Effect of iodinated contrast agents on residual renal function in PD patients

Olivier Moranne¹, Serge Willoteaux², Dominique Pagniez¹, Philippe Dequiedt¹ and Eric Boulanger¹

¹Nephrology Department and ²Radiology Department, University Hospital of Lille II, France

Abstract

Background. Residual renal function (RRF) is an important predictor of outcome in peritoneal dialysis (PD) patients. Although increasing emphasis has been placed on preserving RRF, the nephrotoxicity associated with contrast medium administration in PD patients remains a controversial issue. In the present prospective study, we evaluated the evolution of RRF 2 weeks after iodinated contrast medium administration (ICMA) in a group of stable PD patients, and compared it with that in a non-treated control group of stable PD subjects.

Methods. The study was conducted from January 2003 to October 2004. RRF was quantified by the average of 24 h urinary urea and creatinine clearance and peritoneal creatinine clearance (PcrCl) were analyzed, the levels of which were analyzed prior to and 2 weeks following ICMA in 36 PD patients and also assessed at the same time points in a group of 36 PD non-ICMA control subjects, matched according to RRF characteristics. Two weeks following ICMA, the values for RRF, daily urine volume and PcrCl were assessed against those at baseline, and the evolution of RRF was compared between the two groups. In the ICMA group, this study was performed with adequate pre-hydration and a minimum dose of contrast medium.

Results. Compared with baseline values, RRF, daily urine volume and PcrCl were not found to be significantly different 2 weeks after ICMA (7.0±4.3 vs 7.2±4.3 ml/min/1.73 m², P = 0.12; 1324±696 vs 1360±755 ml/day, P = 0.5; and 41.1±9 vs 40.6±9 l/week/1.73 m², P = 0.6, respectively). Following ICMA, variations in RRF and daily urine volume were found to be comparable with those of the control group (0.1±0.5 vs 0.1±0.5 ml/min/1.73 m², P = 0.9; 36±440 vs 40±493 ml/day, P = 0.8, respectively).

Conclusion. In this study, 2 weeks following ICMA, no accelerated decline in RRF was determined in stable PD patients with adequate pre-hydration, i.e. subjects treated under optimal circumstances compared with the control group.

Keywords: peritoneal dialysis; radiocontrast medium; renal function

Introduction

A number of previous studies have demonstrated that residual renal function (RRF) is conserved to a greater extent and persists over a longer period of time in peritoneal dialysis (PD) than in hemodialysis (HD) patients [1]. The preservation of RRF is an important aspect that contributes to decreased mortality and morbidity in patients on PD therapy [2]. However, it should be noted that renal and peritoneal clearance are not the same; an increase in the exchange volume or frequency of PD cannot completely compensate for a decline in RRF [3]. It is now considered that the preservation of RRF may be particularly important for the effectiveness of long-term PD [4].

Independent factors such as a previous history of diabetes, congestive heart failure, peritonitis or proteinuria are associated with an accelerated decline in RRF in PD patients [5,6]. The effects of sex, age, PD technique, such as automated PD (APD) or continuous ambulatory PD (CAPD), and aminoglycoside administration have been studied and controversially discussed [7]. Diuretics have not been found to affect the evolution of RRF, but have been found to result in increased urinary sodium excretion [8]. However, the use of angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs) or calcium channel blockers has been identified as being associated with a decreased risk of RRF decline [9,10].

Various reports on contrast medium-induced nephropathy in the general population have appeared in the literature: an increase in serum creatinine concentrations begins on day 2 to become maximal
Effect of iodinated contrast agents on RRF in PD patients

Patients and methods

Patients

This single-centre study was performed in accordance with our institution’s rules and guidelines. A total of 36 stable PD patients scheduled to receive ICMA were enrolled in the study over the period from January 2003 to October 2004. All these patients were prospectively matched for RRF characteristics with 36 stable PD control subjects who underwent systematic biannual assessment of dialysis adequacy, and who did not receive any ICMA following the assessments. Patients with <2 months PD follow-up, a 24 h urine clearance of <200 ml or an RRF <2 ml/min/1.73 m² were excluded from the trial. Other exclusion criteria were the following: the occurrence of peritonitis in the 3 month period prior to the study, any modifications in hypertensive and dialysis treatment during the month preceding ICMA or between two RRF assessments, or the patient’s refusal to participate in the trial. To evaluate RRF status at baseline, the following data were recorded for each patient: age, sex, blood pressure (BP), body mass index (BMI), PD method (APD vs CAPD), daily proteinuria, drugs such as ACEI, ARB, calcium channel blocker and diuretics, the possible presence of diabetes and primary renal disease. The latter was diagnosed on the basis of clinical, laboratory, radiological and histological findings. CAPD patients received 3-4 exchanges of 21/day. All APD patients received an 8-10 h nightly regime with one additional 2 l exchange daily for continuous cyclic peritoneal dialysis (CCPD). Radiological investigation was carried out, and the volume and type of iodinated radiocontrast agent (RCA) were also recorded.

