leucocyte counts. In our patients, three out of 23 (13.04%) CAPD patients given lercanidine developed non-infective turbid peritoneal dialysis.

Differential diagnosis of non-infectious cloudy peritoneal dialysate includes cellular causes (i.e. leucocyte, eosinophils, red cells and malign cells) and non-cellular causes (i.e. triglyceride and drugs) [2]. Yoshimoto et al. [1,3] reported that bendipine, manidipine, nisoldipine and nifedipine caused cloudy dialysate on CAPD patients. In their study, it was revealed that the fluid contained an elevated triglyceride concentration. As far as we know this is the first report in the literature that lercanidine causes cloudy dialysate in the CAPD patients.

Conflict of interest statement. None declared.


**Effect of creatinine assay standardization on the performance of Cockcroft–Gault and MDRD formula in predicting GFR**

Sir,

The recent article of van Biesen et al. [1] illustrates the importance of standardization of serum creatinine assays when using formulas to estimate glomerular filtration rate (GFR). We provide further proof of the importance of standardization of creatinine. We previously compared the performance of the modification of diet in renal disease (MDRD) formula and the Cockcroft–Gault (CG) formula in healthy persons and normo-albuminuric diabetic patients [2]. As reported in this Journal, we concluded that the MDRD equation was less accurate than CG formula in predicting GFR (measured by inulin clearance). Our data were based upon a creatinine assay, based on the Jaffé kinetic reaction performed on a Hitachi 747 auto-analysers.

Meanwhile it has been shown that correct use of the MDRD equation necessitates calibration of the creatinine assay against the assay used by the Cleveland Clinic Laboratory [3].

The Cleveland Clinic Laboratory originally used a Beckman modified kinetic rate Jaffé reaction. Recently, samples of the MDRD study were re-analysed and compared with a creatinine assay using isotope dilution mass spectrometry (IDMS) as the gold standard [4]. IDMS results were highly correlated to enzymatic creatinine, measured by Roche technology. Therefore, this enzymatic assay should preferably be used in the MDRD equations.

We recently introduced the Roche enzymatic method in our Hospital. Comparison of the enzymatic method with our former Jaffé method according to an approved evaluation protocol [National Committee for Clinical Laboratory Standards, Evaluation Protocol number 9 (EP-9)] revealed: $y$ (enzymatic creatinine) = 1.266 ($x$ Jaffé creatinine) $– 29$. Based on this formula, we recalculated our creatinine data and applied the new formula [4]:

$$170 \times \left[\frac{\text{[enzymatic creatinine (mg/dl)]}}{0.95}\right]^{-0.999} \times (\text{age})^{0.176} \times \left[\frac{\text{[Serum urea nitrogen (mg/dl)]}}{1.070}\right] \times [\text{albumin (g/dl)}]^{0.318} \times (0.762 \text{ if female;} \times 1.180 \text{ if black}).$$

Results are given in Table 1. It is apparent that the use of standardized creatinine assay has a major influence on the reported differences between the formula-derived GFR and the true GFR. In fact, in contrast to our earlier finding, our recalculated data indicate that the MDRD formula is probably more accurate than the CG formula, also in persons with normal GFR. Reporting of MDRD-GFR using creatinine assays that are not calibrated using a gold standard should be discouraged.

**Conflict of interest statement.** None declared.

**Table 1.** Measured and predicted GFR in healthy subjects and diabetes patients without [2] and with standardization of creatinine assay

<table>
<thead>
<tr>
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<th>GFR (inulin clearance)</th>
<th>Former Jaffé method</th>
<th>New enzymatic method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CG</td>
<td>ΔCG - GFR</td>
<td>MDRD - GFR</td>
</tr>
<tr>
<td>Healthy subjects</td>
<td>107 ± 11</td>
<td>112 ± 17</td>
<td>5.0 ± 18.6</td>
</tr>
<tr>
<td>Diabetic patients</td>
<td>122 ± 18</td>
<td>119 ± 16</td>
<td>−2.8 ± 19.7</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SD; GFR, glomerular filtration rate (ml/min/1.73 m²); CG, prediction of GFR with Cockcroft–Gault formula (ml/min/1.73 m²); MDRD, prediction of GFR with the MDRD formula (ml/min/1.73 m²).
gastrointestinal symptoms and diarrhoea completely disappeared with the new dialyser. The surface-treated AN69 membrane was then reintroduced on 1 December 2004. Less than 1 hr after the beginning of haemodialysis, severe abdominal cramps and diarrhoea occurred again. The patient had diaphoresis but no breathing problems or angiooedema. The blood pressure remained stable. The treatment was immediately stopped. Intravenous diphenhydramine 50 mg and hydrocortisone 100 mg were given. Symptoms resolved rapidly, and haemodialysis was started again with a cellulose triacetate membrane dialyser without any other adverse event. Ramipril was maintained.

