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Review

INSOMNIA IN THE ELDERLY AND CONTEMPORARY TREATMENT METHODS

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ABSTRACT

Introduction: Insomnia is one of the most common health problems of modern times and the third most common reason for presenting to the primary care doctor after headache and gastrointestinal symptoms.

Aim: The aim of this article is to present current treatments for insomnia in older people over 65 years of age, focusing on cognitive-behavioural therapy complemented by pharmacological treatment.

State of the art brief: The prevalence of insomnia can be as high as 19%. The problem mainly affects older people. It is caused not only by the physiological changes occurring in the process of ageing, but also by the numerous diseases from which seniors suffer. Insufficient sleep can lead to many illnesses or aggravate existing ones, which is particularly dangerous for the aforementioned age group. The treatment of insomnia is based on non-pharmacological methods, which include cognitive-behavioral psychotherapy and sleep hygiene education, and on pharmacological treatment, in which a wide range of drugs are used. In daily practice, mainly benzodiazepines and their derivatives, antidepressants and melatonin are used.

Conclusions: Insomnia is a very significant problem worsening daytime functioning, negatively affecting quality of life. Therefore, appropriate diagnosis of sleep disorders is important, as it may facilitate the identification of the potential cause of the disorder and the introduction of appropriate management.

KEYWORDS: insomnia; elderly; cognitive-behavioral therapy; sleep hygiene; treatment.

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1. Introduction

Insomnia is the most common form of sleep disorder in adults, especially the elderly, and is one of the most common causes of health problems in humans. The International Classification of Diseases and Health-related Problems (ICD-10, 10th revision) defines insomnia as an unsatisfactory quantity or quality of sleep. The diagnosis can be made if symptoms occur at least

3 times a week for a minimum of one month [1]. Insomnia can take three different forms, which are defined in the third version of the International Classification of Sleep Disorders (ICSD-3) developed by the American Academy of Sleep Medicine (AASM): difficulty falling asleep, difficulty with maintaining sleep and premature waking up. The first type of disorder predominates in younger people, while the last two forms predominate in older people [2].

An important aspect of insomnia is the fact that it affects the 24-hour functioning of the body. It worsens the quality of life, causes concentration and memory disorders, increases the risk of many diseases, including hypertension, neurological and psychiatric diseases, and may even cause more road accidents [3].

2. Division of insomnia

There are several divisions of insomnia. The first division based on cause can be used (American Classification of Mental Diseases and Disorders - DSM-IV - Diagnostic and Statistical Manual of Mental Disorders [4]), which divides insomnia into:

- primary, i.e. spontaneous, arising without any apparent cause,
- secondary, which is the result of another disease or another specific trigger (e.g. medications).

However, a more practical division is based on the duration of symptoms, according to ICSD-3 (AASM 2014 - American Academy of Sleep Medicine [5]). Classification distinguishes:

- short-term insomnia that lasts less than 3 months; it is usually caused by current life situations or events (e.g. reaction to stress, infection, rapid change of time zones, pain), therefore it is often a secondary disorder,
- chronic insomnia lasting more than 3 months; this type of insomnia is usually associated with chronic diseases and addictions, e.g. to alcohol or psychoactive substances; what is important is the presence of perpetuating factors which, even after the cause of insomnia has ceased, cause it to continue; so chronic insomnia may become an idiopathic disease.

There is another division of insomnia depending on the clinical symptoms and the mechanism of insomnia:

- psychophysiological; involves excessive concentration on problems with falling asleep, which intensifies after going to bed, which increases arousal and makes it difficult to fall asleep,
- reactive; appears suddenly in response to a specific stimulus, e.g. stress, lasts a short time, but may develop into chronic insomnia if perpetuating factors occur,
- paradoxical; the patient's reports are inconsistent with the results of the polysomnographic examination,
- related to poor sleep hygiene; is a behavioral disorder occurring as a result of the patient's inappropriate behavior, e.g. frequent and long naps during the day, use of stimulating substances (caffeine) in the evening, use of electronic devices just before bedtime,
- secondary to medications or psychoactive substances taken; related to intake, withdrawal or poisoning,
- insomnia in the course of somatic or mental diseases, such as depression, anxiety disorders, neurological diseases or diseases involving severe pain,
- idiopathic; without a specific cause, it often begins in childhood [3,6,7].

