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Relationship between Vitamin D and Insomnia in Older Adults

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Abstract:

Vitamin D is one of the common fat-soluble vitamins, which can be obtained from ultraviolet exposure and intake from particular food or supplementation. Insomnia caused by many reasons like diseases or health status, would also increase possibilities of suffering from other diseases, and has a prevalence to be common among all sorts of people, especially in older adults. Researchers found vitamin D associated with neurotransmitters, oxidative stress and inflammation. Many research also suggest vitamin D are relevant to insomnia, people with low serum vitamin D concentration have a higher possibility to suffer from insomnia, after a period time of supplementation of vitamin D insomnia patients, many of them get improved, but there are no significant difference on some on them either. The mechanism about vitamin D improving insomnia symptoms is not clear, there is no determine recommended dose and duration for patient, and also not enough clinical trials for further exploration. As an auxiliary means of insomnia treatment, vitamin D may have a good performance combined with other therapies. The current review summarizes some mechanism of vitamin D, both positive and negative evidence associated with vitamin D improves insomnia symptom, and have an outlook for the future study on insomnia between vitamin D.

Keywords: Vitamin D; insomnia; older adults.

1. Introduction

Insomnia is one of the sleep disorders, characterized by constant difficulty in initiating, maintaining sleep, a low sleep quality and daytime dysfunction, is becoming more and more a common health problem in the society [1]. According to American Psychiatric Association, early morning awakening, difficulties maintaining sleep, difficulties initiating sleep, one or more of these symptoms at least three times a week in three months, and accompanied with the daytime impairment, insomnia can be diagnosed. People are recommended to sleep seven to eight hours every day from the National Sleep Foundation, but less can achieve as many of them are exposed to the high pressure from occupation, family and so on. Through estimating, more than 50% older adults have problem in initiating or maintaining sleep [2,3]. According to the previous study, insomnia is related to different kinds of diseases, such as diabetes,depression [4,5]. It is an increased risk of type 2 diabetes mellitus (T2DM) as important as traditional factors, like an unhealthy weight [6]. The patient who suffered from insomnia had higher risks of exposure to depression and anxiety than the healthy ones, at 9.82 and 17.35 times, respectively [7].The medical treatment to insomnia is sedative or hypnotic drugs mostly benzodiazepines or benzodiazepine receptor antagonists, which have side effects to the patients, such as: daytime drowsiness, risk of abuse and addiction, and rebound insomnia on withdrawal [8,9].

Therefore, it is really important to investigate more therapeutic targets, and develop more effective and safer individual treatments for the disease. Clinical investigations suggest that there are many different factors may lead to the suffering of insomnia, for example, optimal sleep can be maintained and regulate by vitamin D through the increasing researches, vitamin D is connected to the production and secretion of neurotransmitters, and these kinds of neurotransmitters may regulate the sleep cycle. Status of Vitamin D may potentially mediate or elucidate the association between Obstructive sleep apnoea(OSA) and cardiometabolic morbidity [10]. Vitamin D deficiency are common among the insomnia patients through the evidences, but most of them are clinical researches. To find the the frontiers between vitamin D and sleeping performance especially in the older adults, the present review endeavour to provide ideas between vitamin D deficiency and insomnia treatment.

2. Relationship Between Vitamin D and Insomnia

2.1 Vitamin D

Vitamin D which can be ingested from meals and produced by the radiation of ultraviolet-B (UVB) from the

skin. 25-hydroxyvitamin D (25(OH)(2)D(3)) is commonly considered as the best indicator of vitamin D status in the body [11]. According to the definition of the Endocrine Society, the level under 20ng/mL is deficiency; insufficiency is higher than 20 but no more than 29ng/mL; and 30ng/mL can be defined as sufficiency.

