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AST-120 Ameliorates Cognitive and Emotional Dysfunction in a 5/6 Nephrectomy Chronic Kidney Disease Model

DONG JIN LEE[1], Yeon Hee Yu[2], Nam-jun Cho[1], Samel Park[1], Duk-Soo Kim[2], Hyo-Wook Gil[1]
[1]Department of Internal Medicine-Nephrology, Soonchunhyang University Cheonan Hospital, Korea, Republic of
[2]Department of Anatomy, Soonchunhyang University Cheonan Hospital, Korea, Republic of

Objectives : Chronic Kidney Disease (CKD) is intricately associated with cognitive impairment, a connection often attributed to elevated levels of uremic toxins, particularly Indoxyl sulfate. While existing evidence emphasizes the detrimental effects of Indoxyl sulfate on cognitive function in CKD, there is a notable dearth of research investigating the potential cognitive improvements resulting from its reduction. This study aims to address this gap by examining the impact of AST-120, a therapeutic agent known to reduce Indoxyl sulfate levels, on cognitive and emotional functions in a 5/6 nephrectomy CKD model.
Methods : Male Sprague Dawley rats underwent 5/6 nephrectomy, and AST-120 was administered over a 10-week period. Behavioral assessments, including novel object recognition, Y-maze, Barnes maze, and classical contextual fear conditioning, were employed to evaluate cognitive and emotional functions. Immunohistochemical staining, including double immunofluorescent staining for aquaporin-4 and glial fibrillary acidic protein, provided insights into hippocampal alterations. Additionally, electrophysiological recordings of hippocampal field excitatory postsynaptic potential (fEPSP) were conducted.
Results : The CKD model exhibited significant deficits in spatial working memory, learning, memory, and object recognition. Immunohistochemical analyses revealed coexpression of aquaporin-4 and glial fibrillary acidic protein, supporting hippocampal blood-brain barrier changes. AST-120 administration led to a notable reduction in Indoxyl sulfate levels and correlated with improved cognitive and emotional functions, as evidenced by enhanced performance in behavioral assays and normalized fEPSP in the hippocampus.
Conclusions : This study establishes a critical link between elevated Indoxyl sulfate levels in CKD and cognitive dysfunction, emphasizing the potential therapeutic impact of AST-120 in ameliorating cognitive and emotional deficits. By reducing Indoxyl sulfate, AST-120 emerges as a promising intervention to enhance cognitive function in CKD, suggesting avenues for future therapeutic strategies targeting uremic toxins in neurocognitive disorders associated with renal dysfunction.