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Omega-3 fatty acid activates PGC-1α mediated mitochondrial biogenesis and PINK1-dependent mitophagy pathway in kidney and heart of adenine induced uremic rats.

Jung Min Hong[1], Dong Ho Choi[3], Bin Na Park[1], Su Mi Lee[2], Young Ki Son[1], Seung Eun Kim[2], Won Suk An[2]
[1]Department of Internal Medicine-Nephrology, Dong-A University Hospital, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, Dong-A University, College of Medicine, Korea, Republic of
[3]Department of Internal Medicine-Nephrology, Good Moonhwa Hospital, Korea, Republic of

Objectives: Mitochondrial homeostasis is controlled by biogenesis, dynamics, and mitophagy. Mitochondrial dysfunction plays a central role in cardiovascular and renal disease and omega-3 fatty acids (FA) are beneficial for cardiovascular disease. We aimed to investigate whether omega-3 FA regulates the expression of mediators of mitochondrial biogenesis, dynamics, and mitophagy in kidney and heart of adenine-induced uremic rats.

Methods: Sprague-Dawley rats were divided into three groups: normal control, adenine control, and omega-3 FA. Uremia was induced by feeding diets containing 0.75% adenine and 2.5% protein for the first 3 weeks. During next 4 weeks, they were received 2.5% protein with or without omega-3 FA (300 mg/kg/day). The renal and cardiac expression of PGC-1α, SIRT1/3, Nrf2, DRP-1, OPA1, Mfn1/2, PINK1, BNIP3 and NIX were examined by western blot analysis. The qPCR was used to determine mitochondrial DNA (mtDNA).

Results: Compared to normal, serum creatinine and heart weight/body weight in adenine control was increased and improved in omega-3 FA group. Compared with normal, PGC-1α, SIRT1/3, and Nrf2 were down-regulated in kidney and heart of adenine control. PGC-1α expression of kidney and heart was recovered in omega-3 FA group. DRP-1 of kidney was up-regulated but DRP-1 of heart was down-regulated in adenine control. DRP-1 of heart was up-regulated in omega-3 FA group. PINK1, BNIP3 and NIX were down-regulated in heart of adenine control and recovered in omega-3 FA group. PINK1 was down-regulated but BNIP3 and NIX were up-regulated in kidney of adenine control and those were mitigated in omega-3 FA group. MtDNA was decreased in kidney and heart of adenine control group but mtDNA of heart was recovered in omega-3 FA group

Conclusions: DRP-1 related with mitochondrial fission may oppositely work in uremic kidney and heart. Omega-3 FA is beneficial for mitochondrial homeostasis by activating mitochondrial biogenesis and PINK1-dependent mitophagy in kidney and heart of uremic rats

Figure 1. mitochondrial dynamics and mitophagy in heart and kidney