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The Role of Complementary and Alternative Medicine in the Treatment of Insomnia

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Abstract

Insomnia is a frequent condition that can be acute, intermittent, or chronic. It is an unpleasant feeling that makes it difficult to fall asleep. The main aim of the review is to determine the adverse effects of Insomnia drugs and the need to opt for Complementary and alternative medicine (CAM) approach as an adjuvant in treating Insomnia condition with lesser-known side effects. The Methodology involved a detailed literature survey which was performed through an online database, such as Science Direct, Google Scholar, Scopus, Cochrane, and PubMed. The study included original research and book chapters conducted on relation with Insomnia in particular with various therapies used currently and aimed to find possible alternative source which will be effective in treatment as well as with less burden of side effects. The study found that various Insomnia drugs showed adverse reaction and the need of CAM approaches as a beneficial role in the treatment of Insomnia complications was beneficial. We believe CAM therapy could be the most suitable choice in preventing the Insomnia risk with less known side effects in contrast with the existing treatment patterns with plethora of side effects. In Conclusion, CAM approaches as well as proper vitamin intake has beneficial effects on sleep cycle. However, to improve the utility of unconventional approaches, more evidences from in vitro, in vivo, and clinical trials need to be addressed.

Keywords: Complementary and alternative medicine; Insomnia; Barbiturates; Benzodiazepine; Melatonin

Introduction

Insomnia is described as a person's report of difficulties or a lack of sleep. Long sleep latency, frequent awakenings at night, and spells of arousal during the night are all indicators of insomnia. [1] Insomnia can be short-term (a few days or weeks) or long-term (more than a month). There are three forms of insomnia: episodic insomnia, persistent insomnia, and recurring insomnia. Episodic insomnia lasts 1-3 months, but chronic insomnia lasts at least 3 months at a time. Recurrent insomnia is defined as insomnia that happens more than 2-3 times per year. There are different types of insomnia: primary insomnia (sleep issues that are unrelated to any health condition), secondary insomnia (sleep problems that are related to health conditions such as asthma, depression, pain, medication use, and alcohol use), and co-morbid insomnia (insomnia exists in association with another medical condition or psychiatric condition). Insomnia often can worsen a medical or psychological problem and prevent it from being treated. Population-based research have revealed that around 30% of a range of adult samples gathered from various nations suffer one or more symptoms of sleeplessness [2]. Age and gender are the most identified risk factors. Prevalence is higher in women and in older adults. The cause of higher risk in older adults is not defined properly, but it can be due to partial decline in the sleep function that causes insomnia in elder patients. In women insomnia is more prevalent during the onset of menstrual cycle and menopause. [3] Insomnia is also prevalent in people with psychiatric disorders, [4] night work routine. All these factors are not the only factors that independently cause insomnia but these can be a contributing factor. Chronic disorders can be an important risk for insomnia. It is predicted that most of the people with insomnia are at a higher risk of comorbid disorders such as diseases causing hypoxemia, dyspnea, neurodegenerative disease, pain, GRD. In elderly patients, phase advance syndrome results in report of difficulty in initiating sleep, maintaining sleep, early morning awakenings. [5][6] It is approximated that almost 40% of all the people with insomnia have an existing psychiatric condition. [7] Depression is the most common psychiatric disorder. Insomnia is a diagnostic symptom for depressive and anxiety disorder.

Methods

Sources of information and search strategies

A detailed literature survey performed through an online database, such as Science direct, google Scholar, Scopus, Cochrane, and PubMed. The search keywords were [Complementary and alternative medicine OR Insomnia OR Medications OR CAM therapy OR Evidence-based Medicine OR Barbiturates OR Benzodiazepine OR natural supplements]. The literature search was limited to studies published in English with no time limitation.

Study inclusion and type of intervention

The Methodology involved a detailed literature survey which was performed through an online database, such as Science Direct, Google Scholar, Scopus, Cochrane, and PubMed. The study included original research and book chapters conducted on relation with Insomnia with various therapies used currently and aimed to find possible alternative source which will be effective in treatment as well as with less burden of side effects. Studies which did not involve alternative therapies were exempted from study involved.

