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Original article

Fibroblast growth factor is associated to left ventricular mass index, anemia and low values of transferrin saturation

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ABSTRACT

Background: Fibroblast growth factor 23 (FGF-23) is a phosphorus-regulating hormone. In chronic kidney disease (CKD), circulating FGF-23 levels are markedly elevated and independently associated with mortality. Left ventricular hypertrophy (LVH) is a potent risk factor for mortality in CKD, and FGFs have been implicated in the pathogenesis of myocardial hypertrophy. In addition, the effect of anemia on CV disease and LVH is well known in CKD. A relation between iron and FGF-23 metabolism is mentioned in a few studies. The aim of this study was to test the association of FGF-23 levels with echocardiographic (ECHO) and iron parameters in peritoneal dialysis patients (PD).

Methods: In this cross-sectional study, 61 subjects with PD (29 women and 32 men, mean age: 46.9 ± 13.3 years, mean PD vintage: 69.5 ± 39 months) underwent echocardiograms to assess left ventricular mass index (LVMI). Medical treatments and average values of the basic laboratory results of the last 6 months for all patients were recorded. Serum FGF-23 concentrations were measured using intact FGF-23 (iFGF-23) human enzyme-linked immunosorbent assay (ELİSA) kit. According to the median levels of serum FGF-23 the patients were grouped into two (FGF-23 high and low groups).

Results: Significant positive correlation was recorded between serum FGF-23 levels and LVMI ($P = 0.023$). There was also significant difference in terms of hemoglobin (12.1 ± 2 versus 11.0 ± 2, $P = 0.017$), transferrin saturation (TSAT) (24.9 ± 16.8 versus 19.5 ± 10.8, $P = 0.042$) between low and high FGF-23 group. Also in linear regression analysis the negative relation between FGF-23 and hemoglobin is persisted ($r = 0.199$, $P = 0.045$).

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Conclusions: FGF-23 is associated with LVMI, anemia and low TSAT in patients with PD. Whether increased FGF-23 is a marker or a potential mechanism of myocardial hypertrophy and anemia in patients with end-stage renal disease (ESRD) requires further study.

El factor de crecimiento fibroblástico está asociado con el índice de masa ventricular izquierda, anemia y niveles bajos de saturación de la transferrina

Palabras clave:
Factor de crecimiento fibroblástico 23
Índice de masa ventricular izquierda
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Diálisis peritoneal

RESUMEN

Introducción: El factor de crecimiento fibroblástico 23 (FGF-23) es una hormona reguladora del fósforo. En la enfermedad renal crónica (ERC), los niveles de FGF-23 son especialmente elevados y se relacionan de manera independiente con mortalidad. La hipertrofia ventricular izquierda (HVI) es un importante factor de riesgo de mortalidad en la ERC y se ha implicado a los FGF en la patogenia de la hipertrofia del miocardio. Además, se conoce el efecto de la anemia en la enfermedad cardiovascular y la HVI en la ERC. En algunos estudios se menciona una relación entre el hierro y el metabolismo del FGF-23. El objetivo de este estudio fue comprobar la asociación de los niveles de FGF-23 con parámetros ecocardiográficos y de hierro en pacientes con diálisis peritoneal (DP).

Metodología: En este estudio transversal se procedió a realizar un ecocardiograma a 61individuos con DP (29 mujeres y 32 hombres; media de edad: 46,9 ± 13,3 años; DP clásica media: 69,5 ± 39 meses) para evaluar el índice de masa ventricular izquierda (IMVI). Se registraron los tratamientos médicos y los valores promedio de los resultados básicos de laboratorio de los últimos 6 meses de todos los pacientes. Las concentraciones en suero del FGF-23 se midieron con el kit ELISA *(enzyme-linked immunosorbent assay)* de FGF-23 humano intacto (iFGF-23). Según los niveles promedio de FGF-23 en suero, los pacientes se distribuyeron en dos grupos (FGF-23 alto y bajo).

Resultados: Se registró una correlación positiva significativa entre los niveles de FGF-23 en suero e IMVI (P = 0,023). También hubo diferencias significativas en cuanto a la hemoglobina (12,1 ± 2 frente a 11,0 ± 2, P = 0,017) y saturación de la transferrina (TSAT; 24,9 ± 16,8 frente a 19,5 ± 10,8, P = 0,042) entre los grupos de FGF-23 bajo y alto. También en el análisis de regresión lineal se mantuvo la relación negativa entre el FGF-23 y la hemoglobina (r = 0,199, P = 0,045).

Conclusiones: El FGF-23 se asocia con IMVI, anemia y TSAT baja en pacientes con DP. Saber si el aumento del FGF-23 es un marcador o un mecanismo potencial de la hipertrofia miocárdica y la anemia en pacientes con insuficiencia renal terminal exige un estudio en mayor detalle.

Introduction

Cardiovascular disease (CVD) is the most common cause of mortality in patients with end stage renal disease (ESRD)[1]. Besides the well-known traditional cardiovascular risk factors, this population has risk factors specific to chronic kidney disease which results in accelerated atherosclerosis[2]. LVH, commonly exists in patients with ESRD, is a major cardiovascular risk factor and independent predictor of cardiovascular mortality in this population[3].

Hypertension is accepted as the main underlying factor in the development of LVH. However recent studies indicated that FGF-23 may contribute to left ventricular mass enlargement[4,5]. FGF-23 is phosphorus regulating hormone and significantly increased in patients with ESRD. It promotes phosphate excretion and reduces 1-25$(OH)_2$ vitamin D production in the kidney[6]. Independent relation between increased FGF-23 levels and mortality was first reported by Guirez et al.[7] in 2008 in hemodialysis (HD) patients. Even in patients with normal renal functions higher FGF-23 was found to be independently associated with mortality and cardiovascular events[8]. In addition, the effect of anemia on CV disease and LVH is well known in CKD patients[9]. A relation between iron and FGF-23 metabolism is mentioned in a few studies. In studies, it is emphasized that iron deficiency is an important stimulator of FGF-23 transcription[10]. The aim of this cross-sectional study was to investigate the possible relationship between serum levels of FGF-23 with ECHO and iron parameters in PD patients.