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투석 환자에서 만성적 저도의 염증과 선천성 면역 반응 감소에 대한 연구

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Primed Leukocytes: Culprit Underlying Chronic Low Grade Inflammation and Impaired Innate Immune Response in Patients with Hemodialysis

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Although chronic low grade inflammation in ESRD patients is known to contribute to high cardiovascular morbidity and mortality, the pathogenetic mechanism leading to an inflammatory status is not clear. In addition to cardiovascular complications, uremic patients are susceptible to infection, making it the second most common cause of mortality, but it still remains unclear whether frequent infectious complications are caused by impaired innate immune responses. In 35 patients with hemodialysis, we studied basal level of toll like receptor 4 (TLR4) positive CD14 leukocyte population in peripheral blood and compared with that of 26 controls by using 4 color flow cytometry. Prestimulated, proinflammatory CD14low CD16+monocyte populations were also compared. Plasma levels of TNF- α, IL- 1β, IL- 6, IL- 8, IL- 10 and IL- 12 p70 were measured by cytometric bead array (CBA). Monocytes were further stimulated by LPS and percent increase in TLR4+ CD14+ leukocyte population with plasma cytokine changes was also compared between HD patients and controls. In basal status, percentage of peripheral blood TLR4+ CD14+ leukocyte was higher in patients with HD (0.98 vs. 0.36, $p<0.05$). Additionally, prestimulated, proinflammatory CD14low CD16+ monocyte population was also increased significantly in patients with HD compared to control (26% vs. 8.9%, $p<0.01$) and this was accompanied by significantly higher levels of plasma cytokines at basal status, suggesting that preactivated monocytes expressing TLR4 had been responsible for chronic inflammatory status in patients with HD. However, upon stimulation with LPS, percent increase in TLR4+ CD14+ leukocyte population was significantly lower in patients with HD compared to controls who showed marked increase in response to LPS (- 27% vs. 142%, $p<0.05$). This suboptimal response in TLR4+ CD14+ leukocyte population was also accompanied by reduced cytokine response by LPS stimulation (IL- 1β, 21373s. 36 fold increase in HD vs. control), indicating that chronic low grade inflammation in patients with HD can partially account for impaired innate immune response. In conclusion, in patients with HD, peripheral blood leukocyte subsets are thought to be preactivated, and this can lead to the state of chronic low grade inflammation by producing proinflammatory cytokines. This microinflammatory status can also be a mechanism for impaired innate immune response against inflammatory stimuli, resulting in a state being vulnerable to inf

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