Vitamin D and orthostatic hypotension

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Abstract

Introduction: we aimed to investigate on the potential relationship between vitamin D and orthostatic hypotension (OH) in a case–control model in older adults.

Methods: all participants were community-dwelling adults who were not taking vitamin D supplements. Cases were subjects aged 64 or older who were diagnosed with OH at a Falls and Blackout Unit. Controls were age- (within 5 years) and gender-matched subjects who had no history of blackouts, falls or orthostatic dizziness in the preceding year. OH was defined according to standard criteria and was diagnosed with an active stand test. Serum vitamin D [25(OH)D] was measured by radioimmunoassay.

Results: seventy-six subjects were included in the analysis (38 controls and 38 cases). Twenty-four in each group were female and mean age was between 78 and 79 years. Subjects with OH had lower serum 25(OH)D compared to controls (mean difference = 20.6 nmol/l, P = 0.0002). Lower vitamin D status was associated with an increased risk of OH after adjustment for season, body mass index, presence of stroke, diabetes and angina (P = 0.035) but not with impaired orthostatic haemodynamics.

Discussion: findings suggest that vitamin D may play a role in the aetiology of OH. Further studies will be required to explore on this relationship.

Keywords: vitamin D, orthostatic hypotension, orthostatic haemodynamics, older people

Orthostatic hypotension (OH) is common in the elderly and is associated with falls, fractures and significant morbidity and mortality [1]. Vitamin D supplementation has been shown to reduce risk of falls that may be mediated by its effect on muscle strength and balance [2–4]. However, other potential mechanisms for this fall reduction are unclear. It is possible that vitamin D may also play a role in orthostatic hypotension, though evidence is lacking. Vitamin D has been implicated in both systolic and diastolic blood pressure, as well cardiovascular and cerebrovascular disease [5–9]. Vitamin D receptors are found in vascular smooth muscle, endothelial and cardiac cells suggesting that vitamin D could affect vasomotor and cardiac response during orthostasis [10].

We aimed to investigate the hypothesis that lower vitamin D status is associated with orthostatic hypotension in a case–control model involving community-dwelling older adults.

Methods

All participants were community-dwelling adults who were not taking vitamin D supplements. Cases were subjects aged 64 or older who were diagnosed with orthostatic hypotension at the Falls and Blackout Unit at St James’s Hospital, Dublin and were consecutively recruited between January and February 2009. Those unwilling or unable to
give consent or who had an illness in the past month were excluded.

Controls were age- (within 5 years) and gender-matched subjects who had no history of blackouts, falls or orthostatic dizziness in the preceding year and who were participants of the Dublin Healthy Ageing Study (DHAS), details of which have been previously described [11]. This is a community-based study examining physical, psychiatric, cognitive and social health care characteristics of non-demented older people. Subjects in the DHAS who met our criteria were randomly selected from this study database. Blood samples and clinical data from the DHAS were used for comparison with the OH group who attended the Falls and Blackout Unit.

Assessments

Orthostatic hypotension was diagnosed with the use of an active stand test and was defined according to the consensus criteria as a reduction in systolic or diastolic blood pressure of ≥20 and 10 mmHg respectively, within 3 min of assuming an erect posture [12].

The active stand test involves measuring haemodynamic variables while the patient moved from a horizontal to a standing position with or without assistance. Non-invasive continuous plethysmographic measurements of beat-to-beat blood pressure and heart rate were recorded with the use of a standardized device (Finometer®). This converts finger arterial pressures to brachial arterial pressures by a method of brachial reconstruction. Measurements were taken after lying supine for 5 min and then on standing up quickly and continuing to stand for 3 min. Blood pressure and heart rate were noted every 30 s from baseline until the manœuvre was complete.

All subjects had their height (m) and weight (kg) measured and body mass index calculated by standard formula (weight/height²). The Mini-Mental State Examination (MMSE) was administered as a screen of global cognitive function [13]. Non-fasting vitamin D blood samples were drawn, centrifuged within two hours and stored at −20°C until later analysed at St James’s Hospital Biochemistry laboratory. 25-Hydroxyvitamin D status was determined until later analysed at St James’s Hospital.

All participants gave informed consent and ethical approval was granted by the Research Ethics Committee of St James’s Hospital.

Statistical analysis

All data were analysed with the statistical software program JMP® version 8.0 (SAS Institute Inc., Cary, NC, USA). Mean and standard deviation were used as descriptive statistics. Serum 25(OH)D was not normally distributed in the OH group and was logarithmically transformed. Differences in vitamin D status and baseline characteristics between both cohorts were analysed with the unpaired t-test, Mann–Whitney and Fisher’s exact test. The relationship between vitamin D, OH and haemodynamic parameters on the active stand was explored in logistic and multiple linear regression models. Analysis for outliers was performed graphically and with the Cook’s D test and any identified were excluded as appropriate. Statistical significance was accepted when P < 0.05.

