

DOI: <https://doi.org/10.17816/uroved643075>



Anxiety and depressive disorders in patients with primary painful bladder syndrome.

Part 2. Modern treatment approaches

Tatiana A. Karavaeva^{1–4}, Anna V. Vasileva^{1, 5}, Igor V. Kuzmin⁶, Margarita N. Slesarevskaya⁶, Dmitrii S. Radionov¹, Diana A. Starunskaya¹

¹ V.M. Bekhterev National Medical Research Center for Psychiatry and Neurology, Saint Petersburg, Russia;

² Saint Petersburg State University, Saint Petersburg, Russia;

³ St. Petersburg State Pediatric Medical University, Saint Petersburg, Russia;

⁴ N.N. Petrov National Medical Research Center of Oncology, Saint Petersburg, Russia;

⁵ North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russia;

⁶ Academician I.P. Pavlov First St. Petersburg State Medical University, Saint Petersburg, Russia

ABSTRACT

This article presents modern approaches to the treatment of comorbid anxiety and depressive disorders in patients with primary painful bladder syndrome. The pharmacotherapy options and various non-pharmacological methods (psychotherapy, cognitive-behavioral therapy, hypnotherapy) for managing these conditions are detailed. It is noted that treatment targeting only the physical component of chronic pelvic pain is often ineffective. To achieve the desired outcome in some patients, it is also necessary to address cognitive, emotional, and behavioral factors associated with pain syndrome.

Keywords: depression; anxiety disorders; comorbidity; somatoform disorders; painful bladder syndrome; psychotherapy; cognitive-behavioral therapy.

To cite this article

Karavaeva TA, Vasileva AV, Kuzmin IV, Slesarevskaya MN, Radionov DS, Starunskaya DA. Anxiety and depressive disorders in patients with primary painful bladder syndrome. Part 2. Modern treatment approaches. *Urology reports (St. Petersburg)*. 2024;14(4):425–433. DOI: <https://doi.org/10.17816/uroved643075>

Received: 15.12.2024

Accepted: 28.12.2024

Published online: 30.12.2024

DOI: <https://doi.org/10.17816/uroved643075>

Тревожные и депрессивные расстройства у пациентов с первичным синдромом болезненного мочевого пузыря. Часть 2. Современные подходы к лечению

Т.А. Караваева^{1–4}, А.В. Васильева^{1, 5}, И.В. Кузьмин⁶, М.Н. Слесаревская⁶,
Д.С. Радионов¹, Д.А. Старунская¹

¹ Национальный медицинский исследовательский центр психиатрии и неврологии им. В.М. Бехтерева, Санкт-Петербург, Россия;

² Санкт-Петербургский государственный университет, Санкт-Петербург, Россия;

³ Санкт-Петербургский государственный педиатрический медицинский университет, Санкт-Петербург, Россия;

⁴ Национальный медицинский исследовательский центр онкологии им. Н.Н. Петрова, Санкт-Петербург, Россия;

⁵ Северо-Западный государственный медицинский университет им. И.И. Мечникова, Санкт-Петербург, Россия;

⁶ Первый Санкт-Петербургский государственный медицинский университет им. акад. И.П. Павлова, Санкт-Петербург, Россия

АННОТАЦИЯ

В статье представлены современные подходы к лечению коморбидных тревожных и депрессивных расстройств у пациентов с первичным синдромом болезненного мочевого пузыря. Подробно описаны возможности фармакотерапии и различных немедикаментозных методов (психотерапии, когнитивно-поведенческой терапии, гипнотерапии) в лечении данных состояний. Указано, что лечение хронической тазовой боли, направленное только на ее физический компонент, часто оказывается неэффективным. Для получения требуемого результата у ряда пациентов необходимо воздействовать также на когнитивные, эмоциональные и поведенческие факторы, связанные с болевым синдромом.

Ключевые слова: депрессия; тревожные расстройства; коморбидность; соматоформные расстройства; синдром болезненного мочевого пузыря; психотерапия; когнитивно-поведенческая терапия.

Как цитировать

Караваева Т.А., Васильева А.В., Кузьмин И.В., Слесаревская М.Н., Радионов Д.С., Старунская Д.А. Тревожные и депрессивные расстройства у пациентов с первичным синдромом болезненного мочевого пузыря. Часть 2. Современные подходы к лечению // Урологические ведомости. 2024. Т. 14, № 4. С. 425–433. DOI: <https://doi.org/10.17816/uroved643075>

INTRODUCTION

Primary bladder pain syndrome (PBPS) is one of the most common causes of chronic pelvic pain. The condition is characterized by pain or discomfort in the bladder region, with exacerbation during bladder filling, in the absence of infection or another urinary tract involvement [1, 2]. PBPS is 5–10 times more prevalent in women than in men and frequently results in dysuria [3]. The medical and social importance of PBPS is due to its high prevalence, significant negative impact on the quality of life, long periods of disability and often invalidity of such patients, as well as the significant costs of long-term treatment, which is often lifelong [2, 4, 5].

