A Possibility of Correcting Oophorectomy Syndrome by Transplantation of Human Fetal Tissues

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The expression of the main symptoms of postoophorectomy syndrome is studied. Comparative analysis of various corrective methods shows that transplantation of human fetal tissues may be used as an alternative approach in cases where hormone replacement therapy is not indicated.

Key Words: *postoophorectomy syndrome; hormone replacement therapy; transplantation of human fetal tissues*

Surgical interruption of ovarian function in a woman of reproductive age is accompanied by complex reactions of the neuroendocrine system which characterize the adaptation of the female organism to new conditions. Acute estrogen deficiency induces the development of postoophorectomy syndrome, which is variously expressed in 50-80% of patients [2,6], while a long-lasting and severe form of this syndrome is noted in one-quarter of women [1,3,7].

Postoophorectomy syndrome is clinically characterized by neurovegetative (NVS), psychoemotional (PES), and metabolic and endocrine (MES) symptom complexes [4,5].

In NVS the most common disturbances are hot flashes of the head and upper body, sweating, cardiovascular disturbances (tachycardia, arrhythmia, chest pains, arterial hypertension), and peripheral vasospasm (headache and limb numbness).

The psychoemotional disturbances manifest themselves in heightened irritability and fatigue, tearfulness, hypomnesia, depression, and sleep disturbances.

MATERIALS AND METHODS

For objective evaluation of NVS, PES, and MES revealed during patient interviews and objective examination their severity was expressed in points and the total count was presented as the modified menopausal index (MMI).

The above-mentioned symptom complexes were analyzed as follows:

- for NVS an MMI ranging from 0 to 10 points means the absence of manifestations, 11-20 points - a mild, 21-30 points - a moderate, and 31 and over - a severe form of this symptom complex.
- for PES and MES (similarly estimated) an MMI ranging from 0 to 1 point was interpreted as the absence of pathology, 2-7 points indicates a mild, 8-14 points - a moderate, and more than 15 points - a severe form of these symptom complexes.

Using this method we examined 95 patients of reproductive age after bilateral oophorectomy. The patients were assigned to the following groups according to the kind of therapy: group 1 comprised 19 women receiving no therapy, group 2 consisted of 23 women receiving divina, and group 3 consisted of 53 women who had undergone a course of transplantation of human fetal tissues (THFT).

The mean age of the patients was 33.3±2.1 years. All women included in the trial had undergone surgery for benign tumors and tumorlike ovarian neoplasms and benign neoplasms of the uterus. The mean postoperative period was 2-3 (2.4) years.

Tissues for transplantation were isolated from fetuses obtained from healthy women aged 15-40

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years. The indications for terminating pregnancy were social factors (difficult living conditions, broken families). Prior to medical abortion all women were tested for viral infections (hepatitis B, cytomegalovirus, herpes infection, and HIV), chlamydiae, and toxoplasmosis, and the blood was tested for the Wassermann reaction. The gestational age of the fetus was judged from the date of the last menstruation, the fundal height of the uterus, the day of the first fetal movement, and ultrasound data.

The age of the fetuses was 16-20 weeks and their mass ranged from 200 to 450 g.

Sterility of the fetal tissues was monitored during preparation. The tissues were injected subcutaneously in the gluteal area under surgical conditions.

RESULTS

The incidence of manifestations of the postoophorectomy syndrome is presented in Table 1. The most frequent signs of NVS were hot flashes of the head, numbness and pins and needles sensations, and headache.

PES were characterized by diminished ability to work, undue fatigue, irritability, tearfulness, absentmindedness, and memory disturbances.

MES were manifested in weight gain, atrophy of the genital organs, skin dryness, and bone pain. All postoophorectomy symptoms were variously combined, yielding a polymorphous clinical picture.

It was noted that in patients with postoophorectomy syndrome NVS and PES were most strongly expressed, while MES were noted relatively rarely during the first months postoperation. On the other hand, a considerably higher incidence of MES (and their stronger individual expression) against the background of a lower incidence and severity of NVS and PES was characteristic for women at a later period (2-3 years) following surgical termination of ovarian function. Particularly striking is the more frequent complaint of bone pain.

