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MINERAL METABOLISM

SPIRONOLACTONE AND CALCIFICATION

A new study reports that spironolactone-mediated aldosterone blockade reduces vascular and soft tissue calcification *in vivo*. "Our observations suggest that spironolactone might have beneficial vascular effects in patients with end-stage renal disease and other conditions with excessive vascular calcifications," says researcher Florian Lang.

Voelkl and colleagues used klotho-hypomorphic (*kl/kl*) mice to investigate the effect of the mineralocorticoid-receptor antagonist spironolactone on vascular calcification. Similar to patients with end-stage renal disease, *kl/kl* mice have high plasma aldosterone levels and severe vascular and soft tissue calcification, hyperphosphataemia and hypercalcaemia. The researchers found that spironolactone treatment reduced soft tissue and vascular calcification and increased the lifespan of *kl/kl* mice but did not substantially reduce their serum phosphate or calcium levels.

Next, the researchers analysed the expression levels of factors known to be involved in osteogenic signalling. They found that transcript levels of type III sodium-dependent phosphate transporter 1 (*PIT1,* also known as *SLC20A1*), tumour necrosis factor, osteogenic transcription factors and alkaline phosphatase were increased in calcified tissues from *kl/kl* mice compared with tissues from wild-type mice. However, the levels of these transcripts in *kl/kl* mice significantly decreased in response to spironolactone treatment. "These data indicate that vascular calcification in *kl/kl* mice is not simply the passive result of enhanced calcium phosphate concentration but is at least partially due to active aldosterone-driven induction," explains Lang.

Finally, the researchers showed that aldosterone dose-dependently upregulated mRNA expression of *PIT1* and osteogenic transcription factors, and stimulated the induction and activation of alkaline phosphatase in cultured human aortic smooth muscle cells. Both spironolactone treatment and *PIT1* silencing abrogated aldosterone-induced osteogenic signalling. "It would now be exciting to explore whether the onset of vascular calcification in patients with chronic kidney disease could be slowed by spironolactone treatment." says Lang.

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Original article Voelk, J. *et al*. Spironolactone ameliorates PIT1-dependent vascular osteoinduction in klotho-hypomorphic mice. *J. Clin. Invest*. doi:10.1172/JCI64093