Sodium-glucose cotransporter-2 inhibitors

Use in patients with chronic kidney disease

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Clinical question

How do sodium-glucose cotransporter-2 inhibitors (SGLT2Is) affect patient outcomes in chronic kidney disease (CKD)?

Bottom line

For every 100 patients with CKD taking an SGLT2I for 5 years, approximately 3 or 4 fewer will develop end-stage kidney disease and 3 to 4 fewer will die from any cause versus placebo. Sotagliflozin is not better than placebo for these outcomes.

Evidence

Results were statistically significant unless noted.

- Two systematic reviews of relevant RCTs included patients with CKD.[1,2]
  - -In 1 review of 52,827 patients with cardiovascular and CKD risks, among those with CKD at 5 years[1]:
    - —End-stage kidney disease: 8.9% vs 12% (placebo), number needed to treat (NNT)=33.
    - —Cardiovascular death: 11% vs 14% (placebo), NNT=27.
    - —Overall mortality: 19% vs 22% (placebo), NNT=31.
  - -In the other review (8 RCTs) involving 26,106 patients with baseline CKD, at 2.5 years[2]:
    - —Cardiovascular disease: 10% vs 11% (placebo), NNT=91.
    - —Composite kidney outcome (40% to 60% estimated glomerular filtration rate decline, end-stage kidney disease, or renal death): 4.8% vs 6.9% (placebo), NNT=48.
  - -Limitations: included RCTs not specific to CKD patients.
- In 3 industry-funded RCTs (with CKD patients),[3-5] mean estimated glomerular filtration rate was about 40 to 55 mL/min/1.73 m^2, albumin-to-creatinine ratio was about 75 to 105 mg/mmol, and 67% to 100% of patients had diabetes.
  - -In a trial of 4401 patients taking 100 mg of canagliflozin daily,[3] at 2.6 years:
    - —End-stage kidney disease: 5.3% vs 7.5% (placebo), NNT=45.
    - —Cardiovascular death: 5.0% vs 6.4% (placebo), NNT=71.
    - —All-cause mortality: 7.6% vs 9.1% (placebo), NNT=67.
  - -In another trial of 4304 patients taking 10 mg of dapagliflozin,[4] at 2.4 years:
    - —End-stage kidney disease: 5.1% vs 7.5% (placebo), NNT=42.
    - —Cardiovascular death: 3.0% vs 3.7% (placebo), not statistically different.
    - —All-cause mortality: 4.7% vs 6.8% (placebo), NNT=48.
  - -In a third trial of 10,584 patients taking 200 mg to 400 mg of sotagliflozin daily,[5] at 1.3 years:
    - —No differences in composite kidney outcome, cardiovascular death, or all-cause mortality.

Context

- Metformin and SGLT2Is are recommended first-line therapies for those with type 2 diabetes and CKD.[6]

Implementation

On average, SGLT2Is lower systolic blood pressure by about 4 mm Hg in those with CKD taking renin-angiotensin-aldosterone system blockers.[7] Hemoglobin A_{1c} reductions of about 0.3% are seen in patients with CKD initiating SGLT2I therapy (most already using metformin, insulin, or sulphonylureas), while reductions of up to 0.6% or 1.0% are seen in patients with diabetes with less intensive background antihyperglycemic therapy.[7,8] To add an SGLT2I, existing non–renin-angiotensin-aldosterone antihypertensives or antihyperglycemics may need to be minimized.[6]

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Competing interests
None declared

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Can Fam Physician 2022;68:753. DOI: 10.46747/cfp.6810753
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