Results

Seventy-six subjects were included in the analysis (38 controls and 38 cases). Twenty-four subjects in each group were females and had a mean age of between 78 and 79 years. Two subjects had Parkinson’s disease, though their exclusion in an analysis did not change the study findings. Baseline characteristics were otherwise similar in both groups though participants with OH had a higher baseline systolic blood pressure (mean difference 9.9 mmHg, P = 0.03; Table 1).

In the combined group (n = 76), an inverse association was found between serum 25(OH)D and baseline diastolic blood pressure before and after adjustment for season and body mass index (β = −0.13, P = 0.03). While there was a trend for higher systolic blood pressure in those with lower 25(OH)D this was not statistically significant (β = −0.18, P = 0.08).

Subjects with orthostatic hypotension (OH) who were age- and gender-matched had a significantly lower 25(OH)D than controls (mean difference = 20.6 nmol/l, P = 0.0002). In a logistic regression model incorporating 25(OH)D as a continuous variable, an increased risk of OH was found in those with lower levels after adjusting for season, body mass index, history of diabetes, stroke and ischaemic heart disease (β coefficient = −0.03, P = 0.035).

However, lower 25(OH)D in those with OH was not associated with any drops in systolic or diastolic blood pressure, either before or after adjustment for covariates. In fact, those with a greater fall in systolic blood pressure had

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cases</th>
<th>Controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>79.0 ± 6.8</td>
<td>78.2 ± 5.8</td>
<td>0.65&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Body mass index (kg m&lt;sup&gt;−2&lt;/sup&gt;)</td>
<td>25.5 ± 4.0</td>
<td>25.1 ± 3.4</td>
<td>0.66&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>154.6 ± 22.6</td>
<td>144.7 ± 19.3</td>
<td>0.03&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>77.1 ± 11.3</td>
<td>72.6 ± 10.6</td>
<td>0.07&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>2 (5.3)</td>
<td>6 (15.8)</td>
<td>0.26&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>7 (18.4)</td>
<td>2 (5.3)</td>
<td>0.13&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Angina (%)</td>
<td>4 (10.5)</td>
<td>17 (4.3)</td>
<td>0.51&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>MMSE</td>
<td>26.4 ± 2.9</td>
<td>27.2 ± 2.3</td>
<td>0.26&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>25(OH)D (nmol/l)</td>
<td>40.5 ± 22.2</td>
<td>61.1 ± 23.1</td>
<td>0.0002&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Unpaired t-test.
<sup>b</sup>Fisher’s exact test.
<sup>c</sup>Mann–Whitney test.
higher vitamin D status. In addition, no association was found between 25(OH)D and resting heart rate or changes in heart rate in the OH group (Table 2).

Discussion

To our knowledge, this is the first study that has investigated on a relationship between serum 25(OH)D and orthostatic hypotension. The finding that vitamin D levels were lower in subjects with OH raises the possibility that it may play an aetiological role. There is a good biological plausibility underlying the potential affect of vitamin D on blood pressure control and intravascular volume, mechanisms by which it could contribute to OH. Vitamin D has been shown to down-regulate the renin–angiotensin aldosterone system in rodent models and this also appears to be up-regulated in human subjects who have vitamin D deficiency [14, 15]. In addition, it has also been associated with endothelial dysfunction and hence may have the potential to affect vasopressor response [16–18].

We also found a significant association between 25(OH)D and diastolic blood pressure which has been identified in other studies [5, 19]. While no association was found between lower vitamin D status and blood pressure drops or changes in heart rate, the study number was small and so wider conclusions on this cannot be drawn. However, 25(OH)D has been inversely associated with resting heart rates in a large study of community dwelling!US adults, raising the possibility that it may have an effect on autonomic function [20].

Orthostatic haemodynamics appears to be impaired in frailty in older adults and frailty is also associated with lower vitamin D levels [21, 22]. It is possible that frailty and antihypertensive use, which were not adjusted for, may have changed the study findings.

Given that vitamin D deficiency is prevalent in the older population [10] and supplementation is inexpensive, it may provide a practical alternative strategy for treating other non-skeletal conditions like OH. Further larger observational studies and randomised controlled trials will be required to explore on this relationship.

Key points

- Vitamin D levels were significantly lower in patients with OH.
- Lower vitamin D status was not associated with impaired orthostatic haemodynamics.
- Further studies are needed to explore this relationship.

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