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The Effect in Renal Function and Vascular Decongestion in Type 1 Cardiorenal Syndrome Treated with Two Strategies of Diuretics, a Randomized Clinical Trial

NCT04393493

Study protocol

Study participants

This was a prospective single-center double-blind randomized clinical trial that screened all consecutive patients admitted for acute decompensation (ADHF) and acute kidney injury (AKI), who met the criteria of cardiorenal type 1 syndrome (CRS-1) and were evaluated by the Nephrology service at the Hospital Civil de Guadalajara Fray Antonio Alcalde, a large referral hospital that attends patients without health care insurance and low socioeconomic resources in Jalisco, México. Patients were enrolled from July 2017 to February 2020.

The research was conducted in accordance with the World Medical Association Declaration of Helsinki. The study was approved by the Institutional Review Board (HCG/CEI-0550/17), and all patients provided written informed consent. No funding was received to conduct this study. The trial was registered in ClinicalTrials.gov with number NCT04393493.

Definitions

Cardiorenal type 1 syndrome (CRS-1) was defined according to the 2008 classification system by Ronco et al; to meet the criteria of CRS-1, AKI was defined as an increase in serum creatinine (sCr) according to KDIGO and acute heart failure decompensation (AHFD) was defined clinically. Both criteria need to be present at the moment of the initial evaluation.

Chronic kidney disease (CKD) was defined according to the KDIGO guideline. The estimated glomerular filtration rate (eGFR) in ml/min/1.73 m^2 was calculated according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI). Baseline eGFR was considered according to the last sCr (previous 3 months). Renal function recovery was defined as sCr return to baseline value at any point during the trial (complete recovery).

All comorbidities and clinical data were prospectively collected by direct contact with the patient during the first evaluation. Additional data were collected from medical records and the hospital electronic database.

The **primary endpoint** was to assess renal function recovery (*sCr return to baseline value*) after 96 hours, and the **secondary endpoints** were a combination of variables related to vascular decongestion during the treatment and follow up, namely, the change in urinary output, sCr, sCr worsening, in-hospital mortality, mortality during follow up, dyspnea improvement,

dyspnea improvement before day 3, time until dyspnea improved, renal replacement therapy, change in electrolytes and acid-base status. As exploratory endpoints, we evaluated changes in copeptine levels, BNP, BNP reduction and intervention stop because of clinical improvement. Prespecified adverse events were reported.

Randomization and treatments assignments

Patients who met the inclusion criteria were randomly assigned in a 1:1 ratio to the administration of stepped furosemide or combined diuretics. Randomization was carried out by the use of sequentially numbered cases prepared before starting the study by a computerized sequence. A double-blind, double-dummy design was used. All patients received a bolus of furosemide 80 mg every day, a hyposodic diet (<2.4 gr sodium/day), and strict fluid control was prescribed.

The **Stepped Furosemide** (SF) group received a continuous daily infusion of furosemide 100 mg diluted in 100 ml of Hartmann solution during the first day, with daily incremental doses to 200 mg, 300 mg and 400 mg during the second, third and fourth day, respectively.

The **Combined Diuretics** (CD) group was given a combination of diuretics trying to block different tubular segments, similar to the CARRESS-HF trial, including 4 consecutive days of oral chlortalidone 50 mg, spironolactone 50 mg and continuous infusion of furosemide 100 mg diluted in 100 ml of Hartmann for 24 hours**.** In both groups, the assigned treatment strategy was continued until the signs and symptoms of congestion went away or until the end of the trial (96 hours). Inotropes, vasopressors, continuous positive airway pressure ventilation or management of any other comorbid condition were modified at the discretion of the attending physicians, who maintained constant communication with nephrology staff.