COMORBID ANXIETY AND DEPRESSIVE DISORDERS IN PATIENTS WITH PRIMARY BLADDER PAIN SYNDROME

The goal of treatment for PBPS is to reduce and, if possible, eliminate pain and dysuria, ultimately improving the patient's quality of life [1, 2, 4]. Treatment options for PBPS are diverse and include behavioral, physical, and pharmacological therapies, as well as minimally invasive and non-malignant surgical procedures [2, 4, 6–8]. However, despite the variety of treatment approaches, their efficacy is often inadequate, with a significant number of patients with PBPS failing to achieve not only pain relief, but also a reduction in pain severity. These circumstances contribute to the low level of adherence of such patients to medical recommendations and frequent consultations with different specialists. It has been found that patients with PBPS have a very high frequency of combined (comorbid) psychiatric disorders, including depression, anxiety disorders, and social phobias [9–11]. Moreover, there is a direct correlation between the severity of affective disorders and pain intensity [12–14].

In recent years, there is increasing evidence of the contribution of somatoform disorders and associated affective disorders to the persistence of clinical manifestations of PBPS when standard therapy is prescribed [9, 15, 16]. This highlights the need to prescribe appropriate drug and non-drug therapy when the somatoform origin of PBPS is identified. Management of these patients should be based on the biopsychosocial concept of chronic pelvic pain syndrome (CPPS), in which pain is the result of a dynamic interaction of biological, psychological, and sociocultural factors [17]. The involvement of these factors may vary at different stages of the disease progression. Comorbid emotional disorders (primarily anxiety and depressive disorders) that influence the

strategy of drug therapy account for a significant specific weight [18]. Psychological and social components are predominant in somatoform disorders. In this regard, PBPS treatment targeting only the physical component is often ineffective. To achieve success, it is necessary to address not only physiological processes, but also cognitive, emotional, and behavioral factors associated with the pain syndrome [19].

Pharmacotherapy

According to Haase et al. [20] and Zhuo et al. [21], there is a significant decrease in monoamine neurotransmitters in depression and anxiety disorders, which affects both pain and mood regulation in the central nervous system. As chronic pain persists, alterations in monoaminergic transmission become more pronounced and contribute significantly to the sensitization and maintenance of pain, leading to dysfunction of modulatory pathways, decreased inhibition and/or increased pain signals, forming a vicious cycle [22]. Taking into account the clinical and neurobiological overlap between affective disorders and chronic pain conditions, psychopharmacotherapeutic agents are actively used in the treatment of patients with PBPS. Tricyclic antidepressants (e.g., amitriptyline, clomipramine, and imipramine) and new-generation antidepressants, i.e., selective serotonin reuptake inhibitors (SSRIs; e.g., sertraline, fluoxetine, and others), are widely used. Serotonin-norepinephrine reuptake inhibitors (SNRIs, e.g., venlafaxine, duloxetine) are a class of antidepressants that have been demonstrated to potentiate the functioning of the antinociceptive system [23–26]. Duloxetine, a drug included in many international clinical guidelines for the treatment of chronic pain, is especially relevant in this context. Its analgesic effect is associated with its effect on central sensitization, which is mediated through noradrenergic neurotransmission. The limited affinity of SSRIs and SNRIs for muscarinic, histamine, and α_1 -adrenoreceptors, in conjunction with their minimal impact on monoamine oxidase, contributes to a reduction in adverse effects and an enhancement of their safety profile compared with tricyclic antidepressants. Tranquilizers belonging to the benzodiazepine derivatives group are prescribed for patients exhibiting a combination of anxiety and somatic symptom disorders. In recent years, the antiepileptic agents (e.g., gabapentin and pregabalin) have been used to target the neuropathic mechanism of CPPS [27–30]. A potential risk associated with the use of these drugs is the possibility of addiction [22]. As noted by Servais et al. [31], pregabalin abuse in individuals with CPPS is associated with an elevated risk of chemical addiction. In this regard, the importance of collecting a comprehensive and structured medical history to identify risk factors for addiction, including alcohol and/or other substance abuse and comorbid psychiatric disorders, is evident [32].

