MODERN METHODS OF THERAPEUTIC FASTING AS A WAY TO OVERCOME THE PHARMACORESISTANCE OF MENTAL PATHOLOGY

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Abstract. *In recent decades, pharmacotherapy has gained a dominant position in the treatment of any pathology, including mental disorders. The achievements of psychopharmacotherapy have pushed traditional biological treatments into the background, even in many countries their use has been completely rejected. However, in addition to positive results, psychopharmacotherapy in many cases leads to a pronounced negative pathomorphosis of mental disorders, in many cases pharmacoresistance is formed.*

Keywords: *psychopharmacotherapy, pharmacoresistance, treatment, mental pathology.*

Introduction. In recent decades, pharmacotherapy has gained a dominant position in the treatment of any pathology, including mental disorders [1]. Therefore, in their modern modifications, the greater use of traditional biological therapy methods is justified. The history of the use of hunger as a remedy is as old as the world itself. A great deal of experience in the use of RDT has been accumulated in Psychiatric Practice [2, 3]. According to clinical observations and special studies, it was found that the use of this treatment in psychiatric practice is primarily limited to patients who are able to voluntarily refuse to eat for a long time on their mental state and express a desire to be treated with this method [4, 5]. These conditions are satisfied by patients with non-psychotic conditions and borderline mental disorders. The therapeutic effect of dosed fasting is based on the stimulation of reparative processes in the body, low loss and death of "sick" cells, the active elimination of the final products of metabolism ("slags" and endotoxins), including metabolites of medicinal chemical preparations, the elimination of antigenic food load [6]. With long-term fasting, protective inhibition of the central nervous system develops as a protective reaction of the body to the effects of excessive stress [7]. Short periods of therapeutic fasting have a psychostimulating effect, while with longer fasting, a sedative effect is achieved, which is replaced by a stimulating effect again during the recovery (dietary) feeding period. What should be the duration of the RDT unloading period? Naturopaths follow the so-called completed fasting signs when the appearance of a feeling of hunger in this matter indicates the need to stop it [8]. Doctors With an orthodox medical education who use the RDT method in their practice are usually completely satisfied with the clinical remission of pathology and do not strive for a state of "completed fasting" [9]. In this case, the duration of the discharge period is determined individually and largely depends on the clinical characteristics of the disease, the age of the patient, obesity, the nature and amount of comorbid pathology and some other reasons [10]. In the general

complex of RDT, the recovery period is undoubtedly the most important stage of the entire treatment process, since it actually determines its final effect [11]. The main task during the recovery period is the gradual transition of the patient from endogenous ("internal") to exogenous ("external") nutrition using a special diet [12]. The criterion for the correct passage of the recovery period after fasting will be the restoration of independent feces on the 3-4th day of recovery nutrition. This time period should be controlled by the most responsible and treating doctor [13]. Complete elimination of food and water (absolute fasting) has begun to be used in clinical practice in our country in recent years. Currently, there are two methods in clinical practice — hard and soft "dry" fasting [14]. In the first case, contact with water with strict "dry" fasting is completely excluded, i.e. the patient does not drink water, does not wash, does not rinse his mouth with water, does not take any water procedures, does not cleanse the intestines with enemas. In the latter case, toilet and "cleaning" procedures are carried out with gentle "dry" fasting, but the patient does not drink water [15]. Strict" dry " fasting has limited indicators, for example, a pronounced exudative reaction of an allergic nature, pronounced edema syndrome, and in a short time — up to two days. In clinical practice, short-term absolute fasting is usually used for 3-5 days, rarely more than [16]. With absolute fasting, the fasting period goes through the same stages as full fasting, but the time of their onset decreases, especially with severe "dry" fasting. Thus, the stage of" food agitation "lasts for several hours (very individual); the stage of" exacerbation of ketoacidosis " lasts from 1 to 3 days [17]. On the first day of absolute fasting, with its strict method, a ketoacidotic crisis usually occurs, after which the patient's well-being improves significantly (stage of" compensated ketoacidosis") [18]. With absolute fasting, the recovery period is practically no different from complete fasting. During the unloading period, complete ("wet") fasting from absolute ("dry") to the first days (2 to 4) is limited to drinking water up to 10-12 ml/kg of body weight per day; in the next period, the patient should be guided by a feeling of thirst [19]. The recovery period is carried out in the same way as complete fasting. The use of a combination of absolute and complete therapeutic fasting in therapeutic practice allows for a faster transition to endogenous nutrition, i.e. ketoacidotic crisis and ketoacidosis compensation. Using this technique, the unloading period is reduced without harming the therapeutic effect achieved [20]. Among the methods of RdT described above, full (wet) fasting is most often used, this method can even be considered a classic, since it is often used both in our country and abroad; it is therefore very well studied in terms of pathophysiological shifts in the starving body [21]. During full fasting, the duration of the unloading period depends on the presence and nature, as well as the amount of joint pathology (polymorbism), which usually extends the unloading period to 3 weeks or more [22]. Increasing the final effect of RDT is achieved by combining it with non-drug therapy methods, primarily exercise therapy. In many patients, especially in older groups, exercise therapy decreases to possible physical activity during the day [23]. This is a daily walk in the fresh air for hours, accompanied by optional exercises such as "scattered muscle load". Complications with methodically correct execution of RDT are rare. They are not life-threatening, in most cases they can be avoided and, if they occur, are quickly eliminated [24]. Complications can occur not only during the unloading period, but also during the recovery period of RDT. In this case, they can be associated with a violation of the diet regime or a reassessment of physical capabilities [25]. During the RDT course in chronic pathology, the patient must be reliably told that medical recommendations must be strictly followed in order to maintain and adequately maintain his health and quality of life continuously [26]. If the patient has undergone a course of RdT at a satisfactory

