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Original article

A high sodium intake reduces antiproteinuric response to renin–angiotensin–aldosterone system blockade in kidney transplant recipients☆

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ABSTRACT

Background: Post-transplant proteinuria is associated with lower graft and patient survival. Renin–angiotensin–aldosterone system blockers are used to reduce proteinuria and improve renal outcome. Although it is known that a high salt intake blunts the antiproteinuric effect of ACEI and ARB drugs in non-transplant patients, this effect has not been studied in kidney transplant recipients.

Objective: To analyse the relationship between sodium intake and the antiproteinuric effect of ACEI/ARB drugs in kidney transplant recipients.

Methods: We selected 103 kidney transplant recipients receiving ACEI/ARB drugs for more than 6 months due to proteinuria >1 g/day. Proteinuria was analysed at baseline and at 6 months after starting ACEI/ARB treatment. Salt intake was estimated by urinary sodium to creatinine ratio (uNa/Cr).

Results: Proteinuria fell to less than 1 g/day in 46 patients (44.7%). High uNa/Cr was associated with a smaller proteinuria decrease ($r = -0.251$, $p = 0.011$). The percentage of proteinuria reduction was significantly lower in patients in the highest uNa/Cr tertile [63.9% (IQR 47.1%), 60.1% (IQR 55.4%), 38.9% (IQR 85.5%), $p = 0.047$]. High uNa/Cr independently relates (OR 2.406 per 100 mEq/g, 95% CI: 1.008–5.745, $p = 0.048$) to an antiproteinuric response <50% after renin–angiotensin–aldosterone system blockade.

Conclusions: A high salt intake results in a smaller proteinuria decrease in kidney transplant recipients with proteinuria treated with ACEI/ARB drugs.

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La ingesta elevada de sodio disminuye la respuesta antiproteinúrica del bloqueo del eje renina-angiotensina-aldosterona en el trasplante renal

Palabras clave:
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RESUMEN

Antecedentes: La proteinuria postrasplante renal se asocia a una disminución en la supervivencia del injerto y del paciente. Para reducir la proteinuria y mejorar el pronóstico renal se recomienda asociar fármacos bloqueantes del sistema renina-angiotensina-aldosterona (RAA). Aunque en los pacientes no trasplantados se ha demostrado que la dieta rica en sal reduce el efecto antiproteinúrico de los IECA y ARA-II, este efecto no se ha estudiado en los trasplantados renales.

Objetivo: Valorar la relación entre la ingesta de sodio y el efecto antiproteinúrico de los IECA/ARA-II en los trasplantados renales.

Métodos: Seleccionamos a 103 trasplantados tratados con IECA/ARA-II más de 6 meses por proteinuria > 1 g/día. La proteinuria se analizó al inicio del tratamiento y a los 6 meses. La ingesta de sal se estimó con el cociente urinario sodio/creatinina (uNa/Cr).

Resultados: En 46 pacientes (44,7%) la proteinuria disminuyó < 1 g/día. Un uNa/Cr elevado se relaciona con un menor descenso de la proteinuria (r = −0,251; p = 0,011). El porcentaje de reducción de la proteinuria fue significativamente menor en los pacientes en el tercil más alto de uNa/Cr [63,9% (RIC 47,1%); 60,1% (RIC 55,4%); 38,9% (RIC 85,5%); p = 0,047]. Un uNa/Cr elevado se relaciona de forma independiente (OR 2,406 por 100 mEq/g; IC 95%: 1,008–5,745; p = 0,048) a una respuesta antiproteinúrica < 50% tras el bloqueo del eje RAA.

Conclusiones: En los trasplantados renales con proteinuria tratados con IECA/ARA-II una ingesta elevada de sal se asocia con un menor descenso de la proteinuria.

Introduction

The development of proteinuria, even in a small amount, after kidney transplantation is associated with a reduction in graft and patient survival, and so the control of proteinuria is of clinical relevance.[1–3] Unfortunately, a large number of kidney transplant recipients develop proteinuria. In a study of 613 kidney transplants, up to 45% had proteinuria of more than 150 mg/day, and in 65% of these patients proteinuria was below 500 mg/day. Biopsies from patients with proteinuria showed mainly interstitial fibrosis and tubular atrophy, or non-specific findings, except in those with proteinuria above 1500 mg/day, in which glomerular involvement was predominant.[4] The factors inducing the onset of proteinuria include: transplant from a female donor to a male recipient; advanced donor age; kidney function; blood pressure; cell rejection and antibody-mediated rejection; recurrence of glomerulonephritis; prolonged warm and cold ischaemia; and delayed initiation of graft function.[4–6]

The measures currently used to reduce post-transplant proteinuria include strict control of blood pressure, renin–angiotensin–aldosterone system (RAAS) blockade with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor II blockers (ARBs), lipid control, stop smoking and maintaining a healthy weight.[7] Specifically, the KDIGO guidelines recommend using ACE inhibitors or ARBs in patients with recurrent glomerulonephritis and proteinuria and in hypertensive patients with proteinuria ≥1 g/day.[8]

In the general population, RAAS blockade has been shown to be effective in reducing proteinuria, controlling hypertension and reducing the progression of chronic kidney disease (CKD) in patients with diabetic and non-diabetic nephropathy.[9,10] Although some studies have demonstrated the efficacy of the antiproteinuric effect of RAAS blockade in kidney transplantation,[11,12] there is no precise information on the efficacy of proteinuria reduction on preservation of renal function and improvement of graft and patient survival.[12–16]

In non-transplant CKD patients, several factors can reduce the antiproteinuric effect of RAAS blockade.[17–22] Salt intake is one of these factors. One meta-analysis that included 11 studies was able to quantify that albuminuria was decreased by 32.1% for every reduction in sodium intake of 92 mEq/day.[22] None of the cohorts considered in the meta-analysis included kidney transplant patients. The aim of our study was to assess the relationship between sodium intake and the antiproteinuric effect of ACE inhibitors and ARBs in our population of kidney transplant patients.

Methods

Study population and design

We selected 137 patients from a population of 1423 kidney transplants performed at our site between October 1986 and May 2012. Patients included were those: (1) who have been transplanted for more than 3 months (2) had proteinuria greater than 1 g/day; (3) who had been treated with ACE