

Brief review

New oral anticoagulants in patients with chronic kidney disease[☆]

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ARTICLE INFO

Article history:

Received 29 March 2016

Accepted 29 August 2016

Available online 19 May 2017

Keywords:

Oral anticoagulants

Atrial fibrillation

Chronic kidney disease

ABSTRACT

Patients with chronic kidney disease (CKD) develop bleeding and thrombotic tendencies, so the indication of anticoagulation at the onset of atrial fibrillation (AF) is complex. AF is the most common chronic cardiac arrhythmia, and thromboembolism and ischaemic stroke in particular are major complications. In recent years, new oral anticoagulant drugs have been developed, and they have shown superiority over the classical AVK in preventing stroke, systemic embolism and bleeding risk, constituting an effective alternative to those resources.

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Nuevos anticoagulantes orales en pacientes con enfermedad renal crónica

RESUMEN

Los pacientes con enfermedad renal crónica (ERC) tienen tendencias hemorrágicas y tromboticas, por lo que la indicación de anticoagulación ante la aparición de fibrilación auricular (FA) es compleja. La FA es la arritmia cardíaca crónica más frecuente, siendo el tromboembolismo y el ictus isquémico en particular las complicaciones más importantes. En los últimos años se han desarrollado nuevos fármacos anticoagulantes orales que han mostrado superioridad respecto a los clásicos antagonistas de la vitamina K (AVK) en la prevención de ictus, embolismo sistémico y riesgo de sangrado, constituyendo una alternativa eficaz a ellos.

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Palabras clave:

Anticoagulantes orales

Fibrilación auricular

Enfermedad renal crónica

[☆] Please cite this article as: Belmar Vega L, de Francisco ALM, Bada da Silva J, Galván Espinoza L, Fernández Fresnedo G. Nuevos anticoagulantes orales en pacientes con enfermedad renal crónica. Nefrología. 2017;37:244-252.

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Introduction

Patients with chronic kidney disease (CKD) presents a difficult problem in daily clinical practice; these patients have a bleeding tendency due to a primary disorder of haemostasis secondary to platelet dysfunction and an abnormality in platelet/subendothelial interaction¹; the same patients also had a clotting tendency caused by multiple factors, such as endothelial damage, increased coagulation factors and decreased fibrinolytic proteins.² Therefore, in these patients the indication of anticoagulation therapy for atrial fibrillation (AF) is a complex decision, even more so because of the new oral anticoagulants that are now available and which are different in their renal pharmacokinetics.

The purpose of this article is to clarify decisions concerning whether to give anticoagulation to CKD patients who develop AF, and which anticoagulant drug is best in each case.

Epidemiology and predisposing factors of atrial fibrillation in chronic kidney disease

AF is the most common chronic cardiac arrhythmia, and its prevalence in CKD is 10–20 times higher than in the general population.³ In fact, AF and CKD often coincide: one-third of AF patients have CKD, and 15% of CKD patients appear to have AF.⁴ In patients on haemodialysis studied with a Holter ECG monitor, the frequency of AF reaches up to 27%. No accurate data are available in CKD patients who are not on dialysis (Table 1).

CKD patients are at a high risk of developing cardiovascular disease, and at the same time and in the opposite direction, the prevalence of CKD is greater in people with cardiovascular disease than in the general population, which is associated with a worse prognosis. In particular, vascular and valvular calcification, left ventricular hypertrophy, hydroelectrolytic disorders during dialysis and renin–angiotensin–aldosterone system (RAAS) hyperactivity are predisposing factors for AF. Recently, one study showed that RAAS inhibition with ACE inhibitors and/or angiotensin II receptor blockers (ARBs) is effective in the primary prevention of AF in patients on dialysis.⁵

Risk of stroke in chronic kidney disease

The most significant complications of AF are thromboembolism, particularly ischaemic stroke, which are usually more severe in terms of residual disability and short- and medium-term mortality.⁶ The incidence of stroke is higher among patients on haemodialysis than in the general population. In a study conducted in our nephrology department at Hos-

Table 2 – CHA₂DS₂-VASc score for assessing the risk of stroke in atrial fibrillation.

Factor	Points	
C	Congestive heart failure or LV systolic dysfunction	1
H	Hypertension	1
A ₂	Age >75 years	2
D	Diabetes mellitus	1
S ₂	Stroke, TIA or thromboembolism	2
V	Vascular disease (previous AMI, peripheral artery disease, aortic plaque)	1
A	Age 65–74 years	1
Sc	Women	1

TIA: transient ischaemic attack; AMI: acute myocardial infarction; LV: left ventricle.

Maximum: 9 points. Low risk: 0; intermediate risk: 1; high risk ≥ 2 .

Source: Camm et al.¹⁴

pital Universitario Valdecilla, in Santander, the cumulative incidence of cerebrovascular events was 5.8%. The incidence rate during the first year on haemodialysis was 6.5% higher than the mean observed during the study period.⁷ Murray et al.⁸ observed that the number of strokes during the first month on haemodialysis increased by as much as 7 times. The same was observed in a European database of haemodialysis patients.⁹ The reasons for this higher incidence in the early stages of haemodialysis are not clear; suggested as possible factors are decreased cerebral perfusion and blood flow velocity, or, in patients treated with erythropoiesis-stimulating agents (ESA), increased viscosity and vascular resistance that can lead to increases in blood pressure. In the United States Renal Data System (USRDS), the incidence of stroke was 15.1% in haemodialysis, 9.6% in patients with CKD but not on haemodialysis and 2.6% in patients without CKD.¹⁰ In Jaén, Spain, a study by Vázquez et al.¹¹ found a rate of thromboembolic complications of 24% per year in patients on dialysis in AF, compared with 5% in patients with sinus rhythm. In the USRDS,¹⁰ an 80% greater chance of ischaemic stroke is reported in AF patients with a similar incidence of haemorrhagic stroke. A stroke clearly increases mortality in CKD patients compared with those without CKD.³

Risk of stroke in chronic kidney disease with atrial fibrillation, CHA₂DS₂-VASc score vs. risk of bleeding, HAS-BLED score

Among the factors associated with stroke, in our patients we found diabetes, myocardial infarction or angina pectoris, hypertension, arteriosclerosis/intermittent claudication and history of cerebrovascular accident before haemodialysis.⁷ However, we did not find AF to be an associated factor, as in other more recent works,¹² but this may be due to the no differentiation of ischaemic stroke from haemorrhagic stroke. The American Heart Association's¹³ 2014 clinical practice guidelines recommend (1B) using the CHA₂DS₂-VASc score to assess risk of stroke in patients with AF. The majority of kidney patients have a high risk of stroke¹⁴ (Table 2). Also, kidney patients have a high risk of bleeding according to the HAS-BLED score¹⁵ (Table 3).

Table 1 – Prevalence of atrial fibrillation.³

General population <60 years:	1%
General population <80 years:	8%
Patients on peritoneal dialysis	7%
Patients on haemodialysis	13%–27%

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