



Global Trials Focus

January-February 2022

The ISN-ACT (Advancing Clinical Trials) team presents this monthly round up of randomized trials in nephrology. Trials are selected not just for impact, but also to showcase the diversity of research produced by the global nephrology community. Each trial is reviewed in context and has a risk of bias assessment. We hope to drive improvement in trial quality and promote greater engagement in trial activity.

Key to risk of bias assessment

- Random sequence generation
- Allocation concealment
- Blinding of participants/personnel
- Blinding of outcome assessment
- Complete outcome data
- Complete outcome reporting
- No other sources of bias

High risk

Uncertain risk / not stated

Low risk

Do you agree with our trial of the month? Tell us what you think!

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Want to run your own trial?
ISN-ACT Clinical Trials Toolkit
www.theisn.org/isn-act-toolkit

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ISN Academy: [General Nephrology](#)

Combination diuretics had a similar effect on renal function and dyspnoea improvement as stepped doses of furosemide in patients with type 1 cardiorenal syndrome

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

[Chávez-Iñiguez et al. BMC Nephrology \(2022\) 23:3 <https://doi.org/10.1186/s12882-021-02637-y>](#)



Reviewed by A Zykova



Summary: In this double-blind trial, 80 patients admitted to hospital with acute decompensation of heart failure and a concomitant acute kidney injury, and meeting criteria for cardiorenal type 1 syndrome, were randomly assigned to stepped furosemide (SF) or combined diuretics (CD) groups for 4 days. Patients in the SF group received a continuous infusion of furosemide with a stepwise dose increase from 100mg on day 1 to 400mg by day 4. Patients in the CD group received a furosemide infusion at 100mg/24 hours with the addition of oral chlorthalidone 50mg and spironolactone 50mg. All patients also received a daily 80mg furosemide bolus, and were on a <1 litre fluid restriction, and a <2.4g sodium restriction. There was no statistically significant difference in the incidence of renal function recovery after 4 days of treatment (relative risk 1.5, 95% confidence interval 0.4–5.2; p=0.49), although this endpoint only occurred in 8 patients in the SF group and 5 patients in the CD group. After 4 days, the daily urine output had increased by 125mL with stepped frusemide (with a large interquartile range [IQR] of 1662) compared with 200mL with combined diuretics (IQR 988; p for comparison =0.30). There were no significant differences in serum creatinine worsening at 96h, improvement in dyspnoea, in-hospital mortality, mortality at follow-up, or requirement for renal replacement therapy. The rates of hyponatraemia, hypokalaemia and metabolic acidosis were similar between groups. There were more hypotension events with stepped frusemide (10%) compared with combined diuretics (2.5%).

Comment Despite the high frequency of cardiorenal syndrome type 1, a lack of large-scale trials has resulted in ongoing uncertainty about the best evidence-based use of diuretics. Diuretic resistance in acute heart failure is associated with renal impairment, increased risk of rehospitalisation, and mortality. A combined diuretic regimen can potentially overcome this phenomenon and decrease the dosage of loop diuretics to reduce additional RAAS stimulation and further renal impairment. In this trial the sequential blockade of the renal tubule with a combination of diuretics in patients with cardiorenal syndrome was similar to stepped furosemide alone. Further trials with larger sample size may be needed to answer the question of optimal diuretic therapy in type 1 cardiorenal syndrome more definitively.