Dialysis improves endothelial function in humans

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Abstract

Background. Circulating inhibitors of endothelial function have been implicated in the pathogenesis of vascular disease in chronic renal failure. The aim of this study was to determine if lowering the plasma concentration of these and other dialysable toxins improves endothelial function. To do this we compared the acute effects on endothelial function of single episodes of haemodialysis with automated peritoneal dialysis. We hypothesized that endothelial function would improve after dialysis, with a greater effect seen after haemodialysis due to more substantial clearance of endothelial toxins per-treatment.

Methods. Subjects with end-stage renal failure undergoing haemodialysis (n=16) or automated peritoneal dialysis (n=14) were investigated. Endothelial function was determined using vascular ultrasound to measure flow-mediated dilatation of the brachial artery and was compared with the dilatation caused by sublingual glyceryl trinitrate. Endothelial function was assessed before and after a single dialysis treatment. Plasma concentrations of the inhibitors of endothelial function, asymmetric dimethyl-l-arginine and homocysteine were measured. Flow-mediated dilatation was expressed as percentage change from basal diameter and analysed using Student’s t test.

Results. The plasma concentration of circulating inhibitors of endothelial function was reduced after haemodialysis but not peritoneal dialysis. Haemodialysis increased flow-mediated dilatation from 4.0 ± 1.0% to 5.8 ± 1.2% (P < 0.002). These changes persisted for 5 h but returned to baseline by 24 h. Automated peritoneal dialysis had no acute effect on flow-mediated dilatation (5.9 ± 1.1% vs 5.4 ± 0.8% after, P > 0.5). There were no effects of either dialysis modality on dilatation to glyceryl trinitrate.

Conclusions. Short-term reduction of circulating inhibitors of endothelial function by haemodialysis is associated with increased flow-mediated dilatation. These data suggest that dialysable endothelial toxins have deleterious effects on endothelial function that are rapidly reversible.

Keywords: atherosclerosis; endothelial function; hypertension; renal failure; nitric oxide

Introduction

Patients with renal failure have increased cardiovascular risk due to the development of atherosclerosis and its complications. One pathogenic mechanism that might contribute to cardiovascular risk in these patients is endothelial dysfunction. Under physiological conditions, the endothelium synthesizes mediators, including nitric oxide (NO), that have dilator, anti-thrombotic and anti-atherosclerotic properties. Endothelial dysfunction and reduced NO bioactivity occur in patients on haemodialysis (HD) [1], peritoneal dialysis [2] and in those with chronic renal failure prior to the introduction of renal replacement therapy [3]. These studies suggest a possible causal role for endothelial dysfunction, in particular reduced NO bioactivity, in the pathogenesis of vascular disease in these patients.

Endothelial dysfunction in renal failure could be a consequence of accumulation of inhibitors of endothelial function. Water-soluble, dialysable substances (uraemic toxins) have been implicated in the organ dysfunction of renal failure for over 180 years, and their removal by dialysis is thought to account for many of the beneficial effects of renal replacement therapy. Of the many different molecules that have been proposed as possible uraemic toxins [4], some have the potential to inhibit endothelial function, including N¹N¹-dimethyl-l-arginine (asymmetrical dimethylarginine,
ADMA, an inhibitor of endothelial NO production, and homocysteine (tHcy, which directly damages the endothelium and may inactivate NO). If the effects of these, and other as yet unidentified endothelial toxins, were rapidly reversible then their clearance by dialysis would be expected to improve endothelial function. To test this hypothesis, we compared the acute effects of single episodes of haemodialysis with automated peritoneal dialysis on endothelial function. Peritoneal dialysis session, haemodialysis results in larger, more rapid reductions in dialysable compounds than automated peritoneal dialysis (APD). Our hypothesis predicts that endothelial function would fluctuate with clearance of endothelial toxins, with the greatest changes caused by haemodialysis.

Subjects and methods

Subjects

We prospectively studied two groups of adults with end stage renal failure, 16 (8 male) receiving HD and 14 (7 male) receiving APD. Outpatients receiving renal replacement therapy for at least 3 months were recruited. Exclusion criteria included diabetes, age > 70 years, smoking and a fasting cholesterol exceeding 6 mmol/l (recognized independent risk factors for impaired endothelial function). Between 60 and 70% of subjects in both groups were hypertensive with a mean arterial pressure > 100 mmHg despite concurrent treatment with an average of two antihypertensive agents (Table 1). Subjects taking nitrates discontinued therapy 48 h prior to the study but other regular medications were continued. HD patients received dialysis for 4 h three times per week using a cellulosynthetic membrane (Hemophan) and freshly prepared bicarbonate buffer. Dialysate quality was within Renal Association (UK) guidelines (<0.03 endotoxin units/ml and <8 viable bacterial units/ml). Dialysate temperature was maintained at 37°C throughout. A mean of 2.2±0.3 kg was removed during HD (Table 2), 1 kg of fluid was ultrafiltered in the first hour of haemodialysis and the remainder was removed evenly over the dialysis session to achieve the subjects prescribed dry weight. Patients treated with overnight APD received a mean of 12±3 l exchanges (range 10–15 l) using a combination of 1.36, 2.27 and 3.86% PD fluid (Homechoice, Baxter, UK). The study was approved by the local research ethics committee and all subjects provided written informed consent.

Assessment of endothelial function

Endothelial function was determined by recording the dilator response of the brachial artery to increased blood flow generated during reactive hyperaemia of the downstream forearm. Subjects were asked to lie supine in a temperature-controlled laboratory (22–25°C). The brachial artery of the non-fistula (patients on HD) or non-dominant arm was scanned in longitudinal section using a 7 MHz linear array transducer and a XP 128/10 (Acuson), magnified using a resolution box function and gated with the R wave of the ECG. End-diastolic images of the artery were acquired every 3 s using data-acquisition software (Information Integrity, Boston, USA) and stored off-line for later analysis. Arterial diameter over a 1–2 cm segment was determined for each image using automatic edge detection software (Information Integrity, Boston, USA). Analysis was performed by an experienced vascular technician blinded to the subject and order and repeated by a second investigator in a random selection of one third of scans. Blood flow in the brachial artery was recorded continuously throughout the study using pulsed wave doppler. Baseline recordings of arterial diameter in the upper arm were made for one minute before inflation of a blood pressure cuff placed just distal to the elbow. Recording continued for 5 min during cuff inflation to 300 mmHg and for 4 min after deflation. Endothelium-independent dilatation of the brachial artery was assessed by measuring the dilator response to a submaximal dose of the NO donor, glycercyl trinitrate (GTN, 25 μg sublingually), which elicited vascular dilatation of the same order of magnitude as that of the endothelium-dependent flow stimulus. This is important because larger doses of GTN may fail to discriminate between subtle differences of intrinsic smooth muscle reactivity. Mean arterial blood pressure was recorded using an automated oscillometric system (Critikon, Dinamap vital signs monitor 18468X). Readings were taken before and after each scan using the non-study arm or the calf (in the presence of a fistula).

Effect of haemodialysis on brachial artery reactivity

Endothelial function was assessed in HD patients immediately before and after dialysis (n=16), and then sequentially at 5 h (n=11), 7 h (n=7) and 24 h (n=6) after completion of the treatment. In both groups there was a significant drop-out rate at later time points, reflecting the inconvenience to these patients of repeatedly measuring endothelial function. Time-control studies were performed in 5 HD subjects on a non-dialysis day at the pre- and post-dialysis time points.

Effect of APD on brachial artery reactivity

Endothelial function was assessed in APD patients immediately before and after dialysis and then sequentially at 2 h (n=14), 5 h (n=13) and 24 h (n=9) after completion of a dialysis session.

