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### Treatment of insomnia in elderly patients

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Review article

#### Abstract

**Introduction**: Insomnia is one of the most common health conditions amongst the elderly population. It causes suffering and numerous health problems for those affected.

**Objectives**: To review published results of common non-pharmacological and pharmacological interventions of insomnia and to discuss their application in older patient groups.

**Methods**: We conducted a systematic literature review for the topic non-pharmacological treatment of Insomnia in Elderly and non-systematic review on the topic of pharmacological treatment using the electronic databases PubMed, PsycInfo, Google Scholar and Web of Knowledge. Only published articles and reviews were included.

Results: Sleep education can support the onset of sleep. As a simple and side-effect-free measure, sleep education should be offered to all elderly individuals with sleep-onset insomnia including those living in retirement homes. Stimulus control means that the bed or the bedroom should only be visited, if there is sufficient tiredness, or left, when tiredness is not sufficient, which is very challenging and sometimes impossible due to the decreasing mobility of the elderly, especially under treatment with hypnotics. Sleep restriction can be conducted in a moderate way, reducing the time spent in bed every week for 30 minutes. Light therapy supports the regulation of the circadian body rhythm by exposing the patients to bright artificial light during the day. As a simple measure with only a few side effects, it is suitable when treating elderly individuals in institutions. Digital therapies are an emerging trend in the treatment of sleep disorders and require further empirical investigation of their effectiveness in the treatment of insomnia in the elderly. Non-pharmacological therapy should be the first-line therapy according to guidelines. Prescribing of sleep medication should take into account the period of time until the maximum effective level is reached, the half-life of the preparation, the binding behaviour to receptors and the metabolism of the preparation, which is especially relevant for elderly populations due to polypharmacy.

**Conclusion and implications**: A modified, short cognitive behavioural therapy for insomnia combined with light therapy is the treatment of choice for elderly patients. However, a short-term pharmacological therapy is recommended as a temporary solution to immediately reduce high levels of distress. It is suggested to integrate both therapeutic approaches into a comprehensive therapeutic concept for insomnia in elderly people.

Key words: Insomnia, cognitive behavioural therapy for insomnia, CBT-I, Hypnotics, light therapy, elderly

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## Introduction

In the general population insomnia is one of the most common health disorders. Studies show a prevalence of 12 to 40% (Roth et al., 2011). Depending on the sample population, the prevalence increases with age to 20 to 50% (Alessi & Vitiello, 2015, Patel et al. 2018). The incidence of insomnia in the elderly is reported to be about 5% (Geiger et al., 2015). Insomnia is characterised by difficulties falling asleep, sleeping through or waking up early on most days of the week for at least a month, AASM, 2014).

Even at an advanced age, insomnia causes fatigue, drowsiness, impaired attention as well as cognitive and functional impairments (Bloom et al., 2009) to an extent that varies from individual to individual. Moreover, insomnia in the elderly is an independent risk factor for falling (Stone, Ensrud & Ancoli-Israel, 2008). Insomnia is also often associated with other health problems in older people. Sleep disturbances have been linked to increased morbidity and mortality and alteration of biomarkers for diabetes and cardiovascular disease risk (Caroll et al. 2015). Especially in older women, habitual sleep duration predicts the future risk for cognitive impairments including dementia, independent of vascular risk factors. (Chen 2015).

Insomnia disorder can occur as a single or comorbid disease and the basic principles of treatment are the same (Riemann et al., 2017).

This literature review aims to highlight different forms of insomnia treatment and their outcomes and the implications to consider when treating elderly persons with chronic insomnia.

### **Methods**

For the non-pharmacological treatment of insomnia in elderly we conducted a systematic literature review using the electronic databases PubMed, PsycInfo, Google Scholar and Web of Knowledge. Studies were identified by the combination of the keywords: "insomnia", "behavioural therapy", "sleep", "age", "geriatrics" and "non-pharmacological treatment". We only included original research or reviewed articles from 2013 to 2019.

The total number of all identified studies was N=723. Research articles were discarded if the title and abstract were unrelated to the subject of this systematic review and further analysed when the

articles were written in German or English. Twenty three of the identified articles met the inclusion criteria on title and abstract level. They were obtained in full-text and analysed thoroughly. Studies were further excluded either on the basis of date or if the focus on insomnia was insufficient, if there were confusions with pharmacological therapies or other age-related conditions such as dementia were present. In addition, the sample should foremost consist of older populations. The final number of reviewed publications that met the inclusion criteria on text-level is N=10.

