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A Nonsteroidal Mineralocorticoid Receptor Antagonist Ameliorates Vascular Calcification in Chronic Kidney Disease

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Objectives : Aldosterone is implicated in exacerbating vascular calcification associated with chronic kidney disease (CKD), leading to increased morbidity and mortality. This study aims to assess the impact of a novel nonsteroidal mineralocorticoid receptor antagonist, finerenone, on mitigating vascular calcification in CKD.

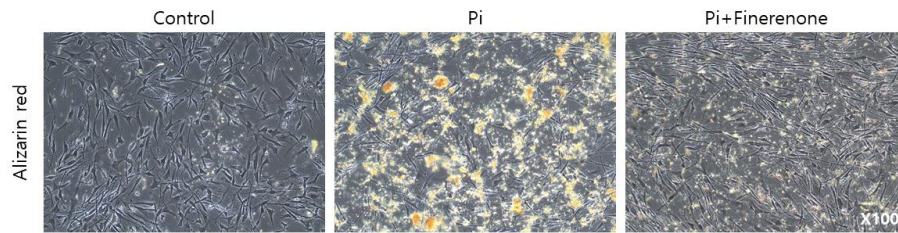
Methods : Vascular smooth muscle cells (VSMCs) were cultured in a high inorganic phosphate environment to induce calcification, reflecting CKD conditions. The impact of finerenone on osteogenically differentiated VSMCs was then evaluated. For the in vivo study, three groups of C57BL/6 mice were fed different diets: standard chow, a 0.25% adenine-enriched diet, and an adenine diet added with finerenone (10 mg/kg) (n = 6–10, each). Following a 6-week diet, the effects of adenine and finerenone on the kidney and aorta were assessed ex vivo.

Results : In vitro, VSMCs under high phosphate conditions exhibited elevated osteogenic gene expressions (BMP2, SOX9) and enhanced calcium deposition. Finerenone treatment reduced SOX9 expression and calcium deposition (Fig. A). In the murine model, mice on the adenine-containing diet showed decreased body weight, increased serum creatinine, and a higher urine albumin-to-creatinine ratio. Notably, finerenone treatment mitigated albuminuria. Additionally, finerenone decreased the expression of osteogenic markers including Sox9 and the senescence marker Cdkn1a in the aorta compared to the adenine-only group. Von Kossa staining of the aorta revealed black granular calcium deposits in mice fed adenine, whereas there was no obvious calcium deposition in mice fed adenine+finerenone (Fig. B).

Conclusions : Finerenone improved osteogenic changes in both in vitro VSMCs and the aorta of a murine CKD model. These findings suggest a potential therapeutic role for finerenone in managing vascular complications in CKD.

Finerenone.png

A.



B.