Table 1. Subject’s antihypertensive medication profile

<table>
<thead>
<tr>
<th>Drugs</th>
<th>HD n (%)</th>
<th>PD n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>α adrenergic blocker</td>
<td>7 (44)</td>
<td>5 (36)</td>
</tr>
<tr>
<td>β adrenergic blocker</td>
<td>10 (63)</td>
<td>7 (50)</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>6 (38)</td>
<td>9 (64)</td>
</tr>
<tr>
<td>ACE I</td>
<td>9 (56)</td>
<td>5 (36)</td>
</tr>
<tr>
<td>Minoxidil</td>
<td>1 (6)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Fruseamide</td>
<td>1 (6)</td>
<td>3 (21)</td>
</tr>
<tr>
<td>Mean antihypertensives per subject</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Data are expressed as absolute number (percentage of whole group). There were no significant differences between the HD and APD groups in medications (P=0.9, Fischer’s exact test). ACE I, angiotensin converting enzyme inhibitor.
Effect of volume expansion on brachial artery reactivity

To determine whether intravascular volume changes might directly alter endothelial function, the effect of volume expansion on brachial artery reactivity was assessed in 7 healthy volunteers, drawn from hospital staff, who were normotensive, non-smokers with a mean fasting plasma cholesterol of 3.9 ± 0.2 mg/dl. Subjects were volume loaded with 11 l of 0.9% saline (w/v) infused intravenously over 30 min. Diameter changes and flow-mediated dilatation (FMD) of the brachial artery were assessed immediately before and after saline infusion.

Biochemical measurements

Blood samples were taken before and after dialysis for analysis of haemoglobin, haematocrit, total cholesterol, creatinine, potassium, glucose and C reactive-protein (CRP). L-Arginine and ADMA were measured by reverse phase high pressure liquid chromatography (HPLC) as described previously [5]. Total plasma homocysteine (tHcy) was measured by ion-exchange chromatography using a Biochrom 20 amino acid analyzer (Pharmacia Biotech, Cambridge, UK) and a high resolution lithium column with a standard physiological separation programme as described previously [6].

Calculations and statistics

The flow stimulus generated by reactive hyperaemia was expressed as the velocity time integral (VTI, the area under the blood velocity/time curve for a complete cardiac cycle) recorded at pre-specified time points at baseline, 5 s after cuff release and subsequently at 15 s intervals for 90 s. FMD was expressed as the percentage change from baseline diameter of the brachial artery (mean ± SEM) and analysed by comparing both the maximal dilatation (mean of three consecutive observations) and the area under the curve (AUC, units of %/min) of dilatation against time. Data were analysed using two-tailed Student’s t test or by analysis of variance of repeated measures as appropriate. Significance was assumed at P < 0.05 (Graph Pad Prism statistical package).

Results

The HD and APD groups were well matched for cardiovascular risk factors (Table 2). No studies were excluded on the basis of technical inadequacy (inter-observer variability of FMD < 1%).

Table 2. Patient clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>HD (n = 16)</th>
<th>APD (n = 14)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43 ± 3.5</td>
<td>44 ± 2.7</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>8/8</td>
<td>7/7</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Months on dialysis</td>
<td>59 ± 14</td>
<td>49 ± 22</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>4.2 ± 0.2</td>
<td>4.2 ± 0.3</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Arterial pressure (mmHg)</td>
<td>108 ± 4.6</td>
<td>102 ± 5.6</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>10.0 ± 0.3</td>
<td>10.7 ± 0.5</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>Weight loss during dialysis (kg)</td>
<td>2.2 ± 0.3</td>
<td>1.8 ± 0.7</td>
<td>&gt; 0.2</td>
</tr>
</tbody>
</table>

The effects of dialysis on brachial artery reactivity

Baseline arterial diameter, blood pressure and heart rate were similar in the HD and APD subjects (data not shown). Arterial diameter during baseline recording was identical before and after both HD and APD (Table 3). HD did not change mean arterial blood pressure (113.9 ± 3.5 mmHg vs 108.6 ± 3.7 mmHg, P = 0.1) or diastolic blood pressure (80.7 ± 2.9 mmHg vs 79.8 ± 2.5 mmHg, P = 0.7) but reduced systolic blood pressure (169.6 ± 4.9 mmHg vs 158.2 ± 5.0 mmHg after HD, P = 0.02). In the APD group, mean arterial pressure (102.7 ± 2.8 mmHg vs 101.6 ± 3.4 mmHg, P = 0.5) and systolic pressure (136.2 ± 3.7 mmHg vs 134.1 ± 4.0 mmHg, P = 0.2) remained constant after dialysis. However, diastolic pressure fell (80.0 ± 2.9 mmHg vs 77.0 ± 2.8 mmHg, P = 0.03). The flow stimuli generated during reactive hyperaemia were similar in both groups before and after treatment (AUC 15.9 ± 2.1 ms vs 15.3 ± 2.3 ms for HD, P = 0.5; 17.1 ± 2.1 ms vs 18.8 ± 2.7 ms for APD, P = 0.5). FMD was increased by HD (4.0 ± 1.0% vs 5.8 ± 1.2%, P < 0.002; Figure 1a) but remained unchanged following APD (5.7 ± 1.1% vs 5.4 ± 0.8%, P > 0.5; Figure 1b). Similarly, the area under the dilatation time curve increased after HD (466 ± 84% vs 657 ± 116%, P < 0.05; Figure 1c) but remained unchanged after APD (638 ± 107% vs 633 ± 111%, P > 0.9; Figure 1d). There were no significant changes in endothelium-independent dilatation in response to GNT after HD (5.9 ± 1.0% vs 6.4 ± 1.1%, P > 0.5; Figure 1a) or APD (6.3 ± 1.2% vs 7.3 ± 1.2%, P > 0.5; Figure 1b). The improvement in FMD after completion of HD persisted for at least 5 h but returned to baseline by 24 h (Figure 2a). Pre-treatment FMD was lower in the HD compared with the APD group (4.0 ± 1.0% vs 5.7 ± 1.1%, respectively; Figure 2a and b), but this did not reach statistical significance (P = 0.2). In 5 patients assessed on a non-dialysis day, there were no time-dependent changes in FMD in the absence of dialysis (4.1 ± 0.7% vs 3.8 ± 1.4% 4 h later, P > 0.5) or GNT dilatation (5.7 ± 1.0% vs 5.5 ± 0.8% 4 h later, P > 0.5).

The effect of changes in plasma volume on brachial artery reactivity

In 7 healthy volunteers, volume expansion had no effect on baseline arterial diameter (3.5 ± 0.3 mm vs 3.5 ± 0.3 mm, P > 0.2), FMD (3.3 ± 0.9% vs 6.3 ± 1.4%,
Table 3. Effects of dialysis on measured parameters

<table>
<thead>
<tr>
<th></th>
<th>HD</th>
<th></th>
<th>P value</th>
<th>APD</th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td></td>
<td>Pre</td>
<td>Post</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>9.7 ± 0.4</td>
<td>9.2 ± 0.5</td>
<td>0.1</td>
<td>11.2 ± 1</td>
<td>11.2 ± 1</td>
<td>0.1</td>
</tr>
<tr>
<td>Haematocrit (mmol/l)</td>
<td>0.30 ± 0.01</td>
<td>0.31 ± 0.01</td>
<td>0.1</td>
<td>0.35 ± 0.02</td>
<td>0.35 ± 0.02</td>
<td>0.3</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>4.2 ± 0.2</td>
<td>3.75 ± 0.3</td>
<td>0.5</td>
<td>4.2 ± 0.4</td>
<td>3.9 ± 0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Urea (mmol/l)</td>
<td>26.4 ± 1.2</td>
<td>9.1 ± 0.6</td>
<td>0.001</td>
<td>21.1 ± 2.4</td>
<td>19.7 ± 2.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Creatinine (μmol/l)</td>
<td>842 ± 46</td>
<td>356 ± 29</td>
<td>&lt; 0.0001</td>
<td>977 ± 59</td>
<td>956 ± 59</td>
<td>0.2</td>
</tr>
<tr>
<td>ADMA (μmol/l)</td>
<td>0.68 ± 0.1</td>
<td>0.43 ± 0.06</td>
<td>&lt; 0.001</td>
<td>0.49 ± 0.1</td>
<td>0.49 ± 0.05</td>
<td>0.9</td>
</tr>
<tr>
<td>Arginine (μmol/l)</td>
<td>35.6 ± 4.7</td>
<td>32.8 ± 4.5</td>
<td>0.6</td>
<td>45.1 ± 12</td>
<td>51.3 ± 12</td>
<td>0.9</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>5.0 ± 0.3</td>
<td>4.9 ± 0.3</td>
<td>0.7</td>
<td>4.7 ± 0.2</td>
<td>4.5 ± 0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>tHcy (μmol/l)</td>
<td>38.3 ± 5.9</td>
<td>23.4 ± 3.0</td>
<td>&lt; 0.001</td>
<td>52.4 ± 15</td>
<td>45 ± 13</td>
<td>0.6</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>12.0 ± 4.2</td>
<td>12.1 ± 4.6</td>
<td>0.5</td>
<td>11.5 ± 4.2</td>
<td>9.8 ± 4.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Baseline arterial</td>
<td>4.3 ± 0.2</td>
<td>4.2 ± 0.2</td>
<td>0.2</td>
<td>4.4 ± 0.2</td>
<td>4.6 ± 0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>diameter (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

