

## INDOLE-3 ACETIC ACID INCREASED RISK OF IMPAIRED COGNITIVE FUNCTION IN PATIENTS RECEIVING HEMODIALYSIS

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**Backgrounds:** Patients receiving hemodialysis have a higher risk of cognitive impairment and dementia than the general population. The accumulation of uremic toxins in the brain causes uremic encephalopathy, however, limited data exists to elucidate the effect of protein-bound uremic toxins on cognitive function. Here we investigate the effect of indole-3 acetic acid and hippuric acid, two different protein-bound uremic toxins from amino acid derivatives, on cognitive function by *Silico* and in a clinical study.

**Methods:** Prevalent hemodialysis patients were enrolled in two independent hospitals. Circulating indole-3 acetic acid and hippuric acid were measured using mass spectrometry. Cognitive performance was measured using Mini-Mental State Examination score, Montreal Cognitive Assessment score, and Cognitive Abilities Screening Instrument score by trained psychologists. Using *silico* data to predict the effect of blood-brain barrier penetration was performed.

**Results:** The *silico* data demonstrated that indole-3 acetic acid and hippuric acid had positive blood-brain barrier penetration ability. Amongst the 230 patients with hemodialysis, circulating indole-3 acetic acid was associated with poor cognitive function but not hippuric acid. After adjustment for demographic characteristics and comorbidities, the association remained statistically significant in Mini-Mental State Examination score ( $\beta = -0.99$ , 95% CI -1.95 and -0.04) and Cognitive Abilities Screening Instrument score ( $\beta = -3.50$ , 95% CI -6.57 and -0.44). Using restricted cubic splines, circulating indole-3 acetic acid levels were related to risk of cognitive impairment. Circulating hippuric acid levels were not associated with cognitive function in patients

with hemodialysis.

Conclusions: Circulating indole-3 acetic acid was associated with cognitive impairment in patients with hemodialysis. Further large scale and prospective studies are needed to confirm our findings.

Key words: indole-3 acetic acid, cognitive function, dementia, chronic kidney disease, hemodialysis