DOI:10.33667/2782-4101-2023-2-4-9

INSOMNIA IN PANIC DISORDER. LITERATURE REWIEW

Korabelnikova E. A.[1,3], Yakovleva E. V.[2,3]

[1]I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation
[2]Private healthcare institution «Central clinical hospital «RZD-Medicine», Moscow, Russian Federation
[3]Russian State Humanitarian University, Moscow, Russian Federation

SUMMARY
Sleep disorders and panic disorder (PD) are often comorbid and closely interrelated. Sleep disorders aggravate the severity of panic disorder, and pathological anxiety worsens sleep. In this regard, the treatment of insomnia in patients with PD is aimed at harmonizing the emotional state and correcting sleep and, along with pharmacotherapy, includes a wide range of psychotherapeutic methods. Successful treatment of insomnia increases the effectiveness of PD therapy, reduces the likelihood of relapse and increases the susceptibility of patients to many anti-anxiety drugs.

KEYWORDS: *sleep; insomnia; panic disorder; panic attacks*

CONFLICT OF INTEREST. *The authors declare that they have no apparent or potential conflicts of interest related to the publication of this article.*
Funding source. *The work was supported by the RSF grant No 22- 28-00540 (https://rscf.ru/project/22-28-00540/). The article was prepared with the support of Krewel Meuselbach Ltd.*

ИНСОМНИЯ ПРИ ПАНИЧЕСКОМ РАССТРОЙСТВЕ

Корабельникова Е. А.[1,3], Яковлева Е. В.[2,3]

[1]Первый Московский государственный медицинский университет им. И. М. Сеченова (Сеченовский университет), Москва, Россия
[2]Частное учреждение здравоохранения «Центральная клиническая больница «РЖД-Медицина», Москва, Россия
[3]Государственный Гуманитарный Университет, Москва, Россия

РЕЗЮМЕ
Нарушения сна и паническое расстройство (ПР) часто коморбидны и тесно взаимосвязаны. Нарушения сна усугубляют тяжесть панического расстройства, а патологическая тревога ухудшает сон. В связи с этим лечение инсомнии у больных с ПР направлено на гармонизацию эмоционального состояния и коррекцию сна и, наряду с фармакотерапией, включает широкий спектр психотерапевтических методов. Успешное лечение инсомнии повышает эффективность терапии ПР, снижает вероятность рецидива и повышает восприимчивость больных ко многим противотревожным препаратам.

КЛЮЧЕВЫЕ СЛОВА: *сон; инсомния; паническое расстройство; панические атаки.*

КОНФЛИКТ ИНТЕРЕСОВ. *Авторы заявляют, что у них нет явных или потенциальных конфликтов интересов, связанных с публикацией данной статьи.*
Источник финансирования. *Работа выполнена при поддержке гранта РНФ № 22-28-00540 (https://rscf.ru/project/22-28-00540/). Статья подготовлена при поддержке Krewel Meuselbach Ltd.*

Introduction

Panic disorder (PD) is a widespread problem in modern society, especially in metropolitan areas. According to different authors, the prevalence of PD in the population is 2–5 %, and it most often develops in young people (the average age is about 25 years) [1].

The modern view on the etiology and pathogenesis of PD suggests the involvement of various factors in it: predisposing (genetic and constitutional), accelerating (provoking) and fixing (*Table 1*) [1].

Clinical manifestations of panic disorder

In ICD-10, PD is coded with the index F41.0 (episodic paroxysmal anxiety) and is included in the class «Neurotic, stress-related and somatoform disorders» (F40-F48) [2]. It manifests as unexplained, distressing attacks of intense fear and/or feelings of internal tension combined with various autonomic (somatic) symptoms that peak within a few minutes. Currently, the DSM–IV and ICD-10 have adopted the following criteria for establishing the diagnosis of PD [2, 3]:

A. Recurrent attacks in which intense fear or discomfort combined with 4 or more of the following symptoms develops suddenly and peaks within 10 min:

- throbbing, palpitations, rapid pulse;
- sweating;
- chills, tremors;
- shortness of breath, dyspnea;

Table 1
Insomnia development factors

Factor type	Factors	Mechanisms
Predisposing	1) Genetics 2) Pathophysiology 3) Personality 4) Environment	• abnormal norepinephrin and GABA metabolism; • abnormal neurodynamics; • medical conditions • early life state • city living
Provoking	1) Mentality	• conflict peak (a divorce, painful discussions, or leaving one'sfamily); • acute and potent stressors (a loved one's death, an illness, or an accident);
	2) Biology	• abstract identification or contraposition (movies, books,e tc.); • hormonal changes (pregnancy, delivery, weaning, or climacteric); • sexual debut, intake of oral contraceptives, or abortion;
	3) Physical health	• menstrual cycle (its disorders or the final phase); • alcohol abuse; • weather effects; • excessive physical exercise;
Fixing	1) Behavioral 3) Cognitive distortions	• avoidance behavior; • perception and thinking distortion that prevents one from normal perception of reality.

