Sir,  

It was interesting to read the letter to the editor commenting on our manuscript recently published in *Nephrology, Dialysis and Transplantation* [1]. The authors of the letter kindly recognize the importance of our contribution to the understanding of potential causes of the inflammatory response observed in chronic kidney disease (CKD) patients. They also comment on our findings of the lack of association between endotoxaemia and the levels of inflammation markers, which we will briefly discuss.  

Initially, it must be emphasized that our study is a clinical observational investigation that was not controlled for many factors. Therefore, as clearly stated in the discussion of our article, the aim of the study was the establishment of associations, and could not safely enter the field of mechanisms.  

In the last part of the letter, the authors correctly observed that most of the values of plasma endotoxin presented in our study appear to be below the detection limit of the method utilized. This was due to an error in the conversion of the units, which will be acknowledged in errata. In the results section, values should have been presented in ng/ml instead of ng/l as presented in the article. The corrected results indicate that most patients in our study present levels compatible to what is considered mild to moderate endotoxaemia. Finally, with respect to our statement, that the lack of correlation between levels of endotoxin and inflammation markers observed in our study could be explained by insufficient amounts of circulating endotoxin, we believe that it is impossible at the moment to present a definitive answer. Although most published data in other populations have not shown a significant correlation between inflammation markers and endotoxin levels [2,3], data on healthy individuals [4] show a significant correlation between endotoxaemia and C-reactive protein after ultra-endurance exercise, in levels (5-15pg/ml) much lower than observed in our CKD patients. Furthermore, raised concentrations (in similar levels when compared with our findings) of endotoxin and cytokines are found in patients with oedematous chronic heart failure, which are normalized after diuretic treatment [5]. In the search for causes of inflammation activation in the progression of CKD, further studies with adequate design will need to address these issues.

Conflict of interest statement. None declared.
Letters

Advance Access publication 25 June 2007

A benefit for renal function after early switch to liposomal amphotericin B from conventional formulation in empirical antifungal treatment

Sir,

Despite its nephrotoxicity, conventional amphotericin B (CAB) is commonly prescribed in immunosuppressed patients because of its lower cost. As a consequence, the rate of nephrotoxicity in haematological patients treated with CAB is 61% for allogeneic stem-cell transplantations and 80% for autologous stem-cell transplantations [1,2]. The study of Meunier et al. [3] demonstrated improvement in renal function after switching from CAB to liposomal amphotericin B (L-AmB). However, there is no consensus on the level of nephrotoxicity in haematological patients that would require a switch to other antifungal treatment. We hypothesized that an early switch to the less nephrotoxic L-AmB, at time when nephrotoxicity is still moderate would avoid more severe nephrotoxicity. In patients with neutropenia and increasing creatinine, we compared two strategies for switching drug regimens.

Patients were eligible for the study if they were 18–75 years old, received an induction or consolidation chemotherapy treatment for haematological malignancy with an expected neutropenia (<500/mm³) of at least 10 days, treated empirically with CAB, had a sCr <110 μmol/l and a calculated sCr clearance >60 ml/min. Patients were excluded in the case of allogeneic stem cell (or solid organ) transplantation or diagnosis of fungal infection.

Before randomization patients received CAB at 0.7–1 mg/kg/day. Thirty-two patients from seven French haematology wards were randomized from October 2003 to August 2005 (16 patients in each group). After randomization, patients in the early switch group were immediately given L-AmB at 3 mg/kg/day, whereas patients in the late-switch group continued CAB treatment and were switched to L-AmB only when sCr increases were >100% (or sCr was >170 μmol/l). Thirty-one patients were analysed (16 patients in early-switch group and 15 patients in late-switch group). Median age of patients was 53 years and 68% were men. The most frequent underlying haematological malignancy was acute leukaemia (94%). Prior to randomization, the mean duration of the initial treatment with CAB was 4.8 days, and this was not different between the two groups. A majority of patients received 1 mg/kg/day (68%). After randomization, the mean treatment duration with L-AmB was 9.2 ± 5.8 days in the early-switch group. For those in the late-switch group, the CAB mean treatment duration was 6.3 ± 5.6 days and the L-AmB treatment duration was 2.9 ± 4.3 days. In this later group, seven patients were switched from CAB to L-AmB treatment following a >100% increase in sCr (the remaining eight patients continued CAB treatment).

The mean changes in sCr from randomization to the end of treatment were −2.3% vs +16.2% (P = 0.04) in early- and late-switch groups, respectively (Table 1). Conversely, the mean changes in sCr clearance were +3.7% in early-switch group vs. −10.3% in late switch group (P = 0.03). These results suggest that L-AmB treatment improved renal function after it had been damaged by CAB.

Conflict of interest statement. None declared.

Shonan Kamakura General Hospital
Hidekazu Moriya
Kamakura, Japan
Email: hidekazu.moriya@tokushukai.jp

doi:10.1093/ndt/gfm756