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Vitamin D as a Molecular Treatment Candidate to Prevent Vascular Access Stenosis in Hemodialysis Patients

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Vascular access is the lifeline for HD patients. Access failure was associated with increased all-cause mortality and CV mortality in patients on maintenance HD. Mechanisms related to stenosis or thrombosis of vascular access are not clearly defined, but various conditions could be risk factors. Neointimal hyperplasia associated with endothelial injury and chronic vascular smooth muscle cell proliferation are prime steps in causing access failure. Impaired reverse cholesterol transportation (RCT) by endothelial macrophages was suggested as a risk factor for AVF stenosis. Furthermore, impaired RCT could be a CV risk factor in the CKD population. Vitamin D affects various immune functions and cardiovascular systems. In many studies, vitamin D deficiency was associated with higher CV morbidity and mortality. Vitamin D deficiency is found in almost all advanced CKD patients. In recent studies, vitamin D deficiency was associated with increased endothelial adhesion molecules or LDL cholesterol. However, whether vitamin D improved microvascular inflammation and stenotic conditions is not known. We investigated whether uremia induced macrophage differentiation and cholesterol efflux. Then, we examined that vitamin D could affect cholesterol efflux and vascular function in CKD conditions. Indoxyl sulfate (IS), known as uremic toxin, induced the differentiation of THP-1 macrophages into M1 or M2 macrophages. Cholesterol efflux was decreased in IS-treated macrophages. Reduced cholesterol efflux in differentiated THP-1 cells was significantly improved by $1,25(\text{OH})_2\text{D}_3$ treatments. In hemodialysis patients, 12-week treatment of paricalcitol improved access flow. IL-6, TNF- α , and LDL cholesterol were decreased after paricalcitol treatment. Cholesterol efflux was slightly ameliorated. These results suggest that vitamin D improves microvascular inflammation. Further studies could elucidate the effects of vitamin D in improving the stenotic vascular condition of CKD.



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