Dapagliflozin reduces the risk of hyperkalaemia in patients with heart failure and reduced ejection fraction: a secondary analysis DAPA-HF

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Background: Hyperkalaemia often limits the use of mineralocorticoid receptor antagonists (MRAs) in patients with heart failure and reduced ejection fraction (HFrEF), denying these patients a life-saving therapy.

Purpose: To determine whether treatment with the sodium-glucose co-transporter 2 (SGLT-2) inhibitor dapagliflozin reduces the risk of hyperkalaemia associated with MRA use in patients with HFrEF.

Methods: The risk of developing mild hyperkalaemia (potassium >5.5 mmol/L) and moderate/severe hyperkalaemia (>6.0 mmol/L) was examined in the Dapagliflozin And Prevention of Adverse-outcomes in Heart Failure trial (DAPA-HF) according to background MRA use, and randomized treatment assignment, by use of Cox regression analyses.

Results: Overall, 3370 (70.1%) patients in DAPA-HF were treated with an MRA. Mild hyperkalaemia and moderate/severe hyperkalaemia occurred in 182 (11.1%) and 23 (1.4%) patients treated with dapagliflozin as compared to 204 (12.6%) and 40 (2.4%) of patients given placebo (Table and Figure). This yielded a hazard ratio (HR) of 0.86 (0.70–1.05) for mild hyperkalaemia and 0.50 (0.29, 0.85) for moderate/severe hyperkalaemia, comparing dapagliflozin to placebo.

Conclusions: Patients with HFrEF and taking a MRA who were randomized to dapagliflozin had half the incidence of moderate/severe hyperkalaemia, compared with those randomized to placebo.

Incident hyperkalaemia in DAPA-HF

	Dapagliflozin		Placebo		HR (95% CI)	P-value
	No. events/patients	Rate per 100py	No. events/patients	Rate per 100py		
Mild hyperkalaemia (>5.5 mmol/L)*						
No MRA at baseline	63/661	7.1	58/684	6.5	1.20 (0.84–1.72)	0.32
MRA treated at baseline	182/1637	8.6	204/1626	9.8	0.86 (0.70–1.05)	0.14
All patients	245/2298	8.2	262/2310	8.8	0.93 (0.78–1.11)	0.42
Moderate/Severe hyperkalaemia (>6.0 mmol/L)**						
No MRA at baseline	13/676	1.4	11/697	1.1	1.17 (0.52–2.62)	0.71
MRA treated at baseline	23/1688	1.0	40/1667	1.7	0.50 (0.29–0.85)	0.010
All patients	36/2364	1.1	51/2364	1.6	0.64 (0.42–0.99)	0.046

Models adjusted for baseline potassium and stratified by diabetes status at randomization. *Excluding those with baseline K+ >5.5 (n=136); **Excluding those with baseline K+ >6.0 (n=16). Abbreviations: CI, confidence interval; HR, hazard ratio; MRA, mineralocorticoid receptor antagonist; PY, patient-years.