level and has a sufficiently good effect, then the duration of clinical remission and/or the possibility of a complete treatment of chronic pathology is fully dependent on him, i.e. from how purposefully and timely he uses the knowledge and skills he acquired while taking the RDT course. Conclusions. RDT can be considered pathogenetically justified, safe and effective as a treatment for mental and somatic pathology, which can be used spontaneously or in combination with other approaches (pharmacotherapy, psychotherapy, etc.), and can also be used to overcome pharmacoresistance in mental and somatic disorders [27]. It is known that fasting is a pathological process that develops due to a lack of nutrients that enter the internal environment of the body in the process of emptying, membrane hydrolysis and absorption of nutrients from the intestinal lumen [28]. Well-known Russian pathophysiologists of the late XIX-early XX centuries S. M. Lukyanov and his pupil E. S. With the efforts of London, it was found that changes in homeostatic processes in the body of hunger are associated with the need to switch to endogenous nutrition, which constitutes the essence of this process [29-30]. Fasting exoidan can be caused by endogenous causes. Endogenous fasting is caused by altered assimilation of nutrients, for example in severe patients; it is often accompanied by a violation of the processes of simultaneous absorption, emptiness, changes in the digestion of membranes, intestinal dyskinesia, etc. [31]. Endogenous fasting is associated with a sharp increase in the body's need for energoplastic substrates due to a stress response, activation of the neuroendocrine catabolic system, and reaction of body systems associated with stress and acute phase response [32]. Many pathological processes are stimulated to activate the central part of the neuroendocrine catabolic system (ventromedial nucleus of the hypothalamus): hypoxia, hypovolemia, pain, sadness [33]. Often substrate-energy deficits are the result of the following diseases and pathological processes [34]:

* digestive disorders;

* chronic and recurrent processes, including infections, fever, cancer and some autoimmune diseases;

* diseases associated with loss of protein and other nutrients, including nephrotic syndrome, chronic obstructive pulmonary diseases, intestinal fistulas, plasmorrhea for burn disease, exudative enteropathy, desquamative dermatitis, etc.;

* endocrine diseases with impaired anabolism and increased catabolism (hyperthyroidism, diabetes);

* psychoneuroendocrine diseases with appetite suppression and eating appetite disorders (anorexia nervosa, psychoses);

* cases with increased nutritional needs (pregnancy, lactation, childhood and adolescence, injuries, surgical interventions, recovery period after acute infections);

* alcoholism and associated temporary hypercortisism;

* drug poisoning;

* parenteral nutrition extended and not adequately adjusted [35-37]. In most cases, both in the past and in the present, fasting is exogenous in nature and has social foundations, for example, during the blockade of Leningrad, the population fasted for a long time: the city developed specific diseases as a result of fasting [38]. Exogenous fasting is the result of a discrepancy between the intake of nutrients into the internal environment and the need for them, such fasting occurs as a result of a complete lack of food or insufficient intake of it, including the ingestion of some of its components into the body (partial fasting, malnutrition) [39]. Nutritional deficiencies can be associated with a small amount of one or more basic nutrients (proteins, fats, carbohydrates), a