3. Insomnia in older people

The problem of insomnia increases with age and affects women more often than men. This is largely due to the physiological changes that occur during the ageing process. Young people sleep on average 7-9 hours a day. However, after the age of 65, the body's need for sleep and its stability decrease. Sleep stages also change [6]. The

number of NREM/REM cycles decreases from 5 to 3, the N1 phase ("semi-sleep", transitional sleep) increases, and the N3 phase (deep sleep) shortens, while the duration of the N2 phase and REM sleep remains relatively constant. In addition, wakefulness during sleep is prolonged (shallow sleep until waking up) and the number of awakenings per hour increases, making it easier to wake up in response to auditory stimuli.

As a result, sleep becomes fragmented because older people, after waking up, have trouble switching from wakefulness to sleep again. The number of awakenings may be up to 30 in people with breathing disorders.

Older people have difficulty maintaining sleep and waking up prematurely, which changes the circadian rhythm and causes them to go to bed earlier and get up earlier in the morning. This often leads to naps during the day, which are not conducive to maintaining proper sleep hygiene. As a result of these processes, deep sleep becomes shorter in favor of longer light sleep, which leads to a decrease in overall sleep efficiency.

In addition, the causes of circadian rhythm disorganization can also include: melatonin secretion disorders; decreased secretion of growth hormone, which affects slow-wave sleep; increased cortisol levels in the evening, which makes it difficult to fall asleep; increased interleukin-6 concentration, which worsens the quality of sleep and reduces its duration; less exposure to light and less activity in seniors, which reduces the need for sleep.

In addition to the influence of physiological processes occurring in the body during ageing, pathological changes, diseases, medications and poor sleep hygiene are also important. They cause secondary sleep disorders and require treatment or modification of medications [1,9].

4. Epidemiology

Insomnia in the elderly is a common problem [1]. The EPESE (Established Populations for Epidemiologic Studies of the Elderly) research, in more than 9,000 ambulatory patients over 65 years of age, difficulty falling asleep or maintaining sleep was reported by 43% of tested, with the disorder increasing in those in poorer health and on multiple medications [10]. The disorders are more common in women, in patients with depression (2.5 times more common), and in those with respiratory diseases (the risk increased by 40%). In addition, studies have noted that the problem of insomnia is growing, and that the use of sleep medications is becoming higher [11]. In the nationwide program of research on cardiovascular risk factors - NATPOL - among nearly 2,500 subjects subjective sleep difficulties were reported by 50.5% of the study population [12]. Subjective insomnia was diagnosed in as many as 50.9% of people between the ages of 60 and 79, the majority of whom were women (74.8%).

The lowest prevalence of insomnia was reported in a study by Schlack et al. in Germany [13]. In contrast, the highest percentage of insomnia was observed by Léger et al. in a study of more than 12,000 people in France, at 19% [14].

Repeated studies in Norway have reported that the prevalence of taking sleep medications increased from 7 to 11% in 14 years [15].

5. Pathomechanism of insomnia

The pathogenesis of the onset of chronic insomnia is explained by the 3P model developed by Spielman and colleagues. This model includes three types of factors: predisposing, provoking and sustaining insomnia. Predisposing factors include age, gender, personality type (neurotic, anankastic), and excessive sympathetic nervous system activity. They have a genetic basis and are subject to little modification. The presence of predisposing factors alone does not lead to insomnia. In combination with provocative factors, they cause acute insomnia. Provocative factors include: severe stress, problems at work, moving house, somatic illness, use of new medications. Once the provoking factors are eliminated, sleep normalizes. However, when sustaining factors emerge, chronic insomnia develops. These factors include daytime naps, taking stimulants before bed, lying in bed for long periods of time, and using sleep medications [3,6,16].

6. Diagnosis

A key element in the diagnosis of insomnia is the history taken from the patient, supplemented by a physical examination and, if indicated, a sleep diary kept by the patient. The history should include information on the nature of the sleep disorder, the patient's general condition, existing somatic and psychological burdens, if any, medications taken, and information on sleep hygiene [3,17].

At the outset, it would be necessary to determine the nature of the existing disorder by determining: the duration of the disorder (acute insomnia, chronic insomnia); whether the disorder involves falling asleep, maintaining sleep or waking prematurely; and whether there are sleep disruptors such as snoring, restless legs syndrome, nycturia, coughing, wheezing, choking, snorting, bruxism, apneic episodes etc. It should also be determined whether the sleep disorder causes poorer daytime functioning, lethargy, impaired concentration, memory and fatigue.

