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ORIGINAL ARTICLE

Inotropes and cardiorenal syndrome in acute heart failure – A retrospective comparative analysis

Marta Madeira[a,b,*], **Francisca Caetano**[c], **Inês Almeida**[a], **Andreia Fernandes**[a], **Liliana Reis**[a], **Marco Costa**[a], **Lino Gonçalves**[a,b]

[a] *Serviço de Cardiologia, Centro Hospitalar e Universitário de Coimbra – Hospital Geral, Coimbra, Portugal*
[b] *Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal*
[c] *King's College Hospital NHS Foundation Trust, Critical Care Department, London, United Kingdom*

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KEYWORDS
Heart failure;
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Abstract
Introduction: Cardiorenal syndrome (CRS) is common in acute heart failure (AHF), and is associated with dire prognosis. Levosimendan, a positive inotrope that also has diuretic effects, may improve patients' renal profile. Published results are conflicting.
Objectives: We aimed to assess the incidence of CRS in AHF patients according to the inotrope used and to determine its predictors in order to identify patients who could benefit from the most renoprotective inotrope.
Methods: In a retrospective study, 108 consecutive patients with AHF who required inotropes were divided into two groups according to the inotrope used (levosimendan vs. dobutamine). The primary endpoint was CRS incidence. Follow-up for mortality and readmission for AHF was conducted.
Results: Seventy-one percent of the study population were treated with levosimendan and the remainder with dobutamine. No differences were found in heart failure etiology or chronic kidney disease. At admission, the dobutamine group had lower blood pressure; there were no differences in estimated glomerular filtration rate or cystatin C levels. The levosimendan group had lower left ventricular ejection fraction. CRS incidence was higher in the dobutamine group, and they more often had incomplete recovery of renal function at discharge. In multivariate analysis, cystatin C levels predicted CRS. The dobutamine group had higher in-hospital mortality, of which CRS and the inotrope used were predictors.
Conclusions: Levosimendan appears to have some renoprotective effect, as it was associated with a lower incidence of CRS and better recovery of renal function at discharge. Identification of patients at increased risk of renal dysfunction by assessing cystatin C may enable more tailored therapy, minimizing the incidence of CRS and its negative impact on outcome in AHF.

* Corresponding author.
E-mail address: marta.jesus.madeira@gmail.com (M. Madeira).

PALAVRAS-CHAVE
Insuficiência cardíaca;
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Dobutamina

Inotrópicos e síndrome cardiorrenal na insuficiência cardíaca aguda – análise comparativa retrospetiva

Resumo
Introdução: A síndrome cardiorrenal (SCR) é comum na insuficiência cardíaca aguda (ICA), associando-se a um prognóstico sombrio. O levosimendano, aliando um efeito inotrópico e diurético, poderá ter melhor perfil renal. A literatura é controversa.
Objetivos: Avaliar em doentes com ICA a incidência de SCR em função do inotrópico utilizado. Determinar preditores de SCR, identificando os doentes que possam beneficiar do inotrópico com melhor perfil renoprotetor.
Métodos: Estudo retrospetivo, incluindo 108 doentes consecutivos com ICA tratados com inotrópicos. Criados dois grupos consoante o inotrópico utilizado (levosimendano e dobutamina). O *endpoint* primário foi incidência de SCR. Realizado seguimento relativo a mortalidade e hospitalização por ICA.
Resultados: O levosimendano foi usado em 71% dos doentes e a dobutamina nos restantes. Sem diferenças na etiologia da IC ou incidência de doença renal crónica. À admissão, o grupo-dobutamina apresentava menor pressão arterial sistólica; sem diferenças na taxa de filtração glomerular (TFG) ou cistatina C. O grupo-levosimendano apresentava disfunção ventricular esquerda mais grave. A incidência de SCR foi maior no grupo-dobutamina, com recuperação incompleta da TFG à alta hospitalar. Em análise multivariada, a cistatina C foi preditora de SCR. A mortalidade intra-hospitalar foi superior no grupo-dobutamina, sendo a SCR e o inotrópico utilizado preditores desta.
Conclusões: O levosimendano parece ter melhor perfil renal, associando-se a menor incidência de SCR, com recuperação da função renal. A cistatina C, ao identificar os doentes em maior risco de disfunção renal, poderá permitir uma terapêutica mais individualizada, reduzindo a incidência de SCR e seu impacto negativo no prognóstico da ICA.

Introduction

Acute heart failure (AHF) remains the single most common admitting diagnosis in industrialized countries, despite significant advances in pharmacologic and device therapy.[1,2] Some degree of renal impairment is present in more than a third of patients with AHF, associated with reduction in renal blood flow and/or elevation in central venous pressure, leading to a decrease in estimated glomerular filtration rate (eGFR).[3–5] Conversely, renal impairment itself may predispose to worsening heart failure (HF), through constant salt and water retention, diuretic resistance and neurohormonal activation, leading to increased cardiac workload.[6,7] In a broad spectrum of patients with chronic HF in the CHARM study,[8] renal dysfunction was independently associated with increased risk of death, cardiovascular death, and hospitalization due to AHF.[9] Furthermore, in advanced chronic HF, renal impairment was a stronger predictor of mortality than either left ventricular ejection fraction (LVEF) or New York Heart Association (NYHA) functional class.[10]

Both dobutamine and levosimendan are inotropic drugs, used specifically to improve cardiac contractility.[11] Through activation of ATP-sensitive potassium channels, levosimendan causes both arterial and venous vasodilation (mainly the latter).[11] This additional effect of levosimendan over dobutamine may be crucial in AHF, since central venous pressure is an independent predictor of cardiorenal syndrome (CRS) in this setting.[12]

However, only a few studies comparing the effects of levosimendan with dobutamine on renal function in patients hospitalized with AHF have been published.[13,14]

We aimed to assess the incidence of CRS according to the inotrope used and to determine its predictors in order to identify patients who could benefit from the most renoprotective inotrope.

The primary endpoint was CRS incidence during hospital stay. The secondary endpoints were recovery of eGFR at discharge, readmission for AHF and mortality during follow-up.

Methods

Population and study design

We retrospectively studied 108 consecutive patients admitted between May 2009 and March 2014 to a single cardiac intensive care unit for AHF with symptoms or signs of severe congestion or low cardiac output requiring inotropes. The diagnosis of AHF was established according to the current European Society of Cardiology guidelines.[15]

Patients with end-stage renal disease on a regular program of renal replacement therapy were excluded.

The sample was divided into two groups according to the inotrope used (levosimendan or dobutamine), prescribed at the discretion of the admitting physician. In the levosimendan group no initial bolus was given and perfusion