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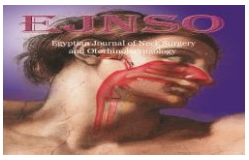

Serum level of vitamin D and its relation to Meniere's disease

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Abstract:

Objectives: To determine the level of vitamin D in Patients with Meniere's disease (MD) and investigate the effect of its supplementation on the frequency and duration of MD attacks.

Patients and methods: A matched case/control study was conducted. Vitamin D serum level was estimated in patients with MD before and 3 months after its administration. The degree of improvement in frequency and duration of MD attacks was calculated.

Results; Our study included 112 persons (28 cases and 84 controls). Low serum levels of vitamin D were detected in MD patients. In addition, we found a significant statistical difference Dizziness Handicapped Inventory (DHI) Questionnaire before and after vitamin D supplementation ($p<0.0001$).

Conclusions: The current study found that MD patients had lower serum vitamin D levels. There appears to be a link between vitamin D and MD, and this study looked at a correlation rather than establishing causation. Also, vitamin D supplementation has a beneficial role in controlling Meniere's disease symptoms and lowering frequency of occurrence of the disease.

Keywords: Meniere Disease-Vitamin D - Vertigo - Ear – Inner

Introduction

The etiology of Meniere's disease (MD) is still unknown, while various explanations have been presented, including genetics, autoimmune, viruses, nutrition, and vascular factors. [1-3] However, the precise process remains uncertain. MD may represent a variety of illnesses with comparable clinical presentations.

Vitamin D has lately received attention for its potential function in a variety of metabolic processes. Vitamin D plays a vital physiological role in calcium control. Because calcium carbonate is a key component of otoconia, there have been numerous studies on the effect of the mineral calcium on the inner ear. According to some research, Vitamin D-related epithelial calcium channel proteins are crucial in vestibular organ physiology, and their absence can lead to impairments in vestibular function. [4]

Several studies on benign paroxysmal positional vertigo (BPPV) and how it relates to metabolism of vitamin D have been carried out. [5] According to some studies, low serum of vitamin D is more relevant in patients complaining of sudden sensorineural hearing loss (SNHL) than in normal hearing people. [6]

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Due to a lack of reports, epidemiologic studies to assess the link between MD and vitamin D are required. In the current study, we wanted to look into the link between serum vitamin D levels and MD.

Patients and methods:

This study was conducted in Sohag University Hospital, Audiology Unit, in the period between August 2022 to June 2023.

Participants:

A matched case-control study was conducted, the serum level of vitamin D was compared between people with MD (case group, number of participants is 28) and people not complaining of MD (control group, number of participants 84) .

Inclusion criteria for definite disease were based on the American Academy of Otolaryngology-Head and Neck Surgery's Equilibrium Committee's revision of the 1995 definition of MD. 7-8 All patients had at least two vertigo episodes lasting at least 20 minutes, in addition to SNHL at low frequencies confirmed by audiometer and intermittent tinnitus or fullness in the ear. The control group included healthy people who had no previous history of hearing problems or vertigo. They were selected during the same time period as the cases in order to control the effect of seasonal sun exposure on vitamin D levels. They were also matched with the MD group (case) in terms of age, gender, occupation, and smoking history. Sun exposure degree, which can alter levels of vitamin D, is affected by the occupation whether is indoor or outdoor. The introduction of 3 controls for each instance increases the power of the study and the precision of the estimates.9

Exclusion criteria included chronic metabolic problems such as malabsorption, surgery of gastrointestinal tract, inflammatory bowel disease, celiac disease, renal impairment, nephrotic syndrome and cystic fibrosis. Patients excluded also if they did, not possess a definite MD, if they were under the age of 20 or above 70, or if they had a history of taking supplements containing vitamin D or medications that could interfere with vitamin D metabolism. (e.g., rifampicin, anticonvulsant as well as antifungal).

Research Ethics:

The study's protocol was approved by the Medical Research Ethics Committee of Sohag university's faculty of medicine (Soh-Med-23-03-15PD).

