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Haemodialysis session: The perfect storm for vascular calcification☆

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ABSTRACT

Introduction: Vascular calcification (VC) associated to chronic kidney disease (CKD) is a complex phenomenon closely related to mineral bone metabolism disorders. Many are the factors implicated, as the drugs used in the treatment of CKD. Some in vitro studies suggest that electrolyte and acid–base disorders induced by haemodialysis (HD) may play a key role in VC.

Methods: We analysed electrolyte and acid–base disorders that occur during an HD session in 26 patients randomly assigned to 1.25 mM or 1.5 mM calcium bath.

Results: There is a calcium load in all the patients, independently of calcium bath concentration or basal serum calcium levels. At the end of the session, 100% of the patients dialysed with 1.5 mM calcium bath have calcium serum levels >1.3 mM. However, this only occurs in 15% of the patients dialysed with 1.25 mM calcium bath. During this calcium load, phosphorus levels persist uncontrolled. Besides, there is a progressive alkalinisation in all the patients. In the end of the session 50% have serum bicarbonate >30 mM and 23% pH >7.5.

Conclusions: During HD sessions occur electrolyte and acid–base disorders that induce VC: calcium load and alkalisation in presence of elevated phosphorus levels. It is necessary to perform studies with kinetic models of calcium load and alkalinisation different from the actual ones.

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Sesión de hemodiálisis: la tormenta perfecta para la calcificación vascular

Palabras clave:
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RESUMEN

Introducción: La calcificación vascular (CV) asociada a la enfermedad renal crónica (ERC) es un fenómeno estrechamente ligado a las alteraciones en el metabolismo mineral óseo. Existen muchos factores implicados, entre ellos los fármacos empleados en el tratamiento de la ERC. Algunos estudios *in vitro* señalan que las alteraciones electrolíticas y ácido-básicas que tienen lugar durante la sesión de hemodiálisis (HD) pueden jugar un papel clave en el proceso de CV.

Métodos: Analizamos las alteraciones electrolíticas y ácido-básicas que tienen lugar durante la sesión de HD en 26 pacientes, empleando de forma aleatorizada concentraciones de calcio en el líquido de diálisis de 1,25 o 1,5 mM.

Resultados: En todos los pacientes, independientemente del baño de calcio empleado, se produce una ganancia de calcio. En el grupo de pacientes dializados con baño de calcio 1,5 mM, el 100% finaliza la sesión con valores de calcio sérico > 1,3 mM, mientras que en el de 1,25 mM, esto solo ocurre en el 15%. Al inicio de la sesión, esta ganancia de calcio coincide con niveles de fósforo aún no controlado. Además, en todos los pacientes se observa una alcalinización progresiva: el 50% finaliza la sesión con cifras de bicarbonato > 30 mM y el 23% con pH > 7,5.

Conclusiones: Durante la sesión de HD se producen cambios electrolíticos y ácido-básicos inductores de CV: ganancia de calcio y alcalinización en presencia de fósforo sérico inicialmente elevado. Son necesarios estudios con modelos cinéticos de ganancia de calcio y alcalinización diferentes a los actuales.

Introduction

Vascular calcification (VC), a process inherent to ageing, is influenced by multiple classical cardiovascular risk factors, such as arterial hypertension, diabetes mellitus, obesity, and dyslipidaemia, amongst others.[1] In the general population, VC takes place in the intimal arterial layer,[2] affecting mainly central arteries (the aorta and its branches) and is linked to systemic atherosclerosis.[3]

Cardiovascular events are the primary cause of morbidity and mortality in patients with chronic kidney disease (CKD).[4] In these patients, 2 patterns of VC have been described: predominantly intimal, and predominantly medial. However, there is much debate regarding the differences between intimal calcification and medial calcification. There is no definitive evidence to suggest that calcification isolated to the media is distinct from the calcification that comes from the natural history of atherosclerosis; nor is there definitive evidence to the contrary.[5,6] What is certain is that it is closely related to the mixture of metabolic and biological abnormalities that accompany CKD,[7,8] notably CDK-mineral and bone disorders. This entity implies abnormalities in the metabolism of calcium, phosphorus,[9] vitamin D,[10,11] FGF23-Klotho, and parathyroid hormone (PTH).[12] To those we must add biological abnormalities such as dysfunctional production of calcification inhibitors by smooth muscle cells, and chronic inflammation.[13] Together, these factors induce physiochemical changes in the smooth muscle cells of the arterial wall, promoting their transformation into osteoblasts,[14] and hydroxyapatite deposition. Classically, the [Ca] × [P] product has been used to determine VC risk in renal patients.[15] However, some in vitro studies have demonstrated that with a stable [Ca] × [P] product, it is the individual concentration of each element that determines the development of VC.[16]

Until now, all therapeutic efforts have been directed at controlling these metabolic abnormalities (essentially phosphate binders,[17] vitamin D derivatives,[18] and calimimetics[19]) and the classical risk factors, with varying and contradictory results. Although some of these treatments can slow progression, none have been demonstrated to reverse VC.[20,21]

In comparison with patients in the early stages of CKD, patients treated with haemodialysis (HD) have higher cardiovascular morbidity and mortality,[22] along with more marked abnormalities in bone metabolism and a greater degree of VC.[23,24] As well as all the previously stated mechanisms, the biochemical changes produced during HD could play an important role in such marked development of VC.[25] In fact, in vitro studies using rat aortas have shown that changes in calcium and phosphorus concentrations and alkalinisation are precipitating factors for VC.[16,26] It is also known that acidosis protects against VC,[27] therefore a high pH could have the unfavourable opposite effect.

Aims

The aim of this study was to analyse the biochemical changes in the parameters of mineral metabolism and acid–base balance that take place during HD.