

Cisplatin 유발 급성신손상의 회복기에서 JAM-C blocking antibody의 역할

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Blocking JAM-C Promotes the Recovery of Cisplatin-induced Acute Kidney Injury

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Background: For resolution of inflammation, infiltrated leukocytes should be removed. Recent studies demonstrating 1) presence of neutrophil transendothelial migration in a reverse direction (rTEM) following ischemia/reperfusion injury (IRI), 2) endothelial junctional adhesion molecule-C being a negative regulator of rTEM, 3) identification of neutrophils that have migrated in a reverse direction by their high expression of ICAM-1 led us to test the effect of JAM-C blocking antibody on the resolution of kidney injury and inflammation in a mouse model of cisplatin-induced acute kidney injury (AKI).

Method: Male C57BL/6 mice (19-23 g) were given a single intraperitoneal (i.p.) injection of cisplatin (18 mg/kg). Monoclonal anti-mouse JAM-C blocking antibody (clone H33; Millipore; Billerica, MA, USA) or control IgG was administered i.p. at 1.5 mg/kg and the injection was delayed until day 4 and 5 following cisplatin injection to restrict the effect of antibodies on recovery phase. Biochemical, histological analyses as well as flow cytometry to detect reverse migrated ICAM-1+ neutrophils were performed at 4, 5 and 6 days after cisplatin injection.

Result: After cisplatin injection, serum creatinine and histologic injury peaked on day 4. Treatment with a JAM-C blocking antibody on day 4 and 5 promoted the functional and histologic recovery of cisplatin induced AKI on day 5 and 6. Facilitating recovery by JAM-C blocking Ab was associated with significantly increased circulating ICAM-1+ Tomm Horsfall protein (THP)+ neutrophils as well as significantly decreased renal neutrophil infiltration, indicating that facilitating rTEM of neutrophils from kidney to peripheral circulation partially mediate resolution of inflammation and recovery.

Conclusion: We suggest that rTEM is involved in resolution of neutrophilic inflammation in cisplatin induced AKI and JAM-C is an important regulator of this process. Therefore, blockade of JAM-C could be considered for the new strategies to facilitate recovery in cisplatin induced AKI.

Key Words: 시스플라틴, 급성신부전, 회복

Cisplatin, Acute kidney injury, Recovery