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MODD STABILIZERS

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Abstract. Mood stabilizers are a group of psychotropic drugs, the main property of which is the ability to stabilize mood in people with mood disorders (affective disorders), in particular bipolar affective disorder, recurrent major depression, cyclothymia, dysthymia, schizoaffective disorder, etc., prevent (completely prevent) or mitigate and shorten relapses (phases) of affective disorders, inhibit the progression of the disease and the development of a “rapid cycle” of phase changes. Normotimics also have the ability to soften the “sharp angles of character”, irritability, quarrelsomeness, short temper, impulsiveness, dysphoria in patients with various mental disorders.

Keywords: psychotropic, normotic medicines, lithium, antiepileptic, antipsychotics.

Lithium salts began to be used for the treatment of manic states in 1949. Only by 1970 was convincing evidence of their high effectiveness obtained and methods for preventing numerous side effects were developed. An alternative to lithium salts for bipolar affective disorder can be antiepileptic drugs (carbamazepine, clonazepam, valproic acid, lamotrigine, topiramate, gabapentin), atypical antipsychotics (olanzapine, quetiapine, risperidone, aripiprazole), calcium channel blockers (verapamil, nifedipine, diltiazem) . In the 19th century Lithium salts were prescribed to patients with gout, since lithium urate is highly soluble in water and excreted by the kidneys. At the beginning of the 20th century. Lithium bromide has become widespread as a sedative and anticonvulsant. Among the indications for its use were manic states. In the 1940s cardiologists have proposed replacing part of the table salt with lithium chloride in the diet of patients with arterial hypertension and heart failure. In many patients this caused

severe intoxication, even death. In 1949, Australian scientist John Cade, having isolated toxic nitroso compounds from the urine of mental patients, studied their effect in an experiment on guinea pigs. At the same time, the animals received lithium salts to increase the solubility of urates. Lithium carbonate caused lethargy in guinea pigs. Lithium is the lightest alkali metal (group Ia). Its chemical properties are the same as those of sodium and potassium. In biological fluids, lithium concentration is determined by flame photometry or atomic absorption spectrophotometry, in the brain - by magnetic resonance spectroscopy. Traces of lithium have been found in mammalian tissues, although its physiological role has not been established. Ionized lithium in therapeutic concentrations does not have a psychotropic effect in healthy people - it does not cause euphoria, sedation or depression. In bipolar affective disorder, lithium exhibits antimanic and normothymic properties - it normalizes mood in mania and depression. Lithium ions entering neurons through fast sodium channels can cause a single action potential. However, lithium is not removed from cells by Na+, K+-dependent ATPase, so the Li+ concentration gradient between the extracellular environment and the cell cytoplasm gradually smoothes out. The retention of lithium ions in cells affects the transmembrane transport of sodium and potassium ions. As a result, electrical processes in the membrane are disrupted. In the central nervous system, lithium inhibits the release of dopamine and norepinephrine caused by depolarization and calcium ions, accelerates the neuronal uptake and presynaptic deposition of these neurotransmitters, and does not affect dopamine receptors and adrenergic receptors. In the hippocampus, under the influence of lithium, the release of serotonin increases and the synthesis of acetylcholine is activated. It is possible that lithium inhibits the catalytic activity of inositol monophosphatase, which reduces the formation of IP3. Lithium also inactivates G proteins that regulate the activity of adenylate cyclase and guanylate cyclase. Enzyme inhibition is accompanied by a decrease in the production of secondary messengers - cAMP and cGMP. Lithium reduces the activity of protein kinase C

in neurons and weakens its effect on a specific protein associated with myristylic acid and rich in alanine. This protein regulates neuronal growth and synapse formation. Lithium also increases the synthesis of the regulatory protein β-catenin. Lithium ions are quickly and almost completely absorbed from the gastrointestinal tract, creating a peak concentration in the blood after 2-4 hours. They do not bind to plasma proteins. Slowly penetrate the BBB. The concentration of Li+ in the brain is 40-50% of the level in the blood. Lithium ions accumulate in the striatum, hypothalamus and pituitary gland. Approximately 95% of a single dose is eliminated in the urine (70% within 6-12 hours, the rest within 10-14 days); 80% is reabsorbed in the proximal convoluted tubule. The half-life of elimination is 20-24 hours. With repeated administration, the excretion of lithium ions accelerates in the first 5-6 days, then a state of equilibrium occurs when intake into the body is equal to elimination. In older people, the excretion of lithium ions is slower. About 1% of lithium ions are excreted through the intestines, 4-5% through sweat. With increased sweating, the removal of lithium ions prevails over the removal of sodium ions. The concentration of Li+ in saliva is twice as high as in plasma; in tears it is the same as in plasma. Lithium passes into breast milk. The volume of distribution and clearance of Li+ changes with hyponatremia (occurs with concomitant diseases, a decrease in the amount of water and electrolytes in the body). Li+ retention is caused by phenylbutazone, indomethacin and diuretics of the thiazide group. Renal excretion of Li+ is accelerated by aminophylline, acetazolamide, osmotic diuretics, and triamterene. Indications for the use of lithium drugs: relief of acute mania and prevention of relapse of bipolar affective psychosis. Therapy is carried out only if there is a sufficient concentration of Na+ in the plasma and normal function of the cardiovascular system and kidneys. During an acute attack of mania, lithium drugs reduce expansive-euphoric mood disorders and excessive urges. The therapeutic effect occurs slowly, after 8-10 days. The preventive action is aimed at lengthening the intervals between the phases of bipolar affective disorder,

