On-line haemodiafiltration decreases serum TNFα levels in haemodialysis patients

Sir,

Blood contact with the dialysis membrane has been documented as a major cause of cytokine activation and release. This interaction is associated with haemodialysis-related acute manifestations, such as fever and hypotension (less frequent at present) [1], and chronic morbidity like inflammation, malnutrition, atherosclerosis, cardiovascular disease, anaemia and even a higher mortality rate [1,2]. Increased cytokine production/activation may also be responsible for bone remodelling, participating in the stimulation/inhibition of osteoclasts and osteoblasts and the aggravation of β-2-microglobulin amyloidosis [3].

The response to erythropoietin in haemodialysis patients also seems to be mediated by various cytokines that participate directly in the erythropoietic process [4]. We had the opportunity to demonstrate that in a group of chronic haemodialysis patients the change from low- to high-flux polysulfone membranes permitted a significant reduction in erythropoietin requirements for the maintenance of a stable haemoglobin at 11.5 g/dl [5]. These results may compensate, by saving erythropoietin, the increased cost associated with the use of high flux membranes and on-line haemodiafiltration.

An increased cytokine activation secondary to blood exposition to bioincompatible dialysis components has been reported by several authors. Different cytokines are involved in the chronic inflammation that results from this bioincompatibility of the haemodialysis treatment. Among the cytokines most widely linked to the inflammatory response has emerged the tumour necrosis factor (TNFα). Unfortunately, most authors compare different types of membranes, with variable degrees of biocompatibility and diffusive/convective properties, making an individual evaluation of each of these properties very difficult as well as of their influence on cytokine activation.

With the purpose of separately evaluating the effects of increased convective capacity on the serum levels of cytokines, we used synthetic membranes of the same type (polysulfone) during low-flux haemodialysis, high-flux haemodialysis and high-flux on-line haemodiafiltration.

A prospective study was carried out in 24 patients who were on intermittent haemodialysis for >3 months. We measured the serum levels of C3c (185 kDa), C4 (205 kDa) and TNFα (19 kDa) at the beginning and end of the ‘mid-week dialysis session’ during three consecutive weeks. TNFα serum levels were measured by quantitative immunoassay RD systems.

During the first week, a low-flux polysulfone was used (ultrafiltration coefficient between 11.1 and 18 ml/h/mmHg); during the second week a high-flux polysulfone was used (ultrafiltration coefficient between 40 and 55 ml/h/mmHg); and finally, during the third week the same membrane as the week before was used but with the on-line haemodiafiltration technique. All of these membranes were steam sterilized and not recycled. The blood pump rate was >300 ml/min and the dialysate pump rate was 800 ml/min. We used
pre-dilution on-line haemodiafiltration, with a reposition volume of 100 ml/min (Hemodiafiltration 4008-H Fresenius monitor). The water used was endotoxin-free (measured by Chromogenic Kinetic LAL assay).

The variations between post- and pre-treatment TNFα serum levels during low-flux haemodialysis, high-flux haemodialysis and high-flux + on-line haemodiafiltration, respectively, are shown in Figure 1. Differences between the three groups were evaluated by Friedman test. Wilcoxon signed ranks test was used for pairwise comparison. A P-value <0.05 was considered statistically significant.

As shown in Figure 1, the serum levels of TNFα increased during the low-flux session, but decreased during the high-flux session and decreased even more during on-line haemodiafiltration. This profile was seen in all of the 24 patients undergoing on-line haemodiafiltration.

The serum levels of C3c and C4 increased during all three types of dialysis, but significantly less so with the on-line haemodiafiltration technique. This points to the importance of ultrafiltration for the removal of these molecules. The increments during the dialysis session of serum C3c and C4 levels were, respectively: in low-flux dialysis, 31.9 and 9.1 mg/dl; in high-flux haemodialysis, 40.1 and 13.8 mg/dl; and in high-flux + on-line haemodiafiltration, 14.3 and 5.3 mg/dl. The increment in C3c and C4 during on-line haemodiafiltration was significantly lower than that observed in high-flux dialysis (P=0.04 and 0.003, respectively) and low-flux dialysis (P=0.004 and 0.003, respectively).

Our results show that the potentiation by on-line haemodiafiltration of the convective effect of high-flux polysulfone membranes optimizes their efficacy in terms of solute removal, as demonstrated by the observed decrease in the serum levels of pro-inflammatory cytokines such as TNFα. Although these results need to be confirmed on a long-term basis and in larger cohort studies, they point to the potential advantages of more convective techniques such as on-line haemodiafiltration in reducing the chronic inflammatory response and the morbidity of chronic haemodialysis patients.