Psychotherapy

Taking into account the important role of psychological mechanisms in the development of CPPS, the main component of personalized therapy is the use of psychotherapeutic interventions [17, 19]. The most commonly used cognitive-behavioral psychotherapies include various relaxation and meditation techniques, biofeedback therapy (BFT), and the recently developed acceptance and commitment therapy (ACT).

Cognitive-behavioral therapy

Cognitive-behavioral therapy (CBT) is a widely used approach to the treatment of various conditions associated with chronic pain [33]. This psychotherapeutic method was initially developed for the treatment of depression; however, it has been adapted for psychiatric disorders and chronic pain conditions since then [34]. CBT is a focused psychological therapy that teaches patients to recognize the impact of their own thoughts and behavior on their pain and functioning, and how to change it. CBT techniques in the treatment of chronic pain include training to identify the relationships between thoughts, emotions, behavior, and the development of physical symptoms; cognitive restructuring and reframing; relaxation techniques to minimize autonomic arousal; stepping and pacing; sleep hygiene; problem-solving strategies; coping and interpersonal skills. There is emerging evidence for the effectiveness of online CBT for chronic pain syndromes using mobile and digital technologies [35–37]. As indicated by Mazzolenis et al. [38], the introduction of artificial intelligence and virtual reality technologies in cognitive therapy for chronic pain seems promising.

Similar to the treatment of genitourinary dysfunction, BFT with parallel electromyography is actively used in the treatment of CPPS [39–41]. This technique is based on a modified system of pelvic floor muscle exercises. The therapeutic and diagnostic hardware used in this procedure includes computerized BFT complexes that facilitate the measurement, reception, and processing of electromyographic signals from the patient during muscle contraction. Furthermore, these complexes enable the supervision of exercise performance by providing feedback in verbal (sound) and/or visual (video) formats [41]. In a comparative study by Cornel et al. [40], 33 patients with diagnosed chronic prostatitis/CPPS were enrolled in the BFT treatment program. According to the results, the mean National Institute of Health Chronic Prostatitis Symptom Index (NIH-CPSI) changed from 23.6 (range: 11–34) at baseline to 11.4 (range: 1–25) after treatment ($p < 0.001$). The mean pelvic floor muscle tone was 4.9 (range: 2.0–10.0) at diagnosis and decreased to 1.7 (range: 0.5–2.8) after treatment ($p < 0.001$).

ACT focuses on observing thoughts and feelings as they are, without trying to change them, and on behavior

that is consistent with values and important life goals. This approach has shown promising results in trials of integrated treatment for chronic pain [42–45]. The data from a meta-analysis of 21 randomized controlled trials by Ye et al. [44] showed a large effect size three months after ACT for individuals with chronic pain. The basic premise of the method as applied to chronic pain is that while pain causes physical discomfort, it is the struggle with pain that causes suffering. In ACT, the sensation of pain itself is regarded as an unconditioned reflex that serves the function of warning the individual of danger or tissue damage, and the sensation of pain is critical for survival.

Hypnotherapy

Although hypnotherapy has not been extensively studied for its efficacy in patients with PBPS, it has been used extensively for pain syndromes [46, 47]. There is evidence that hypnotherapy is an effective approach compared with other non-physical approaches, such as CBT [48, 49]. Thompson et al. [49] conducted a meta-analysis of the data on quantitative assessment of the efficacy of hypnosis for pain reduction and to identify the factors that influence the efficacy of hypnotherapy. A systematic search was conducted in six databases (i.e., PubMed, EMBASE, PsycINFO, CINAHL, CENTRAL, and Web of Science) to identify studies that compared the effects of hypnotic interventions on pain severity, threshold sensitivity, and pain tolerance. The selected studies utilized the models of experimentally induced pain in healthy controls. The researchers identified 85 papers that met the selection criteria, predominantly cross-sectional studies, with a total sample size of 3632 participants ($n = 2892$ for the study group, $n = 2646$ for the control group). A subsequent random-effect meta-analysis revealed the analgesic effects of hypnosis for all types of pain (confidence interval: 0.54–0.76, $p < 0.001$). The efficacy of hypnosis was strongly influenced by hypnotic suggestibility and the use of direct suggestion for pain relief. Specifically, the study found that individuals with high and moderate hypnotizability experienced optimal pain relief through the use of direct analgesic suggestion in hypnosis, demonstrating 42% ($p < 0.001$) and 29% ($p < 0.001$) clinically significant reductions in pain, respectively [49].