Values are mean ± SEM.

Fig. 1. The effect of dialysis on FMD. (a) HD increased FMD but did not alter dilatation to GTN. (b) APD had no effect on FMD or dilatation to GTN. (c) and (d) The profile of FMD for the 4 min period after cuff release is shown for HD and APD. Analysis of area under the dilatation time curves showed improvement after HD (n = 16) but not APD (n = 14).

\( P > 0.2 \), or flow profiles (14.3 ± 2.3 ms vs 14.6 ± 2.46 ms, \( P = 0.5 \)).

The effects of dialysis on plasma biochemistry

HD significantly reduced the plasma concentration of ADMA and tHcy (Table 3). Plasma l-arginine concentration was unaltered by HD (\( P > 0.5 \)), but the ADMA/l-arginine ratio fell significantly after HD (\( P < 0.03 \)). APD did not significantly reduce the plasma concentrations of ADMA, l-arginine or tHcy (Table 3), although levels of methylarginines were lower and tHcy higher than those seen in the HD group. HD resulted in a greater immediate reduction
in plasma creatinine and urea compared with APD but neither treatment affected the plasma concentration of haemoglobin, CRP, glucose, or total cholesterol (Table 3).

Discussion

The purpose of this study was to test the hypothesis that clearance of circulating inhibitors of endothelial function by dialysis improves arterial endothelial function. A single haemodialysis treatment caused rapid clearance of uraemic markers and endothelial toxins, and transiently increased FMD. In comparison, a single APD treatment caused only small changes in these substances and did not acutely alter FMD. Neither treatment altered smooth muscle responsiveness to GTN. These data suggest that acute reduction of the concentration of circulating inhibitors of endothelial function associated with uraemia improves endothelial function in the arterial vasculature.

Dialysis relieves the symptoms of uraemia by removing low to middle molecular weight molecules and the therapeutic effect of renal replacement therapy indicates that these substances contribute to the pathophysiology of chronic renal failure. A variety of candidate toxins have been proposed including products of amino acid and protein metabolism [4]. These include the guanidino compounds ADMA, methylguanidine, and N\(^4\)-monomethyl-L-arginine (LNMMMA) that are excreted by the kidney, and homocysteine, a product of methionine metabolism that requires renal clearance. ADMA, methylguanidine and LNMMMA are inhibitors of NO synthesis and have been shown to reversibly block endothelium-dependent relaxation in vitro and in vivo [7,8]. Homocysteine has been implicated in the generation of oxidative free radicals that might impair endothelial function through inactivation of NO [9]. The accumulation in uraemia of endothelial toxins could contribute to the impaired NO-mediated dilatation reported in patients with renal failure [5].

In the present study, we used FMD of human conduit arteries to assess NO-mediated endothelial function. Dilatation of human conduit vessels is dependent on NO synthesis in the brachial, and coronary vascular beds, because dilatation in response to flow is reduced by inhibitors of NO synthesis [10]. In the present study there was a 45% increase in FMD of the brachial artery after treatment with HD, along with a reduction in plasma concentration of ADMA, homocysteine, creatinine and urea. In contrast, a single treatment with APD had no effect on uraemic markers or FMD. Moreover, there was a strong positive correlation between the reduction in plasma creatinine and increase in FMD (\(r = 0.5, P = 0.01\)) consistent with the concept that removal of dialysable endothelial toxins improves endothelial function.