pronounced lack of vitamins and minerals, a change in the ratio between food substances, for example, the predominance of carbohydrates with a sufficient amount of proteins, etc. for example, the diet of the majority of the city's population in blocked Leningrad was characterized by a general lack of nutrients (proteins)., fats, carbohydrates, vitamins, macro - and microelements) and their uneven depletion [40-41]. Exogenous fasting may be absolute, complete, and incomplete. Absolute" dry " fasting involves exogenous fasting in the complete absence of food and water [42]. Complete exogenous fasting is observed in the absence of absolutely no food, but with drinking water. Incomplete fasting or malnutrition occurs with adequate nutrition that cannot meet the nutritional needs of the body. Quantitative fasting is called Absolute and complete fasting. Qualitative fasting is consistent with partial or incomplete fasting [43-44]. Partial fasting, despite the fact that the body's energy needs are replenished, occurs in people on an unbalanced diet, which is completely excluded from the diet of one of the nutrients or nutrients; this type of fasting includes hypo - and vitamin deficiency. High-quality fasting is also considered accelerated fasting, which occurs in people with limited dietary energy capacity, against the background of the high energy demand of the body observed during mental and physical overload, stresses [45]. The gradual change in metabolism during fasting occurs with a characteristic phase endocrine-metabolic changes and changes in the main energy substrates (table). Complete fasting is divided into periods: emergency adaptation, long-term stable adaptation, decompensation [46]. Each of these periods has its own endocrine-metabolic characteristics. The initial period of emergency adaptation (fig. 1) activation of glycogenolysis, full use of its reserves, stimulation of gluconeogenesis, and fasting for blood glucose levels of 12 to 24 hours is provided by glycogen reserves in the liver. 24 hours after the start of fasting, the liver runs out of glycogen reserves, so in gluconeogenesis, glucose levels in the blood are maintained due to the formation of glycerin, glucogenic amino acids and free fatty acids [47]. 24 hours after the onset of complete exogenous starvation, the body begins to use proteins as a source of energy, enhancing the processes of gluconeogenesis. The first-line Energy Reserve is still the energy accumulated in the liver as glycogen and triglycerides in adipose tissue: in healthy people, triglycerides can be up to 80% of energy reserves, and in obese people, triglycerides of adipose tissue can be up to 95% of the total energy reserve [48]. The lack of glucose in the body that occurs with long-term fasting is complemented by other energy substrates such as ketone bodies. The main role for long-term adaptation of the starving brain is the ability to initiate the absorption of b-oxymasutyric acid. This is characteristic of the fetal brain, but the corresponding mechanisms during fasting only wake up again after 10 days, which leads to a decrease in the need for gluconeogenesis and a slight decrease in the release of nitrogen with urine on 10-14 days of complete fasting. The formation of ketone bodies has two stages: extra-hepatic and hepatic. The extra-hepatic stage leads to an increase in the level of free fatty acids in circulating blood, which leads to their counter insular and arrhythmogenic effect [49-50]; the liver stage is characterized by increased oxidation of free fatty acids in the liver, which are converted into carbon dioxide and ketone bodies [51], part of the lipid material that enters the hepatocytes is excreted by them in the form of lipoprotein of very low density and goes to the needs of other organs, but the lack of important lipotropic substances hepatic steatosis, which is unable to release lipoproteins of very low density [53] . In response to a decrease in glucose, amino acids and free fatty acids in the blood plasma, with a lack of inhibitory impulses from the stomach and other organs of the gastrointestinal tract, the Food Center is excited, which activates the sympathetic part of the autonomic nervous system: the secretion of insulin

antagonist hormones (glucagon, glucocorticoids) increases, and the secretion of insulin itself is inhibited, which leads With intense stress and accelerated fasting, insulin secretion may remain high, but the effect of counter-principles prevails [54-56]. Fasting requires the body to save energy and plastic materials in general. But as with insulin-dependent Diabetes mellitus or severe long-term stress, complete fasting creates a metabolic state of resource redistribution in favor of insulin-independent organs and tissues [57]. Insulin-dependent structures are in the most deprived state. Although Insulin production has decreased, it does not stop. At the same time, the hormonal-metabolic form of fasting is formed under the sign of a sharp predominance of the complex of counter insular regulators [58]. Like the response of the acute stage of physiological stress in injury and inflammation, in fasting conditions, the energy resources of the body's somatic components – skeletal muscle and adipose tissue-are mobilized. But in the acute phase, the immune system and bone marrow interests protect cytokines that redistribute resources for the benefit of these consumers. Without infection, this does not happen with complete fasting. Hematopoiesis is impaired and immunosuppression develops [59]. Amino acids and lipolysis products are used by the liver to synthesize glucose again and to store visceral organ protein to form ketone bodies and to provide the brain's energy needs and a number of vital energy consumers listed above [60]. Sometimes such a counter insulin compensatory redistribution reaction of the body against fasting can be impaired. This is facilitated by the replacement of proteins with low-nutrient carbohydrate foods in a small diet. When taking carbohydrates, it is impossible to adequately suppress insulin production, even if it is not enough to eat. Because of this, resource redistribution is disrupted, which leads to long-term adaptation disorders, early onset of severe complications such as liver function disorders [61]. Without proper allocation of resources from mesenchymal derivatives to visceral organs, the body cannot support the protein-synthesizing potential of the liver, hypoproteinemia accelerates, decreased oncotic pressure in the blood and hungry edema appear [62]. Instead of glucocorticoid, the adrenal cortex mainly gives a mineralocorticoid reaction. This will not help maintain appetite. Such a complex form of Protein-energy deficiency is known as "kvashiorkor" or a swollen form of fasting [63, 64]. Treatment and obesity of such patients is much more difficult than the irreversible (marantic) form of complete fasting, where neither proteins nor carbohydrates are present, and the counter insular response ensures more efficient maintenance of a number of liver functions, glucocorticoids support appetite [65].

Conclusion: as you know today, long-term fasting is a factor that determines deep metabolic and pathophysiological changes aimed at compensating for the lack of nutrients in the body. Understanding metabolic and pathological diseases in a person's long-term hunger is still relevant today, since in many countries the number of hungry people is increasing in the context of natural and social disasters and conflicts, and 1/3 of all financial costs in the world are associated with the development of alimony-related diseases.

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