The State of Autonomic Regulation in Patients with Postcastration Syndrome After Transplantation of Human Fetal Tissues

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The functional state of the autonomic nervous system was evaluated in 38 women after total ovariectomy. Clinical analysis of autonomic disorders and challenging tests indicated the disturbance of autonomic regulation and inhibition of vascular reactivity against the background of total autonomic lability. One month after transplantation of fetal human tissues vascular responses were improved: the number of positive dilatatory reactions increased and moderate pulse waves were recorded. The general condition of the patients improved, their work capacity increased, and sleep patterns normalized, which led to a reduction of anxiety. However, the transplantations had varying effects on hot flashes, which may be associated with their diverse nature. The positive effect that transplantation of fetal human tissues elicited in most patients may be attributed to normalization of their hormonal status.

Key Words: *transplantation of human fetal tissues; treatment of total ovariectomy; autonomic nervous system*

Postcastration syndrome (PS) is a complex of symptoms represented by different psychosomatoautonomic disorders. Therefore, evaluation of the functional state of the autonomic nervous system (ANS) in each patient and determination of the degree of its correction by transplantation of human fetal tissues (THFT) are relevant. Evaluation of the functional state of the ANS not only at rest but also in functional tests allows for the objectivization of results of therapy and determine its duration.

The responses of the ANS to cold (immersion of the hand in 4°C water for 1 min) and mental (multiplication of two-digit numbers) stimuli were studied in 38 women aged 36-43 years. After the baseline record (adaptation of patients to the experimental conditions), the stimuli were introduced successively; the second stimulus was applied only after complete normalization of the curve after the first one. Latency, degree and duration of the reaction, and the nature of the recovery period were analyzed.

Arterial pressure (BP, continuous nonocclusive method, polygraphic recording), heart rate (HR), respiratory rate (RR), and skin-galvanic reflex (SGR) were recorded on a Galileo polyphysiograph prior to, during, and after the loadings. The tests were performed before transplantation of human fetal tissues (THFT) and at the end of each month during a 6-month period.

Psychoemotional status was assessed in the anxiety test of Ch. D. Spilberger with the modifications of Yu. L. Khanin.

Vascular responses varied in a wide range in most of the patients. In addition to complaints

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characteristic of the postcastration syndrome, 17 patients had periodic BP rises (one of them had been suffering from congenital hypertension since she was 16 years old), while conversely 16 women had a tendency toward hypotension. Twenty-three women complained of frequent headaches of varied nature; paroxysmal ANS disorders were observed in 2 women. Hot flashes occurred in 31 patients. In most of them (n=17) these hot flashes were light and infrequent (slight flushing, sweating, vertigo, etc.), in other patients the flashes occurred every 1-1.5 h (fever in the upper part of the body or over the entire body, hyperhydrosis, face reddening, increased HR, "suffocation," weakness, shivering, etc.). In addition to hot flashes and also in their absence the patients complained of general weakness, fatigue, reduced work capacity, increased excitability, depression, sleep disorders, tearfulness, and reduced libido). All these complaints were reflected by the anxiety test: 58.5±5.3 (45-76 points; 45 points indicate a high level of anxiety).

Taken together, these widely diverse vascular and psychoemotional disorders constituted a severe postcastration syndrome. Prior to the treatment, bradycardia occurred in 37 of the patients: 59.6±1.2 (50-63 beats/min), in only 4 it was normal (70-72 beats/min), and in 3 patients HR was increased to 82-84 beats/min. In 12 patients BP was 120/70 mm Hg, in 10 patients it was elevated to 135/80 or 150/90 mm Hg, and in the other 21 patients BP was low-normal (110-100/60 mm Hg) or low (90/60 mm Hg). Thirty-nine patients had a normal respiratory rate: 15.6±2.1 (15-18/min), in 2 patients it was low - 10/min, and in 2 patients it was elevated - 22-24/min.

