APPLICATION OF MIRTAZAPINE IN CHRONIC PAIN SYNDROME

Arslonova Rayhon Razhabboyevna
Samarkand State Medical University, Department of Pharmacology, Assistant
Uzoqova Mehribon Akmal kizi
Samarkand State Medical University Treatment faculty 2of course
Ergashov Saddam Rakhmatovich
Samarkand State Medical University Treatment faculty 3of course

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Abstract: Chronic pain syndrome is a disease characterized by persistent, poorly treatable pain syndrome lasting more than 6 months. Such pain syndrome in most cases is the result of somatic disease or trauma. The main cause of chronic pain syndrome is long-term persistent pain, which causes an imbalance in the peripheral and central nervous system. Neuronal receptors and fibers in this case are subjected to constant activation, which leads to increased stimulation of the central nervous system (spinal cord and brain) by pain stimuli. One of the main causes of chronic pain is the appearance of complexes of hyperreactive neurons at various levels of the CNS. Their pathologic activity is caused by the breakdown of neuronal inhibition mechanisms, increased excitability of neurons and activation of inactive synapses, which unites these neurons into a single focus of excitation with self-sustained ectopic activity. This activity leads to functional, structural, and adaptive (neuroplastic) changes in the brain and spinal cord, causing pain to persist even when its cause is eliminated. There are many medications currently used to treat chronic pain, one of which is the widely used mirtazapine.

Keywords: Chronic pain syndrome, Mirtazapine, Neuronal receptors, antidepressant, sedative and hypnotic drugs.

ПРИМЕНЕНИЕ МИРТАЗАПИНА ПРИ ХРОНИЧЕСКОМ БОЛЕВОМ СИНДРОМЕ

Аннотация: Хронический болевой синдром — заболевание, характеризующееся стойким, плохо поддающимся лечению болевым синдромом, длящимся более 6 месяцев. Такой болевой синдром в большинстве случаев является следствием соматического заболевания или травмы. Основной причиной хронического болевого синдрома является длительно сохраняющаяся боль, которая вызывает дисбаланс в периферической и центральной нервной системе. Нейрональные рецепторы и волокна при этом подвергаются постоянной активации, что приводит к усилению стимуляции центральной нервной системы (спинного и головного мозга) болевыми стимулами. Одной из основных причин хронической боли является возникновение комплексов гиперреактивных нейронов на различных уровнях ЦНС. Их патологическая активность обусловлена нарушением механизмов нейронального торможения, повышением возбудимости нейронов и активацией неактивных синапсов, что объединяет эти нейроны в единый очаг возбуждения с самоподдерживающейся эктопической активностью. Эта активность приводит к функциональным, структурным и адаптивным (нейропластическим) изменениям в головном и спинном мозге, заставляя боль сохраняться даже после устранения ее причины. В настоящее время для лечения хронической боли используется множество лекарств, одним из которых является широко используемый миртазапин.

Ключевые слова: Синдром хронической боли, Миртазапин, Нейрональные рецепторы, антидепрессанты, седативные и снотворные препараты.

INTRODUCTION

Chronic pain syndrome (CPS) is a debilitating condition that persists for more than six months and significantly impairs the quality of life. Unlike acute pain, which serves a protective biological function, chronic pain often continues beyond the healing phase and may exist independently of any ongoing tissue damage. It affects millions of people worldwide and is associated with various physical, emotional, and psychological complications.

The pathogenesis of CPS involves complex mechanisms including peripheral nerve injury, central sensitization, and neuroplastic changes within the spinal cord and brain. These changes lead to an abnormal pain perception and a heightened response to pain stimuli. Traditional analgesics, such as non-steroidal anti-inflammatory drugs (NSAIDs) and opioids, often provide limited relief and can lead to dependence or tolerance over time.

Recent research has highlighted the importance of centrally acting agents, including certain antidepressants, in the management of chronic pain. Among them, **mirtazapine**, a tetracyclic antidepressant, has gained attention not only for its mood-stabilizing effects but also for its ability to modulate pain pathways. Mirtazapine enhances noradrenergic and serotonergic neurotransmission, which are key systems involved in descending inhibitory pain pathways.

This article aims to explore the pharmacological properties of mirtazapine and its potential benefits in the treatment of chronic pain syndrome, emphasizing its role as part of a comprehensive, multidisciplinary approach to pain management.

