



Original article

Aetiology of renal failure in patients with infective endocarditis. The role of antibiotics[☆]

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ABSTRACT

Background and objectives: The possible renal toxicity of certain antibiotics (AB) is well known. The objective of our work is to know the possible effect of AB treatments in the development of renal failure (RF) in patients with infective endocarditis (IE).

Material and method: Collection from a national multi-centre registry of collection on renal function, both prior and its impairment, if any, during the treatment of IE and in relation to possible causative factors, including the use of AB.

Results: Between 2008 and 2012, 1853 episodes of IE reported from 26 Spanish centres were analyzed. Of these, 21.6% had prior RF. They developed new RF or impairment of renal function in 38.7% of the cases. In patients with prior RF, impairment was more frequent (64 vs 31.7%, $p < 0.001$). Overall, patients with RF were older (70.6 vs 67 years, $p < 0.01$), had more comorbidities (Charlson index 5 vs 4, $p < 0.01$), and IE by *Staphylococcus aureus* (32.1 vs 16.5%, $p < 0.01$). Potentially nephrotoxic AB use was only associated with RF in patients without prior RF (aminoglycosides: OR = 1.47 [95% CI 1.096–1.988], $p = 0.010$; aminoglycosides with vancomycin: OR = 1.49 [95% CI 1.069–2.09], $p = 0.019$).

Conclusions: In patients without prior RF, the use of nephrotoxic AB is associated with impairment of renal function. In patients with RF prior to the IE episode, impairment of renal function was more frequent but appears to be more related to the severity of infection.

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◇ The names of the GAMES Group members are available in Annex.

Etiología de la insuficiencia renal en pacientes con endocarditis infecciosa. Papel de los antibióticos

R E S U M E N

Palabras clave:
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Fundamento y objetivos: La toxicidad renal de ciertos antibióticos (AB) es conocida. El objetivo de nuestro trabajo es conocer el posible efecto de los tratamientos AB en el desarrollo de insuficiencia renal (IR) en pacientes con endocarditis infecciosa (EI).

Material y método: Recogida en un registro nacional multicéntrico de los datos referentes a la función renal, tanto previa como su deterioro si existiese, durante el tratamiento de las EI y relacionarlo con los posibles factores causantes, entre ellos los AB.

Resultados: Entre 2008 y 2012 se han analizado 1.853 episodios de EI remitidos desde 26 centros españoles. De ellos, un 21,6% presentaban una alteración previa de la función renal. Desarrollaron IR de novo o un empeoramiento de la función renal previa un 38,7% de los casos. En aquellos pacientes que presentaban IR previa, el deterioro fue más frecuente (64 frente a 31,7%; $p < 0,001$). Globalmente los pacientes con IR tenían más edad (70,6 frente a 67 años; $p < 0,01$) y comorbilidades (índice de Charlson 5 frente a 4; $p < 0,01$), y la EI era por *Staphylococcus aureus* (32,1 frente a 16,5%; $p < 0,01$). El uso de AB potencialmente nefrotóxicos solo se asoció a IR en el grupo de pacientes sin IR previa (aminoglucósidos: OR = 1,47 [IC 95% 1,096–1,988], $p = 0,010$; aminoglucósidos-vancomicina: OR = 1,49 [IC 95% 1,069–2,09], $p = 0,019$).

Conclusiones: En pacientes sin IR previa, los AB nefrotóxicos se asocian a un deterioro de la función renal. En pacientes con IR previa al episodio de EI, el deterioro de renal fue más frecuente, pero parece estar más relacionado con la gravedad de la infección.

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Introduction

Infective endocarditis (IE) is a rare disease, known for more than 4 centuries, characterized, even in our time, by being associated with a significant morbidity and mortality. This association is given by aspects related to the infectious process itself, the treatments or the diagnostic processes used for this disease, plus the fact that it affects patients who are increasingly more elderly and with more underlying diseases. The renal toxicity that occurs in IE is a clear example of the abnormalities that can be caused by both, the infectious process itself (glomerulonephritis, renal infarcts, septic embolism)^{1,2} as well as by the consequences of its treatment (antibiotics, anti-inflammatory analgesics, diuretics, amines) or diagnostic studies (contrast agents).

The possible renal toxicity of certain antibiotics (aminoglycosides, vancomycin) has been well known for decades, but even so, surprisingly, these drugs continue to appear in the recommendations of scientific societies for empirical and even targeted treatment of IE^{3,4} as drugs of choice, despite the existence of other less nephrotoxic alternatives.

The known epidemiological changes that the target population of this disease experiences together with a greater number of comorbidities, including previous renal function abnormalities, also contribute to this renal toxicity.

The objective of our study is to know, in a large, nationwide and multicentre series, the possible effect that antibiotic treatments could have on the development of renal failure in patients with IE and to assess the effect of previous renal disorders.

Material and methods

A prospective registry, containing 148 items, has collected data from all patients diagnosed with IE in 26 Spanish sites between January 2008 and December 2012.

Registration is common practice in all sites, where a multidisciplinary team is in charge of making the diagnosis and recording each case, which is later uploaded to a centralized database.

Definitions

- IE: is defined according to the modified Duke criteria.
- Pre-episode renal function: the registry items referred to the patient's medical history show "baseline creatinine", "mild renal failure", defined as plasma creatinine above 1.4 mg/dl and less than 2.5 mg/dl, and "moderate-severe renal failure" defined by a plasma creatinine higher than 2.5 mg/dl. Whether the patient was previously on haemodialysis or peritoneal dialysis was recorded in this item.
- Kidney failure during the episode: the item "new renal failure?" was included in the complications section, defined as a worsening of baseline creatinine or baseline creatinine clearance by 25% or plasma creatinine above 1.4 mg/dl de novo.

All patients received antibiotics for at least one day.

Cases in which the patient was on haemodialysis prior to the diagnosis of IE and those cases of IE caused by fungi or whose records did not show data on renal function were excluded.

Statistical analysis

Quantitative variables are expressed as mean \pm SD or as median with IQR when appropriate; the qualitative variables are expressed as frequencies and percentages. Continuous variables were compared using the *t*-test and categorical variables using the chi-square test or Fisher's exact test when the first was not applicable.

Odds ratios (OR) and the 95% confidence interval (CI) were calculated to identify worsening or new renal failure predictors by performing a logistic regression analysis using the stepwise exclusion method. The following variables were included: age, history of liver disease, Charlson index, heart failure, new cardiac conduction abnormality, need for mechanical ventilation, septic shock, severe sepsis, cardiac surgery during hospitalization, *Staphylococcus aureus* and having received aminoglycosides alone or combined with vancomycin.

Statistical analyses were performed using the SPSS® version 18 (IBM PASW Statistics 18.0, Armonk, NY, USA) software.

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