慢性腎衰竭病患單核球細胞凋亡標記及單核細胞激素分泌之研究

Study of Monocyte Apoptotic Markers and Monokines in Chronic Renal Failure

中文摘要

慢性腎衰竭病人 (chronic renal failure, CRF)的淋巴球、單核球及嗜中性白血球有細胞凋亡增加之現象。細胞凋亡(apoptosis)的發生會經由不同的因素刺激引起，如DNA 損傷、尿毒毒素、氧化壓力及細胞激素等等的刺激，這些病人免疫功能較一般人差且較容易受到感染，CRF 病人免疫功能不良與細胞激素分泌不平衡(如tumor necrosis factor (TNF-α) 及 IL-2)有關。因此，本論文將針對 CRF 病人中，探討未接受透析之 CRF 患者(non-dialysis CRF, non-D)，與接受腹膜透析(continuous ambulatory peritoneal dialysis, CAPD)或血液透析 (Hemodialysis, HD) 之末期腎病(end-stage renal disease, ESRD)病人之單核球，探討尿毒素、透析方式對單核球細胞凋亡標記及細胞激素分泌之影響。本研究分成 4 組，選擇 10 位未接受透析治療的 ESRD 病人, 14 位 CAPD 病人，16 位 HD 治療的病人，並以 10 位健康自願供血者為對照組，收集單核球用脂多醣 (lipopolysaccharide, LPS)刺激 24 小時，利用酵素免疫分析法(enzyme-linked immunosorbent assay，ELISA)測定細胞激素間白素-10 (Interleukin-10, IL-10) 及間白素-18 (Interleukin-18, IL-18)分泌能力，以及用流式細胞細胞儀 (flow cytometry) 分析細胞凋亡標記的變化。實驗結果顯示經 LPS 刺激後，CAPD 及 HD 之單核球所分泌的發炎性細胞激素 interlukinIL-18 較對照組高 ($p<0.05$)，其抗發炎細胞激素之 IL-10 分泌量也高於未接受治療之慢性腎衰竭病人 ($p<0.05$)。HD 病人單核球細胞表面 CD95 蛋白及 CD120b 蛋白的表現量在HD 病人有明顯增加之情況，同樣地，CD36 及 CD68 在 HD 病人也有表現增加之現象，且 Fas 與 TNFR2 及凋亡清除蛋白 CD68 MFI 間呈正相關，顯示在血液透析時單核球的活化和細胞凋亡及細胞激素系統有密切關係。

英文摘要

In patients with chronic renal failure(CRF), lymphocytes, monocytes and neutrophils undergo accelerated apoptosis. Apoptosis is initiated by a number of different stimuli, including DNA damage, toxins, oxidant stress and cytokines etc. These patients were in immunodeficiency state and more susceptibility to infections. Immunodysfunction in patients with CRF may be resulted in excessed apoptosis of blood cells and imbalanced cytokine systems, such as tumor necrosis factor-[alpha] (TNF-) and interleukin (IL)-2. The aim of the study were to evalue the effect of uremic toxin as well as dialysis modality on the expression of monocyte apoptotic markers and monokine production in CRF patients. Four groups of subjects were evaluated: 10 nondialyzed CRF patients (Non-D, CRF) 14 continuous ambulatory peritoneal

dialysis patients(CAPD), and 16 hemodialysis patients(HD) who were on polysulfone (F80). The control subjects were 10 healthy volunteers(NC). Circulating mononuclear cells were obtained before dialysis and cultured with lipopolysaccharide (LPS) for 24 hrs. IL-10, and IL-18 cytokine were analysis by ELISA kits. The percentage and Mean fluorescence intensity of apoptosis associated markers, CD95, CD120b, CD36 and CD68 on monocytes were analyzed using a FACSCalibur flow cytometer. The data showed that interleukin-18 (IL-18) and IL10 were higher in CAPD and HD patients compared with NC group. The CD95 and CD120b proteins were highly expressed in HD patients compared with other three groups ($p<0.01$). The mean fluorencence intensity (MFI) of CD36 and CD68 also increased in HD group. A positive impact correlation between Fas , TNFR2 and scavenger receptors indicated that there are closed relationship because of the apoptosis of monocytes and cytokine systems in HD patient.