Table 2
PDs classification

Criterion	Variants
1. Based on panic-associated symptoms	• major/massive panic attacks (4 or more symptoms; daily or monthly); minor panic attacks (less than 4 symptoms; several times a day);
2. Based on the main attack component	• vegetative (mostly vegetative disorders with undifferentiated phobias); • hyperventilation (frequent and deep breathing, reflex apnea, paresthesias, and muscle pain associated • with respiratory alkalosis); • phobic (mostly phobias associated with fears in the situations the patient considers as triggers); • conversion (hysterical conversion disorders, often senesthopathies, no or mild fear and anxiety); • senesthopathic (mostly senesthopathies); • affective (pronounced depressive or dysphoric disorders);
3. Typicality-based	• typical panic attacks (all vegetative and affective main symptoms); • atypical panic attacks (no or atypical affective manifestations and some additional symptoms, particularly globus pharyngeus, limb weakness, abnormal vision, hearing, gait, speech, and/or voice, syncope, body bending, cramps, nausea, vomit, and/or abdominal discomfort);
4. Based on presence/ absence of associated agoraphobia	• with agoraphobia; • without agoraphobia.

- respiratory difficulty, a choking sensation;
- pain or discomfort in the left side of the chest;
- nausea or abdominal discomfort;
- dizziness, instability when walking;
- weakness, lightheadedness, fainting spells;
- numbness or tingling sensation (paraisthesis);
- hot and cold flashes;
- feelings of derealization, depersonalization;
- a fear of dying;
- a fear of losing one's mind or acting uncontrollably.

B. The occurrence of panic attacks (PA) is not due to the direct physiological effects of any substance (e.g., drug dependence or medication intake) or somatic disease (e.g., thyrotoxicosis).

C. In most cases, PAs do not arise from other anxiety disorders such as phobias (social and simple), obsessive-phobic disorders, post-traumatic stress disorder.

Different variants of the classification of PDs depending on the parameters taken as a basis [1, 4] are given in *Table 2*.

The main manifestation of PD is PA or vegetative crisis, which are not confined to a particular situation or circumstance and are therefore unpredictable. The attacks (sudden episodes of severe anxiety) usually last from 1 min to 1 hour and occur on average 2–4 times a week.

Panic paroxysms in themselves are not dangerous to life or health, but they frighten the patient to such an extent that he or she loses control over feelings and emotions and becomes completely defenseless. PD patients gradually lose self-confidence and faith in others, the strongest feeling of insecurity does not allow them to communicate normally with other people. A PD patient avoids places where it is difficult to get help, and in congested and crowded places, as well as in confined spaces, he or she prefers to be accompanied by friends or family members (agoraphobia) [5].

Long-term restrictive (selective) behaviour leads to severe social disability or social demoralisation, followed by the development of secondary depression. The fixation on somatic symptoms arising in PA forms in patients' specific fears (of heart attack, stroke, fainting, etc.), often taking on a compulsive character and eventually leading to the development of obsessive-phobic or hypochondriac syndrome.

Comorbidity of panic disorder and insomnia

The study of the representation of insomnia in patients with PD shows, first, a high frequency of their comorbidity [6–8]. According to different authors [9–11], insomnia occurs in 60–80 % of patients with PD. At the same time, both pathological conditions have a more complex interaction rather than a unilateral one.

Firstly, they share common emotional, personal, and biological backgrounds. For example, many people suffering from insomnia have high levels of neuroticism, introversion, anxiety, and perfectionism, which is also characteristic of patients with PD [12–15]. Biological studies have shown the role of polymorphism of certain genes of the serotoninergic system in the pathogenesis of both PD and insomnia [16, 17]. Social and psychological stressors, which are considered the

leading provocateur of insomnia development, also lead to the occurrence or increase in the frequency of PA [18, 19].

Second, PD and insomnia share similar factors and mechanisms of pathogenesis. The modern neurocognitive model of insomnia, like PD, is based on Spielman's 3Ps model (predisposing, precipitating, and perpetuating) [20].

Thirdly, being comorbid conditions, PD and insomnia aggravate and make each other chronic. A clear dependence of disease severity on concomitant sleep disorders has been shown [21, 22]; at the same time, sleep disorders are caused by pathological anxiety, which is manifested by cortical hyperactivation, which, in turn, is the main link in the pathogenesis of insomnia [23].

