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SAFE SLEEP: A MODERN LOOK AT INSOMNIA MEDICATIONS FOR SENIORS

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ABSTRACT

Background. Insomnia is a common and burdensome condition in older adults, marked by difficulty falling or staying asleep, early awakenings, and non-restorative sleep. Its prevalence increases with age and is linked to cognitive decline, depression, falls, and reduced quality of life. Physiological aging and polypharmacy complicate treatment in this group.
Aim. This paper reviews current pharmacological options for managing insomnia in the geriatric population, focusing on efficacy, safety, and adherence to clinical guidelines.
Materials and Methods. A literature review was conducted using PubMed, Scopus, and Google Scholar. Sources included randomized controlled trials, systematic reviews, meta-analyses, observational studies, and guidelines published up to 2024. Keywords included "insomnia," "elderly," "pharmacological treatment," "hypnotics," and related terms. Only studies involving patients aged 65+ were analyzed. Data on efficacy, safety, dosing, duration, and guideline recommendations were extracted.
Analysis of Literature. Current guidelines prioritize non-pharmacological treatments. Pharmacotherapy may be considered when behavioral methods are ineffective or unavailable. Prolonged-release melatonin and low-dose doxepin offer the best safety-efficacy balance. Orexin receptor antagonists show promise but are not yet available in Poland. Sedating antidepressants like trazodone, mirtazapine, and mianserin may be cautiously used in patients with comorbid depression or anxiety. Z-drugs and benzodiazepines, despite their efficacy, pose significant risks such as falls, dependence, and cognitive decline. Antihistamines and antipsychotics are generally not recommended due to unfavorable safety profiles.
Conclusion. Pharmacological treatment of insomnia in older adults should be cautious and individualized. Non-drug therapies remain the first-line option. When medications are necessary, the safest agents should be used at the lowest effective doses for the shortest duration. Ongoing research is essential to expand safe therapeutic options.

KEYWORDS

Insomnia, Geriatric Population, Pharmacological Treatment, Hypnotics, Drug Safety, Sleep Quality

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Introduction.

Insomnia is a non-organic sleep disorder characterized by inadequate quantity or quality of sleep, manifesting as difficulty initiating sleep, maintaining sleep, early morning awakenings, or a subjective sense of unrefreshing rest.[1] This condition significantly impairs quality of life, with affected individuals often reporting daytime fatigue, impaired memory and concentration, and increased irritability.[2] Advancing age is a well-established risk factor for insomnia[1], with prevalence rates estimated to affect up to 50% of the elderly population.[3]

Sleep disturbances in older adults are associated with numerous adverse health outcomes, including cognitive decline, the onset or worsening of depressive symptoms, an elevated risk of falls and fractures, and the exacerbation of comorbid chronic illnesses.[4,5]

Aim

The objective of this paper is to review current pharmacological treatment strategies for insomnia in the geriatric population, with particular focus on their efficacy, safety profiles, and alignment with contemporary clinical guidelines.

Materials and Methods

A comprehensive literature review was conducted to analyze current pharmacological treatments for insomnia in the geriatric population. Scientific databases including PubMed, Scopus, and Google Scholar were searched for articles published up to 2024. The search terms used included combinations of keywords such as

"insomnia," "geriatric," "elderly," "pharmacological treatment," "hypnotics," "melatonin," "benzodiazepines," "sedative antidepressants," "antihistamines," and "antipsychotics."

Inclusion criteria comprised randomized controlled trials (RCTs), meta-analyses, systematic reviews, clinical guidelines, and observational studies focusing on adults aged 65 years and older with insomnia. Articles addressing efficacy, safety, tolerability, and guideline recommendations of pharmacological agents in this age group were prioritized. Publications not available in English or Polish were excluded.

Data extraction included drug types, dosage regimens, duration of therapy, therapeutic outcomes, adverse effects, and guideline recommendations. Special attention was given to medications commonly used or recommended in clinical practice for elderly patients, such as melatonin and its receptor agonists, benzodiazepines, non-benzodiazepine hypnotics, sedative antidepressants, antihistamines, antipsychotics, and orexin receptor antagonists.

