Neuroinflammation in Chronic Renal Disease Associated to Neurodegeneration: Role of Uremic Toxins

Adesso S1, Del Regno M1, Di Iorio BR2, Autore G1, Marzocco S1

1Department of Pharmacy, School of Pharmacy, University of Salerno, Fisciano (SA), Italy
2Nephrology, Medicine Department, A. Landolfi Hospital, Solofra (AV), Italy

Neuroinflammation has been recognized as one of the most common aspects in neurodegenerative diseases. Although the inflammatory process may induce beneficial effects, such as the elimination of the pathogen, uncontrolled inflammation can lead to adverse outcomes through the production of neurotoxic factors able to exacerbate neurodegenerative disease. Astrocytes have been suggested to participate in the induction and the regulation of neuroinflammatory response by responding to the stimulation of exogenous pro-inflammatory molecules or produced by the activated microglia. Neurodegenerative disease can be primary (e.g. Alzheimer's disease) or secondary to some pathological conditions such as chronic renal failure (CKD). CKD is frequently associated with cognitive impairment and, among patients with terminal CKD receiving hemodialysis, more than 85% have been recognized with cognitive deficits. Kidney dysfunction leads to impaired renal metabolic activities and toxins accumulation in patients with CKD; it has been also hypothesized that uremic toxins may play an important role in the etiology of neurological complications associated to uremic syndrome. In this study we examined the effects of the uremic toxin, indoxyl sulphate (IS), on astroglial cells in inflammatory conditions. To simulate the uremic condition, astrocytes were incubated with IS both alone and in presence of a pro-inflammatory agent as Lipopolysaccharide from E. coli (LPS). In this experimental condition, IS significantly increased nitric oxide (NO) release, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) expression and reduced astrocytes mobility. This study will be a step towards elucidating whether uremic toxins, as IS, could be a potential pharmacological therapeutic targets in CKD patients.