Specialists underestimate the problem of insomnia. This is because patients with PD rarely report their sleep disorders to a physician, listing more vivid, dramatic, and frightening PAs in the list of complaints, as well as the fact that physicians rarely actively question patients about their sleep disorders [24–26].

Features of insomnia manifestation in panic disorder

Patients with PD complain of difficulty falling asleep, disturbing thoughts before going to bed, and non-restorative sleep [9].

Only 25% of patients have PAs exclusively during waking hours. The majority of PAs, single or repeated (30–45%), occur during nighttime sleep. More than half (54%) of patients report attacks during both waking and sleeping periods, and in 21% of patients PAs occur only during sleep [9, 10]. PAs arising from sleep exhibit all the symptoms characteristic of PA [27] and at the same time have certain specific features: they are shorter in duration, have more pronounced phobic and psychosensory manifestations, and less pronounced vegetative symptoms in the seizure structure [10]. Fearing the recurrence of PA, patients deliberately deprive themselves of sleep, which aggravates insomnia and generally blight these patients' life. Consequently, nocturnal PAs lead to more pronounced social maladaptation and are considered as an indicator of a more severe course of the disease [9, 10, 27].

M. Van de Laar et al. published data on the fact that in the joint manifestation of PD and insomnia aggravate the disease, reduce the effectiveness of therapy, and increase the probability of recurrence of PD and the risk of suicidal behaviour [13].

Polysomnographic study of patients with PD, according to most studies, reveals increased bedtime, frequent awakenings, decreased sleep efficiency and reduced total sleep duration [23, 28–30]. T. Uhde et al. examined 9 patients with PD who did not take medication for 2 weeks [31]. The authors showed that patients had increased motor activity during sleep, decreased latent period of the sleep phase with rapid eye movements (REM) and decreased REM density (REM frequency per unit time) compared to the corresponding parameters of healthy control subjects. L. Pecknold et al. found poor sleep efficiency in 84 ±12% of patients with PD (n = 44) [28]. A survey of patients with PD conducted by P. J. Hauri et al. showed lower sleep efficiency and increased motor activity, in particular, due to the number of large movements, compared to the control group (*Tables 3, 4*) [29].

Table 3

Sleep of PD patients and healthy subjects [29] (M ± SD)

Parameter	PD patients (n = 24)	Healthy subjects (n = 24)	p
Sleep latent period (before phase 2), min	20.0 ± 10	10.9 ± 5	< 0.001
Sleep effectiveness, min	90.9 ± 4	94.2 ± 6	< 0.01

Table 4

Gross movements in PD patients and healthy subjects during sleep (seconds per sleep hour) [29] (M ± SD)

Sleep phase	PanD patients (n = 24)	Healthy subjects (n = 24)	p
Phase 1	30.3 ± 32	10.9 ± 25	< 0.02
Phase 2	38.3± 37	13.2 ± 21	< 0.01
REM sleep	16.4 ± 19	5.8 ± 11	< 0.05

Only a few studies have polygraphically recorded PAs arising from sleep, and these data, as well as the authors' conclusions about the mechanisms of sleep, are contradictory. I. Lesser et al. recorded PA arising directly from delta sleep, which allowed them to suggest a commonality between the mechanisms of PA during sleep and nocturnal fears [32]. E. Mellman et al. recorded 6 PAs during sleep, all of them arising from the 2nd or 3rd stages of sleep [33]. S. Bell et al. found an increased frequency of nocturnal PAs in patients who also suffered from isolated sleep paralysis, which led the authors to think about a possible connection between nocturnal PAs and REM sleep phases [34].

In the study by R. Hauri et al. [8] PA attacks occurring in sleep were recorded, 6 of them in the transitional phase between stage 2 and stage 3 sleep [29]. According to the authors' observations, these attacks are unique, different from nocturnal fears and from the anxiety state in sleep. Thus, the patient's awakening and the panic paroxysm itself were preceded in most cases by eye movements during slow-wave sleep, muscle twitching, increased muscle tone, and increased EEG frequency up to 21 Hz. According to the authors, nocturnal PAs are more similar to nightmares of patients with posttraumatic stress disorder.

There is an opinion that disorders of the current functional state of the brain in the sleep-wake cycle play a key role in the initiation of PA. The imbalance of inhibitory and activating nonspecific brain systems (excessive activity of the waking system, insufficiency of synchronising mechanisms) is considered as the main pathogenetic factor, which is combined with anxiety-phobic disorders and suprasegmental autonomic activation with hypofunction of predominantly parasympathetic innervation in the cardiovascular system. If we proceed from this point of view, the excessive activity of the waking system can be manifested either during the waking period or during the transition period from daytime wakefulness to sleep during the first and second sleep cycles. This sets the stage for the occurrence of either wakefulness PA, sleep PA, or a combination of the two. This has been confirmed by polygraphic analysis of the cyclic organisation of nocturnal sleep with assessment of the duration and percentage representation of sleep stages, as well as the correlation between electrophysiological parameters and sleep stages [10, 23].

