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CHRONIC KIDNEY DISEASE

Procoagulant microparticles provide a novel pathogenic link between hyperphosphataemia and cardiovascular risk

Hyperphosphataemia is thought to be an important contributor to the increased cardiovascular risk of patients with chronic kidney disease (CKD). The authors of a new study suggest a novel mechanism by which phosphate-induced microparticles might increase thrombotic risk in this population.

"It has long been suspected that an excess of inorganic phosphate increases cardiovascular risk in humans," says researcher Nima Abbasian. "It is also known that cell-derived microparticles circulate in the blood, and that in patients with CKD some of these particles are potently procoagulant. The aim of our study was to link these observations by showing that inorganic phosphate can trigger microparticle release from endothelial cells, and that these microparticles have procoagulant activity."

Abbasian and colleagues report that exposure of cultured human endothelial cells to an excess of inorganic phosphate induced rapid increases in intracellular phosphate levels, plasma membrane blebbing and microparticle release. Lysates of the phosphate-treated cells showed global increases in the levels of phosphoproteins—consistent with an inhibitory effect of inorganic phosphate on phosphoprotein phosphatases—and accumulation of tropomyosin-3, a cytoskeletal regulatory protein that has been implicated in microparticle formation. In a thrombin-generation assay, microparticles derived from the phosphate-treated cells had significantly greater procoagulant activity than those derived from cells exposed to a physiologic level of phosphate. Abbasian states that the phosphate-induced microparticles "strongly resemble" the endothelial microparticles that are observed in the blood of patients with CKD.

> "...an excess of inorganic phosphate can cause a novel form of stress signal inside endothelial cells..."

"Our study demonstrates a mechanism by which an excess of inorganic phosphate can cause a novel form of stress signal inside endothelial cells by inhibiting phosphoprotein phosphatases, resulting in global intracellular accumulation of phosphoproteins and the release of strongly procoagulant microparticles from the endothelial plasma membrane," concludes Abbasian. "These findings suggest that phosphate-induced endothelial microparticles may contribute to thrombotic risk during hyperphosphataemia."

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Original article Abbasian, N. *et al*. Hyperphosphatemia, phosphoprotein phosphatases, and microparticle release in vascular endothelial cells. *J. Am. Soc. Nephrol*. doi:10.1681/ASN.2014070642