Analyze the Role of Vitamin D in the Development of Prehypertension and the Connection with Cellular Ageing

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Abstract

Aim: Evaluate the Role of Vitamin D in pre-hypertension and its association with cellular senescence. Methods: This cross-sectional comparative study conducted in the Department of Physiology, Anugrah Narayan Magadh Medical College, Gaya, Bihar, India, for one year. Inclusion criteria for the pre-hypertensive group (pre-HTN) (n = 50) were both genders between 18 and 27 years of age with SBP between 120 and 139 mmHg and DBP between 80 and 89 mmHg in apparently healthy individuals. The controls (n = 50) population were healthy individuals with 18–27 years of age with SBP between 100 and 119 mmHg and DBP between 60 and 79 mmHg. Results: The study population included 100 apparently healthy individuals. 50 of 100 were pre-hypertensives with the age of 19.11±0.40 and the age of controls was 19.05±0.78. A significant difference was not found between-group differences in height and waist-hip ratio. However, pre-HTN group subject’s BMI (P < 0.0001) and weight (P < 0.0001) was more compared to controls. Mean and standard deviation of various cardiovascular parameters are given in Table 2. In pre-HTN group, significantly higher HR (P < 0.0001), SBP (P < 0.0001), DBP (P < 0.0001), MAP (P < 0.0001), and RPP (P < 0.0001) were seen when compared to controls. No significant difference was seen in PP but it was slightly high in pre-HTN group and negatively associated with Vit-D (r: ‒0.388). The values of Vit-D, telomerase in both groups. Significantly low levels of Vit-D (P < 0.0001) and high telomerase (P < 0.0001) were seen in pre-HTN group when compared to controls. Table 4 shows the correlation of Vit-D and other parameters in pre-HTN group. Low levels of Vit-D have no correlation with BMI, waist-hip ratio, DBP, and MAP. However, significant correlation was seen with HR (r: ‒0.312), SBP (r: −0.554), PP (r: −0.388), RPP (r: 0.478), and telomerase (r: −0.388). Further, as shown in Table 5, high telomerase levels have correlation with waist-hip ratio (r: 0.337), SBP (r: 0.479), DBP (r: 0.446), MAP (r: 0.659), and RPP (r: 0.329) but no significant correlation was seen with BMI, HR, and PP. Conclusion: The reduced Vit-D levels in pre-HTN may cause derangements of cardiovascular homeostatic mechanism, enhance the speed of cellular senescence measured by telomerase.

Keywords: Vitamin D, hypertension, cellular senescence.
Introduction

Vitamin D deficiency has recently emerged as a public health problem, affecting almost 50% of the population worldwide[1]. In addition to the reduced exposition to sunlight[2], also genetic and environmental factors have been suggested as a cause of this pandemic, such as pollution, diet, sedentary lifestyle and stress[3]. Moreover, vitamin D is no longer considered as only a pivotal media-tor of calcium metabolism and skeletal health, but it also regulates several cell functions, including differentiation and metabolism. This aspect may explain the reason why hypovitaminosis D has been proved to be an independent risk factor for overall mortality in various cohort analyses[4], whereas vitamin D supplementation significantly reduced mortality[5]. Moreover, similar data were collected from different clusters of inflammatory and chronic diseases, such as infections[6], autoimmunity[7], neurodegenerative pathologies[8], as well for cancer[9]. However, a special interest was conferred to the potential relationship between vitamin D and cardiovascular (CV) disorders. Although in human cohorts low vitamin D levels were associated with impaired CV outcomes[10], a causal relationship remains unknown, and the general enthusiasm about the benefits of vitamin D supplementation have been recently replaced by words of caution.

On the other hand, novel topics that might address many questions in the field of vitamin D, such as fibroblast growth factor (FGF) 23-klotho axis, non-genomic effects of vitamin D and the paracrine effects of vitamin D (also called “local vitamin D system”) have been identified. In the following paragraphs, we will focus on the mechanisms triggered by vitamin D in arterial hypertension, starting from the complex interplay with the renin-angiotensin-aldosterone system (RAAS) in both basic research and clinical trials.

Material and methods:

This cross-sectional comparative study conducted in the Department of Physiology, Anugrah Narayan Magadh Medical College, Gaya, Bihar, India, for 1 year. Inclusion criteria for the pre-hypertensive group (pre-HTN) (n = 50) were both genders between 18 and 27 years of age with SBP between 120 and 139 mmHg and DBP between 80 and 89 mmHg in apparently healthy individuals. The controls (n = 50) population were healthy individuals with 18–27 years of age with SBP between 100 and 119 mmHg and DBP between 60 and 79 mmHg. Individuals suffering from diabetes, hypertension, endocrine disorders, kidney diseases, and hypertensive patients already receiving medication were not considered to take part in this research.

Methods

The volunteers were asked to not participate in heavy exercises, not drink alcohol and coffee 1 day before the data collection. Baseline, anthropometric parameters were recorded before recording of the BP by sphygmomanometer as per standard protocol[11]. Then, 5 ml of blood was collected, allowed to clot, and subjected to centrifugation to separate the serum. Serum was stored at −80°C for processing of Vit-D and telomerase levels as per the instructions provided in the commercially available kits.