The degree of sleep structure disturbance in PD is different [10]. When PA occurs only in wakefulness, sleep is not grossly altered. In this case, as a rule, there is an increase in nonspecific activation of electroencephalogram (EEG) during wakefulness and sleep. More pronounced sleep disturbances are noted when PA is present during sleep and wakefulness or only during sleep. PAs usually occur in stage 2 sleep and delta sleep. In sleep PA,

there are signs of increased autonomic and EEG activation in relaxed wakefulness, before falling asleep and during spontaneous nocturnal awakenings, and there are characteristic disturbances in the structure of sleep, affecting the REM and delta sleep phases. In the presence of sleep PA and wakefulness PA, maximum disturbances in the sleep structure affecting all stages of sleep (rapid, light and deep slow-wave) were noted.

Hyperventilatory manifestations occurring during sleep PA (awakening from a sensation of inability to inhale or exhale, forcing the patient to jump out of bed, open the window; dizziness and clenching of the fingers, etc.) often give specialists reason to suspect the presence of obstructive sleep apnea syndrome. Diagnostic guidelines in this case are the persistence of the sensation of shortness of breath for more than a few seconds after awakening, the vivid emotional colouring of the attack, and the data on the presence of similar attacks during the day, which makes the diagnosis of «true» sleep apnea unlikely. The final answer is given by nocturnal polysomnography with recording of respiratory parameters during sleep [23].

Approaches to the treatment of panic disorder

Clinical evidence suggests that therapy for PD should take into account its diurnal distribution and the presence and nature of associated sleep disorders.

Traditionally, the treatment of PD consists of several steps:

1. PA management;
2. basic therapy for PD, aimed at preventing recurrence of PA and correcting emotional state;
3. relapse prevention.

Benzodiazepine tranquillisers have the most rapid effect in the treatment of PA, allowing the seizure to be terminated in 15–20 minutes. However, with prolonged use, the dose of the drug has to be increased over time, and irregular use and the associated rebound phenomenon may increase the frequency of seizures over time. Therefore, this group of drugs is not suitable for basic long-term therapy of PD aimed at preventing seizure recurrence and reducing anxiety. Clinical observations show that antidepressants (selective serotonin or serotonin–norepinephrine reuptake inhibitors), which are characterised by high efficacy, good tolerability, ease of prescription, low toxicity in overdose and absence of addiction and dependence effects in long-term use, are the closest to the level of an ideal antipanic drug. Drugs of this group control not only PA, but also other psychopathological syndromes formed in patients with PD [35]. Taking into account these features, the above drugs are recommended as the drugs of choice in PD with or without agoraphobia [36, 37].

In patients with therapy-resistant PD, the 2nd generation antipsychotics olanzapine [38] and risperidone [39] have been shown to be effective. Beta-adrenergic blockers (propranolol and atenolol) are particularly effective in the severe vegetative component of PD, as they block the physical symptoms of chest pain, tightness in the throat and dyspnoea without sedation.

Psychotherapy is an integral component of PD therapy, which is used both independently and in combination with pharmacotherapy. The effect is often achieved only with the help of psychotherapy [40, 41].

Therapeutic tactics are determined by various factors, particularly the severity of the condition. Mild PD (relatively infrequent PAs not accompanied by persistent avoidant behaviour) allows psychotherapy in isolation or in combination with small, fixed doses of daily anxiolytics administered in short courses (no more than 3–4 weeks). Severe PD (more than 4 PAs per month, obvious expectancy anxiety, agoraphobia impairing social adaptation; mild or moderate comorbid depressive disorder) suggests monotherapy for 3–6 months. It is also possible to add a benzodiazepine drug for the initial 2–4 weeks of treatment as an effective «bridge» until the desired effect of selective serotonin reuptake inhibitors is realised [21, 42].

Treatment of sleep disorders in patients with PD

International recommendations for the treatment of insomnia suggest the use of psychotherapy as the leading method of treatment of chronic insomnia, as well as pharmacological agents – not only hypnotics, but also a wide range of anti-anxiety drugs (antidepressants and neuroleptics) that have a positive effect on sleep [43]. Thus, all of the above-mentioned methods of treating PD to a greater or lesser extent influence human sleep by facilitating falling asleep, reducing the number and duration of nocturnal awakenings, and thereby acting on the recovery processes occurring during night sleep.

