Cytokine Levels in Patients with Balkan Nephropathy

M.		Bogićević
R.		Čuićairanović
P.		Vlahović
M.		Mitić
V.		Stefanović

Institute of Nephrology and Hemodialysis, Faculty of Medicine, Nis, Yugoslavia

Prof. Vladislav Stefanović, Institut za nefrologiju i hemodijalizu, B. Tascovića 48, YU-1800 Niš (Yugoslavia)

TNF, pg/ml

Control 7.97 ± 1.12 96.1 ± 7.8

HFM 6.17 ± 1.04 87.7 ± 20.3

BEN 6.79 ± 1.30 34.8 ± 7.6*

BEN-CRF 8.69 ± 1.29 43.8 ± 10.0!

*p < 0.001 vs. control. BEN = Nephropathy patients without renal insufficiency; BEN-CRF = nephropathy patients with chronic renal failure.

Dear Sir,

Two major cytokines, tumor necrosis factor (TNF) and interleukin (IL-1) are mainly produced by monocytes and macrophages, but a variety of certain other cells, including those in the kidney, are also known as their producers. Cytokine levels and production were reported as abnormal in various renal diseases [1, 2]. However, no informations are available concerning cytokine fate and level in patients with Balkan nephropathy, an interstitial kidney disease of unknown etiology [3]. The present study was aimed to determine serum and urine levels of TNF and IL-1 as well as the production of these cytokines by peripheral blood mononuclear cells (PBMC) in patients with Balkan nephropathy.

Thirty-two patients with Balkan endemic nephropathy, 12 healthy members of their families (HFM) and 15 blood bank donors were included in this study. Nephropathy patients were divided into two groups: 16 patients without renal insufficiency and another 16 patients with chronic renal failure, with serum creatinine of $295 \pm 35 \mu\text{mol/l}$ (range 136–492). TNF- α was measured by a radio-immunometric assay kit from IRE-Medgenix (Fleurus, Belgium), and IL-1 α estimations were made by the competitive RIA method with a kit of Amersham (UK).

In order to assess cytokine production, PBMC were isolated from heparinized blood and cultured for 48 h unstimulated and after addition of phytohemagglutinin 125 $\mu\text{g/ml}$ or concanavalin A (Con A) 25 $\mu\text{g/ml}$ into incubation medium [4]. Mean values $\pm$ SEM are presented and the difference between groups was estimated by Student's t test.

Serum levels of cytokines studied were not found altered in HFM and in both groups of patients with Balkan nephropathy (table 1).

Groups

Table 1. Serum and urine levels of TNF and IL-1 in patients with Balkan nephropathy

However, urinary excretion of TNF in Balkan nephropathy patients was markedly decreased. Urinary excretion of IL-1 in patients with renal failure was also decreased, but without a statistical significance. Basal levels of TNF and IL-1 in supernatants of cultured PBMC prepared from patients with Balkan nephropathy and HFM were not found to differ from those in the control group (data not presented). Phytohemagglutinin and Con A provoked a marked increase in cytokine production by PBMC in all groups studied, both when compared to the controls the only alteration observed was a lower stimulation effect of Con A ($p < 0.05$) in renal failure patients. This may imply the interference by some uremic compounds. The methods used are claimed to detect intact cytokine molecules as well as some degradation products and inactive forms of cytokines [5]. Since human urine is the source of TNF and IL-1 inhibitors, further studies are needed to explain the observed decrease of urinary excretion of TNF and IL-1 in patients with Balkan nephropathy.

urine

IL-1, pg/ml

serum

23.2 ± 9.0   21.2 ± 3.6

19.8 ± 1.6   25.0 ± 4.9

26.3 ± 1.9   23.8 ± 2.5

20.8 ± 4.0   14.0 ± 1.9

References

Matsumoto K, Dowling J, Atkins RC: Production of interleukin 1 in glomerular cell cultures from patients with rapidly progressive crescentic glomerulonephritis. *Am J Nephrol* 1988;8:463-470.

Matsumoto K: Decreased production of interleukin-1 by monocytes from patients with lipid nephrosis. *Clin Nephrol* 1989;31:292-296. Stefanovic V, Polenakovic M: Balkan nephropathy. Kidney disease beyond the Balkans? *Am J Nephrol* 1991;11:1-11.

Stefanovic V, Mitic-Zlatkovic M, Cukuranovic R, Miljkovic R, Pavlovic NM, Vlohevic P: β_2 -Microglobulin in patients with Balkan nephropathy and in healthy members of their families. *Kidney Int* 1991;40(suppl 34):S21-S26. Jäätelä M: Biologic activities and mechanisms of action of tumor necrosis factor- α /cachectin. *Lab Invest* 1991;64:724-742.