Methodology:

A. Audiological and vestibular evaluation:
   1. Detailed History: MD patients were asked about audiovestibular symptoms, number of vertigo attacks, attack duration, severity associated symptoms.
   2. Audiometric evaluation: all tests was done in sound treated using then hearing threshold were obtained by (Interacoustics AD 629) coupled with TDH -39 headphone to obtain PTA threshold across the conventional frequency range of the hearing test (0.5 ,1 ,2 ,4 kHz)
   3. Immitancmetry: otoscopic examination and tympanometry were completed to ensure normal middle ear functions by (GSI-39) TympoStar:Grason-Stadler,Inc.,Denmark.
   4. **Questionnaire**: Dizziness Handicapped Inventory (DHI) Questionnaire is composed of twenty-five questions. There are 7, 9, and 9 questions related to physical (DHI-P), functional (DHI-F), and emotional (DHI-E) aspects

of dizziness in MD, respectively, participants were asked to concentrate on their condition over the previous six months. The total DHI score was determined, and the severity was classified as mild (zero-thirty points), moderate (thirty-one-sixty points), or severe (sixty-one-one hundred points).

B. Vitamin D:

Vitamin D level in the serum: The serum vitamin D level was determined using the VIDAS enzyme-linked fluorescent assay. The clinical practice guideline of the European Society of Endocrinology defined vitamin D deficiency as a vitamin D level of twenty ng/mL, insufficient as a level between 21 and 29 ng/mL, and values. Thirty ng/mL was considered normal. [10,11]

Vitamin D supplement: All the participants with vitamin D deficiency were receiving vitamin D oral capsule 50000 IU/week regularly for 3 months.

C. Re-evaluation:

After a full regimen of vitamin D supplementation, all participants with MD and vitamin D deficiency were reevaluated, with improvements in attack duration, frequency, and severity, DHI, and vitamin D assay.

Statistical analysis:

IBM SPSS Statistics for Windows version 23.0 was used to analyze the data. The paired T-test and correlation co-efficient measures were among the statistical tests used in the analysis. P values of 0.05 or less were considered significant.

Results

An entire number of 112 participant were included in our study; 28 adults complaining of MD were included in this study, and 84 controls. Age ranged from 20-50 years with (mean age 34 years SD ±8.8). As regard gender distribution of the study group, there were 19 male (67.8%) and 9 females (33.2%). Age, gender, occupation, BMI, and smoking status were all matched between the study and control groups (Table 1). Based on the inclusion criteria, all patients had vertigo and hearing loss, with hearing loss being bilateral in four (14.2%) patients. Furthermore, tinnitus was reported in 23 (82.1%) cases, with 11 (39.2%) reporting it to be annoying. Twenty-one people (75%) had aural fullness.

Table (1): Demographic distribution of MD patients and controls:

	Case (n = 28)	**Control (n = 84)**	**P value**
Age, y	34±8.8	33.45±8.7	0.7
Body mass index	24.45	25.11	0.68
Sex Male female	67.8% (19) 33.2% (9)	55 % (46) 45% (38)	0.61
Occupation Indoor outdoor	13 (46.4%) 15 (53.6%)	39 (46.4%) 45 (53.6%)	0.58
Smoking Yes no	4 (14.3) 24 (85.7)	12 (14.3) 72 (85.7)	0.608

The mean vitamin D levels in the case and control groups were (18.8 ± 4.7) and (33.6± 6.6) ng/mL, respectively (P<0.0001).

In addition, we found a significant statistical difference DHI before and after supplementation with vitamin D (Table, 2).

Table (2): Paired T test for vitamin D &DHI before and after treatment in MD patients

	Before treatment		**After treatment**		**P value**
	Mean	SD	Mean	SD	
Vitamin D Level	18.8	4.7	41.1	39.9	0.056
DHI	44.68	14.71	33.05	11.85	<0.0001*

Finally, we found a highly significant statistical difference in the duration and frequency of attack before and after vitamin D supplementation (Table 3)

Table (3): Paired t test for frequency &duration of attack in MD before and after treatment.

	Before treatment	After treatment	
Duration			P<0.0001*
<6 Hour	4	19	
6-12 Hour	10	4	
>12 Hour	14	5	
Frequency			P< 0.0001*
<3 attacks per 3 months	7	15	
3-4 attack	8	8	
>4 attacks	13	5	

Discussion:

Meniere's disease progresses slowly, it has a fluctuating course; it is a disease of the inner ear characterized by vertigo attacks, fluctuation in SNHL, tinnitus, and aural fullness. MD is a complicated heterogeneous illness in which many underlying factors interact, including temporal bone anatomical variation, autoimmunity, and altered dynamics of intralabyrinthine fluid due to abnormal ion channel function. However, the precise cause of MD remains unknown. [1-3]

Adding to its typical involvement in homeostasis of mineral, vitamin D has been shown to have unique effects in proliferation and differentiation of the cell, antiaging capabilities, and special effects on neurodegenerative illnesses. [12] In this context, the question is whether deficiency of vitamin D has any effect on function of inner ear function, particularly for MD.

