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조영제 신독성에서 자가포식현상의 역할에 관한 연구

고려대학교 의과대학 내과학교실[1], 고려대학교 신장학 연구소[2]

고강지[1], 배소연[2], 이은아[1], 정미연[1], 표희정[1], 권영주[1]

The Role of Autophagy in Radiocontrast Induced Nephropathy

Gang Jee Ko[1], So Yon Bae[2], Eun Ah Lee[1], Mi Yoen Jung[1], Heui Jung Pyo[1], Young Joo Kwon[1]

Department of Internal Medicine[1] Korea University College of Medicine
Institute of Kidney Disease Research[2]

Introduction: Radiocontrast induced nephropathy (CIN) is the third common cause of acute renal failure among in-patients. Although the number of patients getting the exams using radiocontrast is increasing, little has been progressed in the treatment for CIN. The pathophysiology of CIN was known as tubular injury with direct toxic effect of contrast and oxidative stress. Autophagy, which regulates cell death in physiological as well as pathological conditions, was known to have a role in tubular injury of various acute kidney injury models related to cisplatin and ischemia. We investigated the role of autophagy in radiocontrast induced nephropathy.

Methods: Radiocontrast nephropathy was induced with intraperitoneal injection of iohexol (Omnipaque) in male C57BL/6J mice. Prostanoids and nitric oxide (NO) synthesis was inhibited prior injection of iohexol with indomethacin and NO synthase inhibitor. Mannitol was used for osmotic control of iohexol, and 3-methyadenine (MA) was used for inhibition of autophagy. Tubular injury caused by iohexol was also examined in vitro model using rat tubular cells (NRK-52E)

Results: Increased autophagy after iohexol administration was demonstrated with increased LC3 expression in kidney. Creatinine at 24hrs after iohexol injection was significantly increased compared to controls (saline vs manntol vs iohexol: 0.26±0.01 vs 0.36±0.04 vs 0.91±0.19 mg/dL, $p<0.05$). Autophagy inhibition with 3-MA worsen CIN (1.31±0.40 mg/dL, $p<0.05$). In vitro study also showed that iohexol treatment decreased cell viability measured by MTT assay and increased caspase 3 expression. The injury was augmented with 3-MA pretreatment.

Conclusion: Autophagy was associated with radiocontrast induced tubular injury. Detailed mechanisms should be investigated further.

Key Words: 조영제신독성, 자가포식현상, 급성신부전
Radiocontrast, Autophagy, Acute kidney injury