

The Role of Lithium in Pathogenesis of Bronchial Asthma on the Basis of Studying its Effect on Regulation of Neuro-Immuno-Endocrine Systems

Eka Rodonaia, Tamaz Churadze

Scientific-Research Institute of Pediatrics

Abstract

The aim of presented work was to consider the role of lithium in pathogenesis of bronchial asthma on the basis of studying its effect on regulation of Neuro-Immuno-Endocrine systems. In order to correct errors in the systems the effective method of treatment has been devised. 80 children aged 1-14 years suffering from bronchial asthma have been investigated. All the patients were homogeneous according to their demographic-anamnetic data and studied parameters. Decrease in concentration of lithium ions was registered at the onset of the disease. Dispersal analysis (ANOVA-oneway) revealed existence of statistically reliable correlation between severity of the disease and content of lithium ions - in particular, as severe the disease was, the lower concentration of lithium ions was observed. As a result of basis therapy, concentration of lithium ions remained constant indicating chronisation of the process. It can also be considered as a reason for further relapse. To inhibit the mechanisms leading to the destruction of membranes and to correct abnormalities in Neuro-Immuno-Endocrine regulatory system, lithium carbonate was tested in medical treatment. A new scheme for effective treatment in hospital conditions has been worked out that provides for using lithium carbonate in complex basis therapy under regular control on lithium ions concentration in blood.

Keywords: *neuro- immuno- endocrine system, bronchial asthma, lithium*

The investigations of recent years have underlined significance of the Central Nervous System (CNS), Immune and Endocrine Systems in development and output of nonspecific diseases of the Respiratory System [2]. The following patterns of the disease have been stated: predisposition to frequent relapses and prolonged duration of bronchial and lung diseases on background of the CNS disorders; higher rate of appearance of first signs of the disease at early postnatal stages of ontogenesis; abundance of severe and subsevere development of bronchial and lung diseases; the torrent development of the disease and predisposition to relapses [6].

Manifestation of perinatal disturbance of CNS in the children suffering from bronchial asthma testifies the significant role of failures in the Neuro-Immuno-Endocrine systems in formation of bronchial asthma. In most cases the output of perinatal pathologies is microstructural changes observed in hypothalamus and hypophysis, that are clinically revealed in functional disturbance of vegetative centres and alterations in hormone regulation at a releasing-trophic hormonal level [1]. The hypothalamus via its retro-regulatory relations with the CNS and thymus produces the neuropeptide affecting T lymphocytes. In its turn, the T lymphocyte releases Adrenocorticotropin (ACTP) that affect B-lymphocytes, on the one hand, and suppresses

the α -receptor of mast cell, on the other hand, resulting in CGMP level decrease. The latter leads to the inhibition of degranulating processes in the cell. The T lymphocyte produces IL-6, that through its retro-relation links acts on hypothalamus. The hypophysis-derived hormone ACTH affects adrenocortex that in its turn, produces hydrocortisone that blocks the γ -receptor of mast cell, resulting in CGMP decrease in the mast cell. Above that, the hydrocortisone in combination with a sexual hormone and the insulin acts on the thymus and leads to the decrease of its weight [2]. The lowered level of the thymus hormone launches the increase of adrenalin that stimulates β -receptors of mast cells. As a result of these processes, the rate of CAMP goes up. Any stress can cause production of adrenalin by the sympathetic nervous system; the mediator of the parasympathic nervous system – acetylcholine stimulates the γ -receptor of mast cell and through that causes increase in amount of CGMP, degranulation of mast cells and a bronchial spasm [3].

According to the experimental and clinical data it has been stated, that lithium is capable to restore the balance between α , β , and γ receptors and the cyclic nucleotides. In most cases it can completely relieve the spasm and avoid a repetitive attack [4]. Lithium salts can cause: normal duration of the processes associated with protein catabolism; normalization of triptophan metabolism; decrease of serotonin content in blood and its accumulation in the neural tissue; decrease in releasing of catecholamines from neural endings; acceleration of noradrenaline reduction rate, that might be used for correction the disbalance as a result of adrenal hyperreactivity [5]. Lithium inhibits the synthesis of extra dopamine [8], decreases expression of pre-apoptosis receptors P53 and Bax and increases expression of anti-apoptosis receptor Bcl 12 [7]. At allergic reactions the content of endogenous lithium in blood and in erythrocytes as well, goes down. The ions preferentially accumulate in thymus and in this way restore the balance between the subpopulations of T lymphocytes.

Proceeding from all the above, we set it as an object to evaluate the role of lithium ions in pathogenesis of bronchial asthma by means of studying the regulation of Neuro-Immuno-Endocrine systems and to devise the

effective, in view of pathogenesis, treating method to correct the existed errors.