Cold exposure allowed us to assess not only the tone but also the reactivity of the ANS. Only 15 women developed a pronounced response: by the end of the test their pulse was increased by 12-15 beats/min; however during the neuroreflex phase it increased only by 4-5 beats/min, with the exception of one patient. The response was weak in 13 patients (increase in the pulse rate <10 beats/min). Nine patients developed no response, and in 7 patients the response was paradoxical: the pulse rate decreased by 5-9 beats/min. Generally, the increase in the RR was small: not more than 2-3/min. A decrease in RR was observed predominantly in patients with nonresponsiveness and a paradoxical reaction. In these patients the disturbances in respiratory rhythm were often accompanied by changes in depth of breathing.

The nature of the plethysmogram recorded from the patients with a tendency toward hypotonia testified to vascular hyporeactivity or nonresponsiveness, being indicative of the inertness of the mechanisms regulating vascular tone. Patients with a tendency toward hypertonia or hypertonic patients showed a similar frequency of nonresponsiveness.

The physiological parameter (SGR) and psychological testing confirmed the presence of affective disorders. SGR (a parameter reflecting the function of the emotional-motivational systems of the brain) in response to mental arithmetic was pronounced in patients with increased excitability, emotionality, and impulsiveness. A weak SGR or its absence in response to mental arithmetic correlated with severe emotional disorders (apathy, adynamia, markedly reduced work capacity). The index of personal anxiety in such patients was greater than 60 points.

Thus, clinical analysis of ANS disorders and the results of testing indicate that autonomic regulation is disturbed in PS. A tendency toward hypotonia was revealed in 24 women. It is known that disturbances in vascular reactivity revealed in functional tests and upon loading are the decisive factor in the differentiation between physiological and pathological hypertension. Plethysmographic studies of the response to cold demonstrated inhibition of vascular reactivity against the background of total autonomic lability. Similar changes in vascular reactivity were observed in half of the patients with paroxysmal rises of BP.

The most severe disturbances of ANS were revealed in patients with pronounced hot flashes. They suffered from episodes of breathlessness, and the breathing rhythm was disturbed, deep and shallow breathing alternating, with considerable changes in rhythm and in frequency of respiratory movements even at rest. These patients exhibited vascular shifts in response to cold tending toward hyporeactivity or nonresponsiveness, or else the reaction was paradoxical. It should be mentioned that the respiratory waves on the plethysmogram matched the respiratory movements, indicating a discord in the interaction between the vasomotor and respiratory systems.

Analysis of ANS tests showed that THFT had the maximum effect 1-2 months after the operation. By the 3rd-4th month the ANS parameters tended to return to the baseline values, which were attained by the 5th-6th month.

In those patients exhibiting signs of sympathetic activation after THFT the vascular reaction was improved by the 2nd-4th month judging by the plethysmographic data: the number of positive constriction reactions increased, there were moderate wavelike oscillations in pulse volume appearing

on the initially inert curve, etc. During the first month after transplantation the patients mentioned considerable positive changes in general condition, work capacity, mood, and sleeping; they had ceased to overreact to everyday annoyances, and had stopped concentrating on their disease. This was confirmed by the reduced situational (reactive) anxiety from 20 to 9 points in some patients.

However, THFT had a differing effect on hot flashes, which may be associated with their varying nature. In fact, in patients with climacteric syndrome there was an initial activation of the sympathetic-adrenal division of the ANS followed by a vagoinsular compensatory reaction. It was demonstrated that the nature of the hot flashes and their clinical manifestations were determined by the rise or fall of reactivity and the reserves of one of the two ANS divisions.

Analysis of ANS tests and clinical manifestations of ANS reactions that accompany hot flashes suggest that THFT, which activates the sympathico-adrenal division of ANS, elicits a beneficial effect in patients with functional predominance of the vagoinsular division with its high compensatory capabilities. For a certain type of response of the nonspecific brain systems to internal and external conditions and moderate disturbances, THFT improves the coordinative action of both divisions of the ANS, which normally act in a synergistic manner. Pronounced dysfunction of both divisions was revealed in one patient. By the 6th month this patient demonstrated a paradoxical response to cold, RR and HR had regained the baseline values, and irregular breathing was observed during the entire observation period. Such a response was accompanied by increased personal anxiety from 45 to 59 points.