The gathered evidence was synthesized to evaluate the balance between therapeutic benefits and risks of pharmacotherapy for insomnia in elderly patients, with a focus on adherence to established clinical guidelines and the principle of cautious drug use in geriatric medicine.

Analysis of Literature

Characteristics of Insomnia in the Elderly

With advancing age, physiological changes in both the structure and quality of sleep are commonly observed. Older adults frequently experience difficulties with both sleep initiation and maintenance. The proportion of deep sleep (N3 stage) decreases, while the REM phase is often shortened or fragmented. Circadian rhythm disruptions are also prevalent, and total sleep duration is typically reduced. These changes are partly attributed to diminished melatonin secretion from the pineal gland.[4, 6, 7]

The high prevalence of chronic comorbidities in the geriatric population significantly contributes to sleep disturbances. Cardiovascular diseases (e.g., hypertension, heart failure), respiratory disorders (e.g., chronic obstructive pulmonary disease), neurological conditions (e.g., dementia, Parkinson's disease), and psychiatric disorders (e.g., depression, anxiety) can all negatively impact sleep efficiency.[4, 8, 9]

Pharmacotherapy is another relevant factor. Certain medications commonly used in this age group—such as glucocorticosteroids, beta-blockers, second-generation antihistamines, and statins—may adversely affect sleep architecture or hinder sleep maintenance.[8, 9, 10, 11]

General Principles of Insomnia Treatment in Geriatrics

Current clinical guidelines emphasize two primary strategies for managing insomnia in the geriatric population: non-pharmacological interventions and the treatment of underlying somatic conditions that may impair sleep quality.[8] Non-pharmacological approaches include cognitive behavioral therapy for insomnia (CBT-I), along with patient education on sleep hygiene, regular physical activity, and appropriate dietary habits.[8, 9]

Equally important is the comprehensive and effective management of comorbid conditions, which not only improves the overall health status of patients but also contributes to the alleviation of symptoms that interfere with sleep.[4, 9]

Pharmacological treatment serves as an adjunctive option when non-pharmacological strategies are insufficient or cannot be implemented.[12] Drug selection should be guided by the individual clinical profile of the patient, taking into account contraindications and potential drug–drug interactions.[8] In line with geriatric prescribing principles, the "start low, go slow" approach is recommended—initiating therapy at the lowest effective dose and titrating slowly to achieve the desired therapeutic outcome while minimizing adverse effects.[13]

Pharmacological Groups Used in the Treatment of Insomnia in the Elderly

Non-benzodiazepine Hypnotics (Z-drugs)

Non-benzodiazepine hypnotics, commonly referred to as "Z-drugs," include zolpidem, zopiclone, zaleplon, and eszopiclone. These agents exert their effects by selectively binding to the α1 subunit of the GABA-A receptor, thereby enhancing GABAergic neurotransmission and inducing sedation. In contrast to classical benzodiazepines, Z-drugs demonstrate minimal anxiolytic, amnestic, and anticonvulsant properties.[9]

The table below summarizes the standard dosages and duration of action for each agent:[8,14]

Drug	Dosage	Duration of Action
Zolpidem	5-10 mg	Approximately 6 hours
Zopiclone	3,75-7,5 mg	6-8 hours
Zaleplon	10 mg	2-4 hours
Eszopiclone	1–3 mg (max. 2 mg in older adults)	6-9 hours

Due to their rapid onset of action (15–30 minutes), these medications should be administered immediately before bedtime.

Z-drugs are effective in improving sleep quality, reducing sleep latency, decreasing nocturnal awakenings, and increasing total sleep time.[9] Despite their greater receptor selectivity compared to benzodiazepines, long-term use of Z-drugs carries a risk of tolerance, dependence, and withdrawal symptoms. Consequently, their use should be limited to short-term therapy, typically not exceeding 2–4 weeks.[15]

In the elderly, the risk of adverse effects is heightened and includes impaired balance, dizziness, headaches, morning drowsiness, falls, and cognitive disturbances such as memory impairment. Special caution is required in patients with hepatic impairment, as dose adjustments may be necessary. Numerous potential drug–drug interactions should also be considered.[8]