Psychotherapy is the leading method of therapy for chronic insomnia, which improves sleep no less effectively than medications [44, 45]. At the same time, the effect of medications on sleep often ceases almost immediately after the end of the medication, while the results of normalising sleep patterns with the help of psychotherapy are maintained in the future. In addition, psychotherapy does not cause addiction or side effects, which is often observed with the use of sleeping pills.

Among the psychotherapy methods effective in treating both PD and insomnia, cognitive-behavioural psychotherapy should be highlighted. According to most international guidelines for the treatment of insomnia, cognitive-behavioural therapy for insomnia is the method of choice in the treatment of this category of patients [1, 46]. According to a number of studies, cognitive-behavioural therapy for insomnia comorbid with PD leads to decreased PA and improved sleep [1, 6].

Other non-pharmacological methods effective in the treatment of insomnia include: exposure to bright light during the day; water procedures, especially baths with substances that have a calming effect (pine needles, sea salt, special bath foam, etc.); aromatherapy in the form of massage with essential oils, inhalations, vapours and aromatic baths, sleeping herbal pillows; massage and acupuncture; therapeutic music and «nature sounds». An important and necessary condition for the effectiveness of any therapeutic intervention for insomnia is sleep hygiene [45].

It is important to remember that insomnia itself can increase anxiety and worsen well- being and mood, usually in the morning hours after poor sleep [47]. At the same time, PA in sleep disrupts falling asleep to the point of recurrent sleepless nights. Therefore, short courses of sleeping pills may be justified when the clinical picture is dominated by symptoms of insomnia. Drugs affecting the hamkergic system are more often used, as they facilitate falling asleep, reduce the waking time within sleep, and improve recovery processes during sleep.

The most modern hypnotics are derivatives of cyclopyrrolones (zopiclone), imidazopyridine (zolpidem) and pyrazolopyrimidine (zaleplon). These drugs have, in addition to hypnotic, sedative, anxiolytic, anticonvulsant and myorelaxant action, have a short half-life, with proper use do not cause addiction and daytime wakefulness disorders, unlike benzodiazepines. Nevertheless, given the rapid onset of effect and anti-anxiety effect, in the treatment of this category of patients derivatives of benzodiazepines in some cases it is advisable to use a short course (no more than 2–3 weeks). It should be borne in mind that prolonged use of any sleeping pills, even of the modern generation, can cause addiction and form dependence, as well as contributes to the development of insomnia itself. Therefore, it is not recommended to take sleeping pills for more than 3 weeks.

Alternatives to hypnotics in the modern drug market are non-drowsy drugs of other pharmacological groups positively affecting sleep: anxiolytics, antidepressants and antipsychotics, antihistamines. Low-dose antidepressants and some neuroleptics [48, 49] can improve sleep in patients with anxiety disorders and insomnia without clinically significant depression. Among antidepressants, tricyclic (tetracyclic) nonselective antidepressants (imipramine, clomipramine, amitriptyline, mianserin, maprotiline) and selective antidepressants (selective serotonin reuptake inhibitors – paroxetine, fluvoxamine, sertraline, fluoxetine, citalopram) are used in the treatment of insomnia; among neuroleptics, levomepromazine, chlorpromazine and quetiapine are more commonly used. These drugs do not develop addiction and physical dependence.

Doxylamine succinate (DS), which acts simultaneously on M-cholinergic and H1- histamine receptors in the central nervous system, is often used among drugs with a sedative effect. Such a combined effect on receptors contributes to the enhancement of the sleeping effect and the development of sedative action of DS. Treatment of insomnia with DS is effective and safe, which is shown in many foreign and domestic studies [50, 51, 52]; it is the only sleeping drug that can be used during pregnancy. An examination of 61 patients with various forms of neurotic disorders, including PD with sleep disorders, conducted in the clinic of the Department for the Study of Borderline Psychiatric Pathology and Psychosomatic Disorders of the The Mental Health Research Centre (MHRC) of the Scientific Organizations Federal Agency, showed the efficacy and safety of DS in the treatment of this category of patients [52].

A convenient form of DS is offered by the German company «Krevel Miselbach»: Valocordin-doxylamine – drops for ingestion. 1 ml of the drug contains 25 mg of DS. The drug has a mint smell, giving an additional sedative effect. The advantage of the liquid form is that the drug can be dosed more flexibly than DS in tablets. The possibility to choose an individualised dose contributes to increased compliance. The fractional patented dropper simplifies dosing. The recommended single dose for patients over 18 years of age is 22 drops (corresponds to 25 mg DS). In case of insufficient efficacy of therapy, the dose can be increased to a maximum of 44 drops (50 mg DS).