RELEVANCE

Pain is not only a symptom of most diseases but also a complex psychophysiological phenomenon involving mechanisms of regulation and formation of emotions, motor responses, humoral and hemodynamic manifestations, all of which contribute to pain syndrome. Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or resembling such an experience.End-of-dose pain refers to pain that occurs at the end of the dosing interval when the concentration of an analgesic in the blood falls below the minimum therapeutic (pain-relieving) level. Pain intensity is the primary characteristic that defines the severity of pain as experienced and described by the patient.Short-acting drug formulations are a term used interchangeably with "immediate-release" or "conventional-release" formulations. Neuropathic pain is pain caused by disease or damage to the somatosensory nervous system (either central or peripheral).Chronic pain syndrome is an independent disease. It does not serve a protective function or carry any biological significance. On the contrary, chronic pain leads to maladaptation, abnormal perception of painful and non-painful stimuli, and various dysfunctions of the central nervous system, necessitating correction of the pain syndrome.The primary cause of chronic pain syndrome is prolonged, persistent pain, which disrupts the balance between the peripheral and central nervous systems. Neuronal receptors and fibers undergo continuous activation, leading to increased stimulation of the central nervous system (spinal cord and brain) by pain signals.One of the key reasons for chronic pain is the formation of hyperreactive neuronal complexes at different levels of the CNS. Their pathological activity results from impaired neuronal inhibition mechanisms, increased excitability of neurons, and activation of previously inactive synapses, which group these neurons into a single excitatory focus with self-sustaining ectopic activity. This activity causes functional, structural, and adaptive (neuroplastic) changes in the brain and spinal cord, leading to persistent pain even after its original cause has been eliminated.Chronic pain syndrome is a disease characterized by persistent pain lasting more than six months, which is poorly responsive to therapy. In most cases, this syndrome results from a somatic disease or as a

consequence of trauma. Chronic pain syndrome triggers a series of pathological reactions, including catecholamine release, which leads to pupil dilation, tachycardia, arterial hypertension, and tachypnea, Increases Skeletal Muscle Tone and Induces Convulsive Activity

All these autonomic reactions eventually lead to the body's maladaptation: they disrupt nighttime sleep, significantly reduce appetite, cause depression and psychosomatic disorders, contribute to the development of nutritional deficiencies, and consequently, systemic inflammatory response syndrome. These factors suppress immune function and create an imbalance in neuro-endocrine-immune interactions, further worsening the progression of the underlying pathological process that causes pain.

Mirtazapine is a next-generation antidepressant with a rapid therapeutic effect, minimal adverse effects, and a broad spectrum of action. It replaces sedative and hypnotic drugs and is also used in patients with cardiovascular diseases. According to literature data, it improves survival rates in patients who have suffered a stroke, making it ideal for elderly patients. It also combines well with somatic medications.Mirtazapine is a tetracyclic antidepressant that enhances central adrenergic and serotonergic transmission. It blocks serotonin 5-HT2 and 5-HT3 receptors, meaning serotonergic transmission is enhanced only through 5-HT1 receptors. Both spatial enantiomers contribute to its antidepressant activity: S(+)-enantiomer blocks α2-adrenergic receptors and 5-HT2 serotonin receptors. It moderately blocks H1-histamine receptors, exerting a sedative effect.Mirtazapine has little influence on α1-adrenergic receptors and cholinergic receptors; at therapeutic doses, it does not significantly affect the cardiovascular system. In clinical practice, it also demonstrates anxiolytic and hypnotic effects, making it particularly effective for anxiety-related depression of various origins. Due to its moderate sedative action, it does not exacerbate suicidal thoughts during treatment.Chronic pain syndrome is common in elderly individuals and leads to various complications, contributing to a high mortality rate. This underscores the need for physicians to prescribe effective and safe medications that reduce chronic pain and the risk of complications.

Objective of the Study: To evaluate the effectiveness of mirtazapine in complex therapy for patients with chronic pain syndrome.

METHODS AND RESEARCH MATERIALS

Upon discharge from a medical facility where palliative care was provided in an inpatient setting, patients were prescribed medication at the discretion of the medical institution's head. Prescriptions were issued in the form of an electronic document and/or on paper (except for medications provided free of charge or at a discount). The prescribed medications were either given directly to the patient or their legal representative at the time of discharge Medications, including those containing narcotic and psychotropic substances from Schedules II and III, as well as potent drugs, were prescribed for up to 5 days of use.

The study included 30 patients who received inpatient treatment in the neurology department of the SamMI clinic and were subsequently monitored on an outpatient basis.

Group 1 consisted of 10 patients (33.3%) with post-ischemic stroke pain, Group 2 included 9 patients (30%) with spinal pathology and musculoskeletal pain, and Group 3 had 11 patients (36.7%) with secondary polyneuropathies.Mirtazapine was administered as part of complex therapy at a dose of 7.5–15 mg (¼ to ½ tablet) once daily in the evening.

RESULTS

Dynamic clinical observation of patients with chronic pain syndrome showed that by day 7 of treatment, sleep quality improved, and neuropathic pain subsided, demonstrating the positive

effects of the drug. Long-term use of mirtazapine did not lead to tolerance or resistance. By days 7–12, patients experienced improved sleep, reduced anxiety, and pain relief.

CONCLUSIONS

The obtained data confirm the effectiveness of mirtazapine in the studied patients, supporting its application in individuals with chronic pain syndrome.

The management of chronic pain syndrome remains a complex clinical challenge due to its multifactorial nature and the involvement of both peripheral and central mechanisms. Mirtazapine, originally developed as an antidepressant, has shown efficacy in addressing chronic pain through its modulation of central neurotransmitter systems, particularly by enhancing noradrenergic and serotonergic transmission. Its additional sedative and anxiolytic effects make it a valuable adjunct in patients with comorbid sleep disturbances and mood disorders.

Based on current evidence and clinical observations, mirtazapine can be considered a promising component of multimodal therapy for chronic pain syndrome. However, further large-scale, randomized controlled trials are needed to fully establish its role, optimal dosing, and long-term safety profile in pain management.

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