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Interaction of Phosphate and Uremic Substances on Vascular Calcification

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Objectives : We investigated the involvement of phosphate (P) and indoxyl sulfate (IS), a uremic substance in vascular calcification in renal failure.
Methods : After culturing vascular smooth muscle cells (VSMCs) in a regular media (control) or P- and/or IS-loaded media for 10 days, VSMC calcification and expression of the chronic inflammatory state associated with aging (inflammaging) marker genes were examined by real-time PCR. We also investigated calcification and inflammaging marker gene expression in the aortas of adenine-induced renal injury mice treated with intravenous administration of IS for 10 days.
Results : In studies using VSMCs, IS loading tended to promote the calcification of VSMCs compared with controls (VSMCs cultured with a regular media), and P loading significantly promoted the calcification. No additive promotion of the calcification was observed with the combination of P and IS. Inflammaging maker genes were induced by P loading and IS further accelerated some of the marker genes. Aortic calcification was observed in adenine-induced renal injury mice with hyperphosphatemia, and the calcification was further accelerated when the mice were loaded with IS via a continuous intravenous route for 10 days using an infusion minipump. Markers of inflammaging were induced in the aortic tissue of this model.
Conclusions : In the uremic condition, inflammaging was induced by P in parallel with vascular calcification progression, and it was suggested that loading with IS, a uremic substance, may enhance inflammaging and further promote vascular calcification.