Methods

RRF, urine volume and peritoneal creatinine clearance (PcrCl) analyses were quantified on an out-patient basis 24 h before and 2 weeks after each ICMA (i.e. 36 injections for the ICMA group compared with none for the control group); over the same time period, these values were evaluated once during the systematic biannual measurement of dialysis adequacy and also 2 weeks after this assessment in the non-ICMA control group. To ensure adequate clinical hydration, all ICMA patients were hospitalized 24 h before ICMA and received 11 l of saline intravenously (i.v.) during the 12 h preceding ICMA and after RRF and PcrCl assessment. PD was temporarily discontinued only during abdominal computed tomography angiography (CTA) or femoral vascular access. The type and dosage of oral drugs and PD treatment method were not modified during the study. RRF was quantified as the average of 24 h urinary urea and creatinine clearance [16]. PcrCl was estimated from the total volume of the 24 h dialysate and creatinine levels in the blood following 24 h of dialysis. RRF and PcrCl were normalized to 1.73 m² body surface area and expressed as ml/min/1.73 m² and l/week/1.73 m², respectively.

The primary aim was to determine the differences in RRF prior to and 2 weeks after ICMA, and also the differences in daily urine volume. Differences in PcrCl at 2 weeks were evaluated to confirm the analysis of RRF and daily urine volume levels.

Statistical analysis

Data were expressed as mean±SD for quantitative values and as percentages for qualitative values. For baseline characteristics, quantitative values were compared using the Student’s t-test, and qualitative values were assessed by chi² test. The differences at 2 weeks in values for each group for...
RRF, daily urine volume and PcrCl levels were analysed for significance by paired t-test. The power of the study was 85%, to reveal a mean difference of 0.5 ml/min/1.73 m² RRF after ICMA.

Variations at 2 weeks in RRF, daily urine volume and PcrCl between the two groups were analysed for significance by analysis of variance (ANOVA). All P-values were two-tailed, and values < 0.05 were considered as being statistically significant. Statistical analysis was performed using SPSS statistical software (version SPSS 11.5; SPSS Inc., Chicago, IL).

**Results**

Table 1 shows the baseline characteristics for the study population. No difference in potential factors that might influence RRF was found between the two groups although there was a significant difference between the two groups for patient age, i.e. subjects in the ICMA group were older than those in the control group (Table 1). Here it should be pointed out that in the literature, older age has been reported as a risk factor for contrast medium-induced nephropathy, although it has not been found to be a prognostic factor for accelerated RRF decline in PD patients [7,11].

Table 2 provides a summary of primary kidney diseases in the study population, from which it can be seen that there were no significant differences between the two groups.

Thirty-six ICMA were undertaken for diagnostic purposes, and included the following: 17 coronary angiographies, 10 angiographies of the iliac arteries and lower extremities, four abdominal and four aortorenal CTAs, and one thoracic angiography. Of these 36 investigations, six included interventional procedures consisting of four percutaneous transluminal angioplasties (PTAs) of the coronary arteries with stenting, and two peripheral PTAs of lower limb arteries.

The mean ICMA volume amounted to 104 ± 55 ml. No adverse effects were noted, and all saline perfusions were well tolerated. In 27 cases, the agent used for ICMA was iodixanol, an iso-osmolar non-ionic dimeric agent, and in nine cases iohexol, a low-osmolarity non-ionic monomeric agent.