For the pharmacological treatment of insomnia we included some relevant papers without systematic literature research using the electronic databases PubMed, Google Scholar and Web of Knowledge. Studies were identified by the combination of the keywords "insomnia", "behavioural therapy", "hypnotics", "light therapy" and "geriatrics".

Research articles were discarded if title and abstract were unrelated to the subject of this review and further analysed when the articles were written in German or English. The remaining articles were obtained in full-text and analysed thoroughly. Articles that fit the aforementioned inclusion criteria were included in the analysis.

In view of the different ways of treating insomnia, also taking certain considerations into account when treating the older populations, this review was divided between pharmacological and non-pharmacological approaches.

#### Results

## Non-pharmacological treatment of insomnia

The non-pharmacological therapy of insomnia (cognitive behavioural therapy for insomnia-CBT-I) is evidence-based non-pharmacological therapy of insomnia in young and old populations (Riemann et al. 2017, AASM 2014) and covers different behavioural interventions. All of these non-pharmacological therapy methods improve sleep (effect approx. 40%) and the noctumal awake phases (effect approx. 50%). The total sleep time is less strongly influenced (increase of about 5%) (Geiger-Brown et al., 2015). These effects are also more pronounced than in the case of a sole pharmacotherapy (Sivertsen et al., 2006). Many of these non-pharmacological therapies are used in combination.

## Sleep hygiene (Sleep education)

Sleep hygiene or sleep education is the most basic and simplest behavioural therapeutic measure and can be applied to all sleep disorders and settings including clinics, home care, protected homes or hospital settings (Stepanski and Wyatt, 2003). Sleep education includes behaviours that promote the onset of sleep.

Sleep education measures include:

- after lunch, do not drink caffeinated beverages (coffee, black tea, cola) anymore
- avoiding alcohol as far as possible and never use it as a sleeping aid.
- no heavy meals in the evening
- regular physical activity
- gradual reduction of mental and physical arousal before going to bed
- introduce a personal sleep ritual
- do not stay in bed longer than necessaryno longer than 30 minutes
- provide a pleasant atmosphere in the bedroom (quiet, darkened)
- do not look at the alarm clock or the wristwatch at night
- provide a quiet and well-tempered environment
- do not drink large amounts of water or tea at bedtime

The daily routine should also be structured including a consistent time for getting up and going to bed. Sleep disturbed people often have inconstant rhythms with considerable differences from day to day (Cheek, Shaver & Lentz, 2004). Elderly people should not go too early to bed for sleeping, because getting into bed too early can lead to early awakening between 3 and 5 AM.

Premature awakening in the early morning is the most prominent problem reported by the elderly regarding bad sleep quality.

Particularly in facilities and hospitals, it should be ensured that patients/residents staying in multiple-bed rooms do not interfere directly with each other during the night's rest by watching TV for long periods, listening to music, restlessness or snoring, and indirectly by the heightened need for care.

However, a disregard for sleep hygiene is rarely the sole cause of disturbed sleep. It is therefore not surprising that studies show that sleep hygiene alone is often not sufficient to permanently im-

prove pronounced sleep disorders (Bloom et al., 2009).

Nevertheless, sleep hygiene or sleep education measures should be used as a simple and sideeffect-free basic measure for any form of sleep disorder in elderly people.

### Stimulus control

Stimulus control is considered to be a very effective behavioural treatment method for insomnia. Through operant learning, the ability to fall asleep and to sleep through the night is promoted. Through stimulus control, the day-night rhythm is stabilised and the importance of the bed and the bedroom as a sleeping environment is strengthened (Morin et al., 2006).

The bed should only be visited if tiredness is present. Tiredness indicates that the sleep pressure is sufficiently high. Going to bed without feeling tired leads to frustration, as sleep cannot be forced.

If no sleep occurs about 20 minutes after going to bed, the person should get up out of bed. The duration of 20 minutes should be felt and not "checked" by looking at a clock. A watch should be positioned in the bedroom so that from the bed no direct view of the dial is possible. After leaving the bed, it is important not to carry out any stimulating activities. The bed should not be visited again until there is drowsiness and immediate sleep can be expected. If no sleep occurs again, the bed is left again and this behavioural cycle is repeated.

The time of getting up in the morning should be fixed and should be adhered to regardless of the amount of sleep achieved at night.

This behaviour stabilises the circadian rhythm and sustainably improves sleep efficiency.

Rules of stimulus control (Riemann et al., 2016)

- The bed is only used for sleeping, the only exception is sexual activity.
- Only go to bed when you are drowsy and expect to fall asleep immediately.
- If no sleep occurs after about 15 minutes, the bed should be left again.
- Non-stimulating activities can be performed after leaving the bed
- The bed is only visited again when there is drowsiness and immediate falling asleep is to be expected.
- If sleep does not return after about 15 minutes, the bed should be left again.

