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# SHORT REPORTS

## Peritoneal Transport Function and Endothelium-Dependent Vasodilation

Peritoneal dialysis (PD) patients display significant differences in peritoneal small solute membrane transport (SSMT) (1,2). It has been thought that transport magnitude is dependent upon the ratio of the perfusing vessels and peritoneal membrane surface areas. Local vessels' surface area and permeability may be submitted to endothelial control. Flow-mediated vasodilation (FMD), a surrogate indicator of endothelial-dependent vasodilation, may be estimated by high-resolution ultrasound of peripheral arteries. Reduced nitric oxide (NO) activity, altered endothelial-dependent vasodilation, and endothelial dysfunction have been reported in end-stage renal disease (ESRD) patients (3–6). Small solute membrane transport characteristics and abnormal peritoneal endothelial function may be related. The current study evaluated FMD in stable PD patients allocated to different categories of SSMT based on a peritoneal equilibration test (PET).

### PATIENTS AND METHODS

A cross-sectional study enrolled 31 clinically stable adult PD patients who were free of peritonitis for at least 1 month. Each participant was presented and signed an informed consent; the study protocol was approved by the hospital Research Ethics Committee. A standard PET following an overnight fasting period was used to evaluate SSMT (7,8). In order to allocate a comparable number of individuals to each SSMT category, quartiles of the 4-hour dialysate-to-plasma ratios of creatinine ($D_4$/P creat) were used to classify transport as low (0.39 – 0.50), low-average (0.52 – 0.60), high-average (0.62 – 0.71), and high (0.73 – 0.95). Additionally, the initial and final dialysate sample glucose concentrations were measured to calculate a timed glucose ratio ($D_4/D_0$ glucose). Dialysis adequacy was estimated by a normalized weekly urea clearance (Kt/V). Urea (urease method), creatinine (Jaffé reaction, undeproteinized), and glucose (glucose oxidase) determinations were performed by automated methods (Advia 1650; Bayer HealthCare, Tarrytown, New York, USA). Nitric oxide metabolites [nitrate and nitrite (jointly referred to as $NO_x$)] were measured by chemiluminescence (Nitric Oxide Analyzer, model 280; Sievers Ionics Instrument, Boulder, Colorado, USA) in deproteinized samples of serum obtained for Kt/V and PET estimates (serum, 4-hour and 24-hour dialysate). Duplicate calibration curves (1 – 100 μmol/L; $r = 0.9993$) were used, as previously described (9). Flow-mediated vasodilation was evaluated according to recommendations of the International Brachial Artery Reactivity Task Force, using a 7.0 MHz transducer (Model 128XP/10; Acuson, Mountain View, California, USA) (10,11).

Results are expressed as mean ± standard deviation, median and interquartile range, or percentage. Chi-square (or Fisher exact) test was used in comparisons. ANOVA with Duncan *post hoc* test was employed to localize differences. Associations were explored by Pearson's correlation coefficient and tendencies by linear regression analysis of untransformed and logarithm-transformed data. The software Statistical Package for Social Sciences (SPSS version 11.5; SPSS Inc., Chicago, Illinois, USA) for Windows operating system (Microsoft Corp., Redmond Washington, USA) was used overall.

### RESULTS

The study population characteristics are presented in Table 1. Brachial artery FMD and categories of SSMT are depicted in Table 2. No significant differences in pre-flow-occlusion vessel diameter or FMD among categories were found, albeit FMD in the low transport category seemed to be of greater magnitude. Linear tendency evaluation ($p = 0.052$ and $p = 0.062$ for untransformed and log-transformed data respectively) was also unable to demonstrate differences. Flow-mediated vasodilation was negatively correlated with the initial vessel diameter ($r = -0.443$, $p = 0.013$) and 4-hour ($r = -0.358$, $p = 0.048$) and 24-hour ($r = -0.393$, $p = 0.029$) peritoneal $NO_x$, and positively correlated with $D_4/D_0$ glucose ($r = 0.358$, $p = 0.048$).

### DISCUSSION

Flow-mediated vasodilation was evaluated along different SSMT categories. No significant differences were found, although FMD was higher in the *low* transport

TABLE 1
Study Population Characteristics (*n*=31)

| Variable | Value |
|---|---|
| Demographic | |
| Age (mean±SD) | 49±18 years |
| Female | 52% |
| Caucasian | 87% |
| Clinical | |
| Systolic BP (mean±SD) | 136±22 mmHg |
| Diastolic BP (mean±SD) | 85±16 mmHg |
| Treatment | |
| CAPD | 84% |
| Duration on dialysis [median (IQR)] | 23 (9–50) months |
| Daily ultrafiltration [median (IQR)] | 300 (200–400) mL |
| Residual diuresis [median (IQR)] | 200 (0–500) mL |
| Kt/V (mean±SD) | 1.86±0.33 |
| $D_4$/P creat (mean±SD) | 0.63±0.14 |
| $D/D_0$ glucose (mean±SD) | 0.54±0.11 |
| Biological | |
| $NO_x$ [median (IQR)] | 47 (31–84) µmol/L |
| $D_{4hr}$ [median (IQR)] | 33 (20–46) µmol/L |
| $D_{24hr}$ [median (IQR)] | 40 (23–59) µmol/L |