**Table 1. Baseline characteristics of the study population**

<table>
<thead>
<tr>
<th>Patient (n)</th>
<th>ICMA group</th>
<th>Control group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; mean ± SD)</td>
<td>60 ± 13</td>
<td>54 ± 14</td>
<td>0.02</td>
</tr>
<tr>
<td>Sex ratio (M/F)</td>
<td>25:36</td>
<td>16:36</td>
<td>0.6</td>
</tr>
<tr>
<td>Duration of PD (months; mean ± SD)</td>
<td>16 ± 23</td>
<td>16 ± 13</td>
<td>0.9</td>
</tr>
<tr>
<td>APD (n; %)</td>
<td>4 (11)</td>
<td>6 (17)</td>
<td>0.35</td>
</tr>
<tr>
<td>Diabetes type 1 or 2 (n; %)</td>
<td>18 (50)</td>
<td>16 (44)</td>
<td>0.2</td>
</tr>
<tr>
<td>BMI (kg/m²; mean ± SD)</td>
<td>24.8 ± 4</td>
<td>25.2 ± 4</td>
<td>0.7</td>
</tr>
<tr>
<td>SBP (mmHg; mean ± SD)</td>
<td>133 ± 15</td>
<td>132 ± 13</td>
<td>0.9</td>
</tr>
<tr>
<td>DBP (mmHg; mean ± SD)</td>
<td>74.5 ± 9.6</td>
<td>77.8 ± 11.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Loop diuretics (n; %)</td>
<td>36 (100)</td>
<td>36 (100)</td>
<td>1</td>
</tr>
<tr>
<td>ACEI or ARB (n; %)</td>
<td>28 (78)</td>
<td>31 (86)</td>
<td>0.6</td>
</tr>
<tr>
<td>Calcium channel inhibitor (n; %)</td>
<td>8 (22)</td>
<td>9 (25)</td>
<td>1</td>
</tr>
<tr>
<td>24 h proteinuria (g; mean ± SD)</td>
<td>0.7 ± 0.77</td>
<td>0.9 ± 0.9</td>
<td>0.3</td>
</tr>
<tr>
<td>Initial RRF (ml/min/1.73 m²; mean ± SD)</td>
<td>7.07 ± 4.3</td>
<td>6.5 ± 3.6</td>
<td>0.5</td>
</tr>
<tr>
<td>Initial urine output (ml/day; mean ± SD)</td>
<td>1324 ± 696</td>
<td>1625 ± 779</td>
<td>0.8</td>
</tr>
<tr>
<td>Initial PcrCl (l/week/1.73 m²; mean ± SD)</td>
<td>41.1 ± 9</td>
<td>36 ± 10</td>
<td>0.1</td>
</tr>
</tbody>
</table>

ICMA, iodinated contrast medium administration; APD, automated peritoneal dialysis; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; PcrCl, peritoneal creatinine clearance; RRF, residual renal function.

**Table 2. Primary kidney disease**

<table>
<thead>
<tr>
<th>Disease</th>
<th>ICMA group n (%)</th>
<th>Control group n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephrosclerosis</td>
<td>12 (33)</td>
<td>11 (30.5)</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>16 (44.5)</td>
<td>13 (36)</td>
</tr>
<tr>
<td>Glomerulopathy</td>
<td>4 (11)</td>
<td>6 (17)</td>
</tr>
<tr>
<td>Chronic interstitial disease</td>
<td>2 (5.5)</td>
<td>4 (11)</td>
</tr>
<tr>
<td>Unknown aetiology</td>
<td>2 (5.5)</td>
<td>2 (5.5)</td>
</tr>
</tbody>
</table>

**Table 1. Baseline characteristics of the study population**

**Table 2. Primary kidney disease**
Discussion

Over the last decade, there has been increasing focus on RRF in chronic PD patients, and the preservation of RRF is now considered to be an important predictor of outcome in this patient population [7]. In our study, the analysis of RRF in 36 stable PD patients, prior to and 2 weeks after ICMA, failed to demonstrate that ICMA led to a decline in RRF compared with the results for a control group. The power of this study was > 80% to reveal a mean difference of 0.5 ml/min/1.73 m² RRF over a 2 week period, which limits the type 2 error.

We did not evaluate RRF levels 48–72 h post-ICMA, a procedure which is normally used in the general population to investigate the short-term effect, i.e. the possible presence of contrast media-induced nephropathy. This decision was made in order to better evaluate over the medium term the possible effect of ICMA on the evolution of RRF. In spite of the reported day to day variation in RRF in PD patients, in our study the RRF assessments showed that RRF remained stable in both the ICMA and the control group [7].

In the literature, older age, diabetes and low RRF have been identified as risk factors for decreased renal function following contrast agent administration. However, in the ICMA group in the present study, which included 50% diabetic PD patients with decreased RRF and who were of older age, these findings were not corroborated.

