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ORIGINAL

Association between exposure to angiotensin-converting enzyme inhibitors and angiotensin receptor blockers prior to septic shock and acute kidney injury

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KEYWORDS
Septic shock;
Acute kidney injury;
Angiotensin-converting enzyme inhibitors;
Angiotensin receptor blockers;
Recovery

Abstract
Objective: To evaluate the association between angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) use prior to a septic shock episode and the development, prognosis and long-term recovery from acute kidney injury (AKI).
Design: A single-centre, prospective observational study was carried out between September 2005 and August 2010.
Scope: Patients admitted to the ICU of a third level hospital.
Patients: A total of 386 septic shock patients were studied.
Interventions: None.
Variables of interest: Use of ACEIs/ARBs, AKI development, recovery of previous creatinine levels and time to recovery.
Results: A total of 386 patients were included, of which 312 (80.8%) developed AKI during ICU stay and 23% were receiving ACEIs/ARBs. The percentage of patients on ACEIs/ARBs increased significantly in relation to more severe stages of AKI irrespective of the kind of AKI score. After adjusting for confounders, the development of AKI was independently associated to the use of ACEIs/ARBs (OR 2.19; 95%CI 1.21–3.84; $p = .04$). With respect to the recovery of kidney function, the group of patients on ACEIs/ARBs had significantly higher creatinine levels at ICU discharge and needed hemodialysis more frequently thereafter. However, use of ACEIs/ARBs affected neither recovery of previous creatinine levels nor significantly delayed recovery.

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Conclusions: The use of ACEIs/ARBs before septic shock episodes was correlated to AKI development and severity, but did not affect the recovery of kidney function after sepsis resolution.

PALABRAS CLAVE
Shock séptico;
Fracaso renal agudo;
Inhibidores de la enzima conversora de la angiotensina;
Receptores de la angiotensina 2;
Recuperación

Asociación entre la exposición previa a inhibidores de la enzima conversora de la angiotensina y los antagonistas de los receptores de la angiotensina en pacientes con fracaso renal agudo y shock séptico

Resumen
Objetivo: Evaluar la asociación entre la administración previa a un episodio de shock séptico de inhibidores de la enzima conversora de la angiotensina (IECA) y antagonistas de los receptores de la angiotensina 2 (ARAII) con el desarrollo, pronóstico y recuperación a largo plazo del fracaso renal agudo (FRA).
Diseño: Estudio unicéntrico prospectivo observacional desarrollado entre septiembre de 2005 y agosto de 2010.
Ámbito: Pacientes ingresados en la UCI de un hospital de tercer nivel.
Pacientes: Un total de 386 pacientes en shock séptico.
Intervenciones: Ninguna.
Variables de interés principales: Uso de IECA/ARAII, desarrollo de FRA, recuperación de niveles de creatinina previos y retraso hasta la recuperación.
Resultados: Se incluyeron 386 pacientes, 312 (80,8%) desarrollaron FRA durante su estancia en la UCI, el 23% se encontraban en tratamiento previo con IECA-ARAII. El porcentaje de pacientes en tratamiento con IECA/ARAII se incrementó en relación con el incremento de la gravedad del FRA independientemente de la escala de gravedad utilizada. Tras ajustar por los factores de confusión el tratamiento con IECA-ARAII se asoció de forma independiente al desarrollo de FRA (OR 2,19; IC 95% 1,21-3,84; p = 0,04). El grupo de pacientes en tratamiento con IECA/ARAII tuvo niveles significativamente más altos de creatinina al alta de la UCI y necesitó con mayor frecuencia de hemodiálisis. Sin embargo, su uso no afectó a la recuperación de la creatinina previa ni la retrasó.
Conclusiones: El uso de IECA-ARAII previo al desarrollo de un shock séptico se asoció con el desarrollo de FRA y su gravedad, pero no con su recuperación.

Introduction

Patients with acute kidney injury (AKI) have a higher risk of short-term and long-term mortality and of chronic kidney injury and are also a significant healthcare burden.[1–4] Sepsis is the trigger for AKI development in approximately 50% of critically ill patients.[5] Sepsis-induced AKI increases mortality from sepsis by 50–60% and also extends intensive care unit (ICU) stay.[6] The pathophysiology of septic AKI, although not as yet firmly established, is considered to be different from AKI of other aetiologies. In response to a drop in blood pressure, circulating angiotensin I, under the action of the angiotensin-converting enzyme (ACE), is hydrolysed to angiotensin II, which causes systemic micro-artery contraction, increased peripheral resistance and raised blood pressure. Thus, the renin-angiotensin-aldosterone system could play a key role in sepsis-related AKI.[7]

Renin-angiotensin system blockers, including angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are frequently used in clinical practice.[8] Since angiotensin II constricts efferent arterioles in glomeruli, ACEIs cause efferent arteriolar dilatation. This action mechanism might be hazardous in clinical situations where kidney blood flow is prone to decrease, resulting in further drops in intra-glomerular pressure and the glomerular filtration rate. While ACEIs are known to slow down the progression of chronic kidney disease, their role in AKI remains controversial. Studies of ACEIs and ARBs as used by surgery patients have reported disparate findings.[9,10] Some have demonstrated an increased risk for postoperative AKI, others a decreased risk and others no impact on the risk. In sepsis in particular, the use of ACEIs and ARBs has been identified as contributing to the development of AKI.[11] Thus, National Clinical Guideline Centre recommendations for AKI include temporarily suspending ACEIs and ARBs in adults with sepsis until clinical condition has improved and stabilised.[12] However, the role played by ACEIs and ARBs in long term kidney function recovery has not been extensively evaluated.

The aim of this study was to assess the association of ACEI and ARB use prior to a septic shock episode with development, prognosis and long-term recovery from AKI.

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