Hypnosis for chronic pain usually involves induction with suggestions for relaxation and comfort. Post-hypnotic suggestion is designed to continue pain reduction after the session, or to help the patient easily and quickly achieve comfort through anchoring. In addition, techniques such as gauntlet anesthesia, dissociation, indirect suggestion for pain relief, or scattered suggestion are used. The amnesia phenomenon is used to desensitize the patient to forget the pain, even temporarily.

CONCLUSION

The postulate of multifactorial pathogenesis of PBPS is accepted by the scientific community. The importance of psychogenic causes in the development of urogenital pain syndrome is undisputed. Comorbid anxiety and depressive disorders in patients with CPPS require special therapeutic approaches. In this regard, a psychotherapist or psychiatrist must be included in a multidisciplinary team of specialists involved in the treatment of such patients. The possibilities of modern pharmacotherapy and a variety of non-drug methods allow for the effective treatment of these disorders.

ADDITIONAL INFO

Authors' contribution. All authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study. Personal contribution of each author: T.A. Karavaeva, A.V. Vasileva, I.V. Kuzmin, M.N. Slesarevskaya, D.A. Starunskaya — search and analysis of literary data, editing the text of the manuscript; D.S. Radionov — search and analysis of literary data, writing the text of the manuscript.

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Funding source. The study was carried out within the framework of the state assignment of the V.M. Bekhterev National Medical Research Center for Psychiatry and Neurology for 2024–2026 (XSOZ 2024 0014).

Competing interests. The authors declare that they have no competing interests.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией. Личный вклад каждого автора: Т.А. Караваяева, А.В. Васильева, И.В. Кузьмин, М.Н. Слесаревская, Д.А. Старунская — поиск и анализ литературных данных, редактирование текста рукописи; Д.С. Радионов — поиск и анализ литературных данных, написание текста рукописи.

Источник финансирования. Исследование выполнено в рамках государственного задания ФГБУ «НМИЦ ПН им. В.М. Бехтерева» Минздрава России на 2024–2026 гг. (XSOZ 2024 0014).

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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AUTHORS' INFO

Tatiana A. Karavaeva, MD, Dr. Sci. (Medicine), Professor;
ORCID: 0000-0002-8798-3702; eLibrary SPIN: 4799-4121;
e-mail: tania_kar@mail.ru

Anna V. Vasileva, MD, Dr. Sc. (Medicine), Professor;
ORCID: 0000-0002-5116-836X; e-Library SPIN: 2406-9046;
e-mail: annavdoc@yahoo.com

ОБ АВТОРАХ

Татьяна Артуровна Караваева, д-р мед. наук, профессор;
ORCID: 0000-0002-8798-3702; eLibrary SPIN: 4799-4121;
e-mail: tania_kar@mail.ru

Анна Владимировна Васильева, д-р мед. наук, профессор;
ORCID: 0000-0002-5116-836X; e-Library SPIN: 2406-9046;
e-mail: annavdoc@yahoo.com

AUTHORS' INFO

Igor V. Kuzmin, MD, Dr. Sci. (Medicine), Professor;
ORCID: 0000-0002-7724-7832; eLibrary SPIN: 2684-4070;
e-mail: kuzminigor@mail.ru

Margarita N. Slesarevskaya, MD, Cand. Sci. (Medicine);
ORCID: 0000-0002-4911-6018; eLibrary SPIN: 9602-7775;
e-mail: mns-1971@yandex.ru

***Dmitrii S. Radionov**, MD; address: 3 Bekhtereva st., Saint Petersburg, 192019, Russia; ORCID: 0000-0001-9020-3271;
eLibrary SPIN: 3247-3178; e-mail: dumradik@mail.ru

Diana A. Starunskaya, MD; ORCID: 0000-0001-8653-8183;
eLibrary SPIN: 1478-0297; e-mail: dianastarunskaya@gmail.com

ОБ АВТОРАХ

Игорь Валентинович Кузьмин, д-р мед. наук, профессор;
ORCID: 0000-0002-7724-7832; eLibrary SPIN: 2684-4070;
e-mail: kuzminigor@mail.ru

Маргарита Николаевна Слесаревская, канд. мед. наук;
ORCID: 0000-0002-4911-6018; eLibrary SPIN: 9602-7775;
e-mail: mns-1971@yandex.ru

***Дмитрий Сергеевич Радионов**; адрес: Россия, 192019, Санкт-Петербург, ул. Бехтерева, д. 3; ORCID: 0000-0001-9020-3271;
eLibrary SPIN: 3247-3178; e-mail: dumradik@mail.ru

Диана Андреевна Старунская; ORCID: 0000-0001-8653-8183;
eLibrary SPIN: 1478-0297; e-mail: dianastarunskaya@gmail.com

* Corresponding author / Автор, ответственный за переписку