The patient's general medical history should include information on diagnosed chronic diseases, psychiatric disorders, medications taken (medications with psychostimulant effects include beta-mimetics, selective serotonin reuptake inhibitors, anticholinergics), environmental, occupational, and lifestyle factors. Caffeine, alcohol and nicotine as well as illicit drugs intake should also be inquired about.

The history of sleep hygiene, i.e., bedtimes, daytime naps, stress, physical activity, and stimulants before bedtime, proper sleeping conditions such as a comfortable bed, mattress, proper temperature, and an airy room, is also important [3,18].

The diagnosis of insomnia can be supplemented by keeping a sleep diary for a minimum of 1-2 weeks.

In special situations with difficult diagnosis, the following tests are performed: actigraphic (recording of the patient's motor activity) and polysomnographic (rather not recommended) [1,7].

Chronic insomnia significantly reduces a person's quality of life, results in a reduced sense of well-being and impaired maintenance of attention and concentration,

increases difficulty in performing daily tasks and weakens the immune system. Studies indicate that patients suffering from insomnia have a 2.5 to 4.5 times increased risk of car accidents [19]. Patients struggling with insomnia are much more likely to develop physical problems than patients with depression [1]. Patients show increased fatigue and irritability. Correlations have been noted between insomnia and increased risk of dementia. Insomnia promotes a 3- to 4-fold increase in the development of depression or a 2- to 3-fold increase in anxiety disorders [1]. The association is due to pathophysiological mechanisms responsible for sleep and mood to which excessive cortisol secretion and increased activation of the hypothalamic-pituitary-adrenal axis contribute [19]. There is a disruption of neurotransmitters in the brain by the lack of regeneration of neural tissue as a result of insufficient sleep.

Studies have shown a link between poor cardiometabolic outcomes and sleep problems. Long-term insomnia can lead to the development of hypertension and heart failure mainly in women. The highest probability of developing diabetes or hypertension has been reported in patients who slept less than 5 hours [20]. Reduced sleep slows down metabolism and thus glucose is stored as fat, resulting in obesity. In addition, insufficient sleep decreases levels of leptin, which is responsible for appetite regulation [21].

Insomnia also leads to neurocognitive disorders such as difficulty focusing attention, memory problems or concentration. Patients sleeping less than 6 hours showed poorer scores on tests of information processing speed and visual memory in contrast to those with normal sleep duration. Patients suffering from insomnia show reduced episodic, cognitive and working memory [20]. Thus, short sleep duration can cause cognitive impairment and, in geriatric patients, lead to dementia.

Along with insomnia, a reduction in immunity has been observed due to decreased white blood cell production [19]. As a result, patients are more susceptible to infections, mainly of the upper respiratory tract.

In summary, chronic insomnia and consequently prolonged physiological arousal may predispose to hypertension, risk of depression, diabetes and alcohol abuse.

7. Treatment

Sleep disorders have a number of consequences that include negative effects on overall health and functioning, both in terms of somatic and mental health. For this reason, insomnia should not be underestimated [22].

The treatment of insomnia includes cognitive-behavioral therapy, which is gaining increasing importance, and pharmacological treatment. For patients with short-term insomnia, pharmacological treatment as the first choice is in line with current recommendations. However, for patients struggling with chronic insomnia, cognitive-behavioral therapy should be the first choice [23].

7.1. Non-pharmacological methods

CBT (Cognitive Behavioral Therapy) is a first-line option due to its high efficacy and lasting benefits in treating sleep disorders.

CBT-I (CBT for insomnia) is a primary and mainstream treatment method based on short-term (about 4-8 sessions) psychotherapeutic interactions using one or more strategies to treat insomnia. This includes psychoeducation in stimulus control, sleep hygiene, sleep restriction, and relaxation training.

Stimulus control is a method designed to extinguish patients' negative associations, and pave the way for new correct beliefs on the bed/sleep plane. It recommends:

1. Going to bed only when feeling sleepy or tired.
2. Leaving the bed when one cannot fall asleep, returning to bed when drowsiness arrives.
3. Using the bed only for sleep or sex.
4. Establishing a fixed time for waking and getting up, regardless of the length of sleep achieved the night before.
5. Eliminating naps during the day.

