THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 12 Issue 12

REVIEW ARTICLE

Role of Effective Noninvasive Vagal Stimulation on sleep quality in Patients with Insomnia

Dr Madhusudhan Umesh [1], Dr Vidya Singaravelu [2], Dr Kalpana M [3], Dr Vidya G [1], Dr Archana Gaur [1], Dr Madhuri Taranikanti [3], Dr Nitin Ashok John [4]

[1] Associate professor, Department of Physiology, AIIMS (All India Institute of Medical Sciences), Bibinagar, Hyderabad 508126, Telangana.
[2] Professor, Department of Paediatrics, Malla Reddy Institute of Medical Sciences, Suraram, Hyderabad, Telangana
[3] Additional professor, Department of Physiology, AIIMS (All India Institute of Medical Sciences), Bibinagar, Hyderabad 508126, Telangana.
[4] Professor & Head, Department of Physiology, AIIMS (All India Institute of Medical Sciences), Bibinagar, Hyderabad 508126, Telangana.

OPEN ACCESS

PUBLISHED
31 December 2024

CITATION
Umesh, U., Singaravelu, V., et al., 2024. Role of Effective Noninvasive Vagal Stimulation on sleep quality in Patients with Insomnia. Medical Research Archives, [online] 12(12). https://doi.org/10.18103/mra.v12i12.6132

Doi
https://doi.org/10.18103/mra.v12i12.6132

ISSN
2375-1924

ABSTRACT

The insomnia has negative impact on mental health, physical productivity, and overall quality of life for individuals and communities. Insomnia frequently goes undiagnosed and untreated due to therapies and management barriers. Transcutaneous vagus nerve stimulation is a non-invasive neurostimulation intervention that targets the afferent auricular branch of the vagus nerve in the auricular concha, specifically the cymba concha

Vagus nerve electrical stimulation (VNS) has been used in the treatment of refractory epilepsy, depression, and insomnia. Transcutaneous devices have been deployed successfully in intractable epilepsy, significant depression, post-stroke rehabilitation, and the general geriatric population.

At this moment, treatments for insomnia include cognitive behavioral and pharmacological therapies, including benzodiazepines and non-benzodiazepines, as well as alternative therapies like acupuncture. However, the therapeutic use of medications for sleep disorders must be used cautiously, with obvious worries about the occurrence of side effects such as dependence and drowsiness.

In this review we are exploring the role of noninvasive vagal nerve stimulation as an add on therapeutic tool in insomnia patients.

Introduction:

The term insomnia is used when a patient has difficulty falling asleep or staying asleep despite adequate opportunity and circumstance to sleep, also associated with daytime impairment or distress this occurs 3 times a week and has been constant for at least a month.[1] Sleep-related disorders affect approximately 30% to 35% of the global population, with women having a higher prevalence.[2] It has a negative impact on mental health, physical productivity, and overall quality of life for individuals and communities. Insomnia frequently goes undiagnosed and untreated due to therapies and management barriers [3]

Transcutaneous vagus nerve stimulation is a non-invasive neurostimulation intervention that targets the afferent auricular branch of the vagus nerve in the auricular concha, specifically the cymba concha [4]. The Vagus nerve has a role in the genesis of slow-wave sleep by altering the levels of neurotransmitters like γ-aminobutyric acid (GABA) and norepinephrine.[5] Vagus nerve stimulation (VNS) has been used in the treatment of refractory epilepsy, depression, and insomnia. Transcutaneous devices have been deployed successfully in intractable epilepsy, significant depression, post-stroke rehabilitation, and the general geriatric population.[6,7]

At this moment, treatments for insomnia include cognitive behavioral and pharmacological therapies, including benzodiazepines and non-benzodiazepines, as well as alternative therapies like acupuncture.[8] However, the therapeutic use of medications for sleep disorders must be used cautiously, with obvious worries about the occurrence of side effects such as dependence and drowsiness. [9].

Emotions influence sleep, as do neuronal and humoral regulation, with the vagus nerve playing a significant part in the regulation of sleep and mood due to its broad distribution and functions [10]. Currently, VNS is a successful adjuvant treatment for epilepsy, depression, and insomnia [11]. Some patients who had VNS reported greater sleep and life quality, less daytime tiredness, and a better mood. Furthermore, these alterations occurred in the absence of VNS's anti-epilepsy or anti-depression effects, implying that VNS could control sleep. Furthermore, a previous investigation on the use of VNS modalities for insomnia found that patients experienced increased sleep quality [12]. Taken combined, therapy involving VNS may be more useful to patients.

In this review we are exploring the role of noninvasive vagal nerve stimulation as an add on therapeutic tool in insomnia patients.

