

Phosphate transporter inhibitor reduces renal failure associated aortic valve calcification

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Introduction: Hyperphosphatemia is a major risk factor for aortic valve calcification (AVC) in renal failure population. Previously, we demonstrated that in- vitro inhibition of phosphate transport abolishes mineralization in valvular myofibroblasts. We sought to assess the in vivo effect of Fosarnet (phosphate transporter inhibitor) using our unique animal model of AVC induced by a uremia-inducing diet.

Methods: Aortic valves were obtained from three groups of rats (n=9 each): control valves (group A), Calcified valves- from rats fed with the uremic diet for 7 weeks (group B), and valves from rats fed with the same diet and also received Fosarnet administered intraperitoneal 5mg/kg (group C). Valves were examined using multislice computed tomography (MSCT), histology assessment, and antigen and gene expression analyses.

Results: Histological evaluation of diet group's calcified valves revealed positive staining for calcium deposits and osteoblast's markers.

MSCT of Fosarnet treated rats (group C) showed significant decrease in valve calcification compared with group B (Agatston score 21 ± 5 vs. 34 ± 4 $p < 0.05$). The reduction in AVC due to Fosarnet treatment was confirmed by histology, however valvular osteoblast markers were similar in groups B and C.

Conclusions: Phosphate plays a crucial role in the pathogenesis of AVC. Inhibition of phosphate uptake by fosarnet reduces calcification with no effect on osteoblast transformation; therefore the pro- calcific effect of phosphate is physicochemical and independent of cellular activity. The results are important in the study of renal failure associated ectopic calcification.