According to the 2023 update of the AGS Beers Criteria, published by the American Geriatrics Society, the use of non-benzodiazepine hypnotics is not recommended in older adults due to their unfavorable safety profile in this population.[16]

Benzodiazepines

Benzodiazepines exert their pharmacological effects by modulating GABA-A receptors in the central nervous system, leading to decreased neuronal excitability.[17] This drug class includes agents such as diazepam, lorazepam, alprazolam, and midazolam.[18] In addition to their hypnotic properties, benzodiazepines possess anxiolytic, muscle relaxant, and amnestic effects.[17]

Although benzodiazepines have historically been used in the treatment of insomnia, they are not recommended for use in the geriatric population due to their unfavorable safety profile.[16,17] Older adults exhibit altered pharmacokinetics, including reduced hepatic metabolism and increased pharmacodynamic sensitivity to these agents.[16] These age-related changes significantly elevate the risk of serious adverse events, such as falls, fractures, impaired cognitive function, as well as the development of physical and psychological dependence.[19]

Furthermore, epidemiological studies have demonstrated an association between long-term benzodiazepine use and an increased risk of developing dementia, including Alzheimer's disease.[20] Consequently, leading clinical guidelines, including the AGS Beers Criteria, advise against the use of benzodiazepines in older adults.[16,17]

Sedative Antidepressants

Sedative antidepressants are commonly used in the treatment of insomnia, particularly in patients with comorbid depressive or anxiety disorders.[8]

Special attention should be given to doxepin—a tricyclic antidepressant with additional antihistaminic and α1-adrenergic blocking properties.[21] It is currently the only antidepressant approved by the U.S. Food and Drug Administration (FDA) specifically for the treatment of insomnia.[9] Clinical studies have demonstrated that low doses of doxepin (3–6 mg) exert a selective antagonistic effect on H_1 receptors, resulting in improved sleep quality in older adults without significant next-day residual effects.[8,9,17,22] This favorable profile makes doxepin a unique and recommended option for the long-term management of insomnia in the geriatric population.[23] However, it should be noted that in Poland, the lowest available dose of doxepin is 10 mg, which may limit its use at the optimal therapeutic range for insomnia.[8]

Another agent frequently used in clinical practice is trazodone, a triazolopyridine derivative with anxiolytic, antidepressant, and sedative properties.[24] The recommended dose for insomnia ranges from 25 to 150 mg, administered at bedtime. In elderly patients, trazodone can be considered with caution, but its use is associated with risks such as morning sedation, orthostatic hypotension, cardiac arrhythmias, and, rarely, priapism.[8]

Other antidepressants employed in the treatment of insomnia include mirtazapine and mianserin, both classified as noradrenergic and specific serotonergic antidepressants (NaSSA).[25] These agents may be beneficial in cases of insomnia co-occurring with depression but are not recommended in patients without depressive symptoms.[9] Due to potential adverse effects—including excessive daytime sleepiness, QT interval prolongation, hypotension, and weight gain—close clinical monitoring is necessary during treatment with these medications.[8,26]

Antihistamines and Antipsychotics

First-generation antihistamines are frequently used as over-the-counter sleep aids. Agents such as diphenhydramine and doxylamine are available without prescription in Poland.[8] However, due to their pronounced anticholinergic properties and associated adverse effects—such as daytime sedation, dizziness, cognitive impairment, and increased risk of falls—their use in the elderly is strongly discouraged. Current clinical guidelines recommend avoiding this class of drugs or limiting their use to the lowest effective doses for the shortest possible duration.[8,16,27]

Some atypical antipsychotics, most notably quetiapine, are also prescribed off-label for the treatment of insomnia in older adults.[8] At low doses (25–100 mg), quetiapine exhibits sedative effects due to its antagonism of histamine H_1 and serotonin 5-HT_2A receptors.[28] Nevertheless, the use of quetiapine for primary insomnia is not recommended and should be restricted to patients with clearly defined comorbid psychiatric conditions—such as schizophrenia, mood disorders, or Parkinson's disease–related psychosis.[16,28] This limitation stems from the elevated risk of serious adverse effects in the geriatric population, including metabolic disturbances, extrapyramidal symptoms, cardiovascular complications, and increased mortality.[28]

