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혈액투석 중인 당뇨병성 말기신부전 환자에서 CD39와 CD73 세포의 dysregulated balance

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Dysregulated Balance of CD39 and CD73 Cells in Diabetic ESRD Patients on Hemodialysis

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Introduction and Aims: CD39 and CD73 are an ecto-enzyme that degrades extracellular nucleotides, such as ATP. Recent evidences indicate that CD39 and CD73 expression by regulatory T (Treg) cells contributes to the protective role in renal injury in an animal model of chronic renal injury. In addition, recent studies demonstrate the protective anti-inflammatory role of CD39/CD73 molecules pathway during renal hypoxia. However the role of CD39 and CD73 has yet not to be clarified in diabetic ESRD patients. This study was designed to evaluate the balance and role of CD39/CD73 of Treg cells in diabetic ESRD patients who receiving hemodialysis.

Methods: Fifteen diabetic ESRD patients receiving hemodialysis and 15 healthy controls (HC) were recruited. Peripheral blood mononuclear cells were collected and stained with antibodies to CD4, CD25, FOXP3, CD39 and CD73. The balance of CD39/CD73 Treg cells were measured by using flow cytometry. Intracellular reactive oxygen species (ROS) generation was measured by flow cytometry using fluorescent dye, H2DCF-DA. The frequency of apoptotic cells was calculated by scoring annexin V-binding cells after back-gating of CD16/CD56 cells.

Results: Diabetic ESRD patients had an increased frequency of Treg (HC vs ESRD, 2.57±0.3 vs. 10.04±3.1, p=0.0001) and CD39 cells (HC vs. ESRD, 11.66±2.5 vs. 33.72±6.9, p=0.01) and a decreased frequency of CD73 cells (HC vs. ESRD, 6.56±2.9 vs. 2.23±0.2, p=0.02). Diabetic ESRD patients had an increased frequency of CD39 on CD4 T cell. (HC vs. ESRD, 3.774±0.42 vs. 7.52±3.8, p=0.03) Intracellular ROS generation was significantly increased in diabetic ESRD patients (HC vs. ESRD, 8.84±2.6 vs. 58.25±11.0, p=0.01). In addition, ESRD patients showed a positive correlation between the frequency of ROS and both apoptosis and CD39 cells (apoptosis, r=0.696, p=0.04; CD39, r=0.458, p=0.04).

Conclusion: Tregs isolated from diabetic ESRD patients lacked protective anti-inflammatory activity, suggesting that diabetic ESRD interferes with Treg functionality. The dysregulated balance of CD39/CD73 cells in diabetic ESRD patients provides new insights into an alteration of immunity and the pathogenesis of renal tissue injury in diabetic ESRD patients.

Key Words: T 세포, 당뇨병, 말기신부전
T cell, Diabetes, ESRD