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# Promising role of sodium-glucose cotransporter-2 inhibitors in IgA nephropathy

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News and Views

Nearly 700 million people around the world suffer from chronic kidney disease (CKD) (1). Immunoglobulin A (IgA) nephropathy, as the most common primary glomerular disease, is one of the leading causes of CKD (2). Previous investigations showed the natural history of IgA nephropathy and showed over a 6-year period of study, 30 percent of patients considerably lost their kidney function (3).

The current standard treatment for IgA nephropathy is renin-angiotensin-aldosterone system (RAAS) inhibitors, which are recommended for patients with moderate to mild proteinuria (4). Fish oil has also been recommended as an optional treatment for IgA nephropathy (5). Additionally, immunosuppressive therapy is controversial and can be considered as the last option for patients whose previous supportive treatment was ineffective (6).

Recently much attention has been directed toward the administration of sodium-glucose cotransporter-2 inhibitor in glomerular disease (6,7). Dapagliflozin is a sodium-glucose cotransporter-2 inhibitor (SGLT2i) that has been suggested for patients with IgA nephropathy, either with or without diabetes. Dapagliflozin causes glucosuria and natriuresis by acting on the proximal tubule of nephrons (7).

Wheeler et al conducted the DAPA-CKD study as a multicenter study including 386 study sites in 21 countries between 2017 and 2020 to evaluate the effects of dapagliflozin on the progression of CKD and other kidney complications in IgA nephropathy patients. In this study, 270 patients were randomly selected, from which 254 were diagnosed by biopsy. One hundred thirty-seven patients out of 270 used dapagliflozin 10 mg, and the others took the placebo. Both groups were followed for 2.1 years. Results of this study showed patients who took dapagliflozin in addition to angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers therapy had a lower risk of 50% or more decline in estimated glomerular filtration rate and a lower mortality rate from renal or cardiovascular disease and end-stage renal disease (6).

Another study showed SGLT2i causes reduced intra-glomerular pressure and influence the renin-angiotensin-aldosterone system either local or systemic in diabetic individuals with or without kidney disease (8).

It seems that administration of dapagliflozin to the angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers therapy can remarkably reduce the risk of CKD progression in patients with IgA nephropathy through multiple mechanisms, including a reduction in intra-glomerular pressure, natriuresis, and better blood pressure control, a direct act on endothelial cells, decreasing inflammatory markers, and also diminishing reactive oxygen species (9). Serious considerations must be taken while using SGLT2i in patients with hypovolemic states and those who receive drugs affecting renal function. SGLT2i may be a promising treatment option for patients with (and possibly without) diabetes-associated renal dysfunction (8).

## Authors' contribution

Conceptualization: SZ.
Validation: SS.

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Investigation: SS.
Resources: SZ.
Writing–original draft preparation: SZ.
Writing–review and editing: SZ, SS.
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Supervision: SS.
Project administration: SS.

## Conflicts of interest

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