Melatonin and Melatonin Receptor Agonists

A natural decline in endogenous melatonin production is observed with advancing age, which may contribute to disturbances in the sleep–wake cycle and, consequently, insomnia in older adults.[6] Melatonin supplementation in geriatric patients (over 55 years of age) is considered a safe and effective therapeutic option for insomnia related to circadian rhythm disorders. It is not associated with adverse effects commonly seen with other pharmacological agents and does not induce tolerance or dependence. The recommended regimen includes the administration of 2 mg of prolonged-release melatonin approximately 60 minutes before bedtime. Supplementation should be continued for up to 13 weeks and combined with non-pharmacological interventions.[8]

Another promising therapeutic approach in this patient population involves the use of selective melatonin receptor agonists—specifically those targeting the MT_1 and MT_2 receptors—such as ramelteon. Similar to melatonin, ramelteon has a favorable safety profile and lacks addictive potential.[9] However, ramelteon is currently not approved for use in Europe and is not available in Poland.[8]

Orexin Receptor Antagonists (DORA)

A novel class of hypnotic agents, orexin receptor antagonists (dual orexin receptor antagonists, DORA), exert their effect by selectively blocking the OX1R and OX2R receptors. This blockade inhibits orexin signaling in the hypothalamus, a neuropeptide system essential for maintaining wakefulness.[29]

The first DORA approved by the FDA for the treatment of insomnia was suvorexant. Clinical studies have demonstrated its efficacy in elderly patients, including prolongation of total sleep time and reduction of sleep onset latency.[9] Suvorexant has generally been well tolerated; the most commonly reported adverse effect was increased daytime somnolence, with no other significant side effects observed.[17] Moreover, a meta-analysis by Xu et al. suggested a potential role for suvorexant in reducing the incidence of delirium in the elderly population.[30] Nevertheless, the authors highlighted the need for further research to confirm the long-term efficacy and safety profile of DORA drugs.[29]

Currently, suvorexant is not available in Poland and is not incorporated into the national guidelines for pharmacological treatment of insomnia in geriatric patients.[8,31]

Conclusions

Insomnia represents a significant clinical challenge in the elderly population due to its high prevalence and the wide range of associated adverse health outcomes, including cognitive decline, increased risk of falls, and diminished quality of life. Aging is accompanied by physiological alterations in sleep architecture and heightened vulnerability to factors that disrupt circadian rhythms. Management of insomnia in older adults necessitates a tailored approach that addresses both secondary causes and the limited tolerance to pharmacological interventions commonly observed in this group.

The foundation of treatment should be non-pharmacological strategies, with cognitive behavioral therapy for insomnia (CBT-I) as the first-line intervention, alongside optimization of sleep hygiene and effective management of comorbid conditions. Pharmacotherapy should be reserved for cases where non-pharmacological measures prove insufficient or infeasible and should be administered with caution, for the shortest duration possible, following the "start low, go slow" principle to minimize adverse effects.

Among pharmacological options, prolonged-release melatonin and low-dose doxepin currently demonstrate the most favorable safety profiles in the geriatric population. Orexin receptor antagonists (DORAs) also show promise; however, their limited availability in Poland restricts their clinical use. In selected cases, sedative antidepressants such as trazodone, mianserin, or mirtazapine may be appropriate, particularly for patients with concomitant depression or anxiety disorders. These agents require careful monitoring due to potential side effects, including daytime sedation, orthostatic hypotension, and cardiac arrhythmias.

First-generation antihistamines, despite their easy accessibility, are not recommended for insomnia treatment in elderly patients because of their anticholinergic burden, risk of cognitive impairment, and potential for QT interval prolongation. Similarly, the use of antipsychotics for sleep induction should be confined to clearly defined indications, such as delirium, owing to their unfavorable safety profile and risk of numerous adverse effects.

Benzodiazepines and non-benzodiazepine hypnotics (Z-drugs) should be considered last-resort options due to their association with balance disorders, increased fall risk, cognitive impairment, and potential for dependence.

Given the growing elderly population, further research is essential to better define the efficacy and safety of hypnotic agents in this demographic and to promote the development and dissemination of effective non-pharmacological therapies.

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