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Advancing Sleep Health Worldwide

INTERNATIONAL SLEEP GUIDELINES

Recommendations for Diagnosis & Treatment

Endorsement of European guideline for the diagnosis and treatment of insomnia by the World Sleep Society

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The WSS International Sleep Medicine Guidelines Committee selects, reviews, and publishes guidelines for the prevention and treatment of sleep disorders. These guideline recommendations are written to be applicable to the practice of sleep medicine by the global sleep specialists that comprise WSS membership.

ABSTRACT

The European guideline for the diagnosis and treatment of insomnia (1) was developed by a task force of the European Sleep Research Society, which was composed of 27 experts with clinical experience on insomnia management from different European countries and the European Insomnia Network. The guideline focused on insomnia disorder as defined by ICD-10/ICSD-3. Its starting point was the previously published guideline by the German Sleep Society, which was revised and expanded based on a review of relevant meta-analyses of insomnia therapies published through June 2016. The scope of this guideline was to provide recommendations on the treatment of chronic insomnia disorder. This guideline was selected for review by the World Sleep Society (WSS) Insomnia Task Force and the WSS International Sleep Medicine Guidelines Committee. A task force of content experts from the WSS has reviewed this guideline specifically for its relevance and applicability to the practice of sleep medicine by sleep specialists that comprise its membership.

Endorsement of European guideline for the diagnosis and treatment of insomnia by the World Sleep Society

Task Force Members, Guidelines Committee Members, on behalf of the Governing Council of the World Sleep Society

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PII: S1389-9457(21)00040-X

DOI: https://doi.org/10.1016/j.sleep.2021.01.023

Reference: SLEEP 4734

To appear in: *Sleep Medicine*

Received Date: January 14, 2021

Accepted Date: January 15, 2021

Please cite this article as: Task Force Members Guidelines Committee Members on behalf of the Governing Council of the World Sleep Society, endorsement of European guideline for the diagnosis and treatment of insomnia by the World Sleep Society, Sleep Medicine, https://doi.org/10.1016/j.sleep.2021.01.023.

WSS INTERNATIONAL SLEEP MEDICINE GUIDELINES POSITION STATEMENT

TITLE

Endorsement of European guideline for the diagnosis and treatment of insomnia by the World Sleep Society

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Task Force Members, Guidelines Committee Members, on behalf of the Governing Council of the World Sleep Society

INTRODUCTION

The *European guideline for the diagnosis and treatment of insomnia* (1) was developed by a task force of the European Sleep Research Society, which was composed of 27 experts with clinical experience on insomnia management from different European countries and the European Insomnia Network. The guideline focused on insomnia disorder as defined by ICD-10/ICSD-3. Its starting point was the previously published guideline by the German Sleep Society, which was revised and expanded based on a review of relevant meta-analyses of insomnia therapies published through June 2016. The scope of this guideline was to provide recommendations on the treatment of chronic insomnia disorder.

This guideline was selected for review by the World Sleep Society (WSS) Insomnia Task Force and the WSS International Sleep Medicine Guidelines Committee. A task force of content experts from the WSS has reviewed this guideline specifically for its relevance and applicability to the practice of sleep medicine by sleep specialists that comprise its membership.

METHODS

Following review of the guideline from the Insomnia Task Force, the task force developed this position statement, which was submitted for review and comments to the WSS International Sleep Medicine Guidelines Committee and then to the WSS Governing Council.

This guideline used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system to grade the evidence and guide recommendations (2, 3).

The WSS Task Force made significant efforts to check the availability of management options described in the guideline within all geographic regions included in the WSS membership. However, if this information from a given geographic region was not accessible or available, this prevented the WSS from listing the specific geographic region in the Recommendations below.

RECOMMENDATIONS

Summary

Evaluation and diagnosis of insomnia

An essential step before initiating treatment of insomnia involves adequate evaluation and diagnosis. It should consist of a clinical interview to evaluate the presence of medical and psychiatric comorbidities, as well as other suspected sleep disorders, the use of sleep questionnaires and diaries, a physical exam and, if indicated, laboratory testing (strong recommendation, moderate to high-quality evidence). Actigraphy measurement is recommended in suspected cases of irregular sleep-wake or circadian rhythm disorders. Polysomnography is recommended when there is clinical suspicion of other sleep disorders (periodic limb movement disorders, sleep-related breathing disorders), in cases of treatment resistant insomnia, for occupational at-risk groups, and when substantial sleep state misperception is suspected (strong recommendation, high-quality evidence).