Our findings are in conformity with previous data [2,6,7] on the spontaneous regression of NVS and PES paralleled by a progression of MES in the dynamics of surgically induced postoophorectomy syndrome.

Changes in the degree of expression of the postoophorectomy syndrome after treatment are presented in Table 2. The patients of the different groups are seen to be comparable in terms of the severity of clinical manifestations of the postoophorectomy syndrome.

TABLE 1. Incidence of Pathological Manifestations in Patients after Total Oophorectomy

Symptom	Number of patients	%
NVS		
hot flashes	84	88.4
limb numbness	52	54.7
headache	44	46.3
palpitations	36	37.3
vestibulopathies	28	29.5
low heat tolerance	19	20
chills	21	22.1
altered blood pressure	7	7.4
altered dermographia	27	30.5
PES		
reduced ability to work	92	96.8
undue fatigue	90	94.7
absentmindedness	68	71.6
memory disturbances	59	62.1
irritability and tearfulness	87	91.6
sleep disturbances	42	44.2
poor mood	39	41.1
reduced sex drive	31	32.6
MES		
weight gain	47	49.5
thyroid symptoms	2	2.1
diabetes mellitus	1	1.1
hypoplasia of breast	7	7.4
muscle and joint pains	21	22.1
bone pain	29	30.5
skin dryness	30	31.6
atrophy of genital organs	38	40

TABLE 2. State of MMI against the Background of Different Kinds of Therapy

Points	Control		Divina		THFT	
	abs.	%	abs.	%	abs.	%
NVS						
0–10	2	10.5	2	8.7	7	13.2
11–20	6	31.6	9	42.0	18	33.9
21–30	10	52.6	7	30.2	19	35.8
>30	1	5.3	5	19.3	9	16.9
PES						
2–7	4	21.0	8	34.8	16	30.2
8–14	14	73.7	12	52.2	27	50.9
>14	1	5.3	3	13.0	10	18.9
MES						
2–7	9	47.4	9	39.1	28	52.8
8–14	10	52.6	12	52.2	22	41.5
>14	0	0.0	2	8.7	3	5.7

In patients receiving no therapy during the first year following oophorectomy the expression of NVS and PES tended to decrease, which manifested itself in a decreased total score for NVS and PES (1.4 and 2.6, respectively), while the MES score was somewhat increased (by 1.4 points).

However, the mean values of the MMI characterizing all these three symptom complexes did not differ reliably upon the primary and repeated examinations ($p>0.05$).

In patients receiving hormone therapy the NVS, PES, and MES were reliably less pronounced (by 11.4, 6.5, and 4.3 points, respectively). These data suggest that divina reliably mitigated all three symptom complexes of the postoophorectomy syndrome, being most effective against NVS, somewhat less effective against PES, and least effective against MES.

Transplantation of human fetal tissues affected the spontaneous dynamics of all three symptom complexes, more actively suppressing NVS and PES (by 43.9 and 23.1 points, respectively) in comparison with the effect of divina; however, a reliable suppression of MES (by 4.5 points) should also be noted.

A more pronounced suppression of osteoarticular symptoms of MES (by 4.5 points, $p<0.05$) was noted in the women who had received a fetal tissue transplantant. However, this improvement was relatively transient and 4-5 months following the procedure aggravation of these symptoms was observed.

Thus, our results suggest that hormonal preparations effectively control NVS and PES, especially during the first 1-3 years following oophorectomy, when these symptoms are maximally expressed.

Hormone therapy (divina) resulted in some regression of MES. This is attributed to the fact that female sex steroids exhibit a broad spectrum of physiological effects and have a positive impact not only on bone metabolism but also on metabolic processes in other organs and tissues. However, long-term hormone replacement therapy (HRT) frequently leads to the development of endometrial and breast cancer, induces hemodynamic changes with an increased risk of coronary occlusion, causes a predisposition to stone formation, impairs mood, suppresses adrenal function, and causes breakthrough bleeding, accompanied by discomfort.

Taking into account the above phenomena caused by HRT, THFT can be viewed as an alternative method for treating postoophorectomy syndrome, since there are no contraindications and it produces a more pronounced and long-lasting therapeutic effect.

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