In recent years, scientists have shown great interest in the study of the sleeping properties of melatonin. Synthetic analogues of melatonin allow normalising the level of this hormone in the central nervous system. They are quite effective and harmless sleeping pills, which can be recommended in all cases of sleep disorders, in patients of any age and with any concomitant pathology without visible negative effects and with a high degree of tolerability [44].

Among other drugs with a sleeping effect for the treatment of insomnias, remedies based on individual herbs or herbal compilations, which are the basis of combined phytopreparations, are prescribed.

The treatment regimen is determined individually depending on the nature and severity of the symptoms of PD and insomnia. The use of drug-free methods should be considered a priority in treatment. Drug therapy should be used if non- pharmacological correction is ineffective. In milder variants of PD, treatment of insomnia should preferably begin with psychotherapy in combination with herbal sleeping pills and melatonin preparations. They are the group of choice for young people, cause the least problems for the patients taking them and can be easily discontinued later. If these drugs are ineffective within 3–5 nights, they are replaced by more potent – modern sleeping pills with minimal risk of drug dependence and addiction (doxylamine, zopiclone, zolpidem, zaleplon). Use immediatelymedication treatment should be used in patients when the rapid onset of effect is important. For more severe symptoms, a combination of psychotherapy and psychopharmacotherapy is recommended, including drugs from the groups of antidepressants and neuroleptics, whose therapeutic targets are both PD and sleep disorders, and which are acceptable for long-term use without the risk of addiction and dependence.

Successful treatment of insomnia has been shown to increase the efficacy of PD therapy, reduce the likelihood of relapse, and increase patients' susceptibility to many anti-anxiety medications [53].

Thus, the treatment of insomnia in PD consists of a set of measures aimed at harmonising the emotional state, the autonomic nervous system and the management of PA and insomnia as syndromes. The key to successful therapy of sleep disorders in PD is a comprehensive approach, including, along with pharmacotherapy, a wide range of psychotherapeutic methods.

REFERENCES

1. *Korabelnikova EA. Sleep disturbances in panic disorders. S. S. Korsakov Journal of Neurology and Psychiatry. Special issues. 2018; 118(4–2): 99–106. (In Russ.) DOI: 10.17116/jnevro20181184299*
2. *WHO. ICD-10. International statistical classification of diseases and related health problems (10th revision). Classification of mental and behavioral disorders.*
3. *DSM–IV. Diagnostic and Statistical Mannual of mental disorders. Washington; 1990.*
4. *Dyukova G. M. Panic disorders in the practice of a neurologist. Remedium Privolzh'e. 2017; 2(152): 21–24. (In Russ.)*
5. *Shin J., Park D., Ryu S. et al. Clinical implications of agoraphobia in patients with panic disorder. Medicine (Baltimore). 2020; 99(30): e21414. DOI: 10.1097/MD.0000000000021414*
6. *Cousineau H., Marchand A., Bouchard S. et al. Insomnia symptoms following treatment for comorbid panic disorder with agoraphobia and generalized anxiety disorder. J. Nerv. Mental Dis. 2016; 4: 267–273. DOI: 10.1097NMD.0000000000000466*
7. *Brook A., Marcks B., Weisberg R. Co-occurrence of insomnia and anxiety disorders: a review of the literature. Am. J. Lifestyle Med. 2009; 3(4): 300–309. DOI: 10.1177/1559827609334681*

