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SGLT-2 INHIBITION: POTENTIAL DANGERS FOR RENAL FUNCTION AND INTEGRITY

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Sodium-glucose co-transporter-2 inhibitors (SGLT2i) provide outstanding long-term cardiovascular and renal protection in high-risk patients with type 2 diabetes mellitus. Yet, despite encouraging renal safety outcome reported in the EMPA-REG study, scattered reports suggest that there might be a risk for acute kidney injury (AKI) which may occasionally be lethal or might require renal replacement therapy. We propose that two mechanisms could lead to AKI with SGLT-2 inhibition. The first one might be an exaggerated alteration of glomerular hemodynamics in volume-depleted states and perhaps in patients on RAAS blockades. The second one might be related to a drop in medullary oxygenation due to enhanced solute delivery to the distal nephron, with intensified medullary oxygen expenditure, predisposing to hypoxic tubular damage. While the former mechanism conceivably reflects an overacting inherent function of SGLT-2 inhibitors, reducing trans-glomerular pressure, which is responsible for their long-term renal protection, accumulating information suggests that indeed intensified medullary hypoxia takes place as well. Additional experimental and clinical studies are required to validate these preliminary data. Meanwhile, clinical guidelines are proposed to avoid AKI in patients on SGLT-2 inhibition, namely awareness regarding hydration status, and caution with RAAS blockade, as well as with the concomitant exposure to agents compromising medullary oxygenation, such as NSAIDs or radio contrast agents.