5 Things You Need to Know About SGLT2-I Use in the Elderly

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SGLT2 inhibitors perform well in older patients and cause minimal hypoglycemia. But caution is advised and here are 5 reasons why.

The challenge of treating diabetes in this section of population is to avoid hypoglycemia; this SGLT2 inhibitor is associated with only a minimal tendency toward hypoglycemia. Caution, however, is advised as it causes a drop in blood pressure and its use in the elderly needs to be closely monitored. Also it needs to be titrated renally. It has a tendency to cause mycotic infections in the genital area and causes recurrent urinary infections, which may cause many unwanted side effects, especially in elderly women.
1. Renal Insufficiency

Dose adjustment may be required to offset declining glomerular filtration rate (GFR) and higher rates of nephropathy, especially among those with longstanding diabetes

- Canagliflozin has been safely used in stage 3 CKD²
- GFR <60 mL/minute/1.74 m²: dose reduction recommended²
- Maximum recommended dose with GFR <60 mL/minute/1.74 m²: 100 mg daily²
- GFR <45 mL/minute/1.84 m²: Canagliflozin not recommended²
- Potential for increased side effects in renal insufficiency³

Renal dosing may be required due to declining glomerular filtration rate and higher rates of nephropathy found in the elderly, especially among those with longstanding diabetes.

2. Volume Depletion and Cardiovascular Effects

- Canagliflozin seems to be associated with a low incidence of orthostatic hypotension, with increased adverse events related to osmotic diuresis⁴
- Monitor for hyperkalemia, hypermagnesemia, and hyperphosphatemia³
- Monitor LDL, HDL, and TG: all tend to increase³,⁵
- Reduced blood pressure could potentially exacerbate CHF³
- Cardiovascular safety trials are ongoing

Analysis of pooled data from a canagliflozin FDA briefing document stated that volume depletion-related adverse events, most commonly hypotension, occurred in 1.2% and 1.3% of
canagliflozin 100 mg and 300 mg groups, respectively, versus 1.1% in placebo groups; furthermore, none of these events in the canagliflozin groups were serious or led to study discontinuation.

3. Mycotic Genital and Urinary Tract Infections

- High levels of glucose in the genital tissues associated with canagliflozin use promotes Candida growth
- Incidence higher in women\(^5\)
- Up to one-third of mycotic genital infections recur in both women and men\(^5\)
- About one-half of UTIs recur\(^5\)

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| Genital mycotic infections| Women: 4%  
Men: 1.4% | Women: 24%  
Men: 6% |
| Urinary tract infections  | 15%         | 17%       |

High levels of glucose in the genital tissues associated with canagliflozin use promotes attachment and growth of Candida. The incidence of mycotic genital infections is higher in women and up to one-third of these infections recur in both men and women. Approximately one-half of UTIs recur.
4. Fractures and Changes in Bone Metabolism

- Canagliflozin 300 mg: 4% of elderly patients had fractures over 104 weeks
- Canagliflozin 100 mg: Almost 3% of elderly patients had fractures over 104 weeks

Mechanistically, the connection makes sense because SGLT2 inhibitors are associated with an increase in concentrations of phosphate in serum, probably via increased tubular reabsorption, which can adversely affect bone.

5. Polypharmacy and Drug Interactions

- Canagliflozin may interact with medications commonly used to treat conditions in the elderly, in whom polypharmacy is common.
- UGT inducers (rifampin, phenytoin, phenobarbital and protease inhibitors) can potentially render canagliflozin subtherapeutic.
- UGT inhibitors (eg, digoxin) may render canagliflozin supratherapeutic. Digoxin levels may need to be monitored.
- Loop diuretics can worsen volume depletion and metabolic derangements associated with canagliflozin.

UGT, UDP-glucuronosyltransferase
Canagliflozin can potentially interact with medications commonly used to treat conditions in the elderly, in whom polypharmacy is common. UGT inducers (rifampin, phenytoin, phenobarbital and protease inhibitors) can potentially render canagliflozin subtherapeutic while UGT inhibitors like digoxin can potentially render canagliflozin supratherapeutic. Digoxin levels may need to be monitored. Loop diuretics can worsen volume depletion and metabolic derangements associated with canagliflozin.

In May 2013 the FDA approved canagliflozin, the first sodium glucose cotransport 2 (SGLT2) inhibitor on the market, for use in mono- or combined therapy in patients with T2DM. SGLT2 inhibitors block the reabsorption of glucose through the proximal renal tubule, leading to decreased HbA1c levels and modest reductions in weight and blood pressure.

Canagliflozin has been shown to be well tolerated in the elderly, with minimal tendency to cause hypoglycemia—a primary challenge in treating diabetes in this population. Because it acts independently of insulin levels and is not affected by beta cell function or insulin sensitivity, it can be used at all stages of diabetes.

There are important cautions to be observed, however. The slides above offer snapshots of the specific issues about using canagliflozin in the elderly. Links to additional information can be found in the reference list below.

References


Source URL: http://www.psychiatrictimes.com/diabetes/5-things-you-need-know-about-sglt2-i-use-elderly

Links: