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## **EDITORIAL**

## Vitamin D and the kidneys: a fascinating relationship

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The complexity of the physiological system that controls serum calcium levels is remarkable. In the **Figure** we present a very simplified view of this system, stressing the crucial role of vitamin D and the kidneys in the overall complex. No wonder, the system without normal renal function turns out to be highly deranged. Chronic kidney disease (CKD) is, unfortunately, very frequent, and metabolic bone disease, the result of specific alterations in calcium and phosphorus metabolism, one of its main complications<sup>(1)</sup>. The availability of kidney transplantation provided a real step forward in CKD patients' survival and quality of life. For the majority of transplant patients, a return to nearly normal renal function is the more likely result<sup>(2)</sup>.

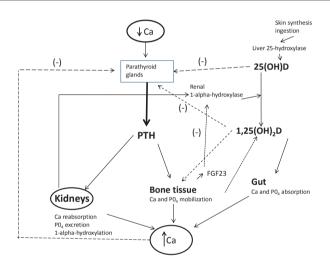


FIGURE — Schematic layout of the complex mechanism that controls calcium levels. The important roles of the kidneys and vitamin D metabolites are clearly seen

PTH: parathyroid bormone; Ca: calcium; FGF23: fibroblast growth factor 23; 25(OH)D: 25-bydroxyvitamin D; 1,25(OH)D: 1,25-dibydroxyvitamin D; (-): inhibition.

Other players in this system that have been more and more emphasized are the vitamin D metabolites 25-hydroxyvitamin D (25(OH)D) and 1,25-dihydroxyvitamin D  $(1,25(OH)_2D)^{(3)}$ . These steroid hormones of ubiquitous activity are key participants in calcium metabolism, and loss of glomerular filtration and tubular cell activity greatly affects their metabolism and action. Since the implications of  $1,25(OH)_2D$  levels in the control of parathyroid function were revealed<sup>(4)</sup>, new knowledge leading to a better clinical approach in the treatment of chronic renal disease patients has been remarkable.

Rocha and Andriolo<sup>(5)</sup> publish, in this number of Jornal Brasileiro de Patologia e Medicina Laboratorial (JBPML), interesting data on the biochemical profile of a group of Brazilian patients with end-stage renal disease in the pre-transplant period and three months after a successful procedure. Their very interesting findings confirm and stress several characteristics of this group of patients. First, normal renal function achieved after successful transplantation tends to normalize serum levels of phosphate and parathyroid hormone (PTH), even considering the short-time (three months) follow-up. Longer observation times may have shown lower PTH levels. Another very interest observation is their data on vitamin D: most of the patients, based on their 25(OH)D levels, were deficient pre- and post-transplant. Pre-transplant levels of 1,25(OH)<sub>2</sub>D are low due to the loss of 1-alpha-hydroxylase activity of renal tubular cells as well as the decline in glomerular filtration, since the delivery of precursor 25(OH)D depends on a complex megalin-associated vitamin D-binding protein

transport<sup>(6)</sup>. The finding of low 25(OH)D levels in most of the patients may not be surprising, because in the Brazilian population with normal renal function the incidence of vitamin D deficiency is more usual than it would be expected<sup>(7)</sup>. As the authors point out, patients with end-stage renal disease have several other reasons to be vitamin D deficient. The implications of a low substrate in the deficiency of  $1,25(OH)_2D$  is an interesting point, especially when 25(OH)D is extremely low, as in one of the patients studied. The post-transplantation remarkable increase in  $1,25(OH)_2D$  levels denotes the recovery of normal renal function and is implicated in the tendency toward normalization of PTH function.

An important point that needs attention when analyzing the data published by Rocha and Andriolo is the analytical difficulty of some of the hormones studied. PTH is quite heterogeneous in circulation, and, in patients with end-stage renal disease, the accumulation of inactive metabolites is well-known<sup>(8)</sup>. 1,25(OH)<sub>2</sub>D circulates in very low concentrations, together with the presence of high concentrations of vitamin D-binding protein and a high concentration of a potential cross-reactant, 25(OH)D, making the assay one of the most demanding in terms of sensitivity and specificity. Despite potential methodological difficulties, the published data highlights a very important practical problem: the biochemical modifications related to calcium metabolism observed after a successful renal transplantation.

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