ACEI and ARB administration is known to have a positive effect on preserving RRF, but can also alter residual glomerular filtration rate (GFR) during pathological states such as dehydration or renal macro- and

---

**Fig. 1.** Evolution of RRF, daily urine volume and PcrCl 2 weeks post-ICMA in the contrast medium-treated group and after 2 weeks in the non-ICMA group. Compared with baseline, there was no significant variation in RRF, daily urine volume or PcrCl (7.07 ± 4.3 vs 7.20 ± 4.3 ml/min/1.73 m², *P* = 0.12; 1324 ± 696 vs 1360 ± 755 ml/day, *P* = 0.5; and 41.1 ± 9 vs 40.6 ± 9 l/week/1.73 m², *P* = 0.6, respectively) in the ICMA study group 2 weeks after treatment, or in the control group for RRF, daily urine volume or PcrCl (6.5 ± 3.6 vs 6.62 ± 3.6 ml/min/1.73 m², *P* = 0.12; 1625 ± 779 vs 1665 ± 862 ml/day, *P* = 0.64; and 41 ± 9 vs 40.6 ± 9 l/week/1.73 m², *P* = 0.5, respectively).
micro-perfusion. To avoid a decrease in GFR, it is recommended to discontinue loop diuretics, and ACEI or ARB administration over the period of ICMA in the general patient population [17]. ACEI or ARB treatment is extremely common in our PD unit, as we consider that these drugs have a positive effect on the preservation of RRF and a positive vascular effect in diabetic patients. Loop diuretics are systematically introduced early on to favour a larger daily urine volume. However, in this study, no modification in the treatment schedule was made for any of the patients.

In the ICMA group, it is possible that the absence of alteration in RRF following ICMA could be explained by optimized i.v. hydration before each injection, but also by the stable haemodynamic state of these PD patients, and the systematic use of loop diuretics.

To avoid the risk of nephrotoxicity, one of the recommendations is to administer a minimum volume, i.e. <200 ml of iodinated contrast medium per radiological investigation [14]. Our institution has also adopted this recommendation, and close teamwork has been established between nephrologists, radiologists and cardiologists aimed at achieving minimum ICMA, particularly by omitting a ventriculogram at coronary angiography, which is not systematically required in this particular patient population.

The influence of PD technique on the preservation of RRF has been controversially reported in the literature, and has been identified as being associated with a more rapid decline of RRF [18]. In our study, a subgroup consisting of APD patients (four ICMA vs six non-ICMA subjects) on CCPD displayed stable levels of RRF 2 weeks following ICMA and at the same time point in the control group, respectively, but the number of patients was too limited for the data to be analysed.

In another subgroup of diabetic patients, 2 weeks after ICMA the evolution of RRF did not differ significantly between the ICMA group and the non-ICMA group (i.e. 18 ICMA vs 16 non-ICMA control subjects; data not shown).

Last-generation iodinated contrast medium was used preferentially in the present study, as it is associated with significantly reduced nephrotoxicity in patients with chronic kidney disease [19]. We did not find any significant variation in RRF after 2 weeks in the ICMA subgroups in which iso-osmolar and hypo-osmolar contrast agent was used; data not shown [19].

Cardiovascular disorders are frequently associated with end-stage renal disease, and it is thus vital to make an evaluation of the PD patient’s vascular status before performing kidney transplantation. As first-line investigation, magnetic resonance imaging (MRI) should be carried out, as it ensures an absence of nephrotoxicity if low amounts of gadolinium (Ga) contrast agent is used. However, MRI is not feasible in patients with pacemakers and metal implants, and is not consistently the most reliable of methods for the investigation of vascular or digestive disorders. As far as coronary angiography is concerned, MRI is still under investigation. The use of CTA rather than MRI can be justified by its more widespread availability, its better spatial resolution and its capacity to detect vascular calcification [20].

A reanalysis of the CANUSA study reported worse patient survival associated with a decline in RRF, which could partly be due to the decreased clearance of small and larger molecular weight uraemic toxins and also to the impaired renal contribution to the maintenance of euvoaemia [2].

The preservation of RRF is an important aim, and in the present work we have shown that ICMA can be safely used under optimal treatment conditions in stable PD patients, i.e. with contrast medium administered at a minimum dose and with adequate pre-hydration of ICMA patients without the risk of an accelerated decline in RRF.

Conflict of interest statement. None declared.

References

in patients 70 years of age or older. A prospective study. Arch Intern Med 1990; 150: 1237–1242

Received for publication: 4.8.05
Accepted in revised form: 18.11.05