There is a wealth of scientific evidences indicating that vitamin D are essential in sleep regulation. Some of the researchers considered it may due to the expressions of vitamin D receptors(VDRs) in the brainstem, the prefrontal cortex, the hippocampal dentate gyrus, the lateral geniculate nucleus, VDRs can be found in these kinds of areas which is relevant to sleeping, may have the ability of regulating the release of factors about sleep cycle [12,13]. Vitamin D might play an effective role on several mechanisms about sleeping, including induction of neuroprotection, modulation of oxidative stress, regulation of calcium homeostasis, and suppression of inflammation. The lack of vitamin D may lead to oxidative stress and inflammation. When cells are under the environment of inflammation, the procedure of activating vitamin D will obviously faster, this is one of the crucial part to improve the function of oxidation of mitochondria in skeleton muscles, and decrease the oxidative stress in mitochondria at the same time. Factors like cyclooxygenase-2 and nuclear factor kappa B(NF-κB) will be released more when facing oxidative stress, and this would cause nitrosative stress, then lead to the cell damage and apoptosis. Vitamin D enhances the expression levels of antioxidant agents and reduces cytokines production by exerting inhibitory effects on the activation and expression of NF-κB and other associated genes [14]. Vitamin D improve the antioxidant ability through regulating of nuclear factor erythroid 2-related factor 2 (Nrf2) and klotho, Nrf2 which related to promote the transcription of antioxidant-related genes and klotho which also called “longevity protein”, the combination of Nrf2-klotho increase the cellular concentration of antioxidant, therefore maintain a healthy environment for cells against the oxidative stress. Chronic vitamin D deficiency adjusts the nuclear mRNA to decline the ability of mitochondrial respiration, which is relevant to conplex I of the electron transport chain, and the generation of adenosine triphosphate (ATP) [15]. Moreover, low concentration of electron transport chain will increase the possibility of oxidative stress. Specifically, it has been found to exert its effects by decreasing the levels of prostaglandin D2 and various cytokines in the body. This mechanism suggests that Vitamin D may help to alleviate inflammatory responses and promote a more favorable environment for sleep.

2.2 Vitamin D Level among Insomniacs

Through the investigation over the world, more and more citizens are facing the problem of vitamin D deficiency, because of the daily habits, which are more likely to stay indoor from sunrise to sunset, and consistently supports the notion that vitamin D deficiency in older adults may be significantly related to increased odds of experiencing reduced sleep performance and heightened daytime sleepiness. Chronic insomniacs with onset in spring and winter have the problem of low vitamin D concentration level, at about 15.72 ng/mL while the healthy ones are 3 ng/mL higher, and insomniacs are as twice possibility of suffering from vitamin D deficiency as healthy controls, low sleep performance, more severe anxiety, depression and somatization symptoms are facing by patients at the same time [16]. A research found response to sleep medicines maybe correlated to the serum 25(OH)D concentrations, that chronic insomniacs also the non-response patients are around 20 ng/mL, significantly lower than those of healthy control subjects, also the response group [17]. 50 insomniacs study found that all their patients were suffering from the deficient state of vitamin D, and ladies are less likely to this problem [18]. A research analyzed 105 old adult patient and concluded a result of positive correlation between Vitamin D and total sleeping [19]. A finding with over 3000 samples of elder adults living in a community found that their poor quality of sleeping associated to low level serum vitamin D. Lower serum vitamin D level, more anxiety and depression are easier to detect in patients with worse sleep quality. And excessive daytime sleepiness in old adults is also significantly connected to the deficiency of vitamin D, too much daytime sleeping which means patients are more likely to face a higher possibility of sleep disorder at night, and this would form a vicious cycle [20].

3. Impact from the Vitamin D Supplement

During the pharmaceutical treatment, there were most of higher vitamin D serum concentration among response patients than the non-response ones. The probability of treatment non-response was independently associated with vitamin D deficiency. A double-blind clinical trial demonstrated that the use of vitamin D supplementation, administered at a dosage of 50,000 IU every two weeks for a period of 8 weeks, significantly facilitated improvements in sleep duration and quality among individuals with sleep disorders [21]. Oral supplementation of 50,000 IU vitamin D for 9 weeks in adolescent girls, can not only lighten the influence of insomnia, but also enhance the cognitive ability, such as paying attention, remembering, learning. When combining vitamin D with antihypertensive medications, the combination can make a difference to the high blood pressure also the insomnia, headache and so on [22].

According to a clinical research, insufficient and deficient serum vitamin D level veterans after different dosage of vitamin D for 1200 IU per day and 50,000 per week of intake, were less likely to feel pain and suffer from the insomnia [23]. A study focuses on cognitive impairment of older adults, suggests that with a efficient serum vitamin D level, adults are less likely to suffer from cognitive impairment, also indicates that vitamin D may play a critical role in the etiology of cognitive impairment, Alzheimer's disease, and all-cause dementia.

