5. Thornton SN. Hypovolaemia-induced mild hypoxia produces subchronic metabolic dysfunction. Int J Obes (Lond) 2009; 33: 605

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Reply

Dear Sir,

We thank Dr Thornton for his interest in our work. We share his interest in the diuretic effects of RAAS blockade, and actually were among the first to describe this more than 20 years ago [1]. With RAAS blockade, after an initial period of negative sodium and water balance, steady state is restored at a lower extracellular volume with restoration of urine volumes towards baseline.

In the current study [2], data were obtained after 6 weeks of treatment, i.e. during steady state. Steady-state urine volumes were higher during high sodium intake, but were unchanged by losartan and/or hydrochlorothiazide (Figure 1). Dr Thornton suggests that haemodilution may be present and may account for changes in haemoglobin and erythropoietin, but no signs of haemodilution were present in our study. Actually, all data pointed towards haemoconcentration as apparent from increased plasma levels of creatinine, urea, uric acid, albumin and renin, and decreased body weight and blood pressure [3]. Thus, the reduction of erythropoietin and haemoglobin by hydrochlorothiazide added to losartan in our proteinuric renal patients with preserved renal function occurred despite the simultaneous presence of haemoconcentration, suggesting that the reduction of absolute erythropoietin and haemoglobin levels may even be underestimated. In line with animal studies [4,5] we hypothesize that erythropoietin reduction by hydrochlorothiazide is caused by a decrease in renal oxygen requirement, which is the main stimulus for erythropoietin production, due to the inhibition of active tubular sodium reabsorption.

Furthermore, Dr Thornton points to the tight relationship between oral fluid intake and urine concentration, probably during steady state, which should be accounted for when measuring proteinuria. We fully agree on this issue and consistently assessed proteinuria in 24-h collections of urine, with proteinuria reported as protein excretion per 24 h (gram per 24 h) as well as protein–creatinine ratio (milligram per milligram) [3]. This minimizes the risk of underestimation of proteinuria in comparison with spot urine analysis and makes it possible to correct for collecting errors.

To conclude, erythropoietin and haemoglobin levels were reduced by hydrochlorothiazide added to losartan in our study population, without signs of haemodilution.

Conflict of interest statement. None declared.

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Fig. 1. Data are shown as mean ± SEM. Losartan/HCT, losartan plus hydrochlorothiazide; #P < 0.05 versus same treatment on high sodium diet (effect of low sodium diet). Steady-state urine volumes were higher during high sodium intake, but were unchanged by losartan and/or hydrochlorothiazide.


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