Dear Sir,

Patients with severe atherosclerosis are generally accepted for chronic treatment of end-stage renal failure by dialytic techniques [1,2]. In these patients atherosclerotic complications are the most common cause of mortality [3] and peripheral arterial disease an important cause of disability, probably exacerbated by the accelerated atherosclerosis described in dialysis patients [4]. Surgery is usually unsuitable for these patients because of extensive arterial disease and/or general debility, and conventional medical management is often unsuccessful or contraindicated. So, the results of clinical trials suggesting that prostacyclin (PGI₂), a potent vasodilator and anti-platelet agent [5], can be useful in the medical treatment of peripheral arterial disease [6–8], prompted us to assess the effectiveness of this new promising treatment in dialysis patients with peripheral arterial disease.

Five male patients (table 1) with stable intermittent claudication (no changes in walking distance during the previous 3 months) were randomly allocated, in a double-blind crossover placebo-controlled trial, to receive an 8-hour intravenous infusion each day for 3 consecutive days either of PGI₂ (Wellcome Foundation, Rome, Italy; 2–10 ng/kg/min) dissolved in glycine buffer or of glycine buffer alone. After a 3-month interval each patient crossed over to the other arm of the trial. The diagnosis of peripheral arterial disease was based on typical history, clinical examination and angiography. The following were evaluated both before and after each infusion: skin color, foot temperature (as mean of hallux, medial and lateral malleolar, and interdigital temperatures), hallux oscillography – basal and after 40 min of indirect warming (IW) -, walking distance and platelet aggregation. Platelet aggregation was studied 24 h and hallux oscillography and walking distance 1 week after the end of the infusion. Blood pressure and heart rate were monitored during the infusions. Data were analyzed by two-way analysis of variance using Tukey-Cicchetti test for multiple comparison.

At the end of the study, no patient was assessed as having improved skin color after either treatment. The mean increases in foot temperatures after PGI₂ and glycine infusion were not significantly different. Room temperature was constant during the entire study period. Basal hallux oscillography showed a significant increase in hallux arterial pulse after IW only in the less involved side before either PGI₂ (pre IW: 3.7 ± 1.2 mm, post IW: 13.5 ± 7 mm; p < 0.05)
and glycine buffer (pre IW: 2.8 ± 2.7 mm, post IW: 10.1 ± 4.7 mm; p < 0.05) infusion. Both PGI2 and glycine infusions were unable to induce significant changes in basal and post-IW hallux arterial pulse.

Walking distance (table 1) increased after PGI2 infusion in patients No. 1–3, and after glycine infusion in patients 2 and 3. No effects were observed in patients 4 and 5. No changes were observed in platelet aggregation after the two treatments.

Every patient experienced facial flushing and mild headache during PGI2 infusion, but only in 1 patient did the dose have to be reduced (7 ng/kg/min) because of nausea and vomiting. Four patients experienced mild pain referred to the region of the masseter during PGI2 treatment.

Blood pressure did not change, while heart rate increased of about 10 beats/min during PGI2 infusion.

In conclusion, we were unable to demonstrate any effect of PGI2 with regard to pain relief additional to the marked placebo response relief observed after glycine buffer infusion. No significant vasodilatory effect of PGI2 was found in dialysis patients with peripheral arterial disease, even when a functional response to IW was observed. This could explain why we were unable to demonstrate any effect of PGI2 with regard to improvement in walking distance.

References