Sleep hygiene education is based on informing the patient about distractors such as environmental factors (influence of light, temperature, noise) and behavioral factors (lifestyle, physical activity, diet, psychoactive substances used) that significantly disrupt sleep.

Sleep restriction is a method of adjusting the time spent in bed, according to the expected duration of sleep. The evaluation is made on the basis of records in sleep diaries kept by the patient. The level of sleep efficiency is calculated and the time frame is determined based on it. The initial time frame is approximated by the average number of hours the patient sleeps. The time frame is successively lengthened or shortened until satisfactory results are achieved. The mild sleep deprivation used in this method results in an increase in the number of hours slept and facilitates falling asleep.

Relaxation training is a set of techniques aimed at reducing psychosomatic tension. It consists of progressive muscle relaxation, breathing exercises, mindfulness training, autogenic training, meditation, and progressive muscle relaxation [24].

7.2. Pharmacological methods

In pharmacotherapy, benzodiazepines (BDZs), nonbenzodiazepine hypnotics (Z-drugs), antidepressants, antipsychotics, antihistamines with sleep-inducing effects, and melatonin receptor agonists have found particular use in the treatment of insomnia.

7.2.1. Benzodiazepines and nonbenzodiazepine hypnotics

Both BDZs and Z-drugs bind to the GABA-ergic A receptor, enhancing its activity. BDZs bind to the α subunit of subtypes 1, 2, 3 and 5 of the GABA-A receptor, while Z-drugs are more specific, having a higher affinity for the $\alpha 1$ subunit [24]. Both groups of drugs induce sleepiness, reduce the frequency of awakenings, prolong sleep duration and improve sleep quality. In addition to their common sleep-inducing effect, the selectivity of the Z-drugs manifests itself in a more effective effect on shortening sleep latency. Z-drugs have no anti-anxiety, myorelaxant or anticonvulsant effects compared to BDZs [25].

Zolpidem binds selectively to the $\alpha 1$ and $\alpha 5$ subunits of the GABA-A receptor complex. The drug's action is thought to facilitate falling asleep, reduce the number of awakenings during the night, extend the length and improve the quality of sleep. The use of zolpidem is

associated with an increased risk of falls and drowsiness, but still less than when using drugs from other groups. Subsequent side effects of the drug include hallucinations, increased suicidal tendencies, dependence, rebound insomnia, obstructive sleep apnea and cognitive impairment the following day [26,27].

Eszopiclone is the S isomer of the racemic zopiclone and belongs to the Z-drug group. It acts through the $\alpha 1$, 2, 3 and 5 subunits of the GABA-A receptor. It is effective in facilitating sleep, prolonging sleep time, improving function, alertness, and concentration during the day. Side effects include unpleasant taste, dry mouth, drowsiness, headache and dizziness [27,28].

The choice of drug is influenced by its pharmacokinetic properties. Drugs with a shorter half-life (zolpidem: 2-3 hours) have a lower risk of side effects than those with a longer half-life (zopiclone: 5-6 hours). The expected effects of the applied pharmacotherapy in the form of fewer awakenings, easier falling asleep, increased sleep duration and quality can be achieved with drugs that have a longer duration of action. The results of studies report that zopiclone has comparably good or better effects compared to BDZs [25].

In short-term treatment, BDZs and Z-drugs are recommended for a period of 2 to a maximum of 4 weeks. This duration is dictated by the high risk of substance abuse, dependence, development of tolerance to the drug, rebound insomnia, coordination and cognitive dysfunction [24].

The use of BDZs and Z-drugs among the elderly population has comparable risks. Patients suffering from kidney or liver disease deserve special attention, as this results in prolonged time of action, elimination, metabolism of the drug from the system. The higher sensitivity of GABA-A receptors in the elderly means that even small doses can generate potential side effects such as cognitive or balance disorders. The risk of hip fractures due to falls when the drug is switched on and off after long-term (more than one month) use increases by 50% [25].

Despite the restrictions, these preparations are widely and long-term used in the population suffering from sleep disorders. Studies show that in European countries the duration of treatment of insomnia with BDZs and Z-drugs is statistically 15.2 weeks, and they are prescribed in 92% of all pharmacotherapeutic treatment attempts [29].

