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МАТЕРИАЛЫ КОНФЕРЕНЦИИ И ШКОЛЫ

THE TECHNOLOGY FOR CREATING AN INTEGRATED ANALGETIC AND ANTI-ITCHING THERAPY BASED ON UNDERSTANDING MECHANISMS OF DRUG ACTION: IN SILICO–IN VITRO–IN VIVO–CLINIC

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Introduction. Neuropathic pain and itching accompany diabetes mellitus and chronic renal failure. The relationship of mental disorders of a depressive and anxiety nature with chronic pain and itching syndromes has been clinically proven. For such patients, psychotropic drugs are recommended that have their own analgesic and antipruritic efficacy due to interaction with secondary targets in the central nervous system. One of these targets is postsynaptic ionotropic NMDA glutamate receptors of the type involved in the transmission of pain signals.

Methods. A comprehensive chemical-pharmacological approach, including electrophysiological and model methods, clinical testing.

Results. Inhibition of NMDA-receptor, leading to the relief of pain and itching by psychotropic drugs, occurs according to the potential-and magnesium-dependent mechanism. The molecular model of the productive interaction of psychotropic molecules with the NMDA receptor has been constructed, the structural criterion for the selection of effective drugs has beens created: V-shaped group of aromatic rings and a positively charged amide group at a distance of 5A. Psychotropic drugs with analgesic and antipruritic efficacy have been identified, adjuvant therapies have been created and clinically confirmed for patients with diabetes mellitus and chronic renal failure using antidepressants mianserin, tianeptine and atomoxetine; and also for patients with diffuse total pruritus syndrome based on the antidepressant trittiko and antipsychotic chlorprotixen.

The target of pain therapy is also the sodium-calcium exchanger (NCX), which plays a key role in the process of calcium-dependent inactivation of NMDA receptors. The advantage of the target is that, unlike ion channel blocking, which has strong side effects, the regulation at a finer level via NCX is less traumatic.

Conclusions. The results obtained allowed to explain the better tolerance of amitriptyline compared to desipramine by the fact that amitriptyline at therapeutically relevant doses affects the ionic conductivity of the NMDA receptor indirectly through interaction with the NCX, without blocking the NMDA-receptor channel, and desipramine at low therapeutic concentrations directly blocks the receptor.

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