- This cycle is repeated as often as necessary.
- The time to get up in the morning is determined and adhered to.
- Sleep during the day should be avoided

Stimulus control has also been shown to be very effective in the elderly (Cochen et al., 2009), but often meets its limits in this patient group. For example, the requirement to leave the bed is perceived as too annoying and is therefore often omitted. Similarly, immobility, pain or muscle weakness often make it impossible to leave the bed despite the patient's willingness to do so.

Due to these practical problems, the method has been modified with the counter-control method that also allows less mobile patients to apply these principles (Spira et al., 2016). Instead of getting up, patients are encouraged to free themselves mentally from the compulsion to want to sleep and, in case of insomnia, to sit up and read, listen to music or watch TV until they are expected to immediately fall asleep again. This modified procedure has proven to be effective, but did not achieve the effectiveness of the actual stimulus control. Therefore, this modification should only be applied to patients who are unable to get out of bed especially for the residents in retirement homes.

### **Sleep Restriction**

According to the rules of Sleep Restriction, the time spent in bed should be equal to the average estimated sleep time (Spielmann 1987). Thus, the sleep pressure increases within the restricted time in bed which leads to a better quality of sleep. But in reality, the rigid and for younger people, very effective method cannot be used in such a rigid format for elderly residents in retirement homes.

Therefore, the method of sleep compression can be implemented so that the total time spent in bed is reduced on a weekly basis for 20-30 minutes. Within several weeks, the time in bed will almost reach the average sleep time with a sleep efficiency of over 85% (Kenneth et al. 1988).

### Light therapy

The brightness of the environment plays a fundamental role in the regulation of the circadian rhythm. Therefore, light plays an important role in the treatment of sleep disorders (McCurry et al., 2011). Light plays an important role in stabilising the day-night rhythm. Bright daylight is one of the most important timers. Sufficient exposure to light

during the day increases the amplitude of the circadian rhythm and stabilises the phase. The time and intensity of light exposure play an important role (Figueiro, 2017; Richter et al. 2014).

Already dark rooms in the afternoon, no light exposure during the day, brightly lit rooms for care at night, bright illumination when going to the toilet, the nocturnal use of smartphones or watching television at night are negative examples of how sleep can be disturbed by light exposure. Recognising this and applying this knowledge in everyday life is a sustainable measure to improve the sleep of older individuals.

Although the results of therapy studies on the effect of light therapy in people with Alzheimer's dementia are predominantly contradictory for methodological reasons, overall positive effects tend to emerge. In one study, for example, people with Alzheimer's disease experienced an improvement of seasonal mood swings under light therapy (Hickman et al., 2007). Therefore, light therapy is a therapeutic option for people with dementia and circadian rhythm disorders, especially due to its low side-effect rate (Richter, Myllymaeki et al., 2014).

The efficacy of light therapy is well documented for exposure of 10,000 lux for half an hour or 2,500 lux for two hours (Schneider, Härter & Schorr, 2017). Light therapy can be applied in various forms. The decisive factors are the intensity, timing and duration of application. The simplest form of light therapy is to go outdoors.

If an artificial light source is used, the patient should not sit more than 50-80 cm away from it. It is vital that the light falls on the retina. Therefore, the eyes must be open and must not be covered by sunglasses for example. However, the patient should not look directly into the light source.

Alternatively, a light box can be used, which is set approximately one metre away from the patient, or lights can be installed in the ceiling. It is better to integrate lighting systems into a communal room. This allows light therapy to be applied simultaneously with other activities. This sustainably promotes compliance (Bloom et al., 2009).

Using a combination of methods including Elements of CBT-I, Light Therapy and physical activity can also improve the depressive mood in elderly individuals with chronic insomnia and depression (Richter et al. 2018)

### Digital treatment of Insomnia

In the course of the digitalisation and virtualisation of therapeutic measures in the field of insomnia through virtual coaches (Peter et al. 2019), online treatment and online-guided interventions, the effectiveness of such measures must also be examined here. A systematic literature review in which numerous studies on the insomnia treatment of older persons by new communication technologies were examined shows that sleep quality can be improved (Salvemini et al., 2019). This is also important because the availability of behavioural intervention methods for the elderly is still too limited.

#### Medications for the treatment of Insomnia

In the elderly, benzodiazepines and benzodiazepin receptor agonists are equally effective for short-term treatment.