TREATMENT OF INSOMNIA

Cognitive-Behavioral Therapy for insomnia (CBT-I) is recommended as the first-line therapy for chronic insomnia disorder in adults of any age. This recommendation received the strongest level of endorsement (Strong recommendation, high-quality evidence). CBT-I is a multi-component intervention aimed at modifying maladaptive sleep habits, regulating sleep-wake schedules, and altering unhelpful thoughts and worries that contribute to perpetuate insomnia. It may include several of the following components: sleep hygiene education, behavioral sleep scheduling interventions such as sleep restriction and stimulus control procedures, cognitive restructuring therapy, and relaxation-based interventions. CBT-I is effective, produces durable sleep improvements (up to 24 months after therapy), and is well accepted by patients.

Side effects of CBT-I have not been thoroughly investigated, although some evidence suggests that sleep restriction, one component of CBT-I, may lead to transient daytime sleepiness/fatigue and may impair vigilance.

Pharmacological therapy is a recommended alternative option, only if CBT-I is not effective or not available. This broad class of therapies include the following substances: Benzodiazepines (BZD) and other GABA-A receptor agonists (e.g., zolpidem, eszopiclone, zopiclone), sedating antidepressants, orexin antagonists, antihistamines, antipsychotics, melatonin (MT) receptor agonists, and phytotherapeutic substances (e.g., valerian, medicinal cannabis). The extent of evidence supporting or against using these therapies varies considerably across substances.

WORLD SLEEP SOCIETY

Most hypnotics with indication for insomnia have been tested and approved for short-term use (< 4 weeks). Safety and efficacy of long-term studies (> 6-months of treatments), either placebo-controlled or open label, have been conducted with zolpidem, eszopiclone, MT receptor agonists, and doxepin for the treatment of chronic insomnia. Side effects have been reported, including hangover, nocturnal confusion, falls, rebound insomnia, tolerance and dependency. Of note these side effects may be aggravated by polypharmacy, especially in older individuals.

- BZD (e.g., nitrazepam, flurazepam) and GABA-A agonists (e.g., zolpidem, zopiclone) are effective in the short-term treatment of insomnia (≤ 4 weeks) (high-quality evidence). Those with shorter half-lives may have fewer side effects related to morning sedation, and should be preferred.

- Several antidepressants are used in the treatment of insomnia in doses smaller than those used for treating depression (e.g., amitriptyline, doxepin, mirtazapine, trazodone, trimipramine), but only two (e.g., doxepin, trazodone) have been investigated and found effective in the short-term treatment of insomnia, and at doses smaller than those used for treating depression. Contraindications have to be considered carefully (moderate-quality evidence).

- Although some studies have examined the long-term effects of some agents (eszopiclone, zolpidem SR, suvorexant, ramelton), there is not enough evidence to recommend long-term use of these agents for insomnia; in addition, there are concerns about possible side-effects/risks (strong recommendation, low-quality evidence). Low dose scheme or intermittent use is an alternative treatment regimen, although very few studies have evaluated such a treatment strategy. Such a strategy is suggested for GABA-A agonists (e.g., zolpidem, zopiclone)*.

- The use of antipsychotic agents is not recommended for the treatment of insomnia due to lack of evidence and concerns about potential side effects. This recommendation is particularly true for patients with insomnia and with no evidence of any comorbid psychiatric disorder (strong recommendation, very low-quality evidence).

- Melatonin is not recommended for the treatment of insomnia due to low efficacy (weak recommendation, low-quality evidence).

- MT receptor agonists (ramelteon, tasimelteon) are only available in some countries, and have shown mild to moderate effect on difficulty initiating sleep. They are an option to shorten sleep latency and for the treatment of circadian phase delayed disorder (weak recommendation, low-quality evidence).

