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Original article

Differences between 2nd and 3rd generation seric parathormone determination methods on mortality in haemodialysis patients☆

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ABSTRACT

Parathormone plays a key role in controlling mineral metabolism. PTH is considered a uremic toxin causing cardiovascular damage and cardiovascular mortality in dialysis patients. There are two different assays to measure PTH called 2nd generation or intact PTH (iPTH) and 3rd generation or bioPTH (PTHbio).

Objective: To evaluate the differences in mortality of dialysis patients between both assays to measure PTH, as well as the possible prognostic role of the PTHbio/iPTH ratio.

Methods: 145 haemodialysis patients were included with 2-year monitoring including baseline laboratory test and annually thereafter.

Results: 21 patients died in the first year and 28 in the second. No correlation was found between PTH, PTHbio and PTHbio/iPTH ratio with mortality. Both PTH have a perfect correlation between them and correlate similarly with other molecules of the mineral metabolism. The extreme baseline values of PTH are those of higher mortality. In survival by iPTH intervals (according to guidelines and COSMOS study), a *J* curve is observed. When iPTH increases, the ratio decreases, possibly when increasing fragments no. 1–84. There is no greater

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prognostic approximation on mortality with PTHbio than PTHi. There was also no difference in mortality when progression ratio PTHbio/PTHi was analysed.
Conclusions: We didn't find any advantages to using bioPTH vs. PTHi as a marker of mortality. BioPTH limits of normality must be reevaluated because its relationship with iPTH is not consistent. Not knowing these limits affects its prognostic value.

Diferencias entre los métodos de determinación de 2.ª y 3.ª generación de la parathormona sérica sobre la mortalidad en el paciente en hemodiálisis

Palabras clave:
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RESUMEN

La paratohormona tiene un papel fundamental en el control del metabolismo mineral. Además es considerada como una toxina urémica al originar daño cardiovascular e influir en la mortalidad cardiovascular del paciente en diálisis. Existen dos métodos de medición denominados de 2.ª generación o PTH intacta (PTHi) y de 3.ª generación o bioPTH (PTHbio).
Objetivo: Evaluar las diferencias en la mortalidad del paciente en diálisis entre ambas formas de medición de PTH, así como el posible papel pronóstico de su cociente.
Métodos: Se incluyeron 145 pacientes en hemodiálisis con un seguimiento de 2 años con determinación analítica basal y posteriormente de forma anual.
Resultados: Veintiún pacientes fallecieron el primer año y 28 el segundo. No se encontró correlación entre PTHi, PTHbio y cociente PTHbio/PTHi con la mortalidad. Ambas PTH tienen una buena correlación entre ellas y correlacionan de manera similar con otras moléculas del metabolismo mineral. Los valores basales de PTH extremos son los de mayor mortalidad. En la supervivencia por tramos de PTHi (según guías y estudio COSMOS) se observa una curva en J. A mayor aumento de PTHi el cociente desciende, posiblemente al aumentar los fragmentos no 1-84. No existe una mayor aproximación pronóstica sobre mortalidad con PTHbio que con PTHi. No se observan diferencias en el valor predictivo del cociente sobre la mortalidad. Tampoco hubo diferencias en mortalidad cuando se analiza la progresión del cociente PTHbio/PTHi.
Conclusiones: No encontramos ventajas en la utilización de PTHbio sobre la PTHi como marcador de mortalidad. Se deben reevaluar los límites de la PTHbio pues su relación con la PTHi no es constante. El no conocer esos límites condiciona su utilidad pronóstica.

Introduction

The Parathyroid Hormone (PTH) is a 84 amino acids protein with a established role in the regulation of mineral metabolism; main target organs are the bone and kidneys among others. In spite of being a hormone, in the case of the renal patient, it is classified as a true uremic toxin because it increases progressively with the progression chronic kidney disease (CKD), and it responsible for multiple systemic effects.[1,2] It is included as one of the uremic toxins that cause cardiovascular damage.[3,4]

The control of PTH is important for the adequate treatment of the abnormalities of mineral metabolism in CKD. Therefore much of the therapeutic efforts aimed at controlling these alterations are dedicated to an adequate control of PTH. Nevertheless, in hemodialysis patients PTH is a poor marker of mortality. Only large studies have revealed that high PTH values that are related to higher mortality. And in these studies the results are variable.[4–8] However, other molecules such as calcium and phosphorus have shown a better prognostic significance on mortality, along with vitamin D, although with the later the results have been less conclusive.[9,10]

Circulating PTH includes a mixture of peptides such as the whole molecule 1–84 and smaller fragments resulting from the catabolism of PTH, these are called non-1–84 or carboxyterminal fragments. Only PTH 1–84 (whole protein) exert biological activity. Some of the carboxyterminal fragments have a PTH antagonistic action. PTH is cleared by the kidney and the proportion of these PTH peptides varies according to the CKD stage. The methods currently used to measure PTH in clinical practice are of two categories. The so-called 2nd generation that measures the intact 1–84 PTH (PTHi) and multitude of fragments no 1–84. The 3rd generation method, also called PTHbio, recently marketed, quantify the PTH 1–84 only, although its use is not generalized yet.[11,12]