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Effect of indoxyl sulfate on endoplasmic reticulum stress in human astrocytes

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Objectives: Chronic kidney disease has emerged as a possible new risk factor for cognitive impairment. Indoxyl sulfate (IS) accumulates with the progression of chronic kidney disease (CKD). IS has been shown to be toxic to the kidneys, vascular system, and bones. Recent studies show that astrocytes play an important role in neurodegenerative disease. However, little is known about the neurotoxicity of IS on astrocytes.

Methods: The toxicity of IS on astrocytes was investigated through the use of the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay and flow cytometry. We evaluated the expression of endoplasmic reticulum stress-related mRNA in IS-treated control astrocytes.

Results: IS is toxic to astrocytes in a dose- and time-dependent pattern. The expression of spliced Xbp1 (IRE1 pathway), CHOP (PERK/eIF2α pathway), ATF6α (ATF6α pathway), ATF4 (PERK/eIF2α pathway), and BiP (IRE1α /ATF6α pathway) increased significantly following IS treatment of astrocytes. Tauroursodeoxycholic acid, an ER stress modulator, attenuated IS-induced ER stress and apoptosis in astrocytes .

Conclusions: In conclusion, IS can induce neurotoxicity in patients with CKD, and this pathogenesis involves cell apoptosis through ER stress in human astrocytes