Treatment with vitamin E-coated membrane dialysers and cardiovascular protection in dialysis patients

Sir,
The paper by Kirmizis et al. [1] reports significant reduction of inflammation and oxidative stress (OxSt) markers in haemodialysis (HD) patients treated with a vitamin E-coated cellulose membrane dialyser (Clirans E, CL–E) (VEM) for 6 months, which might provide evidence in these patients for potential cardiovascular protection.

We would like to suggest that the results of our studies in VEM-treated HD patients provide additional evidence, also on a clinical ground, for potential cardiovascular protection exerted by VEM use.

In 2004 [2], we documented in HD patients upon VEM treatment using a molecular biology approach, in which mononuclear cell gene expression of p22phox and haeme oxygenase (HO)-1 were reduced and increased, respectively. A subunit of NADPH oxidase, p22phox, is essential for the final electron transport to molecular oxygen in generating superoxide [3], while HO-1 increases and protects from OxSt, and also possesses anti-inflammatory, anti-proliferative and anti-apoptotic effects [3]. The reduction of mononuclear cell p22phox and increase of HO-1 not only suggest reduced OxSt but also the inhibition of leukocyte activation, which strengthens the evidence for a beneficial effect on OxSt and cardiovascular risk in HD patients.

A reduced plasma hydroperoxide level and increased plasma antioxidant power after 1 year of VEM use were also shown in HD patients [2].

We have reported on 23 HD patients treated for 1 year with the newest and more biocompatible version, VEM, than Clirans E (no longer produced), Vitabran E (ViE; Asahi Medical, Tokyo, Japan) (Vitamin E-coated on a polysulfone membrane). We found not only reduced p22phox and increased HO-1 protein levels [3] but also a reduced plasminogen activator inhibitor (PAI)-1 and phosphorylated extracellular signal-regulated kinase (ERK) 1/2 protein expression and plasma oxidized LDL (oxLDL). Furthermore, the analysis of carotid artery intima–media thickness, an indicator of atherosclerosis and coronary atherosclerosis in HD patients, showed a trend toward reduction after 1 year of VEM treatment [3].

PAI-1, a recognized part of the OxSt-related response, is linked to inflammatory cytokines which promote vascular inflammation and atherosclerosis and is induced by oxLDL [3]. ERK1/2 eliciting transcriptional reprogramming and altering gene expression associated with hypertension is recognized as an OxSt-related effector for cardiovascular remodeling and atherosclerosis [3].

The combination of our data and those of Kirmizis et al. [1] including now >80 HD patients, approximately half of them treated for 1 year, confirms the beneficial effects of VEM treatment on OxSt, inflammation and atherogenesis. The support of a molecular biology approach to OxSt and inflammation-related protein assessment and the reduced ERK1/2 phosphorylation state we showed was associated with improvement of inflammation and OxSt markers as we, Kirmizis et al. and others [1–4] have reported. These data have also the clinical correlate of a trend toward reduction of vascular remodeling [3] and strongly indicate as highly likely that VEM treatment induces cardiovascular protection in HD patients.

Conflict of interest statement. None declared.

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Reply

Sir,
We appreciate Dr Calò’s comments regarding our study and the anti-inflammatory and antioxidative effects of vitamin E-coated membrane dialyser (VEM) use. After several years in which the topic has remained rather in quiescence, the newer evidence provided by both groups [1–3] brings again the beneficial potential of VEM use to the surface. Apparently, what Dr Calò’s group found after 1 year of VEM use in haemodialysis (HD) patients was an increased plasma antioxidant power. One point of concern regarding the use of VEM, however, is the fact that its preventive effects, whichever they might be, cannot be applied at early stages of chronic kidney disease and, thus, to atherosclerosis. Anyway, in view of the potential cardiovascular prevention exerted by this approach, the need seems imperative now, for larger randomized controlled studies and studies investigating the probable effects on morbidity and mortality with the use of VEM in end-stage renal disease (ESRD) patients as early as possible in their disease course. In parallel, as we have further analysed in our recent paper [1], we believe there are significant lessons to be learnt from the effects of VEM use in ESRD patients, regarding the beneficial effects of vitamin E supplementation in the general population. Thus, we believe that the benefits from vitamin E supplementation could be observed in selected patient groups with high degrees of oxidative stress and chronic