80 children at the age of 1-14 years have been examined. The concentration of lithium ions in a patient's blood serum was measured in dynamics: in the morning on an empty stomach before and after receiving the agent. Proceeding from treating principles, two studied groups were identified. The first group of patients was treated according to the basis therapy, while another group was given lithium carbonate in combination with the basis therapy. The doses of lithium carbonate was varying and depended on the concentration of lithium ions in blood sera and on the weight and other individual characteristics of a patient. The treating scheme was worked out and it envisaged the 5-day course of getting in lithium carbonate at the dose of 8-10 mg/kg.

The obtained results were statistically worked up using the statistic program SPSS/V10.0. The investigated cohorts were homogeneous according to their demographic-anamnetic data and the studied parameters. For each parameter the coefficient C of contingency and the value of statistic probability (P) were estimated. At the initial stage of the disease lowered level of lithium ions was observed – $M = 0.34$, $N = 0.7-1.2$ mmol/l. We also studied the correlation between lithium concentration and the severity of disease duration in the patients. The dispersal analysis (ANOVA-oneway) showed correlation between the development of disease and the concentration of lithium ions.

Above that, we have studied the clinical characteristics – symptom appearance rate per month and the night symptom rates in every three years – in dynamics in correlation with applied methods of treatment. We revealed the treatment with lithium carbonate in combination with basis therapy to be rather successful in comparison with the single basis therapy.

Our data have demonstrated the necessity of correcting the failures in the Neuro-Immuno-Endocrine systems for effective preventive treatment, since they represent one of the main links in formation of bronchial asthma.

References

1. Shabolov N.P. - Bronchial asthma // S-P., Meditsina, 1999, 334-336.
2. Playfair J. - Immunology at a glance // S-P., Meditsina, 1999, 1-95.
3. Sokolov E.I., Glan P.V., Grishna T.N. - Immunity and stress // Moscow, Meditsina, 1999, 90 - 93.

4. Tab-a-Tabai S.A., Tagdisi D.G., Musaev I.T., Panahi M.A. - Seeking the effective adrenergic means at bronchial asthma // Intern J. of Immuno-rehabilitation, 1999, 14, 31.
5. Knox A.J., Higgins B.G., Hall I.P., Tattersfield A.E. - Effect of oral lithium on bronchial reactivity in asthma // Clinical Science, 1994, 82 (4), 407 - 412.
6. Bankova V.V., Studenikin M.Ja., Balabolkin I.I. - Allergic diseases in children // Moscow, Meditsina, 1998, 1-352.
7. Chen R.W., Chuang O.M. - Long term lithium treatment suppresses P53 and Bax expression but increases Bcl-expression // Intern. J. of Biological Chemistry, 1999, 274 (10), 6039 - 6042.
8. Carli M., Morissette M., Hebert C., Pi Paolo T. - Effects of a chronic lithium treatment on central dopamine neurotransmitters. // Biochemical Pharmacology, 1997, 54 (3), 391 - 397.

Роль лития в патогенезе бронхиальной астмы путем регуляции нейро-иммуно-эндокринной системы

Эка Родонаия, Тамаз Чурадзе

Научно-исследовательский институт педиатрии

Р Е З Ю М Е

Целью работы являлось установление роли лития в патогенезе бронхиальной астмы путем регуляции нейро-иммуно-эндокринной системы; разработка патогенетически оправданного метода лечения для коррекции имеющихся в данных системах нарушений. Под наблюдением находились 80 детей с бронхиальной астмой в возрасте 1-14 лет. Исследуемые когорты по демографическим и анамнестическим данным, а также по исследуемым параметрам были гомогенны. В начале лечения наблюдалось снижение концентрации ионов лития. В результате проведенного дисперсионного анализа выявлена статистически достоверная связь между тяжестью течения болезни и изменениями концентрации ионов лития: чем тяжелее течение болезни, тем ниже концентрация ионов лития в крови. После проведения базисной терапии концентрация ионов лития остается неизменной, что можно рассматривать в качестве одной из причин хронизации процесса и очередного рецидива. С целью ингибирования процессов, приводящих к мембранодеструкции, а также коррекции существующего в нейро-иммуно-эндокринных системах дисбаланса был использован карбонат лития. Разработана патогенетически оправданная схема лечения с использованием карбоната лития в комплексе мер базисной терапии, и обязательным учетом концентрации ионов лития в крови в стационарных условиях.

Ключевые слова: *нейро-иммуно-эндокринная система, бронхиальная астма, литий*