

Letter to the Editor

Vitamin-D and Cardiac Dysfunction in Parkinson's disease: Beginning to Close the Evident Gaps

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We read with great enthusiasm the opinion paper by Kim *et al.* who postulated appropriately that vitamin-D plays a role in the pathogenesis of olfactory dysfunction in Parkinson's disease (PD) [1].

PD, one of the most frequent age-related neurodegenerative disorders, affects millions of people globally, there is no cure, and its prevalence will double by 2030 [2]. In addition to these perspectives, a complicating issue not frequently discussed in the neuroscientific community is the mortality in PD [3]. Unfortunately, PD can be considered a malignant disease because it is associated with higher mortality rates compared to the general population [3, 4]. Clearly, the main causes of death in PD are pneumonia, cerebrovascular and cardiovascular diseases [5]. Additionally, sudden unexpected death in PD (SUDPAR) is increasingly discussed as a contribution to mortality in DP [3, 6].

Didactically, SUDPAR is defined as unexpected death of a patient with PD without any satisfactory cause of death as determined by autopsy [3, 6]. Until now, causes of SUDPAR remain elusive [3,6]. Anyway, the results of previous experimental and clinical studies suggest that cardiac abnormalities and autonomic dysfunction play key roles in SUDPAR [6]. Furthermore, a number of risk factors may be directly associated with SUDPAR such as age at onset, duration of PD, gender, motor severity and drug treatment (polypharmacy) [3, 6], but these factors require further investigations in translational studies. In addition, it is well discussed that low vitamin-D levels and PD are considered bad fellows [7]. In these lines, systematic reviews and meta-analyses of observational studies have shown that low vitamin D levels are more prevalent in PD patients compared to healthy individuals, and low serum or plasma vitamin-D may be a predictive marker for risk and severity of PD [8].

Despite all these proposals, important studies in the last two decades have shown that vitamin-D is involved in the regulation of the cardiovascular system. In this way, a growing body of data clearly indicate that vitamin-D deficiency is related in the genesis of coronary heart disease, cardiovascular dysfunction, and hence sudden cardiac death [9, 10, 12]. Thus, it has been determined that vitamin-D deficiency is associated with arterial hypertension, left ventricular hypertrophy, congestive heart failure, and chronic vascular inflammation [9-12].

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Based on clinical evidence that clearly points to vitamin-D-mediated cardioprotection, is it possible that vitamin-D concentrations can be considered an interesting biological indicator for possible cardiac abnormalities in PD patients and even SUDPAR? In the near future, probably yes.

In a study of 145 PD patients serum vitamin-D levels were significantly lower as compared to age-matched controls [13]. This may have implications in terms of bone health and fracture risk [13]. This study also provided evidence that the outcome of PD patients with vitamin-D deficiency is worse as compared to those with normal vitamin-D values. Thus, vitamin-D serum levels should be determining in all PD patients and supplementation initiated. However, there are also studies, which did not show a significant role of vitamin-D in the pathogenesis of PD [14].

Overall, there is a long way to go. First, more well-delineated experimental and clinical studies are needed to establish the effect of vitamin-D on PD. As previously has been suggested, human neuroprotection studies are needed, but probably not feasible until better biomarkers are established [7]. Second, we must be attentive and improve impaired cardiovascular functions in PD. Finally, we will also have to explore the specific mechanisms of action that vitamin-D plays, in order to improve cardiac function and to prevent the possible cardiac abnormalities present in patients with PD.

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