Insomnia patients are always with depression at the same time, which may have a poor sleep performance because of the mood. When suffering from depression, patients may get improvement on their moods after the supplementation of vitamin D, which may be associate with the serotonin synthesis and neuroinflammation reduction [24].A eight weeks research indicates that young bipolar disorder patients after vitamin D3 reduced manic and depressive symptoms and got a higher brain gamma-aminobutyric acid (GABA) concentrations [25]. GABA is one of the common dietary supplement aims at improving sleep performance. GABAergic neurons are primarily located in the basal forebrain and the anterior hypothalamus. Cells with arousal functions are inhibited during sleeping by releasing a high level of GABA [26]. This shows that vitamin D may not have an impact solely on insomnia, other neurotransmitters like GABA would be regulated by vitamin D, which indicate a further mechanism of vitamin D help improve sleep performance.

Meanwhile, some of the researches indicate that there may be no efficacy on the patients after the different dose(high or low) supplementation of vitamin D [27]. It may due to the sensitivity to vitamin D on different people, high sensitive patient would show more reaction to the using, and low sensitive patient may have no reaction on vitamin D or need to try another higher level dosage of vitamin D. Different sensitivity of vitamin D may be related to VDRs, which widely located at the the sleep related areas, some patient may have less VDRs than normal or healthy person, their VDRs may be captured by other neurotransmitters, or irreversibly damaged for some illnesses before, consequently lead to their low active factors. Moreover, vitamin D are associated with many of other nutrients, maybe the synergy of several nutrients, such as calcium, magnesium, and zinc. Many of these metal ions are the enzyme during the biochemical reactions, patients also probably suffer from the deficiency of them, then lead to ineffective results. Study shows that magnesium deficiency may be related to the abnormal function of vitamin D, and it plays a role on the activation and inactivation of vitamin D.

4. Combination Therapy with Vitamin D

Many researches shows that vitamin D may have the sleeping performance improved, but as an auxiliary means, combining with other therapies may increase the common treatment effectiveness of insomnia.

The therapies of insomnia mostly been used might be divided into two different parts: pharmaceutical treatments such as: benzodiazepines(BZ), benzodiazepine receptor agonists(BZRA), Sedating antidepressants, Antipsychotics, Antihistamines, Melatonin receptor agonists; and non-pharmaceutical treatments which includes cognitive-behavioural therapy, other cognitive-behavioural/psychotherapeutic interventions, exercise, light therapy, music and non-invasive brain stimulation [28]. Among the non-pharmaceutical treatments health education would be often ignored, though it also play an important and significant role on the patients. Insomnia patients suffer from the disease for a long time, and are prone to anxiety, irritability and other emotions and high pressure in lives. Therefore, during health education, it is necessary to understand the patients' mental state, listen patiently to the their real needs, and eliminate their worries and doubts about the insomnia. At the same time, explain the disease-related knowledge to the patients, clarify the impact of negative emotions on their disease, and guide them to make self-psychological adjustments and maintain an optimistic and positive attitude towards treatment.

5. Conclusion

Quite a lot of studies suggest that the supplementation of vitamin D can help insomnia patients increase their serum concentration level then improve their quality of life. As a auxiliary means of treatment, vitamin D has a promising future in improving the insomnia symptoms, such as better sleep performance, longer sleep duration. The improvement in insomnia is important because insomnia may be associated with many health problems. Though there are quite a lot of researches indicated that insomnia is related to the deficiency of vitamin D, the effectiveness of vitamin D between insomnia is still unclear, and the mechanism to insomnia is also needed to be explored. Moreover, some of the research found that there is no significant difference after the supplementation of vitamin D. The reasons for these results might due to differences in the health status of different patients, some of them may also suffering from other severe disease which is the main cause of the insomnia; study duration and dose of the vitamin D, some low dose of vitamin D may not be effective in a short time, this kind of researches should have a longer observation for another re-evaluation on patients.

There is not a determine recommended dose and duration of vitamin D for sorts of patients, and the duration of supplementation. More clinical trials are required to investigate the problems facing by vitamin D to improve the insomnia symptom.

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