Five patients responded to the treatment in a different manner. Two patients with the hypertonic type of vascular dystonia were of particular interest. In both of them BP was elevated (150-140/100-90 mm Hg), and the response to cold was moderate. There were no substantial changes in the background parameters during the therapeutic action of THFT, with the exception of RR, which tended to increase. The nature and intensity of the response to cold were similar. In one of these women hot flashes were infrequent and light, while in the other they were frequent and severe. We managed to record a hot flash during which the ANS parameters changed markedly: the pulse rate increased by 18 beats/min, RR increased by 4-5/min, and SGR increased 500%. These levels were maintained for a 50-sec period followed by a slow recovery. This testifies to functional predominance of the sympathico-adrenal division of the ANS. The treatment had no effect on the frequency and intensity of the hot flashes, althought the general condition of the patients was improved, which correlated with a decrease in situational (reactive) anxiety (by 4-5 points). However, by the 5th-6th month of treatment this parameter tended to increase, and personal anxiety rose 5-7 points compared to the baseline values. This may be explained by unfulfilled hopes for a considerable improvement in general condition, particularly on the part of the patient with severe hot flashes.

The poorest response to treatment was shown by a patient with congenital hypertensive disease. This patient had a history of 6 cesarean sections. Prior to the treatment she had bradycardia and elevated BP (150/100 mm Hg) and developed no response according to the cardiovascular parameters. By the 2nd month HR increased 7 beats/min and BP to 200/120 mm Hg; the response to cold became paradoxical. Situational anxiety increased from 41 to 68 points and vasomotor manifestations were more pronounced.

Thus, this study clearly demonstrates that THFT is contraindicated in hypertensive patients. It can be recommended to patients with autonomic vascular dystonia accompanied by the asthenic syndrome (weakness, fatigue, poor work capacity, etc.) but only with a close follow-up. THFT had no effect on hot flashes with the predominance of functional activity of the sympathico-adrenal division of the ANS.

Judging from the ANS tests, THFT had no effect in a patient with nocturnal autonomic crises of vagoinsular nature with an initial discord in cardiovascular and respiratory parameters (infrequent pulse and low BP with rapid breathing) and nonresponsiveness to cold. At the same time, the general condition of the patient did improve (subjectively) and nocturnal crises disappeared. The parameters of situational and personal anxiety remained practically unchanged, which may be associated with chronic difficult family problems.

A patient with severe psychoautonomic syndrome and complaints of an astheno-hypochondriac nature (she considered herself an invalid after ovariectomy) had, prior to the treatment, hypotonia, bradycardia, and a paradoxical response to cold, which indicate the predominance of vagoinsular activity. After treatment her general condition improved, and the headaches became less frequent. This was reflected by a decrease in situational anxiety (5-6 points). By the 6th month this parameter remained unchanged, while personal anxiety increased from 56 to 76 points.

These observations indicate that in patients with serious psychoautonomic disorders and a psychologically unfavorable situation THFT should be accompanied by psychotherapy and medication.

Thus, depressive sympathico-vascular disorders are major symptoms occurring in patients with postcastration syndrome. Cardiovascular disorders were identified by BP and vascular reactivity studies, which revealed reduced vascular tone and inhibited vascular reactivity. Sympathico-vascular disorders were accompanied by vestibular, visceral (cardiac, respiratory, etc), and thermoregulatory (hot flashes) disturbances of a permanent or paroxysmal nature.

The positive effect that THFT elicited in most patients may be related to normalization of hormonal interplay, specifically with estrogens. Estrogens are known to exert a direct effect on the functional activity of the CNS. This effect is realized via stimulation and inhibition of brain amines (a decrease in the formation of enzymes inhibiting dopamine synthesis, reduction of MAO and COMT, the enzymes catalyzing degradation of catecholamines and serotonin, blocking of the reverse uptake of norepinephrine at the level of synapses, etc.). A rise of the estrogen level leads to a rise of both catecholamines and serotonin, which was confirmed by the study of ANS regulation and mental tests.

The differences in changes of autonomic regulation occurring in some patients after THFT may be due to individual peculiarities of the initial functional state and responsiveness of nonspecific brain systems to internal and external conditions.

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