- Antihistaminergic agents are not recommended for the treatment of chronic insomnia due to lack of evidence for efficacy, as well as tolerance and long-term side effects.

- Phytotherapeutic agents, including valerian and medicinal cannabis, are not recommended for the treatment of insomnia due to poor evidence derived from studies examining these agents (weak recommendation, low-quality evidence).

WORLD SLEEP SOCIETY

- The hypocretin antagonist suvorexant has been approved by the FDA for the treatment of insomnia in the USA, but it is currently available in very few other countries. Several other hypocretin antagonists are under investigation, and they may be available in the future. Suvorexant is effective to treat insomnia, although the optimal therapeutic dose for safety and efficacy is still in question. No recommendation in the European Guidelines was made.

* Some hypnotic drugs (e.g., zolpidem) may be available in different pharmaceutical formulations in different countries, such as sublingual, oral tablets, spray, modified release, etc. It is important to note that some of these will have higher or lower effect on each of the insomnia symptoms. Also, Eszopiclone, available in the USA and some other countries, has a slightly longer half-life compared to zolpidem and zaleplon.

Light therapy and appropriately-timed exercise may be useful as adjunct therapies (weak recommendation, low-quality evidence), but additional studies are needed to document their clinical benefits for chronic insomnia disorder.

Complementary and alternative therapies (CAM) are not recommended for the treatment of insomnia due to lack/poor evidence (weak recommendation, very low-quality evidence). CAM therapies may include but are not limited to acupuncture (possibly effective, but the quality of the studies is weak), aromatherapy and homeopathy (no evidence for benefit, poor quality of studies), music therapy (possibly effective, but the quality of the studies is weak), foot reflexology, moxibustion and meditative movement therapies (including yoga) (possibly effective, but the quality of the studies is weak).

Treatment recommendations for chronic insomnia should consider the presence of comorbidities (psychiatric or medical conditions). For most insomnia therapies, in the presence of comorbidities, treatment should target both insomnia and the comorbid condition, although clinical judgement should determine which condition is treated first, or whether both conditions are treated concurrently.

CAVEATS

Regarding evaluation, actigraphy assessment is not reimbursed by medical insurance in most Asian countries including Japan and is also not reimbursed in Australia and in France. PSG can be reimbursed for the differential diagnosis of sleep apnea and narcolepsy, but is not reimbursed for the sole purpose of confirming a diagnosis of insomnia.

The main caveat with regard to CBT-I is that there are few clinicians (i.e., psychologists or other mental-health practitioners) with adequate expertise to deliver this treatment compared to the large burden of disease within the community. Increasing the breadth of training in CBT-I among different practitioners is a priority for the field, to improve access. In addition, CBT-I has been tested primarily for persistent insomnia, but not with acute, situational insomnia.

WORLD SLEEP SOCIETY

For pharmacological treatment of chronic insomnia, we included a list of drugs available worldwide, however, some of the drugs may be available in different formulations, while others, as modified molecules, according to the geographical region. In addition, other molecules such as hypocretin antagonists and eszopiclone are not available in many countries outside USA.

Melatonin is a more complex issue, since in many countries it is available as an over the counter or food supplement, while in others it is available with prescription only. For instance, it is not currently available in the UK and Brazil.
Finally, with regard to the phytotherapeutics marketed for insomnia, most systematic reviews and meta-analyses conclude there is a lack of standardization of compounds formulation, which makes difficult studies comparison.

With regard to Complementary and Alternative Therapies, availability of some of these treatments may vary widely across countries.

Long-term treatment of insomnia with BZD or other GABA-A agonists is generally not recommended because of a lack of evidence about long-term efficacy and potential side effects and risks of tolerance (strong recommendation, low-quality evidence). In patients using medication on a daily basis, reduction to intermittent dosing is recommended (strong recommendation, low-quality evidence).

Geographic Regions Included in these Recommendations
USA, Canada, European countries, Asia, Australia/ New Zealand, India, South and Latin American countries, and some parts of Africa (e.g., South Africa, Egypt).

CONCLUSION

The WSS Governing Council hereby endorses with caveats described above in this guideline by the European Sleep Research Society as relevant and applicable to the sleep medicine practices of its members within the geographic regions listed above.

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