Almorexant as an dual orexin receptor and Suvorexant as an orexin receptor antagonist and antagonist approved for treating insomnia at doses of 10-20 mg which generally improves sleep maintenance and onset over 3 months are both well-tolerated in elderly patients with insomnia (Herring et al. 2017, Roth et al.2017).

The range of medications for the treatment of insomnia is broad. The clinical decision for a particular drug depends on the type of treatment:

- from the period of time until the maximum effective level is reached
- the half-life of the preparation
- the binding behaviour of the preparation to receptors
- the metabolism of the preparation

The time it takes to reach the maximum effective level determines when a medication should be taken and whether it can be used as a sleeping pill or as a sleeping through pill. If, for example, the maximum effect level is reached after more than two hours, such a preparation is less suitable as a sleeping pill.

The half-life of a drug, on the other hand, allows the duration of effectiveness to be estimated and possible transition phenomena to be anticipated. Such relationships between pharmacokinetics and pharmacodynamics are well established for benzodiazepines and Z-substances. For other substances, the relationship is more complex. For doxepin, for example, the maximum clinical effect occurs sev-

eral hours after reaching the maximum serum level (Hajak, 2001).

The binding profile of the hypnotics to the various receptors is responsible for their effect, but also for their side effects. *Table 1* shows a selection of substances with sedative properties and their effect profile on the various receptors.

Knowledge of receptor occupation is important for these preparations, as it provides information on the expected side effect profile. Binding to benzodiazepine receptors shows a dose-response relationship with effects such as sedation, but also dizziness, forgetfulness, ataxia and dependence (Bent, Padula, Moore, Patterson & Mehling, 2006). The undesired effects are less pronounced with the so-called Z-substances, but are also present.

Anticholinergic effects are xerostomia, dizziness, constipation, accommodation disorders and urinary retention. The drugs that show these adverse effects include tricyclic antidepressants, but also the over-the-counter drugs diphenhydramine and doxylamine. It is interesting in this context that doxepin in a low dosage of 3 mg is approved as a hypnotic in the USA and shows practically no anticholinergic effects (Krystal et al., 2010).

A blockade of the histamine H1 receptor causes sedation. Examples of this effect are the preparations doxepin, amitriptyline, mirtazapine, quetiapine, diphenhydramine blocking have among others amitriptyline, doxepin, trazodone, quetiapine, olanzapine and risperidone. The atypical neuroleptics risperidone, olanzapine and quetiapine have a dose-dependent blocking effect on the dopamine receptor. Clinically, this blockade causes- albeit rarely - extrapyramidal movement disorders such as tardive dyskinesia or akathisia. All of these adverse effects are dose-dependent. Therefore, it is recommended to start with the lowest possible dose and slowly increase it while monitoring the effects and side effects (Reinbold & Assion, 2009).

The type of metabolism of the respective substances is particularly relevant in the context of the polypharmacy of older people. High serum levels can be produced and undesirable effects can occur as a result of the over division of degradation pathways between different substances.

Randomised and placebo-controlled studies of hypnotics are essential to assess the efficacy and potency of medications. In these studies - discrepant to the clinical reality of demand - predominantly middle-aged people and rarely seniors (65+) were examined. In summary, the changes in sleep latency and nocturnal wakefulness obtained by means of self-assessment (sleep diary) or measurement in the sleep laboratory by hypnotics are in the range of 10 to 30 minutes. These values are sobering. However, it must always be taken into account that the significance of such an improvement can already mean a relevant improvement for the individual patient, which increases his quality of life. Therefore, the therapeutic effect of hypnotic therapy cannot be assessed solely on the basis of objective parameters (Kaufmann, Spira, Alexan-

der, Rutkow & Mojtabai, 2016). Herbal preparations also show positive effects when evaluated by the patient, even if no significant differences can be demonstrated with objective procedures compared to a placebo (Bent et al., 2006; Glass, Sproule, Herrmann, Streiner & Busto, 2005).