Insomnia:

Insomnia is the most prevalent sleep problem, and primary insomnia refers to insomnia that has no identifiable explanation. Short-term insomnia can cause fatigue, daytime sleepiness, and work inefficiency [13]. Meanwhile, long-term insomnia can lead to mental instability and increased risk of chronic diseases such as cardiac disease and cancer, as well as higher mortality.[14-16] At present, treatment measures to counter against insomnia comprise cognitive behavioral and medical therapies, including benzodiazepines and non-benzodiazepines, together with alternative therapy such as acupuncture However, clinical use of medical drugs for sleeping disorders is often practiced cautiously with apparent concerns regarding the incidence of adverse events such as dependency and drowsiness .[17-18]

Based on anatomy, it has been proposed that stimuli to the parasympathetic system activate the solitary tract nucleus and project fibers to central sleep structures such as the parabrachial nucleus, ventrolateral hypothalamic preoptic area, anterior median nucleus locus ceruleus, raphe nucleus, reticular structure, thalamus, and so on [19]. Among these, stimulation of the reticular structure may result in the development of slow-wave sleep. Vagus nerve stimulation can regulate sleep by altering the levels of neurotransmitters such γ-aminobutyric acid (GABA), norepinephrine (NE), and 5-hydroxytryptamine (5-HT). Vagus nerve electrical stimulation (VNS) has been utilized to treat refractory epilepsy, depression, and insomnia [20-21].

Insomnia is associated with an elevated cardiovascular risk. Non dipping status, hyperarousal, increased blood pressure, and decreased heart rate variability are common.[22] Furthermore, the frequent arousals associated with sleep problems can cause tachycardia or bradycardia, which is followed by elevated sympathetic and baroreceptor tone, potentially impairing the ANS. [23-24] A cardiovascular investigation confirmed the link between extreme sleep deprivation and sympathovagal imbalance.[25] The study discovered that patients who slept for fewer than 6 hours had higher mean heart-rate variability measurements and lower parasympathetic activity than the general population. Other investigations have also found indications of autonomic dysfunction in the form of hyperarousal, or the "tired but wired" condition that prevents patients from falling asleep despite exhaustion.

Hypermetabolism in the hypothalamus and the associated efferent projections of arousal networks, along with excessive cortical activity during sleep, have been found on positron-emission tomography in patients with insomnia. These findings ultimately lead to hypertension.[26] Similarly, sleep-deprived individuals may experience an atypical sympathetic drive that makes them more vulnerable to autonomic issues.

Sleep problems can have an impact on autonomic functions, whereas autonomic deficits change the physiology of sleep. However, neither the diagnosis and prognosis of sleep disorders, nor the treatments for sleep disorders, have been thoroughly examined with a focus on this bidirectional relationship. Medicinal interventions are commonly used to treat sleep disorders, with the purpose of assisting patients in falling asleep by raising their GABA levels. However, these drugs improperly change the autonomic tone, and their long-term usage accentuates the fall in systolic blood pressure while increasing the heart rate.[27]

Current neuromodulation approaches are helpful for restoring regular sleep patterns while avoiding addiction. Repetitive transcranial magnetic stimulation lowers

cortical hyperexcitability and rebalances neurotransmitter release by engaging the local neural network with alternating currents, whereas LF (25 Hz) deep-brain stimulation of the PPT prolongs REM sleep. However, these methods of neuromodulation do not balance turbulent autonomic fluctuations associated with disturbed sleep physiology. [28-29]

Vagal Nerve Stimulation (VNS)

Vagus nerve stimulation is a neuromodulatory approach that has been widely utilized to treat a variety of clinical illnesses, including epilepsy [30] heart failure [31], depression [32] and inflammatory bowel disease. [33]

Insomnia is frequently associated by an autonomic nervous system imbalance, with symptoms mostly presenting as sympathetic hyperexcitability and vagal hypoactivity [34] In contrast, increased vagal activity can help relieve insomnia symptoms. Currently, VNS has been proved to be a successful supplementary therapy for epilepsy, depression, insomnia, and other conditions. Many studies have demonstrated that VNS can act directly on the vagus nerve ear branch to regulate changes in the levels of various neurotransmitters linked with sleep and influence brain activity to control sleep conditions.[35]

A recent study that focused on the use of the VNS technology to treat insomnia found that patients' sleep quality improved significantly following VNS treatment [36.] Similarly, Marta Jackowska confirmed the favorable effect of VNS on sleep in a healthy community group [37]. This demonstrates the high efficacy of VNS therapy for improving sleep. [38] VNS is a non-invasive method for controlling nerve activity that involves providing an electrical current to the auricular nail via the vagal reflex [38].

The potential pathways by which VNS promotes outcomes in patients have been investigated., VNS causes extensive brain activity alterations in areas such as the solitary nucleus, locus coeruleus, raphe nuclei, insula, and sensory cortex [39] Second, researchers discovered that vagal afferents triggered the ascending reticular activating system, which is essential for promoting and maintaining consciousness, from the periaqueductal grey and raphe nuclei to the thalamus [40]. Furthermore, VNS boosted brain activity and connection throughout the external network via the norepinephrine and orexin/hypocretin pathways [41].

Transcutaneous vagus nerve stimulation for insomnia is very beneficial because it is non-invasive. Unlike surgical vagus nerve stimulation, transcutaneous VNS stimulates the nerve through the skin's surface, making it a safer and more accessible treatment option for patients.

Conclusion

To summarize, the review presented above provides persuasive evidence that transcutaneous vagus nerve stimulation is a viable and effective therapeutic option for people suffering from primary insomnia. The good findings in sleep quality, anxiety, and depression symptom scores provide hope for patients who have struggled to obtain relief with traditional therapy. More research in this field is needed to understand the long-term consequences and best application of vagus nerve stimulation for sleep problems. With continuous advances in neuroscience and medical technology, VNS has the potential to further transform how we treat and manage sleep disorders, enhancing the lives of countless people everywhere.

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