Should I start an SGLT-2 inhibitor in my patient with heart failure and chronic kidney disease?

To the Editor: The article by Sekerak and colleagues[1] is an excellent highlight of the sodium-glucose cotransporter 2 (SGLT-2) inhibitor family's pluripotent cardiorenal impacts. I offer several suggestions to optimize the utilization of this therapeutic class.

First, regarding dosing, while dapagliflozin 5 mg is approved by the US Food and Drug Administration for glycemic control, the heart failure and chronic kidney disease trials were done exclusively with 10 mg, which is the only approved dose for these indications. Similarly, empagliflozin 25 mg is intended for intensification of glycemic control. Use of 10 mg of either agent up front, irrespective of indication, fosters a "set it and forget it" approach that has been beneficial in uptake of this class, particularly in heart failure and chronic kidney disease.

Second, the authors write that clinicians should monitor for hyperkalemia. However, contemporary studies have allayed concerns about hyperkalemia. In patients with diabetes, SGLT-2 inhibitors have been shown to reduce the risk of hyperkalemia without increasing the risk of hypokalemia.[2] In EMPEROR-Reduced (Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Reduced Ejection Fraction), there was no difference in rates of hyperkalemia,[3] and in FIDELIO-DKD (Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease), use of SGLT-2 inhibitors decreased the rate of hyperkalemia associated with finerenone use.[4]

Third, the authors' recommendation to check a basic metabolic panel 2 to 4 weeks after initiating SGLT-2 inhibitor therapy may not be universally necessary, although it could be reasonable in elderly patients or if there are significant clinical concerns regarding volume status or other factors. As articulated by some experts,[5] contemporary studies have alleviated concerns regarding acute kidney injury, highlighting that the physiological dip in the estimated glomerular filtration rate (eGFR) induced by SGLT-2 inhibitors does not correlate with kidney injury and that, despite this dip, therapy should be continued. Therefore, for most patients, it seems reasonable to check laboratory values at the next routine round of laboratory testing rather than 2 to 4 weeks after initiation. This approach could reduce patient burden and prevent the misinterpretation of an expected eGFR dip leading to interruption of this critical therapy.

Taher Modarressi, MD
Princeton Cardiometabolic Health,
Pennington, NJ

REFERENCES

1. **Sekerak R, Ben-Ami Lerner J, Prasad P, Prasad M.** Should I start an SGLT-2 inhibitor in my patient with heart failure and chronic kidney disease? Clev Clin J Med 2023; 90(10):607–609. doi:10.3949/ccjm.90a.23004
2. **Neuen BL, Oshima M, Agarwal R, et al.** Sodium-glucose cotransporter 2 inhibitors and risk of hyperkalemia in people with type 2 diabetes: A meta-analysis of individual participant data from randomized, controlled trials. Circulation 2022; 145(19):1460–1470. doi:10.1161/CIRCULATIONAHA.121.057736
3. **Packer M, Anker SD, Butler J, et al.** Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med 2020; 383(15):1413–1424. doi:10.1056/NEJMoa2022190
4. **Agarwal R, Joseph A, Anker SD, et al.** Hyperkalemia risk with finerenone: Results from the FIDELIO81 DKD trial. J Am Soc Nephrol 2022; 33(1):225–237. doi:10.1681/ASN.2021070942
5. **Heerspink HJL, Cherney DZI.** Clinical implications of an acute dip in eGFR after SGLT2 inhibitor initiation. Clin J Am Soc Nephrol 2021; 16(8):1278–1280. doi:10.2215/CJN.02480221

doi:10.3949/ccjm.91c.02001