Statistical Analysis

To study the between-group differences, independent t-test, to assess the correlation of Vit-D with telomerase and other parameters, Pearson’s correlation coefficient analysis was applied.

Results

The study population included 100 apparently healthy individuals. 50 of 100 were pre-hypertensives with the age of 19.11±0.40 and the age of controls was 19.05±0.78. Among 50 in each group, 32
males, 18 females in pre-HTN group and 26 males, 24 females in the control group. Table 1, a significant difference, was not found between-group differences in height and waist-hip ratio. However, pre-HTN group subject’s BMI ($P < 0.0001$) and weight ($P < 0.0001$) was more compared to controls. Mean and standard deviation of various cardiovascular parameters are given in Table 2. In pre-HTN group, significantly higher HR ($P < 0.0001$), SBP ($P < 0.0001$), DBP ($P < 0.0001$), MAP ($P < 0.0001$), and RPP ($P < 0.0001$) were seen when compared to controls. No significant difference was seen in PP but it was slightly high in pre-HTN group and negatively associated with Vit-D ($r: -0.388$).

Table 1: Comparison of anthropometric characteristics between pre-HTN and controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-HTN ($n=50$)</th>
<th>Controls ($n=50$)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>19.11±0.40</td>
<td>19.05±0.78</td>
<td>0.45</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>32/18</td>
<td>26/24</td>
<td>NA</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.55±7.58</td>
<td>163.11±7.88</td>
<td>0.42</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.63±11.89</td>
<td>55.73±9.65</td>
<td>0.0001</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>24.86±3.52</td>
<td>21.24±4.29</td>
<td>0.0001</td>
</tr>
<tr>
<td>Waist to hip ratio</td>
<td>0.84±0.05</td>
<td>0.83±0.11</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Table 2: Comparison of cardiovascular parameters between pre-HTN and controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-HTN ($n=50$)</th>
<th>Controls ($n=50$)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (BPM)</td>
<td>87.88±3.85</td>
<td>79.77±3.13</td>
<td>0.0001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>124.24±4.39</td>
<td>117.5±4.15</td>
<td>0.0001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>84.54±3.40</td>
<td>75.51±3.66</td>
<td>0.0001</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>39.75±6.43</td>
<td>38.19±4.24</td>
<td>0.181</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>97.75±2.11</td>
<td>88.21±3.03</td>
<td>0.0001</td>
</tr>
<tr>
<td>RPP</td>
<td>10814.83±725.51</td>
<td>9141.80±485.90</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Table 3: Comparison of Vitamin D and telomerase levels between pre-HTN and controls

Table 3 depicts the values of Vit-D, telomerase in both groups. Significantly low levels of Vit-D ($P < 0.0001$) and high telomerase ($P < 0.0001$) were seen in pre-HTN group when compared to controls. Table 4 shows the correlation of Vit-D and other parameters in pre-HTN group. Low levels of Vit-D have no correlation with BMI, waist-hip ratio, DBP, and MAP. However, significant correlation was seen with HR ($r: -0.312$), SBP ($r: -0.554$), PP ($r: -0.388$), RPP ($r: 0.487$), and telomerase ($r: -0.388$). Further, as shown in Table 5, high telomerase levels have correlation with waist-hip ratio ($r: 0.337$), SBP ($r: 0.479$), DBP ($r: 0.446$), MAP ($r: 0.659$), and RPP ($r: 0.329$) but no significant correlation was seen with BMI, HR, and PP.

Table 4 shows the correlation of Vit-D and other parameters in pre-HTN group. Low levels of Vit-D have no correlation with BMI, waist-hip ratio, DBP, and MAP. However, significant correlation was seen with HR ($r: -0.312$), SBP ($r: -0.554$), PP ($r: -0.388$), RPP ($r: 0.487$), and telomerase ($r: -0.388$). Further, as shown in Table 5, high telomerase levels have correlation with waist-hip ratio ($r: 0.337$), SBP ($r: 0.479$), DBP ($r: 0.446$), MAP ($r: 0.659$), and RPP ($r: 0.329$) but no significant correlation was seen with BMI, HR, and PP.