SD = standard deviation; BP = blood pressure; CAPD = continuous ambulatory peritoneal dialysis; IQR = interquartile range; Kt/V = normalized weekly urea clearance; $D_4$/P creat = dialysate-to-plasma ratios of creatinine; $D/D_0$ glucose = timed glucose ratio; $NO_x$ = serum nitric oxide metabolites; $D_{4hr}$ = 4-hour dialysate NO metabolites; $D_{24hr}$ = 24-hour dialysate NO metabolites.

category. Also, linear regression analysis was unable to unravel significant differences, suggesting that peritoneal membrane transport function and FMD may be unrelated in peritonitis-free patients on PD. Alternatively, the results could be the effect of other factors upon endothelial or peritoneal function, such as diet, levels of L-arginine and its analogs, blood pressure control and drugs, fluid status, presence of atherosclerosis, and the cause of renal failure. Reduced total NO production and impaired endothelial function were detected in ESRD and continuous ambulatory PD patients respectively (3,4,12), yet were apparently not linked to SSMT. Flow-mediated vasodilation was negatively correlated with 4-hour and 24-hour peritoneal $NO_x$, albeit not with serum $NO_x$. Lack of correlation between FMD and plasma NO has been reported in healthy individuals and in patients with systemic sclerosis (13,14). Apparently, correlation between brachial artery FMD and peritoneal NO levels has not been previously explored: no study in ESRD or dialysis patients could be found. The weak positive correlation between $D_4/D_0$ glucose and FMD may reflect a tendency to higher FMD in the *low* transport group. Negative correlation between FMD and resting artery diameter has been previously found in individuals with cardiovascular risk (11,15), yet a positive correlation has been observed in hemodialysis and PD patients, suggesting that other factors, dependent on dialysis or ESRD, may be contributory, but no such factors could be identified in the current study (5,11,16). In addition to vascular reactivity, other factors may affect SSMT. Nitric oxide-mediated peritoneal vascular changes may be local events, thus far undetectable from a distance (the brachial artery).

Results of the current study suggest that a relationship between peritoneal membrane transport function and endothelial-mediated vasodilation was not apparent in peritonitis-free patients on PD.

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TABLE 2
Brachial Artery Diameter Changes and Transport Categories (*n*=31)

| | PET categories | | | | | |
|---|---|---|---|---|---|---|
| | High (*n*=8) | High-average (*n*=9) | Low-average (*n*=8) | Low (*n*=6) | Total | *p* Value[a] |
| IAD (mm) | 3.7±0.6 | 4.3±0.8 | 3.9±0.6 | 3.6±0.5 | 3.9±0.7 | 0.119 |
| FMD (%) | 12.3 (1.6–14.2) | 13.5 (3.7–19.0) | 9.6 (4.5–14.2) | 19.8 (10.9–28.4) | 12.8 (5.1–17.8) | 0.070 |

PET = peritoneal equilibration test, classified by quartiles of small solute membrane transport; IAD = initial artery diameter; FMD = flow-mediated dilation.
[a] ANOVA, with *post hoc* Duncan.
Data are presented as mean±SD, or median (interquartile range 25–75).

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## Spectrum and Sensitivity Pattern of Gram-Negative Organisms Causing CAPD Peritonitis in India

Peritonitis remains the most important cause of morbidity and mortality in patients on continuous ambulatory peritoneal dialysis (CAPD), despite reductions in the rates in recent years (1). With improved quality of exit-site care, gram-negative bacteria have emerged as major organisms causing peritonitis. Antimicrobial use for gram-negative cover in the initial empirical treatment varies according to the spectrum of organisms causing peritonitis, as well as their sensitivity patterns. Hospitals worldwide are facing rapid emergence and spread of antimicrobial-resistant bacteria. For patients with end-stage renal disease (ESRD), this not only translates into prohibitive costs of hospitalization, but also increases morbidity and mortality (2). There is a general consensus in the medical community that antimicrobial resistance has emerged as an important variable influencing patient outcomes and overall resource utilization (3). We studied the spectrum and sensitivity patterns of gram-negative organisms causing peritonitis in ESRD patients on CAPD at a large tertiary-care public-sector hospital in India.

MATERIALS AND METHODS

Patients symptomatic with features suggestive of peritonitis between January 2000 and July 2004 were