Serum Interleukin-6 in Continuous Ambulatory Peritoneal Dialysis in Patients

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Dear Sir,

Recently, Cavaillon et al. [1] reported elevated serum levels of the cytokine interleukin-6 (IL-6) in long-term hemodialyzed patients compared to healthy donors. Although lower than in the long-term group, statistically significant higher serum levels of IL-6 were also found in nondialyzed uremic patients. Similar findings were reported by Herbelin et al. [2]. These studies suggest that renal failure itself may lead to accumulation of IL-6 in the circulation. However, this hypothesis is in contradiction with the observations of other authors. Goldman et al. [3] could not demonstrate detectable IL-6 levels in the serum of 6 infection-free patients treated with continuous ambulatory peritoneal dialysis (CAPD) for 6-77 months. Nakahama et al. [4] were able to measure detectable plasma IL-6 levels in only 1 of 21 infection-free CAPD patients treated for 3-96 months. Possibly, the observed discrepancies are due to the use of different bio- and Elisa assays with varying sensitivity and/or specificity. More efficient elimination of IL-6 by the peritoneal membrane – in comparison to the membranes used in hemodialysis – cannot explain this difference; based on a molecular weight of 26 kD, a peritoneal clearance by diffusion between only 0.09 ml/min (albumin, MW 69,000) and 0.81 ml/min (β₂-microglobulin, MW 11,800) can be expected [5].

To determine whether serum IL-6 activity could be detected in our CAPD population and furthermore, whether the amount of serum IL-6 was dependent on the duration of treatment, we compared 15 recently started CAPD patients (treated for less than 1 year: range 1-11 months, mean 5) with 12 treated for more than 4 years (range 48-112 months, mean 72). Residual urine production ranged from 150 to 2,000 ml/24 h (median 700) in the short-term group and was 0 in the long-term group except for 1 patient who still had a urine production of 100 ml/24 h. Both groups were free of peritonitis at least 3 weeks before and after the time of study. IL-6 activity was measured with a bioassay using the B 13.29, subclone 9.9 cell line [6]. Values exceeding 13 pg/ml are considered elevated in our laboratory.

Results are shown in figure 1. IL-6 levels were 11.1 ± 5.53 pg/ml (mean $\pm$ SD) in the short-term group versus 21.9 ± 15.9 pg/ml in the long-term group ($t = 2.48$, $p = 0.02$). In only 2 of the 15

short-term patients, IL-6 values exceeding 13 pg/ml were observed. In contrast, 7 of 12 long-term patients showed elevated IL-6 levels ($\chi^2 = 6.075$, $p < 0.02$). Four patients, 3 in the recently started patients and 1 in the long-term group, were studied weekly during 2 months [7]. Variability of serum IL-6 ranged from 5 to 20% in these patients. Serum IL-6 levels never exceeded 13 pg/ml in the 3 patients treated for less than 1 year, whereas they ranged from 29 to 43 pg/ml in the one patient treated for 69 months. IL-6 concentrations correlated inversely with residual renal function (Spearman rank, $n = 27$, $r = 0.552$, $p = 0.005$). No relationship existed between serum IL-6 and the acute-phase protein-C-re-

CAPD < 1 year CAPD > 4 years

Fig. 1. Serum IL-6 levels in recently started CAPD patients compared to those treated for a longer time. — = Upper level of normal values in our laboratory. The difference between the means was significant ($t = 2.48$, $p = 0.02$).

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active protein ($n = 27$, $r = -0.021$, NS). This is in agreement with the observation of Cavail-
lon et al. [1] and Nakahama et al. [4].

It is concluded that IL-6 activity was present in the serum of our CAPD population. Recently started patients tended to have lower levels than those treated for a longer time. Although the liver is the major site of IL-6 metabolism (80%), it has been demonstrated in rats that the kidney is involved in its clearance as well (10-15%) [8]. In our population, loss of residual renal function appeared to contribute to the increment of IL-6 activity in the circulation. Although unlikely, it cannot be excluded that repeated exposure to unphysiological dialysis solutions, containing high glucose concentrations, a high osmolarity and low pH, could lead to activation of monocytes and subsequently to production of IL-6 in serum.

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