Table 3: Comparison of Vitamin D and telomerase levels between pre-HTN and controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-HTN ($n=50$)</th>
<th>Controls ($n=50$)</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D (ng/ml)</td>
<td>17.57±4.88</td>
<td>20.65±7.79</td>
<td>0.052</td>
</tr>
<tr>
<td>Telomerase (IU/ml)</td>
<td>37.17±17.66</td>
<td>7.79±3.55</td>
<td>0.0001</td>
</tr>
</tbody>
</table>
Table 4: Correlation between Vitamin D and other parameters in pre-HTN

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Vitamin D (ng/ml)</th>
<th>r-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td>0.105</td>
<td>0.52</td>
</tr>
<tr>
<td>Waist hip ratio</td>
<td></td>
<td>0.216</td>
<td>0.17</td>
</tr>
<tr>
<td>HR (BPM)</td>
<td></td>
<td>-0.312</td>
<td>0.052</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td></td>
<td>-0.554</td>
<td>0.0001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td></td>
<td>0.230</td>
<td>0.131</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td></td>
<td>-0.388</td>
<td>0.015</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td></td>
<td>-0.100</td>
<td>0.519</td>
</tr>
<tr>
<td>RPP</td>
<td></td>
<td>0.487</td>
<td>0.001</td>
</tr>
<tr>
<td>Telomerase (IU/ml)</td>
<td></td>
<td>-0.388</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Table 5: Correlation between telomerase and other parameters in pre-HTN

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Telomerase</th>
<th>r-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td>0.231</td>
<td>0.16</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td></td>
<td>0.337</td>
<td>0.024</td>
</tr>
<tr>
<td>HR (BPM)</td>
<td></td>
<td>0.132</td>
<td>0.37</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td></td>
<td>0.479</td>
<td>0.001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td></td>
<td>0.446</td>
<td>0.003</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td></td>
<td>0.053</td>
<td>0.68</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td></td>
<td>0.659</td>
<td>0.000</td>
</tr>
<tr>
<td>RPP</td>
<td></td>
<td>0.329</td>
<td>0.036</td>
</tr>
<tr>
<td>Vitamin D (ng/ml)</td>
<td></td>
<td>-0.398</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Discussion

This study volunteers had no statistically significant variations in their age, height, and waist-hip ratio. Weight and body mass index were significantly high in the pre-HTN group when compared to age- and gender-matched controls. HR, SBP, DBP, PP, MAP, RPP, and telomerase levels were high, Vit-D levels were low in the pre-HTN group. Low Vit-D levels were negatively correlated with telomerase, HR, SBP, and PP and it was independent of age, gender, BMI, and waist-hip ratio.

Earlier reports have shown that higher Vit-D is related to longer telomere length, which underscores the conceivably advantageous impacts of this hormone on cell senescence and age-related conditions. In this study, cellular senescence was assessed using telomerase. This enzyme attempts to inhibit the process of telomere shortening. Since the cell telomere loss appears to result from cell division just to a fractional degree, different components, particularly oxidative stress, were attested to assume a job in the expanded rate for shortening of telomeres. The exact mechanism by which lower Vit-D levels are associated with this cellular senescence is hypothesized dependent on the perceptions recommends that the degrees of the telomerase may really be related to oxidative stress, with higher oxidative stress prompting higher telomerase levels. Cells of nearly complex organism may not have an ability to divide. This marvel was depicted by Hay flick in 1961. The quantity of potential divisions around fifty was named the “Hay flick Limit” and at times is called cell senescence. Just because it was valued that cells could be mortal (typical cells) or unfading (tumor cells). The results of our study showed an association between Vit-D and BP is consistent with previously
conducted studies[18,19] and stretch out the relationship to pre-HTN, a prior stage when essential anticipation is powerful. Zhao et al.[20] in an ongoing report detailed a positive relationship between Vit-D and hypertension and pre-HTN. Forman et al.[18] reported a positive relationship between Vit-D and self-revealed occurrence hypertension among 38,388 men from the Health Professionals’ follow-up study and 77,531 females from the Nurses’ Health Study; a positive affiliation was likewise detailed between Vit-D and hypertension in a subsample of members. Further, a study concentrates from the second Nurses’ health study detailed a positive relationship between serum Vit-D and hypertension among 1484 young females[18]. In the NHANES, SBP was demonstrated to be conversely connected with Vit-D among 12,644 participants[19]. Notwithstanding, not all investigations have indicated a reliable positive relationship between low Vit-D and BP. In a planned report directed in the UK, Forouhi et al.[21] did not locate a huge relationship between serum Vit-D and BP in a moderately aged associate of 524 non-diabetic people. In another examination led by Jorde et al.,[22] serum Vit-D levels were emphatically connected with SBP yet had no prescient incentive for the improvement of hypertension or changes in BP. Hardly any intercession preliminaries have announced that Vit-D supplementation did not diminish BP in explicit populaces, including postmenopausal[23] and overweight individuals[24]. Several mechanisms have been proposed to explain the relationship between lower Vit-D levels and pre-HTN. Earlier reports have demonstrated the expanded enactment of the renin-angiotensin-aldosterone framework in Vit-D receptor[25]. Low Vit-D likewise advances insulin resistance, endothelial dysfunction, production of pro-inflammatory cytokines, hyperparathyroidism, and hypocalcaemia influencing vascular smooth muscles[26]. Based on our results, we conclude that reduced Vit-D levels in pre-HTN may cause derangements of cardiovascular homeostatic mechanism, enhance the speed of cellular senescence measured by telomerase. Nevertheless, since this is a preliminary investigation, larger investigations with varied aged groups, across geographical distribution, professional, and socioeconomic differences.

**Reference**

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