Sleep Cycle

The oscillation or transition between the slow wave and REM phases of sleep is referred to as the sleep cycle. To distinguish it from the circadian shift between sleep and alertness, it is referred to as the ultradian sleep cycle, sleep dream cycle, or REM-NREM sleep. This cycle should take between a span of 70 and 110 minutes.

Role of Melatonin in sleep

5-methoxy-N-acetyltryptamine is another name for melatonin. It was found and isolated from bovine pineal. [8] The pineal gland produces melatonin and is also found in the retina, platelets, skin, lymphocytes, and cerebellum, mostly in the GIT [9][10][11][12][13]. Melatonin concentrations in the GIT exceed blood levels by 10-100 times, and the GIT contains about 400 times more melatonin than the pineal gland. Melatonin levels in human breast milk have a diurnal cycle, with high levels at night and undetectable during the day. There was no association observed between gestational age and melatonin levels. Human colostrum contains immunological competent cells that can produce melatonin in an autocrine way after 4-5 days of childbirth. [14] Darkness promotes melatonin production and secretion, whereas light inhibits it. [15][16] SCN transmits luminal information from the retina to the pineal gland (suprachiasmatic nucleus). In humans, secretion begins about dusk, peaks around midnight, and steadily diminishes through the second half of the night. During the night, over 80% of melatonin is generated. The serum concentrations range from 110 to 130 pg/ml. During the day, serum concentrations might reach 10-20 pg/ml. [17][18] Role of vitamins (Fat and water soluble) along with its maximum dietary allowance and its sources is mentioned in Table 1

Table 1: Vitamins and its role in health

`VITAMIN	BENEFITS	INTAKE AMOUNT	GOOD SOURCES
Vitamin A (retinol and beta carotene)	Essential for vision, keep tissues and skin healthy, lower lung and prostate cancer risk	M:900mcgW:700mcg	Carrot, spinach, liver, sweet potatoes
Vitamin B1 (thiamine)	For healthy skin, hair, brain and convert food as energy, it is also critical for nerve function.	M: 1.2mgW: 1.7mg	Pork, whole grains, lentils, spinach, nuts, cauliflower
Vitamin B2 (riboflavin)	For healthy skin, hair, blood. Convert food to energy.	M: 1.3mgW: 1.1mg	Broccoli, green leafy vegetables, salmon, eggs, milk
Vitamin B3 (niacin)	Reduce fatigue and tiredness, transfer electrons during metabolic reactions	M: 16mgW: 14mg	Peanut, cereals, beef liver, wheat bran
Vitamin B5 (pantothenic acid)	Participate in oxidation of fatty acid and carbohydrates. Participate in synthesis of amino acids, ketone bodies, cholesterol	M: 5mgW: 5mg	Broccoli, sweet potatoes, mushroom, tomatoes
Vitamin B6 (pyridoxine)	Lowers homocysteine levels, reduce risk of heart disease	For 31-50 years M: 1.3mgW: 1.3mgFor 50+ yearsM: 1.7mgW: 1.5mg	Fishes like (snapper, tuna) poultry, tofu, bananas, cottage cheese
Vitamin B12 (cobalamin)	Helps with RBC production and prevents anemia, may support bone health and prevent osteoporosis	M: 2.4mcgW: 2.4mcg	Beef liver, tuna, milk, egg, yoghurt, nutritional yeast
Vitamin C (ascorbic acid)	Strengthen body's defense, manage high blood pressure, reduce risk of heart disease, blood uric acid levels, prevent gout attack	M: 90mgW: 75mg	Citrus fruits, blackcurrants, bell peppers, kiwi, strawberries

Vitamin D (calciferol)	Important for maintaining healthy bones and teeth, supports immune system, manage blood sugar levels and prevent diabetes	31-70 years: 15mcg70 above: 20mcg	Rainbow trout, salmon, yoghurt, orange juice, sardines
Vitamin E (alpha-tocopherol)	It prevents cataract formation and it prevents the formation of wrinkles	M: 15mgW: 12mg	Sunflower seeds, almonds, peanuts, avocado, spinach, rice bran oil
Vitamin K	Keeps blood pressure lower. It maintains the bone strength, improves bone density, decreases the risk of fractures.	M: 120mcgW: 90mcg	Soyabean oil, parsley, spinach, grapes, hard boiled eggs