suppressing both the manic and depressive phases. Only 60-80% of patients are sensitive to lithium therapy. Lithium preparations have a small breadth of therapeutic action, so it is necessary to monitor the concentration of Li+ in plasma (analysis is carried out 8-10 hours after administration). For effective and safe treatment of acute mania, it is necessary to maintain a Li+ concentration of 0.9-1.1 mEq/L; to prevent relapse of bipolar affective psychosis - 0.6-0.75 mEq/L. Intoxication can occur when the therapeutic concentration is exceeded by 2-3 times. The Li+ concentration is determined for the first time on the 5th day after the start of treatment, since during this period it becomes stable. When increasing the dose, the concentration study is also repeated after 5 days. Once the optimal therapeutic dose has been established, tests are performed less frequently. Discontinuation of lithium maintenance therapy may be accompanied by relapse of mania. Lithium preparations are also used for repeated exacerbations of depression, schizoaffective disorders, and chronic alcoholism. Lithium preparations are taken orally in tablets and capsules. The most popular is lithium carbonate. This salt is characterized by low hygroscopicity and mild irritating effect on the intestines. Side effects of lithium drugs: nausea, vomiting, diarrhea, drowsiness, peripheral edema, acne-like rash, allergic reactions (dermatitis, vasculitis). In rare cases, benign diffuse hyperplasia of the thyroid gland develops without significant disruption of hormonal function. The secretion of thyroid-stimulating hormone and the absorption of iodine by the thyroid gland increase, the content of iodine-binding protein and thyroxine in the blood decreases moderately. It is believed that lithium interferes with the iodination of tyrosine. Lithium can cause symptoms of hyperfunction of the parathyroid glands and nephrogenic diabetes insipidus (the sensitivity of kidney adenylate cyclase to the action of vasopressin decreases, thirst and polyuria appear). Long-term therapy with lithium drugs creates a risk of developing chronic interstitial nephritis (renal failure, as a rule, does not occur), neutrophilic leukocytosis, and sexual dysfunction in men. In rare cases, an insulin-like effect appears and the T wave

on the ECG becomes flattened. A mild degree of lithium intoxication, occurring at the peak of therapeutic concentration in the blood, is manifested by sedation, tremor, nausea, vomiting, abdominal pain, and diarrhea. Severe poisoning is characterized by confusion, hyperreflexia, severe tremor, dysarthria, ataxia, convulsions, focal neurological signs, arrhythmia, arterial hypotension, albuminuria, uncontrollable vomiting, profuse diarrhea. Coma may develop with a fatal outcome. The most effective way to treat lithium intoxication is hemodialysis. Taking lithium drugs during pregnancy is dangerous for the mother and fetus, especially when combined with diuretics and following a salt-free diet. Newborns are diagnosed with reversible functional disorders: central nervous system depression, muscle hypotension, heart murmurs. Treatment of women with lithium in early pregnancy is accompanied by the development of Ebstein's cardiovascular anomaly (tricuspid valve deformity, atrial septal defect) in children. The incidence of this anomaly in the population is 1 case per 20,000 live full-term newborns, with lithium therapy - 1 case per 5000. The diagnosis can be made perinatally using ultrasonography. Ebstein's anomaly can be corrected surgically. In addition, alternative agents (carbamazepine and valproic acid) have a greater fetotoxic effect than lithium preparations. Lithium preparations are contraindicated for diseases of the cardiovascular system, kidneys, liver, peptic ulcers, cholecystitis, thyroid dysfunction, cataracts, hypersensitivity, and pregnancy. Stop breastfeeding for the period of treatment.

References

1. Машковский М.Д. Лекарства XX века. - М.: Новая волна, 1998. - 320 с.
2. . Машковский М.Д. Лекарственные средства. - 16-е изд. - М.: Новая волна, Издатель Умеренков, 2010. - 1216 с
3. Клиническая фармакология / Под ред. В.Г. Кукеса. - 4-е изд. - М.: ГЭОТАР-Медиа, 2008. - 1056 с