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## **Clinical Consideration in Using MRAs**

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Stimulation of mineralocorticoid receptor (MR) causes angiosclerosis and microangiopathy in renal blood vessels. Aldosterone accelerates glomerular filtration deterioration, worsens glomerulosclerosis, and increases protein excretion via podocyte injury. In this regard, mineralocorticoid receptor antagonists (MRAs) have demonstrated therapeutic actions in chronic kidney disease (CKD), diabetic nephropathy, renal fibrosis, and drug-induced renal injury.

The first MRA, spironolactone, was developed almost 60 years ago to treat primary aldosteronism and pathological edema. It increases sodium excretion and decreases potassium excretion in the kidney. It improves not only blood pressure control, but also renal inflammation, and renal damage after ischemic injury. However, as a competitive antagonist of the MRs, spironolactone inhibits other related receptors such as glucocorticoid receptors, androgen receptors, and progesterone receptors, it also shows undesirable effects like gynecomastia, dysmenorrhea, or impotence. Thus, novel nonsteroidal MRAs were currently developed and have been pharmacologically characterized in comparison to classical steroidal MRAs.

MRAs therapies reduce the risk of dialysis in acute kidney injury patients, and it decreases protein excretion and blood pressure in patients with CKD. Moreover, MRAs such as spironolactone, eplerenone, and finerenone showed not only a dose-related reduction in albuminuria in diabetic nephropathy patients but also decreased CKD progression and cardiovascular disease-related death. Given the critical role of MR signaling in kidney disease, MRAs can significantly retard kidney disease progression. The renoprotective mechanisms exhibited by MRAs are complex and partially beyond their blood pressure lowering effects. Novel nonsteroidal MRAs are very selective and specifically inhibit MR, causing minimal hyperkalemia. The recent clinical trials of finerenone and esaxerenone in patients with kidney disease indicated a potential therapeutic role of nonsteroidal MRAs in nephropathy patients.