Is C0 better than C2 as a determinant of rejection in renal transplant recipients?

To the Editor: During the past years C2 monitoring of cyclosporine microemulsion (CsA) has been focused on as a new, improved, and possibly more "correct" monitoring regimen in transplant recipients [1–3]. I read with great interest the publication by Perico et al [4] in *Kidney International*. They concluded that among serial daily CsA measurements post-transplant, a CsA trough blood concentration of 300 to 440 ng/mL (and not C2) taken as early as day 2 has by far the highest capacity to predict rejection episodes. These results diverge from most recent publications. I register, however, that it is not stated in the text or in the tables or figures how many patients that were actually included in their final analysis. When reading the article, one gets the impression that 224 patients (334 patients minus 110 patients with delayed graft function) were included. From Table 3, which only includes data from 16 patients, one can calculate that the total material analyzed seems to be from only 39 patients [group below: 10 patients = 76.9% (i.e., *13 patients* = 100%); group within:1 patient = 14.2% (i.e., *7 patients* = 100%); group above: 5 patients = 26.3% (i.e., *19 patients* = 100%)]. This is definitely not clear in the text and dramatically lowers the quality of the study. In Table 2, patients with no rejection have a C0 of 539 ± 250 ng/mL compared to patients with rejection having a C0 of 335 ± 248 ng/mL ($N = 39$?). How one can conclude from these data that a C0 on day 2 between 300 to 440 ng/mL is the best predictor needs to be explained.

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About the mechanisms of renoprotective effect of angiotensin inhibitors on lupus nephritis

To the Editor: We read with interest the paper by Alves de Albuquerque et al [1] reporting on beneficial effects of angiotensin-converting enzyme (ACE) inhibitor treatment on the development of nephritis in NZBxNZW F1 and MRL/lpr mice. They showed that captopril treatment decreased transforming growth factor-β1 (TGF-β1) and TGF-β2 expression, and postulated effects of ACE inhibition on immunologic parameters. We recently reported on the beneficial effects of treatment with either ACE inhibitor (enalapril) or angiotensin receptor antagonist (candesartan) on nephritis development in MRL/lpr mice [2]. In spite of comparable anti-DNA antibody titers and glomerular immune complex deposition, proteinuria and histology were markedly ameliorated by either treatment, and the decreased inflammatory cell infiltrate was associated with decreased renal expression of chemokines such as CCL4 and CCL2. These effects cannot be directly related to decreased TGF-β expression, as TGF-β is known to inhibit chemokine expression, and thus, lowered TGF-β would result in increased chemokine expression [3]. Similar to Alves de Albuquerque et al, our data also indicate effects of angiotensin on the local, intrarenal inflammatory process, but most likely on steps influencing inflammatory cell infiltrates. The reduced TGF-β expression observed by Alves de Albuquerque et al might then be a result of decreased cell infiltration, and further influence downstream processes. Taken together, our results also support an immune modulatory role for angiotensin in the course of murine lupus nephritis.

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