

Soluble α -Klotho treatment protects adenine-induced uremia rats from sciatic nerve damage.

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Abstract

Neurologic involvement is the most threatening complication of uremic syndrome. Currently, the main treatment of complicated neuropsychic symptom in end-stage uremia is depended on the advent of dialysis and transplant programs, which may associated with many other complications. Effective therapy for this serious and debilitating condition is needed. This study was aimed to elucidate the roles of exogenous α -Klotho (α -KL) on the recovery of injured sciatic nerve induced by uremia. Hematoxylin-eosin staining was carried out to observe histopathologic changes between the groups. Neurocytes activity was assessed by measuring ATPase, Na⁺, K⁺-ATPase, Succinate Dehydrogenase (SDH) activity levels, and NADH as well as NADPH concentrations. NF- κ Bp65 was assessed to indicate inflammatory. Caspase-3 level was evaluated to indicate the apoptotic pathway. We found that in a damaged nerve induced by uremia, obvious decreased ATPase and Na⁺, K⁺-ATPase were observed demonstrating the dysfunction of nerve system conduction, and significant decreased SDH activity, while increased NADH and NADPH levels were observed demonstrating the mitochondrial ROS generation that directly associated with oxidative stress injury and apoptosis, moreover the activation of NF-KBp65 and Caspase-3 signaling pathways were observed demonstrating that inflammatory and apoptosis were involved after sciatic nerve being injured. α -KL was effective in the recovery of nerve system conduction, played anti-oxidative stress, anti-inflammatory and anti-apoptosis roles in damaged sciatic nerve, besides promoted the regeneration of peripheral nerve at histopathologic levels. We therefore concluded that α -KL may serve as a potential therapeutic agent for uremia-induced sciatic nerve injury.

Keywords: α -KL, Uremia-induced sciatic nerve injury, Physiology, Histopathology, Inflammatory, Apoptosis.

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Introduction

Advanced renal failure leads to uremia. The term "Uremia" refers to illness accompanying kidney failure, which cannot be attributed to derangements in extracellular volume, absence of known renal synthetic products, or inorganic ion concentrations [1]. Some groups with uremia are more prone to associate with nervous system dysfunction [2-6]. Reasons of neuropsychic symptom in end-stage uremia were related to multiple factors such as uremia toxin storage, metabolic acidosis and electrolyte disturbance. Patients often become confused, due to being affected by cognitive impairment [7,8]; stroke [9]; somnolence, or seizures [10] and peripheral neuropathies [11,12]. Uremia has always been reported as serious problem that threatened the whole public health around the world.

Dialysis and kidney transplantation have revolutionized the outcome of patients with progressive renal disease. However, current treatment with dialytic therapy or kidney

transplantation may even carry a high price and induce neurological complications or other related diseases. Dialysis therapy for uremic neuropathy has itself been associated with Central Nervous System (CNS) disorders such as dialysis disequilibrium syndrome, dialysis dementia, and progressive intellectual dysfunction [2]. Moreover, patients undergoing dialysis have a "residual syndrome" including partially treated uremia; dialysis related effects, for example extracellular fluid volume fluctuation; exposure to biological incompatible materials and residual inorganic ion disturbances [13]. As for kidney transplantation, there is less frequent use because of a short supply of donor. Besides, psychiatric or neurological disorders; infectious, gastrointestinal, vascular and urologic complications are common after renal transplantation [14-19]. Due to the shortcomings of the above two treatment methods, searching for other more effective therapeutic agents for the treatments of uremic neuropathy is very important and urgent.

Known as an anti-aging gene, α -Klotho (α -KL) is a protein mainly produced in the kidney and its circulating form (soluble