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ORIGINAL ARTICLE

Continuous infusion or bolus injection of loop diuretics for patients admitted for severe acute heart failure: Is one strategy better than the other?

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KEYWORDS
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Abstract
Introduction and Objectives: Intravenous loop diuretics are an essential part of acute heart failure management; however, data to guide their use is sparse. Our aim was to compare continuous intravenous infusion of loop diuretics with intravenous bolus administration in terms of efficacy and adverse events in patients admitted with severe acute heart failure.
Methods: Over a period of three years, 110 patients were admitted to our cardiac intensive care unit with acute heart failure. Clinical, laboratory and prognostic parameters were compared according to the diuretic strategy used and mortality and readmission for acute heart failure during follow-up were analyzed.
Results: Previous medical history was similar in the two groups. At admission, the continuous infusion group met criteria for worse prognosis: lower systolic blood pressure (p=0.011), more severe renal injury (p=0.008), lower left ventricular ejection fraction (p=0.016) and higher incidence of restrictive pattern of diastolic dysfunction (p=0.032). They were more often treated with vasopressors (p=0.003), inotropes (p=0.010), renal support therapy (p=0.003) and non-invasive ventilation (p<0.001). They had longer hospitalizations (p=0.014) and a higher incidence of cardiorenal syndrome (p=0.009); however, at discharge, there were no differences in renal function between the groups. In-hospital mortality was similar, and during follow-up there were no differences in mortality or readmission for acute heart failure.
Conclusions: Continuous infusion was preferred in patients presenting with worse clinical status, in whom renal dysfunction was transiently worse. However, in-hospital mortality and creatinine at discharge were similar. Continuous infusion thus appears to counteract the initial dire prognosis of more unstable patients.

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PALAVRAS-CHAVE
Diuréticos;
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Diuréticos da ansa em doentes com insuficiência cardíaca aguda: perfusão contínua ou bólus – uma estratégia melhor do que a outra?

Resumo
Introdução/objetivos: O uso de diuréticos da ansa é essencial no tratamento de doentes com insuficiência cardíaca aguda; contudo existe pouca evidência para guiar o seu uso. Neste trabalho comparámos a eficácia e efeitos adversos do uso de diuréticos em perfusão contínua com bólus em doentes com insuficiência cardíaca aguda.
Métodos: Análise de 110 doentes admitidos por insuficiência cardíaca aguda, ao longo de três anos, numa unidade de cuidados intensivos cardíacos. Parâmetros clínicos, analíticos e prognósticos foram comparados de acordo com a estratégia diurética utilizada. Realizado seguimento referente a mortalidade e reinternamento por insuficiência cardíaca aguda.
Resultados: A história médica prévia era semelhante. À admissão, o grupo da perfusão contínua reunia critérios de maior gravidade: pressão arterial sistólica mais baixa (p=0,011), lesão renal mais grave (p=0,008), menor fração de ejeção do ventrículo esquerdo (p=0,016) e maior incidência de padrão restritivo de disfunção diastólica (p=0,032). Foram tratados mais frequentemente com vasopressores (p=0,003), inotrópicos (p=0,010), terapêutica de suporte renal (p=0,003) e ventilação não invasiva (p<0,001). Tiveram internamentos mais prolongados (p=0,014) e maior incidência de síndrome cardiorrenal (p=0,009); contudo à alta não houve diferença na função renal entre os grupos. A mortalidade hospitalar foi semelhante; no seguimento não houve diferenças na mortalidade ou nos reinternamentos por insuficiência cardíaca.
Conclusões: A utilização de diuréticos da ansa em perfusão contínua foi preferida em doentes com critérios de maior gravidade à admissão. Transitoriamente apresentaram maior agravamento da função renal; contudo, a mortalidade hospitalar e a função renal à alta foram semelhantes. Assim, a perfusão contínua poderá ser uma opção em doentes mais instáveis.

List of abbreviations

AHF	acute heart failure
ALT	alanine transaminase
AST	aspartate transaminase
BUN	blood urea nitrogen
CRS	cardiorenal syndrome
eGFR	estimated glomerular filtration rate
HF	heart failure
IV	intravenous
LOS	length of hospital stay
LVEF	left ventricular ejection fraction
MDRD	Modification of Diet in Renal Disease
PASP	pulmonary artery systolic pressure
BP	blood pressure

Introduction

Hospitalizations for acute heart failure (AHF) have increased over time. Costs related to hospitalizations account for around 75% of the total cost of heart failure (HF) care.[1] The prognosis of patients with AHF remains poor, with in-hospital mortality of 4%[2] and a 30-day rehospitalization rate of 23%.[3]

Fluid retention and congestion are responsible for 90% of HF hospitalizations,[2,4] and greater severity of congestion is associated with worse outcomes.[5]

Intravenous (IV) loop diuretics are a mainstay of the pharmacological treatment of AHF. Despite the ubiquitous use of these agents, uncertainties about appropriate dosing and overall safety profile persist.[6,7] As a result, clinical practice varies widely across sites and countries with regard to both mode of administration and dosing.

Theoretically, continuous infusion of a loop diuretic, maintaining stable blood levels, should allow more sustained diuresis, avoiding large swings in intravascular volume and secondary neurohormonal activation. Continuous IV infusion with appropriate dosing may also prevent high or even toxic levels being reached, thereby causing fewer and less severe side effects.

Studies comparing the efficacy and safety of continuous and intermittent IV infusion of loop diuretics in AHF have yielded conflicting results and have been underpowered to address clinical questions, and thus no specific recommendations can be made.[8]

A recent randomized trial, the Diuretic Optimization Strategies Evaluation (DOSE) trial, challenged the existing clinical dogma concerning the optimal method of IV diuretic administration in hospitalized patients.[9] However, criticisms have been made due to the low dosage of the diuretic regimens used. Also, more than 25% of patients included in this trial had left ventricular ejection fraction (LVEF) of 50% or greater, and exclusion criteria included systolic blood pressure (BP) <90 mmHg, serum creatinine >3.0 mg/dl (265 μmol/l) and need for IV vasodilators or