**Case 2**

A 47-year-old man on chronic haemodialysis 4 h three times a week since October 2003 was known to have type 2 diabetes. He was dialysed using a surface-treated AN69 membrane since the first dialysis treatment. His medication included metoprolol, calcium carbonate, aspirin, alfacalcidol, glicazide, furosemide, temazepam and enalapril 2.5 mg four times a week. Enalapril was prescribed from 2003 but compliance was variable. From August to December 2004, enalapril was taken less than once a week. After January 2005, he took enalapril 2.5 mg four times a week, more regularly. In September 2004, he presented two episodes of massive diarrhoea in the first hour of dialysis treatment, associated with a drop of his blood pressure. Starting early January, these symptoms occurred with almost every treatment, corresponding to his improved compliance to enalapril. On 25 February 2005, the dialyser was changed for a haemophan membrane (GFS® 20, Gambro) for this problem. Since then, he has had no diarrhoea during the treatment and no initial fall in blood pressure has been observed. Enalapril was continued without any problem.

In *vitro* studies showed that increasing the membrane electronegativity enhances bradykinin generation [3]. The angiotensin-converting enzyme degrades bradykinin; consequently, ACEIs reduce this process and favour bradykinin build-up. AN69 membrane is one of the membranes with the highest electronegative surface. A surface-treated AN69 membrane with polyethyleneimine(PEI) has recently been made available. The polycationic saline solution (PEI) reduces the surface electronegativity and therefore the bradykinin production [3]. Surface-treated AN69 membrane was reported safe in patients receiving ACEI [4]. However, an anaphylactoid reaction after a single dose of captopril during haemodialysis was previously reported [2]. Our patients presented more subtle symptoms. In case 1, the patient presented a more rapid and severe reaction upon rechallenge, suggesting a real AN69-associated reaction in presence of ACEI. Surface-treated AN69 membrane or ACEI not used concomitantly in this case was tolerated without any problem for many months. In the second case, ACEI and a surface-treated AN69 membrane used concomitantly seemed to have been well-tolerated at first, when compliance to enalapril was questionable. No other explanation was found for the abdominal symptoms in January than a reaction to the filter, since the symptoms suddenly ceased after the dialysate was changed. We felt that challenging this patient again with a surface-treated AN69 membrane would have been dangerous and unethical.

Even if surface-treated AN69 membrane was shown to be less electronegative, the coating of PEI may not cover perfectly all electronegative charges. Variability within dialysers or between fibres filaments is possible.

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**Intestinal manifestations with a surface-treated AN69 membrane and ACEI during haemodialysis**

Sir,

AN69-associated reactions in haemodialysed patients receiving angiotensin-converting enzyme inhibitors (ACEI) are well-documented [1]. The negatively charged AN69 membrane is thought to activate the bradykinin system. Moreover, ACEI reduces bradykinin inactivation. Surface-treated AN69 is considered to be safer in that regard. To our knowledge, only one case of anaphylactoid reaction induced by ACEI during haemodialysis with a surface-treated AN69 membrane has been reported [2]. We report here two patients who had a more subtle presentation with predominantly intestinal manifestations.

**Case 1**

A 54-year-old male with end-stage renal disease (ESRD) consequent to IgA nephropathy had been on chronic haemodialysis (4 h, three times per week) for 2 years. He was dialysed using a surface-treated AN69 membrane (Nephral ST® 500, Gambro) for 4 months. His medication included metoprolol, furosemide, amiodarone, calcium carbonate, sevelamer, allopurinol, oxybutinin, eпоetin-α, calcitomin, warfarin and naproxen. On 8 November 2004, ramipril 2.5 mg once daily was initiated for hypertension and cardiovascular protection. At the next dialysis, the patient presented moderate abdominal cramping and diarrhoea during haemodialysis. These symptoms did not recur until 19 November. They were present on 22 and 24 November, when medical attention was first requested. At this time, the working diagnosis was viral gastroenteritis. However, by caution, the dialyser was changed for a cellulose triacetate membrane (Exeltra® 210, Baxter). Abdominal