Sleep Deprivation

Consequences of sleep deprivation

Sleep plays crucial roles in regulating the operations of numerous other physiological systems in addition to maintaining appropriate brain function, which is especially clear in sleep-deprived situations. It is becoming abundantly obvious that cutting back on total nocturnal sleep hours can have major negative effects on practically every biological system and function. Overall, immunity declines, [19] a condition of systemic inflammation with elevated inflammatory markers develops, [20,21] and numerous hormones become out of control. [22] Individuals that stay up late could also engage in harmful practices when it comes to eating and drinking. [23] Clinical studies have shown that those who lack sleep have an increased chance of acquiring [24] diabetes mellitus, [25] depression, [26] obesity, [27] hypertension, [28] dyslipidemia. (10) According to recent research, sleep loss raises a person's daily energy expenditure. [29] Sleep deprivation is not confined to a specific population, nation, gender, or age range. Instead, millions of people and children around the world are exhibiting this brand-new human behavior. Additionally, a number of epidemiological studies have shown a connection between reduced sleep time and higher death. [30] Circadian rhythm is also known to be altered in ADHD (Attention deficit hyperactivity disorder) as assessed by sleep and other parameters. [31] Numerous authors have made the grave epidemiological observation that exceeding what is regarded as "normal" sleeping hours is linked to higher all-cause death. [32]

Causes of sleep deprivation

Sleep loss can have numerous reasons and is typically complex. Sleep apnea, insomnia, RLS, parasomnias, mood disorders, psychosis, and other psychiatric, neurological, and medical problems are all prevalent causes of sleep loss. It is crucial to directly treat any of the underlying causes when determining the cause(s) of sleep loss. If physicians find an underlying, curable problem, they should not treat the symptoms. Primary insomnia is the default diagnosis if the clinician is unable to pinpoint any underlying causes. Elderly populations are most likely to experience primary insomnia. Changes in sleep architecture caused by ageing resulted in a decrease in delta-wave (or deep) sleep and an increase in the amount of time spent in lighter sleep, resulting in more sleep disruptions. Sleep duration diminishes with ageing as well. Comorbid medical problems can both induce and result in persistent sleep loss. [33]

Treatment For Insomnia

Benzodiazepine receptor agonists

There are both benzodiazepine and non-benzodiazepine drugs in benzodiazepine receptor agonists. Even though all of these medicines bind to the gamma aminobutyric acid (GABAA) receptor complex, their affinity for binding sites varies. BZDs exhibit

nearly same selectivity for alpha subunits 1, 2, 3, and 5, but non-BZDs bind more preferentially to alpha 1. The muscle relaxant, sedative-hypnotic, anxiolytic, and anticonvulsant actions of benzodiazepine receptor agonist is mediated by various GABAA receptor subunits. Furthermore, non-BZD selectivity for the alpha 1 subunit is thought to have less deleterious effects on the central nervous system and a lower potential for misuse when compared to benzodiazepines. [34]

Five benzodiazepines are FDA-approved for the treatment of insomnia. They are triazolam, estazolam, temazepam, quazepam, and flurazepam. The fundamental difference among these BZDs is the duration of action. Triazolam is short-acting. Estazolam and temazepam belong to intermediate-acting category. Temazepam is the common choice of BZD in the treatment of insomnia. Quazepam and flurazepam are long-acting. The optimum BZD should be selected depending on the desired onset and duration of effect. Because patients have developed resistance to the sedative effects of BZDs, long-term use of these medications is not advised. BZDs improved overall sleep duration and decreased sleep latency in over 2,600 people. However, because the experiments were all short-term (14 days or fewer), the researchers were unable to assess tolerance to the medicines' hypnotic characteristics. [35]

Barbiturates

Barbiturates cause CNS depression that can vary from moderate drowsiness to anaesthesia. Hypnotic dosages of these medicines can minimize sleep latency and nighttime awakenings. [36] They are FDA approved drugs for patient with insomnia. They are not recommended because of their adverse drug reactions like, fatal overdose, low therapeutic index, potential for tolerance and dependence. [37] Various drugs are involved in treating insomnia with its own plethoric adverse effects which includes CNS related effects which might be harmful and its list is mentioned in Table 2