Antihistamines, antipsychotics and antidepressant medication which can have anticholinergic side effects should be carefully considered. Low doses of Doxepin in doses from 3 to 6 mg per day could be a feasible treatment option (Fraase et al. 2019, Hertenstein et al. 2017)

**Table 1**Drug groups and their effects on individual sleep parameters

Drug group	SL	TST	REM	WASO	N1/N2	N3	OSAS	PLMS
BZD	$\downarrow$	<b>↑</b>	$\downarrow$	$\downarrow$	<b>↑</b>	$\downarrow$	1	
Z-Substances	$\downarrow$	<b>↑</b>		$\downarrow$				
Antihistamines	$\downarrow$		$\downarrow$					
Melatonin	$\downarrow$			$\downarrow$				
Alcohol	$\downarrow$		$\downarrow$	<b>↑</b>		1	1	

**Table 2**Antidepressants and their effects on individual sleep parameters (according to Riemann et al. 2019)

Drug group	Sleep contiunity	Slow wave sleep	REM sleep
TCA	<b>↑</b>	$\uparrow$ $\longleftrightarrow$	$\downarrow$
SSRI	$\downarrow$	?	$\downarrow$
Trimipramin	<b>↑</b>	$\longleftrightarrow$	
Trazodon	<b>↑</b>	<b>↑</b>	<b>←</b>
Mirtazapin	<b>↑</b>	$\iff$	$\longleftrightarrow$

SL: Sleep latency, TST: Total Sleep Time, REM: paradox sleep (with rapid eye movements), WASO: Wake Time After Sleep Onset, N1/N2: Light sleep, N3: slow wave sleep, OSAS: obstructive sleep apnea syndrome, PLMS: periodic limb movements of sleep, BZD: benzodiazepines, Z substances: Non-benzodiazepine agonists, TCA: tricyclic antidepressants, SSRI: selective serotonin reuptake inhibitors (antidepressants), ↑: increased/amplified, \preduced. \leftarrow: no changes

When treating Insomnia with medication, seven essential points should be considered (Reinbold & Assion, 2009).

- prescribe the lowest effective dose
- intermittent use (2-4x per week)
- use for a short period of time (3-4 weeks)
- gradual termination of therapy to avoid rebound insomnia
- prescription of drugs with short half-lives
- proof the interaction with other drugs
- be aware of the anticholinergic effects

The selection of the medication should be based on the presence and the extent of the impaired daily well-being, and also possible effects on various sleep parameters as listed in *Table 1* should be taken into account. Most of the drugs presented in *Table 2* are off-label, but still used on a daily basis. The expected effect should improve sleep and well-being during the day. It is particularly important to agree on a time-limited and intermittent prescription with the patient at an early stage so that pharmacotherapy can be discontinued after the treatment phase (Reinbold & Assion, 2009). Such an agreement made in advance before the start of therapy reduces the probability of long-term use and abuse.

The indication for drug treatment of insomnia is given when the disorder is severe and a treatment

period of two to four weeks is planned. The lowest possible dose should always be chosen.

The strength of the effect of the most frequently prescribed hypnotics - benzodiazepines and Z-substances - on subjective sleep quality is moderate. The assessment of the effects of benzodiazepines in elderly people is further complicated by the fact that the studies on their efficacy often included only a few patients, who were also selected by rigorous inclusion and exclusion criteria. There are no long-term studies on the efficacy of hypnotics in the elderly.

In light of the currently available data, it is still not possible to make a reliable estimate of how long pharmacological treatment of Insomnia is required. Nonetheless, the necessity of the continuation of therapy with hypnotics should always be discussed with the patient. If a slow reduction of the dose does not lead to a recurrence of the symptoms, a therapy with hypnotics that has been discontinued once should not be started again. However, if the initial symptoms reappear or the patient's quality of life deteriorates, a resumption of the therapy should be considered.

### Conclusion

In conclusion, the cognitive behavioural therapy for insomnia (CBT I) of Insomnia is also the intervention of choice for older people according to the guidelines (Riemann, Baum et al., 2017, Riemann, Baglionni et al. 2017, AASM 2014). However, the patient must be aware that the desired effect is not immediate when applying behavioural measures and that there are some limitations and obstacles for the implementation of stimulus control and sleep restriction in elderly individuals and residents in retirement homes. Stimulus control can be modified to allow the elderly and often multi-morbid patients to stay in their bed in a sitting position to avoid falling in the night. The sleep restriction may be modified into sleep compression. Light Therapy can complete the non-pharmacological measures. Pharmacological measures should be the second and last choice of treatment considering that their benefit in long-term use is very restricted and can lead to dependency, falling during the night and to a worsening of the cognition. They should only be used in the short term to reduce distress and should be integrated into an overall therapeutic concept. Anyway, because of their potential for tolerance and dependence especially in the elderly, they are only recommended for a treatment period up to four weeks. Low doses of sedating antidepressants are commonly prescribed for treating chronic insomnia and have shown promising results in clinical trials. Melatonin and ramelteon can be more efficacious in elderly patients. Antihistamines, antipsychotics and antidepressant medication can cause anticholinergic side effects and should be administrated carefully and in low doses.

# **Conflicts of interests**

Authors declare no conflict of interests.

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