Association of Vitamin D levels and Cognitive function in Postmenopausal women

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Abstract

Background: Vitamin D deficiency (VDD) is a major health concern in India, especially in elderly individuals and is adversely associated with neurocognitive function.

Aims and Objectives:
1. To assess the 25hydroxy vitamin D [25(OH)D] levels in postmenopausal women and compare it with premenopausal women.
2. To study the association of 25(OH)D levels with markers of cognitive impairment, that is Mini-Mental State examination (MMSE) and Addenbrooke’s Cognitive Examination – Revised (ACE-R) score in postmenopausal women.

Materials and Method: A cross sectional study was conducted on 40 postmenopausal women and 40 premenopausal women as controls. The study subjects were analysed for 25(OH)D levels by ELISA and Cognitive function was assessed by using the MMSE and ACE-R score. Appropriate statistical analysis was done.

Results: Serum 25(OH)D levels (22.3±13.58 ng/ml Vs 32.4±12.4 ng/ml) in postmenopausal women were significantly lower (p-value = 0.03) when compared to the premenopausal women. A significant positive correlation was found between the 25(OH)D levels and the markers of cognitive decline (i.e) MMSE (r = 0.40) and ACE-R score (r = 0.61) in postmenopausal women. Even though the vitamin D levels in premenopausal women were higher than postmenopausal women, a significant proportion (60%) had vitamin D inadequacy.

Conclusion: A significantly lower 25(OH)D levels, MMSE and ACE-R scores were observed in postmenopausal women when compared to premenopausal women. 25(OH)D levels were significantly associated with markers of cognitive decline. These results suggest a potential role of Vitamin D in cognitive dysfunction in postmenopausal women and can be considered as an early marker for cognitive decline.

Keywords: Cognitive Function, Vitamin D, Postmenopausal Women, Neurocognitive Function.

Introduction

Vitamin D, popularly known as sunshine vitamin is both vital and indispensable for human beings. Vitamin D, a fat soluble steroid hormone is involved in numerous metabolic processes especially calcium and bone metabolism.1 Despite abundant sunshine, Vitamin D deficiency is documented across all age groups and both sexes from India.2 A study conducted in Delhi in healthy Indians above 50 years has reported that 91.2% subjects had VDD.3 Vitamin D deficiency is not only related to fractures, but also increases the probability of stroke, diabetes and hypertension which leads to dementia4,7 and may also be directly associated with the onset of neurodegenerative diseases.8 Association of VDD with Cardiovascular diseases has been consistently proven globally.9

A growing body of evidence emphasizes the role of vitamin D in cognitive function10-12 the results of which suggest that lower vitamin D concentrations are associated with poorer cognitive function and a higher risk of Alzheimer’s disease (AD).12 More precisely, numerous preclinical and clinical studies suggest that hypovitaminosis D may be associated with increased risk of developing AD and dementia, without being a causal agent. Inducing genomic and non genomic effects, vitamin D plays a role on calcium homeostasis, neurotransmission, vascularization, Aβ and Tau accumulation, oxidative stress, and inflammation, all of which are disturbed in AD.13

Menopause is permanent cessation of menstruation following loss of ovarian activity, which has considerable impact on social, reproductive, physical and psychological health. Women in India are prone to an earlier menopause and all its implications on their health at an earlier age than their counterparts in the industrialized world.14 Studies across the world have reported a high prevalence of Vitamin D deficiency in postmenopausal women.15-18 Studies on postmenopausal women have also associated VDD with osteoporosis, obesity, cardiovascular risk and diabetes.19 An observational study has reported that vitamin D deficiency was associated with increased risk of mortality, MI, HF or stroke in healthy postmenopausal women.20 82% of the postmenopausal women had varying degrees of low 25(OH)D levels in a study conducted in South India.21

As the role of vitamin D in skeletal health has been established, there is continued interest in vitamin D’s broad spectrum of health benefits and outcomes. Although extensive research has been conducted on this arena, mixed results have been reported. Based on this background, our study analyzes the association of vitamin D levels with cognitive function in postmenopausal age group. Vitamin D’s association with cognitive dysfunction in the postmenopausal women...
may have significant implications in their health care, who are often the neglected part of the community.

Materials and Methods

The present cross sectional study was conducted over a period of 6 months from January 2015 to June 2015 at Vinayaka Missions Kirupananda Variyar Medical College. After obtaining the Institutional Ethical Committee clearance and informed consent from the patients, the study was initiated. A total of 80 women were considered for the study which includes 40 post menopausal women and 40 premenopausal women attending the Gynaecology Out Patient Department. Postmenopausal status is defined as cessation of menstruation for atleast one year. Those women who were on drugs like oral contraceptives, statins, anticonvulsants, vitamin D or calcium supplemnetations and women with endocrine disorders, chronic liver or kidney disease were excluded.

Demographic and anthropometric data were collected from all the women. Body mass index (BMI), Waist Hip ratio (WHR) and blood pressure (BP) were recorded. All the women answered a questionnaire assessing the cognitive function by Mini-Mental State examination (MMSE) and Addenbrooke's Cognitive Examination – Revised (ACE-R) score.

In MMSE, functions such as registration, attention, calculation, recall, language (comprehension, reading, writing and naming), ability to follow simple commands, and orientation were examined. For MMSE, scores above 27 are considered normal and scores below 24 indicates impairment in cognition. The ACE-R is a brief cognitive test that assesses five cognitive domains, namely attention/orientation, memory, verbal fluency, language and visuospatial abilities. Total score is 100, higher scores indicates better cognitive functioning. Administration of the ACE-R takes, on average, 15 minutes. ACE scores 90 or above indicates normal cognition and scores below 90 indicates cognitive impairment. ACE-R accomplishes standards of a valid dementia screening test, sensitive to early cognitive dysfunction.

