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Original article

The renin–angiotensin–aldosterone system blockade in patients with advanced diabetic kidney disease☆

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ABSTRACT

Background and objectives: Diabetic kidney disease is the leading cause of end-stage chronic kidney disease (CKD). The renin–angiotensin–aldosterone system (RAAS) blockade has been shown to slow the progression of diabetic kidney disease. Our objectives were: to study the percentage of patients with diabetic kidney disease treated with RAAS blockade, to determine its renal function, safety profile and assess whether its administration is associated with increased progression of CKD after 3 years of follow-up.

Materials and methods: Retrospective study. 197 diabetic kidney disease patients were included and divided into three groups according to the treatment: patients who had never received RAAS blockade (non-RAAS blockade), patients who at some point had received RAAS blockade (inconstant-RAAS blockade) and patients who received RAAS blockade (constant-RAAS blockade). Clinical characteristics and analytical variables such as renal function, electrolytes, glycosylated hemoglobin and glomerular filtration rate according to CKD-EPI and MDRD formulas were assessed. We also studied their clinical course (baseline, 1 and 3 years follow-up) in terms of treatment group, survival, risk factors and renal prognosis.

Results: Non-RAAS blockade patients had worse renal function and older age ($p < 0.05$) at baseline compared to RAAS blockade patients. Patients who received RAAS blockade were not found to have greater toxicity or chronic kidney disease progression and no differences in renal prognosis were identified. Mortality was higher in non-RAAS blockade patients, older patients and patients with worse renal function ($p < 0.05$). In the multivariate analysis, older age and worse renal function were risk factors for mortality.

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Conclusions: Treatment with RAAS blockade is more common in diabetic kidney disease patients with eGFR ≥ 30 ml/min/1.73 m^2. In our study, there were no differences in the evolution of renal function between the three groups. Older age and worse renal function were associated with higher mortality in patients who did not receive RAAS blockade.

Bloqueo del sistema renina-angiotensina-aldosterona en pacientes con enfermedad renal diabética avanzada

Palabras clave:
Diabetes mellitus
Enfermedad renal diabética
Bloqueo del sistema renina-angiotensina-aldosterona
Enfermedad renal crónica

RESUMEN

Antecedentes y objetivos: La enfermedad renal diabética es la primera causa de enfermedad renal crónica terminal en nuestro medio. El bloqueo del sistema renina-angiotensina aldosterona (BSRAA) enlentece la progresión de la enfermedad renal diabética. Nuestros objetivos son: estudiar pacientes tratados con BSRAA, comparando su evolución según el filtrado glomerular, su perfil de seguridad y si se asocia a una progresión mayor de la enfermedad renal crónica.

Materiales y métodos: Estudio retrospectivo de 197 pacientes con enfermedad renal diabética. Se dividieron en tres grupos según tratamiento: pacientes que no recibieron BSRAA (no BSRAA), pacientes que en algún momento lo recibieron (BSRAA discontinuado) y pacientes que recibieron BSRAA (BSRAA mantenido). Se estudiaron características clínicas y analíticas: función renal, ionograma, hemoglobina glicosilada, filtrado glomerular según CKD-EPI y MDRD. Analizamos su evolución (basal, año y 3 años) en relación con el grupo de tratamiento, supervivencia, factores de riesgo y pronóstico renal.

Resultados: Los pacientes no BSRAA presentaron en el momento basal peor función renal y edad más avanzada ($p < 0,05$) en comparación con los que recibieron BSRAA. Los pacientes que recibieron BSRAA no mostraron mayor toxicidad, ni más progresión de la enfermedad renal crónica, y no evidenciamos diferencias en el pronóstico renal. La mortalidad fue mayor en pacientes no BSRAA, de mayor edad y peor función renal ($p < 0,05$). En el análisis multivariado los factores de riesgo de mortalidad fueron edad avanzada y peor función renal.

Conclusiones: El tratamiento con BSRAA es más frecuente en pacientes con FGe ≥ 30 mL/min/1,73 m^2. No observamos diferencias en la evolución de la función renal entre los tres grupos. La mayor mortalidad observada en pacientes que no recibieron BSRAA se relacionó con la edad avanzada y peor función renal.

Introduction

Diabetes mellitus (DM) is a pandemic disease affecting 415 million people worldwide. According to the projections of the International Diabetes Federation, the number of affected individuals is expected to increase to 642 million by 2040, the vast majority of which are in developing countries.[1]

Life expectancy is reduced in patients with DM and cardiovascular disease is the main cause of mortality.[1,2] Thirty percent of DM type 1 patients and 10–40% of patients with type 2 DM will develop diabetic kidney disease (DKD) that may lead to advanced chronic kidney disease (CKD) requiring renal replacement therapy (RRT).[1] In fact, DKD is one of the main causes of advanced CKD and RRT. In Catalonia, it is the second leading cause of RRT, with an incidence of 22%.[3] Ten years after being diagnosed of DM2, 25% will present microalbuminuria, 5% will present macroalbuminuria and 0.8% will have an increase in serum creatinine or advanced kidney failure.[4]

The renin–angiotensin–aldosterone system (RAAS) is involved in cardiorenal regulation of patients with DM. Angiotensin II, acting on type 1 receptors (AT1), have multiple effects: induces vasoconstriction, increases the tubular reabsorption of Na^+, increases oxidative stress, and favors renal production of fibrogenic and inflammatory cytokines. Thus, the inhibition of Angiotensin II production or blocking the type 1 receptor of angiotensin II have been shown to be beneficial for cardiorenal protection in the patient affected with DKD.[5–7]

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARB) reduce mortality, cardiovascular risk and slows down the progression of kidney disease; therefore, most guidelines recommend the use of these drugs as a first option in diabetic patients with CKD.[1,8–10] In DKD patients, the renoprotective effects of RAAS blockade (RAASB) are superior to other antihypertensive drugs. The