Table 2: Insomnia Drugs and its adverse effects

Name of the drug	Dose	Half-life (hours)	ADR	Additional consideration
Triazolam	0.25mg	1.5-5.5	DizzinessDrowsiness	Older adults at high risk of increased plasma concentration
Flurazepam	Women:15mgMen:15/30mg	47-100	AtaxiaDizzinessStaggering	Caution with alcohol useContraindicated in pregnancy
Ramelteon	Should not exceed 8mg	1.0-2.6	NauseaFatigueDizzinessExacerbated insomnia	Avoid alcoholTake 30 minutes before bedtimeNot recommended for patients with hepatic impairment
Suvorexant	10mgShould not exceed 20mg/day	10-22	Headachedizziness	Alcohol intake should avoidContraindicated in patients with narcolepsyNot recommended for patients with hepatic impairment

Butabarbital	50-100mg	100	Confusionagitation	Avoid alcohol usePregnancy category DReduce dose in case of patients with hepatic impairment
Secobarbital	100mg in adults	15-40	somnolence	Caution with alcohol usePregnancy category DReduce dosage in elderly patients and with patients with hepatic impairment
Doxepin	6mg in adults 3mg in elder patients	15.3	URTINauseasedation	Be cautious with alcohol usePregnancy category CShould not be taken within 3 hours of mealExtensive CYP2C19 and CYP2D6 metabolism
Diphenhydramine	50mg in adults	8-17	Dry mouthDizzinesssomnolence	OTC drugElderly patients may be susceptible to ADRCaution with alcoholPregnancy category B
Doxylamine	25mg in adults	10-12	somnolence	Take 30 minutes before bedtimeCaution with hepatic impairment and alcohol

Long Term Usage of Insomniac Drugs

Barbiturates

The use of barbiturates started declining in the mid-twentieth century, as their negative side effects and the risk of lethal overdose became better understood. [38] Cardiorespiratory adverse effects became frequent including decreased cardiac output, hypotension, and increased intrapulmonary shunt and that led to cases of hypoxia. High dose barbiturates lower intracranial pressure in two different ways: by inhibiting metabolism and modifying vascular tone. [39–41]

Benzodiazepines

Long-term benzodiazepine usage has been associated to withdrawal symptoms, therapeutic dose dependency, relapse anxiety, falls and fractures, and a decline in long-term cognitive performance (which might last for months after benzodiazepines have been discontinued). Old age is one of the most reliable indicators of benzodiazepine long-term use. Prior studies demonstrates that people with somatic disorders and persistent pain are more likely to use benzodiazepines long-term. [42] Additionally, those with somatic conditions and/or chronic pain may struggle with sleep more than healthy people, which may help to explain why benzodiazepines are more likely to be used long-term in older age. [43] We should seek non-pharmacological therapies as the first line of treatment for insomnia given the possibility for substantial side effects of hypnotics use in people. In addition to having

fewer side effects, non-pharmacological treatments are also better able to maintain long-term benefits than pharmacological ones.

Complementary and Alternative Medicine Therapy

Complementary and alternative medicines (CAM) are practiced from a really long time for the treatment of sleeping disorders. Valerian was prescribed for insomnia by an ancient Greek physician Claudius Galenus during the 2nd century. [44] The National Center for Complementary and Alternative Medicine defines CAM treatments as "a range of different medical and health care systems, practises, and products that are not currently regarded to be part of traditional medicine." [45][46] Various CAM therapies associated with treatment of Insomnia is established in Table 3.

