensive decrease in component “arousal” and “autonomic reaction” was detected in women of IC subgroup than in persons of IIC subgroup. The proposed therapy led to reduction of these components from “moderate” to “subtle” symptoms, respectively by 49.46 % (p<0.001) and 49.88 % (p<0.001), and traditional therapy – to “weak” manifestations, and its reduction was respectively by 17.33 % (p=0.003) and 11.70 % (p=0.018). Also persons in IC subgroup were characterized by greater dynamics decrease in components “negative affect” and “impaired concentration” compared with the patients in IIC subgroup. In IC subgroup these parameters from “weak” reached level “subtle” manifestations after treatment decreasing by 42.27 % (p<0.001) and 46.55 % (p<0.001). In individuals in IIC subgroup reduction of these components intensity was not significant, namely by 13.33% (p=0.028) and 10.31 % (p=0.116), respectively.

In women with crisis form of PMS differentiated therapy led to significant decrease in intensity components of R. Moos scale compared to traditional therapy. Reduction from "expressed" manifestations to "weak" symptoms of components "pain" by 41.60 % (p=0.001), "autonomic reaction" by 50.00 % (p=0.001), "behavior change" by 48.37 % (p=0.001) and "arousal" by 36.80 % (p=0.001), level of component "control" decreased from "expressed" till "subtle" symptoms on 53.25 % (p=0.001) was observed in patients of IC subgroup. The proposed treatment reduced the component "negative affect" from "moderate" to "subtle" manifestations by 49.02% (p=0.001), the component "impaired concentration" from "weak" by 42.20 % (p=0.001).

Traditional therapy did not significantly influence on severity of manifestations in patients with crisis form. Reduction of such components as "impaired concentration" (9.91 %, p=0.068), "behavior change" (12.66 %, p=0.018), "autonomic reaction" (13.40 %, p=0.018), "control" (13.62 %, p=0.018) and "pain" (16.60 %, p=0.008) was mild. The intensity of last four components was rated as "moderate" manifestations even after treatment. Decrease in severity of such components as "arousal" and "negative affect" was also low, namely 16.97 %, (p=0.008) and 17.09 % (p=0.018) from "moderate" to "weak" manifestations in IIC subgroup.

Conclusions

PMS treatment should have differentiated individual character depending on the clinical form and severity of the disease. Traditional therapy is effective for correction of psychological and somatic manifestations in patients with mild course of neuropsychical and edematous forms of PMS and is not effective in patients with severe course of these forms and persons with cephalgic and crisis forms of PMS.

Use of combined oral contraceptives containing drospirenone in patients with neuropscyhical and edematous forms of PMS and use of selective serotonin reuptake inhibitors in women with cephalgic and crisis forms of PMS significantly help to reduce the intensity and leveling of symptoms compared with traditional therapy. Vitex agnus castus extract is effective in correction of symptoms in women with mild neuropsychical form of PMS.

Prospects for further research

The obtained results encourage studying the influence of differentiated approach to treatment of PMS on the hormonal status of the patients.

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