7.2.2. Antidepressants

Trazodone is a weak serotonin reuptake inhibitor and antagonist of 5-HT_{1A}, 5-HT_{1C}, 5-HT₂, $\alpha 1$ and $\alpha 2$ receptors. Doses of 25 mg to 100 mg are used to treat insomnia [27]. Side effects among the elderly include dizziness, cardiac disturbances, and orthostatic hypotension [24].

Mirtazapine is a potent 5-HT₂ receptor antagonist. It is recommended for the treatment of insomnia in the presence of depression [24]. Side effects include the occurrence of daytime sleepiness and cognitive impairment [30].

Doxepin, from the group of tricyclic antidepressants, in low doses shows antagonism to the H₁ receptor causing sedation and prolonging sleep time. Studies conducted on

side effects have shown nausea, headache and somnolence [24].

7.2.3. Antihistamines

This includes doxylamine, diphenhydramine, and hydroxyzine, but their use is not recommended due to the numerous side effects shown in clinical trials [31].

7.2.4. Antipsychotic drugs

Quetiapine is a potent histamine H1 receptor agonist. It is effectively used in the off-label treatment of insomnia, among other conditions. The most important side effects of quetiapine are orthostatic hypotension, weight gain, hyperlipidemia, hyperglycemia. The drug is well tolerated at a dose of 25 mg to 75 mg for 2 to 6 weeks [30,31].

7.2.5. Melatonin and melatonergic drugs

Melatonin is a natural hormone produced in the human body by the pineal gland. Acting on MT1 and MT2 receptors, it controls the diurnal rhythm, facilitates falling asleep and sustaining sleep, thus maintaining its quality at an appropriately high level. Thus, it can be used as a chronobiotic that determines the appropriate time of sleep [2]. Synthetic melatonin and melatonin receptor agonists are used if sleep disturbances are due to a dysregulated circadian rhythm [33]. The exception is elderly people over the age of 65, in whom melatonin production declines due to changes in the ageing process [2]. It is the safest form of therapy in the elderly in terms of side effects (balance disorders, falls). It has no addictive properties and no build-up of tolerance is observed even during long-term use [33]. The maximum effect is achieved around 13 weeks of use, and higher doses have greater effects.

Melatonin can be divided into those with prolonged release (PR) and immediate release. PR melatonin seems to be more practical for treatment, due to its longer half-life. It is more effective because the effect does not depend on the correct time of administration of the drug and prevents midnight awakenings [17].

Among the melatonergic drugs are ramelteon (not available in Poland), which has a higher affinity for receptors MT1 and MT2 than melatonin; agomelatine, also used to treat depression; and tasimelteon [35].

7.2.6. Sleeping drugs of the new generation

These are OX2R and OX1R orexin rec. antagonists. Orexins have functions in the body that regulate appetite and wakefulness. Drugs that block the aforementioned receptors include suvorexant, lemborexant and daridorexant. Studies by Herring et al. [36] have shown the beneficial effects of suvorexant on the quality of sleep and the shortening of the transition time from the waking state to sleep. They may be an alternative to benzodiazepines, which cause many side effects. Despite the approval of these drugs by the FDA (U.S. Food and Drug Administration), in 2014 suvorexant, 2019 lemborexant and 2022 daridorexant, respectively, they have not yet been approved for marketing in Poland [33,37].

7.3. Herbs

Currently, there is a lack of authoritative research on the effectiveness of herbs in combating insomnia. To date, studies have shown rather mediocre improvements after their use. However, due to the subjective feeling of an increase in sleep quality, patients still readily turn to these specifics. Among the most commonly used are valerian root (valerian), lemon balm, common chamomile and hops. Valerian and lemon balm exhibit agonist effects on the GABA-ergic system, hops contains bitter compounds that have a sleep-inducing effect, and common chamomile exhibits agonist effects to benzodiazepine receptors [33].

7.4. Over-the-counter (OTC) medications

These include the previously discussed immediate-release melatonin and herbs, doxylamine and diphenhydramine [9].

8. Summary

In summary, insomnia is an important health problem that should not be underestimated, as if left untreated it leads to many disorders and diseases. It is a pathological condition that should be treated, as only in rare cases does it resolve spontaneously. A review of the research and literature shows that cognitive-behavioral therapy techniques are effective in the treatment of insomnia, and medications, due to their many side effects, should be used on a short-term basis.

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