

The safety of in-hospital initiation of SGLT2 inhibitor with MRA therapy in patients hospitalized for heart failure with a reduced left ventricular ejection fraction and chronic kidney disease

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Deferring in-hospital initiation of guideline-recommended medications in HFrEF has a few chances they will be initiated ambulatory, especially in the case of coexisting HFrEF and chronic kidney disease (CKD).

The aim was to investigate the safety of in-hospital initiation of SGLT2i with MRA therapy for patients hospitalized for HFrEF and CKD 3.

Methods: 88 patients with HFrEF (on top of standard therapy ACE-I/ARB, B-blockers) and CKD (baseline eGFR between 30 and 60 ml/min) were included in the study. The potassium (K), creatinine (C), uric acid (UA) levels were estimated at baseline and week 12. After biochemical evaluation, patients started on spironolactone (SP) treatment with a median dose of 20 mg daily (titrated) and dapagliflozin (D) with a dose of 10 mg daily (D+SP). Blood pressure (BP), K, and renal function (RF) were checked at weeks 1 (in-hospital), 2, 4, 6, 8, 12 (ambulatory), and more frequently as necessary.

Results: After the start of therapy D+SP mean eGFR decreased significantly at week 1 from 51.14 ± 9.18 to 46.26 ± 7.91 ml/min/1.73m² ($P < .0001$) and at week 2 to 44.18 ± 6.51 ml/min/1.73m² (-2.08 ± 1.2 ; $P < .001$). At week 4 mean eGFR decreased to 42.73 ± 6.86 ml/min/1.73m² (-1.45 ± 1.1 ; $P < .05$). So, a significant decrease in eGFR was observed only during the first month with no significant decrease at 6 and 12 weeks after the start of therapy. Six patients (8%) experienced a significant decline in RF resulting in temporary withdrawal of SP.

At week 2 mean K level increased significantly from 4.56 ± 0.63 to 5.07 ± 0.57 mmol/L ($P < .001$). At weeks 4, 6, 8 K levels remain stable. At week 12 mean K level decreased significantly compared with week 2 (to 4.92 ± 0.57 mmol/L, $P < .05$). The incidences of severe hyperkalemia (HK) (K ≥ 6.0 mmol/L) were in three patients $< 2\%$, and moderate HK (K 5.5–5.9 mmol/L) occurred in ten patients (11%). Patients who experienced inpatient hyperkalemia had a significantly lower eGFR than patients without episodes of HK (38.70 vs. 55.21 mL/min/1.73 m²; $P < .0001$). Episodes of HK were predicted by baseline K ≥ 5.0 mmol/L and eGFR ≤ 40 ml/min/1.73m². Additionally, there was a significant improvement in blood UA (-1.53 ± 0.49 mg/dL, $P < .01$).

By multivariate analysis older age, diabetes, low diastolic BP (< 60 mm Hg), eGFR ≤ 40 ml/min/1.73m² at baseline were associated with decreased RF (0.378, $P < .01$; 0.632, $P < .001$; 0.771, $P < .0001$; 0.397, $P < .01$; respectively), whereas episodes of HK were predicted by baseline K ≥ 5.0 mmol/L and eGFR ≤ 40 ml/min/1.73m² (0.785, $P < .0001$; 0.542, $P < .001$; respectively).

Conclusion: Initiation of SGLT2i with MRA in patients hospitalized for HFrEF and CKD 3 was mainly safe although it caused an early drop in eGFR. Importantly, a fall in eGFR was observed during the first month. Concern about the reduction in eGFR should be in older diabetic patients with eGFR ≤ 40 and low diastolic blood pressure. Although hyperkalemia was common, the occurrence of it was predicted by baseline potassium level and eGFR.