8. Hauri P., Friedman M., Ravaris C. Sleep in patients with spontaneous panic attacks. Sleep. 1989; 12(4): 323–337. DOI: 10.1093/sleep/12.4.323
9. Kovrov G. V., Lebedev M. A., Palatov S. Yu. et al. Sleep disorders in anxiety and anx- iety-depressive disorders. Russian Medical Journal. 2015; 10: 530–536. (In Russ.)
10. Mishiev V. D. Sleep disorders in certain mental disorders: a modern approach to choosing a hypnotist. News of Medicine and Pharmacy. 2007; (3): 9–11. (In Russ.)
11. Na H. R., Kang E. H., Yu B. H. et al. Relationship between personality and insomnia in panic disorder patients. Psychiatry Invest. 2011; 8(2): 102–106. DOI: 10.4306/pi.2011.8.2.102
12. Uhde T., Cortese B., Vedeniapin A. Anxiety and sleep problems: emerging concepts and theoretical treatment implications. Curr. Psychiatry Rep. 2009; 11(4): 269–276. DOI: 10.1007/s11920-009-0039-4
13. Van de Laar M., Verbeek I., Pevernagie D. The role of personality traits in insomnia. Sleep Med. Rev. 2010; 14(1): 61–68. PMID: 19897388. DOI: 10.1016/j.smrv.2009.07.007
14. Belleville G., Marchand A., Poitra J. et al. Do treatments for panic disorder improve sleep in patients with unexplained chest pain. Arch. Sci. Psychol. 2015; 3: 93–100. DOI: 10.1037/arc0000018
15. Zugliani M., Martin-Santos R., Nardi A., Freire R. Personality traits in panic disorder patients with and without comorbidities. J. Nerv. Ment. Dis. 2017; 205(11): 855–858. DOI: 10.1097/NMD.0000000000000745
16. Perlis R., Mischoulon D., Smoller J. et al. Serotonin transporter polymorphisms and adverse effects with fluoxetine treatment. Biol. Psychiatry. 2003; 54(9): 879–883. DOI: 10.1016/s0006–3223 (03) 00424-4
17. Brummett B., Krystal A., Ashley-Koch A. et al. Sleep quality varies as a func- tion of 5-HTTLPR genotype and stress. Psychosom. Med. 2007; 69(7): 621–624. DOI: 10.1097/PSY.0b013e31814b8de6
18. Yumatov E. A., Glazachev O. S., Bykova E. V. et al. Relationship between emo- tional stress and sleep. Vestnik MAN RS. 2016; (1): 5–14. (In Russ.)
19. Vorobyeva O. V. The role of emotional stress in the development of panic disorder. Mental disorders in general medicine. 2008; (4): 48–51. (In Russ.)
20. Poluektov M. G., Buzunov R. V., Averbuh V. M. et al. Draft clinical guidelines for the diagnosis and treatment of chronic insomnia in adults. Neurology and Rheu- matology. 2016; (2): 41–51. (In Russ.)
21. Vorobyeva O. V. Panic disorder–principles of therapy. Russian Medical Journal. 2008; 6: 362–365. (In Russ.)
22. Zinkovsky A. K., Yurov I. E. Personality features and psychovegetative status of patients with panic and generalized anxiety disorder. Social and Clinical Psychia- try. 2001; (2): 44–48. (In Russ.)
23. Poluektov M. G. Sleep disorders in the practice of a psychiatrist. Modern therapy of mental disorders. 2012; (4): 11–17. (In Russ.)
24. National Institutes of Health. National Institutes of Health State of the Sci- ence Conference statement on Manifestations and Management of Chronic In- somnia in Adults. Sleep. 2005; 28(9): 1049–1057. DOI: 10.1093/sleep/28.9.1049
25. Sateia M., Doghramji K., Hauri P., Morin C. Evaluation of chronic insomnia. Sleep. 2000; 23(2): 243–308.
26. Morin C. Cognitive-behavioral approaches to the treatment of insomnia. Clin. Psychiatry. 2004; 65(Suppl 16): 33–40.
27. Golubev V. L., Bashmakov M. Yu. Panic attacks and a night's sleep. Russian Med- ical Journal. 1999; 2(1): 3–6. (In Russ.)
28. Pecknold J., Olha A., Chang H. et al. Sleep architecture in patients with panic disorders. Proceedings of 1 meeting of the Collegium Intenationale Neuro-Psy- chopharmacologicumin. San Juan; 1986.
29. Hauri P., Friedman M., Ravaris C. Sleep in patients with spontaneous panic attacks. Sleep. 1989; 12(4): 323–337. DOI: 10.1093/sleep/12.4.323
30. Hoge E., Marques L., Wechsler R. et al. The role of anxiety sensitivity in sleep disturbance in panic disorder. J. Anxiety Disord. 2011; 25(4): 536–538. DOI: 10.1016/j.janxdis.2010.12.008
31. Uhde T., Roy-Byrne P., Gillin J. et al. The sleep of patients with panic disor- der: a preliminary report. Psychiatry Res. 1985; 12(3): 251–259. DOI: 10.1016/0165–1781 (84) 90030-1
32. Lesser I., Poland R., Holcomb C., Rose D. Electroencephalographic study of nighttime panic attacks. J. Nerv. Ment. Dis. 1985; 173(12): 744–746. DOI: 10.1097/00005053-198512000-00007