The present study does not provide data to support a direct role for ADMA or homocysteine in the determination of FMD before and after dialysis. There was no correlation between the plasma concentration of these substances and FMD, which might be explained by the relatively low numbers of patients studied, confounding by other unidentified dialysable inhibitors of endothelial function, or a non-linear relationship between plasma concentration and FMD. Rather, the data support the hypothesis that the total burden of circulating inhibitors contributes to impaired conduit artery function in renal failure.

There are other possible explanations for our observations. HD was associated with a modest, though statistically insignificant increase in haematocrit (Table 3). It is difficult to predict the effect of increased haematocrit on FMD, which could augment FMD by increasing blood viscosity and luminal shear stress, or reduce FMD through increased NO scavenging by haemoglobin. Perhaps because of these opposing effects, blood transfusion to increase haemoglobin does not alter FMD in humans [11] and we think it unlikely that the small changes in haematocrit that we recorded contributed to the increase in FMD after HD. Both dialysis treatments caused similar weight loss, suggesting that changes in blood volume did not explain the increase in FMD observed after

Fig. 2. The effect of dialysis on the 24 h time course of FMD. (a) FMD remained elevated for 5 h after completion of haemodialysis but had returned to baseline levels by 24 h. (b) There were no changes in FMD after automated peritoneal dialysis.
HD. This conclusion is further supported by the observation that rapid volume expansion does not alter FMD in healthy volunteers. Elevation of core body temperature during HD (due to peripheral vasoconstriction and reduced heat loss) has been implicated in increased NO production and dialysis associated hypotension [12]. This is unlikely to explain the increase in FMD that we observed because there were no changes in basal forearm blood flow or basal arterial diameter after HD. Although mean arterial blood pressure did not change in the present study, there was a reduction in systolic pressure following HD that could alter FMD. However, the relationship between endothelial function and short-term changes in blood pressure is unclear [13,14], and systolic blood pressure changes did not correlate with change in FMD. The profile of antihypertensive medication was similar between the two groups (Table 1) and unlikely to explain the differential effects of dialysis on endothelial function. Other factors known to affect endothelial function such as plasma glucose, CRP and cholesterol were unaffected by either mode of dialysis.

Our findings contrast with a previous report demonstrating that HD is detrimental to FMD of the brachial artery, an effect ascribed to oxidative stress associated with dialysis [15]. This discrepancy might be explained by methodological differences, including the use of less biocompatible and potentially more pro-oxidant cellulose membranes in that study. Whilst further work is necessary to resolve these discrepancies, our results are consistent with the demonstration that HD improves endothelium-dependent dilatation in hand veins [16].

Our data do not suggest that APD is a less effective form of dialysis. Indeed the APD group had slightly greater baseline FMD than the HD group, although this did not reach statistical significance, probably because of the relatively small number of patients studied. This difference was not explained by baseline differences between the two groups in known determinants of endothelial function. It is possible that the higher pre-treatment FMD in the APD group indicates that the APD dialysis schedule maintains endothelial function without rebound between treatments, at a level that HD only achieved for the few hours immediately after a dialysis session. This conclusion is supported by previous studies where FMD of the brachial artery has been reported to be 5.7 ± 1% in patients on peritoneal dialysis [2] and between 3.5 ± 1.2% [17] and 3.7 ± 1.1% [1] in haemodialysis patients. Whether this effect of APD is mediated by a differential effect on the clearance of larger molecular weight toxins remains to be seen [18]. What is clear from this study is that HD is associated with greater swings in dialysable endothelial toxins and endothelial function when compared with APD.

In conclusion, there is increasing evidence that the presence of endothelial dysfunction reflects increased cardiovascular risk [19]. Our data show that endothelial dysfunction is present in uraemia and that it can be corrected acutely, if temporarily, by haemodialysis. These findings have implications for the concept of dialysis adequacy, particularly when therapy is directed towards reduction of cardiovascular morbidity and mortality in this high risk group.

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