Venous blood samples were collected in the morning after an overnight fast of 8-12 hours. Fasting blood glucose (FBG), triglycerides (TG), Total cholesterol (TC), HDL-cholesterol were analysed by Glucose oxidase peroxidase, Glycerol oxidase peroxidase, Cholesterol oxidase peroxidase and Direct method respectively. LDL-cholesterol levels were calculated by Friedwald formula. Serum 25-(OH) vitamin D was estimated by Enzyme linked immunosorbent assay (ELISA). Measurement of 25(OH)D in the circulation is the best diagnostic test to determine the vitamin D status of a person. Several Indian studies have used the following cut off levels for VDD. The vitamin D levels are considered normal when it is >30ngms/ml and it is insufficient when the level is between 20 – 30ngms/ml and deficit when it is less than 20ngms/ml.

Statistical Analysis: Statistical evaluation was performed using the Statistical Package for Social Sciences (SPSS) software. Values were expressed as Mean ± Standard deviation. Student’s t-test was used to compare the premenopausal group with the premenopausal group. Correlation between two variables was assessed by using the Pearson’s correlation coefficient. A p-value of <0.05 was considered as statistically significant.

Results

A total of 80 women were studied in this cross sectional study. The women were categorized into 2 groups, premenopausal and postmenopausal group. Table 1 shows the demographic and anthropometric details of the study subjects. Table 2 shows the markers of cognitive function in pre and postmenopausal women. The markers of cognitive function were significantly decreased in postmenopausal women. As shown in Table 3, vitamin D levels were significantly low in postmenopausal women when compared to the premenopausal women. Table 4 depicts the correlation of Vitamin D levels with the MMSE and ACE-R scores in which a positive correlation was noted between them in postmenopausal women.

Table 1: General characteristics of study subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Post-menopausal women (M±SD)</th>
<th>Pre-menopausal women (M±SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number(n)</td>
<td>40</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>59.71 ± 5.27</td>
<td>40.84 ± 2.24</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>29.9 ± 2.42</td>
<td>24.5 ± 3.33</td>
<td>0.032*</td>
</tr>
<tr>
<td>WHR</td>
<td>0.84 ± 0.03</td>
<td>0.78 ± 0.04</td>
<td>6.24</td>
</tr>
</tbody>
</table>

BMI – Body Mass Index, WHR – Waist Hip Ratio, *statistically significant

Table 2: Markers of cognitive function in study subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Post-menopausal women (M±SD)</th>
<th>Pre-menopausal women (M±SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>21.6 ± 4.97</td>
<td>25.42 ± 1.65</td>
<td>0.01*</td>
</tr>
<tr>
<td>ACE-R</td>
<td>78.65 ± 11.02</td>
<td>83.11 ± 5.63</td>
<td>0.04*</td>
</tr>
</tbody>
</table>

MMSE - Mini-Mental State examination, ACE-R - Addenbrooke’s Cognitive Examination – Revised score *statistically significant

Table 3: Laboratory data of study subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Post-menopausal women (M±SD)</th>
<th>Pre-menopausal women (M±SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D</td>
<td>22.3±13.58</td>
<td>32.4±12.4</td>
<td>0.03*</td>
</tr>
</tbody>
</table>
of Cognitive decline.\cite{22,23} Markers of cognitive dysfunction were significantly decreased in postmenopausal women when compared to the premenopausal women. Also, our observations show a significant positive correlation of 25(OH)D levels with the MMSE and ACE-R scores. This is in agreement with Yelena Slinin et al,\cite{10} where very low 25(OH)D levels among older women were associated with higher odds of global cognitive impairment. Other studies which have found an association with vitamin D levels and risk of cognitive decline are Tejal Kanhaiya Vedak et al,\cite{11} Llewellyn et al,\cite{27} Babak Hooshmand et al,\cite{28} CL Chei et al,\cite{29}

Several mechanisms have been suggested linking the role of vitamin D and risk of cognitive dysfunction. The active form vitamin D is a seco-steroid with multiple neurotrophic and neuroprotective functions in the central nervous system. Vitamin D plays a pivotal role in the development of brain as well as in adult brain function. All the cell types within the brain have the ability to synthesize active vitamin D. Both the vitamin D receptor and the enzyme required for the synthesis of active vitamin D are found in the adult human brain. At the molecular level, the brain has the ability to synthesize the active form of vitamin D within many cell types and regions with predominance in the hypothalamus and the large neurons within the substantia nigra.\cite{30} Vitamin D contributes to neuroprotection by modulating the production of nerve growth factor (NGF), neurotrophin, glialcell-derived neurotrophic factor (GDNF), nitric oxide synthase (NOS), and choline acetyltransferase.\cite{12}

Strength of this study is that, it is done at an earlier stage before the onset of cognitive dysfunction. Quality of life of postmenopausal women can be improved when VDD can be timely prevented, early diagnosed and adequately managed.

**Limitations**

The study was a cross-sectional study with small sample size. The study is also based only on a single measurement of Vitamin D and it would have been ideal if follow up studies were done and also, calcium and parathyroid hormone levels were evaluated.

**Conclusion**

These results suggest a potential role of Vitamin D in cognitive dysfunction in postmenopausal women suggesting vitamin D as an early marker for cognitive decline. These findings may be helpful in designing the preventive measures of cognitive dysfunction in postmenopausal women who often seek health care rarely.

**References**