33. Mellman T., Uhde T. Sleep-related panic. Proceedings of 42nd Annual Conven- tion of the Society for Biological Psychiatry. Chicago; 1987.
34. Bell C., Dixie-Bell D., Thompson B. Panic attacks: relationship to isolated sleep paralysis. Am. J. Psychiatry. 1986; 143(11): 1484. DOI: 10.1176/ajp.143.11.1484a
35. Wade A. Antidepressants in panic disorder. Intern. Clin. Psychopharmacol. 1999; 14(2): 13–17.
36. DeVane C. The place of selective serotonin reuptake inhibitors in the treat- ment of panic disorder. Pharmacotherapy. 1997; 17(2): 282–292.
37. Roy-Byrne P., Craske M., Stein M. Panic disorder. Lancet. 2006; 368(9540): 1023–1032. DOI: 10.1016/S0140–6736(06)69418-X
38. Sepede G., De Berardis D., Gambi F. et al. Olanzapine augmentation in treatment-resistant panic disorder: a 12-week, fixed dose, open-label trial. J. Clin. Psychopharmacol. 2006; 26(1): 45–49. DOI: 10.1097/01.jcp.0000195108.01898.17
39. Simon N., Hoge E., Fischmann D. et al. An open-label trial of risperidone augmentation for refractory anxiety disorders. J. Clin. Psychiatry. 2006; 67(3): 381–385. DOI: 10.4088/jcp.v67n0307
40. Wayne A. M. Panic attacks. Guide for doctors. Moscow; 2004. (In Russ.)
41. Korabelnikova E. A. A modern approach to the diagnosis and therapy of panic disorder. Polyclinic. 2016; (3–4): 31–36. (In Russ.)
42. Breilmann J., Girlanda F., Guaiana G. et al. Benzodiazepines versus placebo for panic disorder in adults. Cochrane Database Syst. Rev. 2019; 3(3): CD010677. DOI: 10.1002/14651858.CD010677.pub2
43. Riemann D., Baglioni C., Bassetti C. et al. European guideline for the diag- nosis and treatment of insomnia. J. Sleep Res. 2017; 26(6): 675–700. DOI: 10.1111/jsr.12594
44. Zakharov A. V., Khivintseva E. V. Clinical use of melatonin in the treatment of sleep disorders. Effective pharmacotherapy. 2019; 15(44): 42–47. DOI 10.33978/2307-3586-2019-15-44-42-47
45. Korabelnikova E. A. Psychotherapy of insomnia: the role of the somnologist and psychotherapist. Effective pharmacotherapy. Neurology and psychiatry. Special issue "Sleep and its disorders". 2014; (12): 38–44. (In Russ.)
46. Qaseem A., Kansagara D., Forciea M. et al. Management of chronic insom- nia disorder in adults: a clinical practice guideline from the American College of Physicians. Ann. Intern. Med. 2016; 165(2): 125–133. DOI: 10.7326/M15–2175
47. Medic G., Wille M., Hemels M. Short- and long-term health consequences of sleep disruption. Nat. Sci. Sleep. 2017; 9: 151–161. DOI: 10.2147/NSS.S134864
48. Mendelson W. A review of the evidence for the efficacy and safety of trazo- done in insomnia. J. Clin. Psychiatry. 2005; 66(4): 469–476. DOI: 10.4088/jcp.v66n0409
49. Everitt H., Baldwin D., Stuart B. et al. Antidepressants for insomnia in adults. Cochrane Database Syst. Rev. 2018; 5(5): CD010753. DOI: 10.1002/14651858.CD010753.pub2
50. Burchakov D. I., Tardov M. V. Insomnia in the practice of a therapist: the role of doxylamine. Medical advice. 2020; (2): 45–53. (In Russ.) DOI: 10.21518/2079–701X-2020-2-45-53.
51. Allison M., Hale C. A phase I study of the pharmacokinetics and pharma- codynamics of intranasal doxylamine in subjects with chronic intermittent sleep impairment. Drugs R D. 2018; 18(2): 129–136. DOI: 10.1007/s40268-018-0232-1
52. Smulevich A. B., Zheleznova M. V., Pavlova L. K. The use of "Donormil" in the treatment of sleep disorders of moderate and mild severity in the practice of a psychiatrist. Psychiatry and psychopharmacotherapy. 2006. 8(1): 21–28. (In Russ.)
53. Asnis G. M., Caneva E., Henderson M. A. Treatment of insomnia in anxiety disorders. Psychiatric Times. 2012; 29(1).

Received 10.05.2023
Revised 31.05.2023
Accepted 10.06.2023

INFORMATION ABOUT THE AUTHORS

Korabelnikova Elena Alexandrovna, *neurologist, MD, professor, Department of nervous diseases, I. M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation; Russian State Humanitarian University, Moscow, Russian Federation. ODCID ID: https://orcid.org/0000-0003-4548-0012. Tel. +7-910-414-09-34, e-mail: e_korabel@mail.ru*

Yakovleva Elena Vyacheslavovna, *neurologist, private healthcare institution «Central clinical hospital «RZD-Medicine», Moscow, Russian Federation; Russian State Humanitarian University, Moscow, Russian Federation. ODCID ID: https://orcid.org/0000-0002-23704540. Tel. +7-919-047-95-32, e-mail: alena_yakovleva_00@mail.ru*