There is paucity of evidence in publications about the link between MD and vitamin D. But there were multiple researches on other inner ear disorder have been conducted in this area. BPPV is a peripheral vestibular illness that has been linked to vitamin D in multiple studies. A number of studies have found that osteoporosis and osteopenia are linked to BPPV [13-14], however, a number of authors argue that this is just a concurrence. [15] A recent meta-analysis of 18 researches on this topic found that vitamin D insufficiency is an independent hazardous factor for benign paroxysmal positional vertigo. [15]

Furthermore, the recurrence of BPPV has been linked low serum vitamin D content. [16] Otoconia separation could be a pathogenic mechanism for Meniere's disease. Meniere's disease has a similar age of onset to BPPV, implying that there may be a similar pathophysiologic basis in this regard. [17-19]

There is also a proof has associated between blood levels of otolin-1 (an otoconia-derived protein) and vitamin D. [20,21] Patients with MD, in contrast, had higher blood levels of otolin1. [19] Upcoming research is needed to see if the otolithic hypothesis of MD is linked to low serum level of vitamin D. The problem can also be handled from the standpoint of autoimmunity, previous viral infections and autoimmune illnesses have been hypothesized to explain the Meniere's disease ‘s physiopathology. [22-23]

Based on the discovery of demyelination in the vestibular nerve, it has been proposed that immune-mediated mechanisms, like those found in multiple sclerosis and Guillain-Barre syndrome, play a role in MD. [24]

Furthermore, vitamin D has an immunoregulatory property, and the epidemiological studies show that low serum level vitamin D is frequent among immune system disorders and certain infectious diseases. [17,25,26] The adaptive immune system is also inhibited by vitamin D. [27] Normal vitamin D levels have been shown to inhibit the production of

proinflammatory cytokines in patients complaining of congestive heart failure and inflammatory bowel disease. [28,29] Vitamin D is thought to influence the proinflammatory mediator genes expression (such as 5-lipoxygenase or cyclooxygenases), interactions with transcription factors (such as NF-kappaB), and signaling cascade activation (such as mitogen-activated protein kinase), all of which are involved in inflammatory responses. 30 In vitro studies have shown that carriers of genotype-selected lymphoblastoid cells can develop NF-kappaB-induced inflammation in MD patients. [31] According to Buki et al, vitamin D may be able to prevent a final post-viral autoimmune response. Vitamin D's anti-oxidative activity and role in endothelial cell stabilization could explain this beneficial effect. [32]

Aside from surveys aimed at possible pathophysiology, researches evaluating the prevalence of occurrence of MD with that of vitamin D deficiency might be an interesting issue for future projects. That will be a very informative and helpful study, and it is possible that the potential role of direct sunlight exposure/latitude will be revealed. However, determining the incidence and prevalence of MD is difficult due to differences in diagnostic criteria among publications. MD is estimated to affect 190 to 218 people per 100,000 in the United States. [33-36] Mehdi et al found a low serum vitamin D level in patients with MD. [37] and this agree with our results as we found that there was significant statistically low serum of vitamin D in MD patients and we found that there was significant statistically improved in symptoms in MD as regards decrease in frequency of occurrence of attack and decrease in its severity and duration. We found that vitamin D level was (18,8±4,7) in MD, on the other hand vitamin D was 33.6±6.6 in the control and so vitamin D was significantly lower in patients with Meniere's disease. In addition, we found that DHI score was 44.68 ± 14.71 and it became 33.05 ± 11.85 after vit D supplementation and p value was $p<0.0001$ which mean that vit D helps improving symptoms of MD. Also there was significant statistically difference in frequency and duration of attacks of MD which means that vitamin D have beneficial effect in controlling MD attacks.

Conclusion:

The present research found that MD patients had lower serum vitamin D levels. There is a correlation between vitamin D deficiency and MD. Vitamin D supplementation has a beneficial role in controlling MD symptoms and lowering frequency of occurrence of the disease.

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Conflicts of interest: No

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