Table 3: CAM Therapy and its Insomnia outcomes

S.no	Cam Therapy	Study Method	Inference	Reference
1.	Musical Therapy	De Niet et al- In a meta-analysis study of 5 studies and 170 participants, they discovered that music-aided relaxation had a positive influence on sleep quality.	The study's findings indicated that calming music improved sleep quality, which is consistent with previous research.	[47]
2.	Valerian	Valerian has been investigated in a number of randomised, placebo-controlled trials at dosages ranging from 400 mg to 900 mg.	Subjective measurements improved in 18 patients who did not have sleep issues.	[48]
3	Acupuncture	Acupressure has been researched in institutionalized elderly persons using a randomized method.	The Pittsburgh Sleep Quality Index improved statistically significantly in this research (as primary outcome measure).	[49]
4	Yoga	In 69 elderly adults, a randomised, parallel group trial during a 6-month treatment period compared yoga (60-minute session 6 days a week, with a 15-minute evening session), Ayurvedic therapy, and a wait-list control were compared.	Self-reported sleep metrics revealed a 1-hour increase in total sleep time compared to pretreatment, which was substantially greater than increases in the wait-list or Ayurveda groups.	[50]
5	Tai Chi	A study evaluating the benefits of Tai Chi (three 60-minute sessions per week for 24 weeks) on 118 aged people.	Tai Chi enhanced self-reported sleep duration by 48 minutes when compared to low-impact exercise.	[51]

Musical Therapy

Psychological disorders and problems like stress, depression, anxiety, sorrow, distress, pain and nausea show an improvement when the person is undergoing Musical therapy and is exposed to various melodies. [52,53] Various studies have been conducted that had shown positive effects in various patients diagnosed with insomnia and schizophrenia. [47] A study conducted by Tan et al., [54] primary school students listened more to sedative music. He concluded that sedative music has a significant good influence on the sleep quality of youngsters. Music therapy is an inexpensive, safe, and painless treatment with no side effects; hence, it can be a feasible non-pharmacological strategy to improve sleep quality and can be utilised in any area of health.

Valerian

Valerian, particularly Valeriana officinalis and Valeriana edulis, is the primary source of the components in valerian. These constituents can be further distinguished in the following subcategories like valepotriates, sesquiterpenes and amino acids.

Valepotriates and sesquiterpenes are the volatile compounds that account for the unpleasant Odour of Valerian. The amino acids include glutamine and g-amino butyric acid. [55]

Acupuncture

Acupuncture, which falls under the category of alternative medical approaches, affects health by acting on meridian points. [56] The majority of acupuncture research used subjective metrics or had a placebo control, which makes it challenging to interpret the results. [56] Utilizing polysomnography, only a few research have looked at how acupuncture affects insomnia. [57,58] Despite the fact that both studies showed signs of better sleep, one was pilot research that lacked a placebo control. Furthermore, as compared to pretreatment levels, this study found an increase in nocturnal melatonin secretion as well as a decrease in stress and anxiety ratings. Acupuncture has also been studied as a therapeutic option for sleep disturbance caused by various illnesses, such as post-stroke insomnia and postmenopausal symptoms. [59] Fibromyalgia [59,60] and sleep apnea are two other sleep disorders that have been treated with acupuncture [60].

Meditation

The type of meditation that is most frequently practiced is mindful meditation. The majority of research showing enhanced sleep during meditation treatment has been done as stress reduction studies. Stress reduction may be one of the processes by which meditation might have a positive impact on sleep. It can be applied as a component of a cognitive treatment strategy in this regard. It's possible that meditation affects slow-wave sleep differently in addition to reducing stress. [61]

Yoga

Anxiety levels and physiological arousal have been proven to decrease with yoga. According to studies, yoga helps chronic insomniac patients report having better sleep overall. [62] Additionally, it has been discovered that practicing yoga helps postmenopausal women with both subjective and objective insomnia problems. [63]

Tai Chi

Tai Chi is a low- to moderate-intensity Chinese workout that incorporates meditation. Tai Chi began as a martial art in China, emphasizing on the mind and body as an integrated system, breathing, and maintaining a peaceful state of mind with the objective of reaching profound levels of relaxation. It dramatically improved sleep quality in both healthy people and those with chronic health issues, indicating that it may be used as an alternative psychological therapy to treat insomnia. [64]

Conclusion and Future Perspectives

It was observed from various studies that reported CAM approaches showed a beneficial role in the treatment of Insomnia complications. We believe CAM therapy could be the most suitable choice in preventing the Insomnia risk with less known side effects in contrast with the existing treatment patterns with plethora of side effects. However, to improve the utility of unconventional approaches, more evidences from in vitro, in vivo, and clinical trials need to be addressed.

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