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ORIGINAL ARTICLE

Digoxin in advanced heart failure patients: A question of rhythm

Elisabete Jorge*, Rui Baptista, Hélia Martins, Fátima Saraiva, Susana Costa, Henrique Vieira, Lourenço Coelho, Pedro Monteiro, Fátima Franco, Luís A. Providência

Hospitais da Universidade de Coimbra e Clínica Universitária de Cardiologia da Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal

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KEYWORDS
Advanced heart failure;
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Abstract
Background: The impact of digoxin on outcomes of patients with advanced heart failure (HF) remains uncertain and its effect may be different for patients in atrial fibrillation (AF) or sinus rhythm (SR).
Objectives: To determine the impact of digoxin on outcomes of advanced HF patients and to assess whether prognosis differs in patients in AF and SR.
Methods: A total of 268 consecutive patients admitted to an intensive care unit with decompensated HF were evaluated. Patients were divided into two groups: A – patients with AF (n=89), and B – patients in SR (n=179). For each group we compared patients medicated and not medicated with digoxin. A mean follow-up of 3.3 years was performed.
Results: Addition of digoxin to contemporary standard HF therapy showed no impact on mortality of patients in group B (all-cause mortality in follow-up: 19.1% vs. 22.5%, p=0.788). Regarding group A, we observed significantly lower medium-term mortality for patients on digoxin therapy (18.6% vs. 46.6%, p=0.048). Digoxin therapy did not influence readmissions for decompensated HF. Among AF patients, no differences were found regarding demographic, clinical, echocardiographic and laboratory variables between patients medicated and not medicated with digoxin.
Conclusions: Digoxin therapy may improve the prognosis of advanced HF patients with AF under optimal medical therapy. However, no benefit of digoxin was demonstrated for patients in SR. These results may help to improve patient selection for digoxin therapy.
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* Corresponding author.
E-mail address: elisabetejorge@gmail.com (E. Jorge).

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PALAVRAS-CHAVE
Insuficiência cardíaca avançada;
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Digoxina na insuficiência cardíaca avançada: uma questão de ritmo

Resumo
Introdução: O impacto prognóstico da digoxina na insuficiência cardíaca (IC) avançada permanece mal esclarecido. A relevância da terapêutica digitálica pode ser diferente na fibrilhação auricular (FA) relativamente ao ritmo sinusal (RS).
Objectivos: Determinar o impacto prognóstico da digoxina na IC e verificar se este é diferente consoante se encontrem em FA ou em RS.
Métodos: Estudaram-se 268 doentes internados numa unidade de cuidados intensivos por IC descompensada. Dividiu-se a população em dois grupos: A – 89 doentes em FA; grupo B – 179 doentes em RS. Para cada grupo compararam-se os doentes medicados com os não medicados com digoxina. Realizou-se um seguimento clínico com a duração mediana de 3,3 anos.
Resultados: A digoxina não teve impacto na mortalidade dos doentes com IC avançada que se encontravam em RS (mortalidade a 3,3 anos: 19,1% *versus* 22,5%, p = 0,788), adicionada à terapêutica médica otimizada. Nos doentes em FA observou-se uma redução significativa da mortalidade nos doentes medicados com digoxina (18,6% *versus* 46,6%, p = 0,048). A digoxina não alterou a taxa de reinternamentos por IC descompensada. No grupo A não se verificaram diferenças entre os doentes medicados e não medicados com digoxina relativamente aos parâmetros demográficos, clínicos, ecocardiográficos ou laboratoriais.
Conclusão: Este estudo sugere que a digoxina pode melhorar o prognóstico dos doentes com IC avançada e FA, sob terapêutica médica optimizada. Contudo, esta não demonstrou benefício nos doentes em RS. Estes resultados podem contribuir para uma melhor seleção dos doentes a medicar com digoxina, otimizando a relação risco/benefício desta terapêutica.
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Introduction

Despite more than 200 years of research, the role of digoxin in heart failure therapy remains controversial. The American College of Cardiology and American Heart Association (ACC/AHA) guidelines for the management of patients with heart failure (HF) recommend the use of digoxin, unless contraindicated, for persistent symptoms after optimal medical therapy.[1] Digoxin use is also endorsed by the European Society of Cardiology guidelines.[2] Although widely accepted, these recommendations are derived mainly from short-term studies assessing non-mortality outcomes.[3–8] The Digitalis Investigator Group (DIG) study,[9] a large randomized trial, showed no impact on all-cause or cardiovascular mortality with digoxin in oligosymptomatic male HF patients in sinus rhythm (SR). However, a reduction in hospitalizations due to worsening HF and an improvement in quality of life were reported.[10] Two other trials showed that withdrawal of digoxin resulted in worsening HF symptoms.[6,7] Although more than 90% of patients were receiving angiotensin-converting enzyme inhibitors (ACEIs) in the DIG trial,[9] the use of beta-blockers and aldosterone antagonists was not reported and likely was very limited. Similarly, improved outcomes are also seen with cardiac devices, which are now widely used in HF patients. A recently published study suggests no benefit of digoxin in advanced HF patients on contemporary medical therapy.[11] In this report, HF patients in SR treated with digoxin had a worse prognosis than those who were not. However, this did not appear to be true for patients in atrial fibrillation (AF). In patients with AF, the beneficial role of digoxin is widely accepted, mainly to optimize ventricular rate control, and the Carvedilol Atrial Fibrillation Evaluation (CAFE) study suggests that there may be synergistic benefits between digoxin and carvedilol.[11]

In our study, we sought to determine the impact of digoxin therapy in advanced HF patients on optimal contemporary medical therapy, and to assess whether prognosis differs according to the presence of AF.

Methods

Patient population and data collection

This single-center study included 268 consecutive patients admitted to an intensive care unit between January 2003 and June 2006 due to decompensated HF in New York Heart Association (NYHA) class III or IV. Standardized records were used to describe the study population in terms of clinical and demographic characteristics, cardiovascular risk factors and comorbidities. The records also showed HF etiology, hemodynamic status on admission, laboratory parameters, electrocardiographic and echocardiographic data, and treatment. Renal dysfunction was defined as creatinine clearance of <60 ml/min calculated by the Cockcroft–Gault formula. Ischemic cardiomyopathy was defined as left ventricular dysfunction associated with significant coronary disease (>70% stenosis in at least one major epicardial coronary artery and/or >50% left main stenosis). In the minority of patients without coronary angiography (4%) the diagnostic criterion of ischemic heart disease was prior myocardial infarction (history of infarction or infarct scar on ECG). Non-ischemic cardiomyopathy was defined as left ventricular dysfunction in the absence of the above alterations. Coronary angiography was performed in 70% of this group; an

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