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Nephrology
Dialysis
Transplantation

Letters and Replies

Reply

Sir,

We thank Zitta *et al*. for their critical comments. The authors raise the question as to which method might be most appropriate to measure glomerular filtration rate (GFR) and renal plasma flow (RPF), thereby challenging the method of constant infusion technique for measurement of GFR and RPF which we used in our study [1]. The main concern was that the clearance of the tracers [inulin and para-aminohippuric acid (PAH)] would be obtained at a time point when plasma inulin and PAH concentrations are not in a steady state. A recent study by Van Acker *et al*. [2] presented data showing that plasma inulin and PAH concentrations did not become completely constant over 24 h, especially when the clearance was low. These data were obtained in patients with chronic renal failure, having reduced GFR and RPF. Thus in these patients, half-time of inulin and PAH excretion were markedly prolonged, thereby explaining a long interval until steady state conditions were achieved. Furthermore, circadian rhythms of renal haemodynamics and functions were predominant mechanisms explaining the fluctuation and variation of GFR and RPF measurements [2]. We avoided these co-factors by applying constant infusion techniques of GFR and RPF always at the same time of the day and by including only patients with normal renal function [1]. Buclin *et al*. [3] compared a different method of measuring GFR. These authors concluded that the constant infusion technique was reliable when the clearance was obtained 2 h after the start of inulin infusion. In particular, the administration of a loading bolus and the dynamic study, secured an early steady state in the plasma concentration of inulin. Therefore, the method of constant infusion technique used for the assessment of GFR and RPF seems to be appropriate in terms of steady-state conditions.

Changes of RPF and GFR due to well-defined, pharmacological infusions take place within minutes and new steady-state conditions of inulin and PAH concentrations take place within 20–25 min [1]. The pharmacokinetic method of dynamic renal function testing used by Zitta *et al*. [4] is inappropriate to assess changes of GFR and RPF within such a short period of time.

The effects of protein ingestion on GFR in hypertensive patients seem to contradict our findings. However, our study and the one of Zitta *et al*. investigated different study

populations, namely patients with hypertension *vs* patients with hypercholesterolaemia. Hypertension involves the kidney and its function, whereas hypercholesterolaemia *per se* does not involve renal function directly. Secondly, we focused on the renal NO system and stimulated NO synthase by infusion of L-arginine directly, whereas the approach of protein ingestion is a rather unspecific way of stimulating GFR.

Finally, not in 'contrast to study ...' but quite in accordance with clinical and experimental data, our data point to a distinct, different endothelial function in the renal vasculature. Carroll *et al*. [5] could demonstrate that cholesterol feeding did not alter haemodynamic responsiveness to acetylcholine and angiotensin II in hypercholesterolaemic rabbits. Consistently in patients with arterial hypertension, the vasodilatory response to acetylcholine, a test for NO stimulation of the endothelium, was not found to be altered [6], in contrast to the study by Zitta *et al*. [4]. In six patients we investigated the endothelial function of the human forearm and renal vasculature and found a clear-cut, blunted response in the forearm but a well-preserved L-arginine-induced vasodilatation in the renal circulation. Thus, our data support the hypothesis of a distinct endothelial function of the renal vasculature.

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