

Abstract Submission No. : 2447

Protective Effect of Heparan Sulphate Derivative against Glycocalyx Damage-induced Renal Fibrosis in Aging Mice

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Objectives: Aging-related glycocalyx loss causes renal fibrosis in aging kidneys. Heparan sulphate (HS) derivative was anticipated overcoming diabetic nephropathy model. Sulodexide is a well-known HS derivative. We investigated the effects of SDX on the PI3K/Akt pathway as a renoprotective pathway in a mouse model of aging.

Methods: C57BL/6 mice were divided into four groups according to age and SDX administration for six months: the eight-month-old mice with vehicle (YM group, n= 10), the eight-month-old mice with SDX (YM+SDX group, n=8), the twenty four-month-old mice with vehicle (AM group, n= 10), the twenty four-month-old mice with SDX (AM+SDX group, n=8). SDX was administered to 10 mg/kg per oral daily for six months. We compared the following parameters between the groups: renal function, blood pressure, renal pathology, activities of the PI3K-Akt-MMP2 and MMP9-Syndecan4 in renal tissue.

Results: Renal function was improved based on serum creatinine and 24 hours albuminuria in AM+SDX group compared with the AM group ($p < 0.05$ for all), but it was not different between the YM group and the YM+SDX group. Areas of renal fibrosis and expressions of protein related to fibrosis significantly reduced in the AM+SDX group compared with the AM group ($p < 0.05$), but the YM+SDX group was similar with the YM group. In protein related with PI3k-Akt pathway, the AM+SDX group showed significantly lower expression of PI3K, phosphorylated Akt, MMP2, MMP9 and syndecan4 than the AM group ($P < 0.05$ for both), but the YM+SDX group was not different compared with the YM group.

Conclusions: SDX, which is a HS derivative, alleviated the protein expression associated with PI3k-Akt pathway in kidneys of aging mice, but those changes were not observed in that of young mice. SDX may provide renoprotective effects via PI3k-Akt pathway in aging kidneys.