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Original article

Hypogonadism associated with muscle atrophy, physical inactivity and ESA hyporesponsiveness in men undergoing haemodialysis

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ABSTRACT

Background: Testosterone deficiency (hypogonadism) is common among men undergoing haemodialysis, but its clinical implications are not well characterized. Testosterone is an anabolic hormone that induces erythrocytosis and muscle synthesis. We hypothesized that testosterone deficiency would be associated with low muscle mass, physical inactivity and higher dosages of erythropoietin-stimulating agents (ESA).

Methods: Single-center cross-sectional study of 57 male haemodialysis patients. None of the patients was undergoing testosterone replacement therapy. Total testosterone was measured in serum. Body composition (by bioelectrical impedance analysis) and physical activity (by the use of pedometers) were assessed. Patients with testosterone levels below the normal range were considered hypogonadal.

Results: Mean testosterone level was 321 ± 146 ng/dL; 20 patients (35%) were hypogonadal. Hypogonadal patients were older and had lower mean arterial blood pressure, higher interleukin-6 levels, lower lean body mass and higher fat body mass. A negative association between testosterone and normalized ESA dose was found in uni- and multivariate regression analyses. Testosterone levels directly correlated with lean body mass regardless of confounders. Hypogonadal patients had lower physical activity than their counterparts [2753 ± 1784 vs. 4291 ± 3225 steps/day ($p = 0.04$)]. The relationship between testosterone and physical activity was independent of age, comorbidities and inflammatory markers, but dependent on the proportion of muscle mass.

Conclusion: Hypogonadism is common in our male haemodialysis population and is associated with higher ESA doses, reduced muscle mass and lower physical activity. The link

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between low testosterone levels and physical inactivity may conceivably relate to reduced muscle mass due to inadequate muscle protein synthesis.

Hipogonadismo asociado a atrofia muscular, inactividad física e hiposensibilidad a FEE en varones sometidos a hemodiálisis

Palabras clave:
Hemodiálisis
Actividad física
Testosterona

RESUMEN

Antecedentes: La deficiencia de testosterona (hipogonadismo) es frecuente en varones en hemodiálisis, pero sus consecuencias clínicas no se han caracterizado satisfactoriamente. La testosterona es una hormona anabólica que provoca eritrocitosis y síntesis muscular. Nos planteamos la hipótesis de que la deficiencia de testosterona pudiera estar asociada a una masa muscular baja, a la inactividad física y a dosis más altas de fármacos estimulantes de la eritropoyesis (FEE).

Métodos: Estudio transversal de un solo centro de 57 pacientes varones en hemodiálisis. Ninguno de ellos estaba recibiendo tratamiento sustitutivo con testosterona. La cantidad total de testosterona se midió en el suero. Se evaluaron la composición corporal (mediante un análisis de impedancia bioeléctrica) y la actividad física (mediante el uso de podómetros). Los pacientes con concentraciones séricas de testosterona por debajo de los límites de normalidad se consideraron hipogonadales.

Resultados: La concentración media de testosterona fue de 321 ± 146 ng/dl; 20 pacientes (35%) se consideraron hipogonadales. Los pacientes hipogonadales eran de edad avanzada y presentaban una presión arterial media más baja, concentraciones más altas de interleucina 6, masa corporal magra más baja y masa corporal grasa más alta. Se observó una asociación negativa entre la dosis de testosterona y de FEE normalizada en análisis de regresión univariante y multivariante. Las concentraciones de testosterona estaban directamente correlacionadas con la masa corporal magra, independientemente de los factores de confusión. Los pacientes hipogonadales presentaban una actividad física más baja que sus homólogos (2.753 ± 1.784 frente a 4.291 ± 3.225 pasos/día; p = 0,04). La relación entre la actividad física y la testosterona fue independiente de la edad, las comorbilidades y los marcadores de inflamación, pero dependían de la proporción de masa muscular.

Conclusión: El hipogonadismo es frecuente en la población de varones en hemodiálisis y está asociado a dosis más altas de FEE, masa muscular reducida y actividad física baja. El vínculo entre las concentraciones bajas de testosterona y la inactividad física está posiblemente relacionado con la masa muscular reducida debido a una síntesis de proteínas musculares insuficiente.

Introduction

Chronic kidney disease (CKD) involves alterations in body homeostasis and metabolic disturbances (including hormone secretion disorders and altered response to hormones in target tissues), resulting in endocrine dysfunctions that may contribute to the increased mortality in CKD patients.[1] Hypogonadism, hallmarked by testosterone deficiency is a common endocrine disorder among men undergoing dialysis, with a prevalence ranging from 35 to 50% in recent studies.[2–4] Various studies link hypogonadism with mortality risk among hemodialysis patients,[5,6] but the pathways by which this risk may be mediated are not well known.

The clinical implications of hypogonadism among dialysis patients are not well characterized. Testosterone is a steroid hormone that has an important anabolic function influencing among others muscle mass, increasing both strength and size.[7] In the general population, testosterone deficiency that accompanies aging has been linked to decreased physical performance and its consequent limitation of mobility.[8] In non-dialysis CKD patients, endogenous testosterone is a strong determinant of both muscle mass and strength.[9] It is unknown if this is still the case in individuals undergoing dialysis.

Furthermore, testosterone induces erythrocytosis[10,11] and testosterone deficiency has been associated with anemia and increased resistance to erythropoietin-stimulating agents (ESA) in dialysis patients.[2] However, this finding has, to date, not been confirmed. The objective of our study was to assess the prevalence of hypogonadism among men undergoing dialysis at our center. Further, we explored the clinical phenotype

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