Clearance of Magnesium in Peritoneal Dialysis Patients: A Single-Center Study

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Keywords

Peritoneal dialysis · Serum magnesium · Peritoneal dialysate magnesium concentrations · Clearance

Abstract

Objective: This retrospective study aimed to investigate the clearance of magnesium (Mg) in peritoneal dialysis (PD) patients and its influencing factors. **Methods:** The demographic information, clinical characteristics and laboratory data of the patients were collected. According to the corrected serum Mg (cS-Mg) concentration, patients were divided into 3 groups including hypomagnesemia ($\text{Mg}^{2+} < 0.77$ mmol/L, group A), normal serum Mg concentration ($0.77 \text{ mmol/L} \leq \text{Mg}^{2+} \leq 1.03$ mmol/L, group B), and hypermagnesemia ($\text{Mg}^{2+} > 1.03$ mmol/L, group C). **Results:** One hundred and fifteen patients were enrolled, and their mean 24 h-peritoneal Mg clearance was 39.75 ± 17.42 mg. The mean normalized peritoneal Mg clearance rate was 1.82 ± 0.82 L/day/1.73 m². Twenty-four-hour peritoneal Mg clearance of group A was significantly lower than that of group C ($p < 0.05$). Bivariate correlation analysis showed that cS-Mg was positively correlated with peritoneal dialysate Mg concentration ($p < 0.01$). cS-Mg was negatively correlated with the normalized peritoneal Mg clearance rate ($p < 0.05$). The normalized peri-

toneal Mg clearance rate was positively correlated with pre-albumin ($p < 0.05$), daily peritoneal protein loss ($p < 0.01$) and the normalized PD-creatinine clearance rate ($p < 0.01$). The normalized peritoneal Mg clearance rate was also negatively correlated with the normalized renal-creatinine clearance rate ($p < 0.01$). Furthermore, cS-Mg of patients with continuous ambulatory PD (CAPD) was significantly lower than that of patients with daytime ambulatory PD (DAPD, $p < 0.01$). The normalized peritoneal Mg clearance rate of patients with CAPD was significantly higher than that of patients with DAPD ($p < 0.01$). Moreover, among the patients with different peritoneal transport characteristics of peritoneal equilibration test, the normalized peritoneal Mg clearance rate of high average transport patients was significantly higher than that in those with low transport, low average transport and high transport ($p < 0.05$). **Conclusions:** Serum Mg could be partly cleared by PD. The peritoneal Mg clearance was positively related with serum Mg concentration, which was concentration-dependent. Peritoneal Mg clearance was negatively correlated with the residual renal function, while being positively correlated with the nutritional status and daily peritoneal protein loss. Peritoneal Mg clearance was higher in patients with high transport characteristics or CAPD.

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Introduction

Magnesium (Mg) is the fourth most abundant mineral in human body and the second most abundant in the intracellular space. Its homeostasis is maintained by intestine, bone, and kidneys. In patients with end-stage renal disease, losing the regulatory role of kidneys can significantly affect the balance of Mg. Both hypomagnesemia and hypermagnesemia have been correlated with all-cause mortality, cardiovascular mortality, and sudden death [1–4]. However, there were few studies about the peritoneal Mg clearance. Our study aimed to investigate the clearance of Mg in peritoneal dialysis (PD) patients and its influence factors.

Patients and Methods

Patients

PD patients who underwent urea kinetics or peritoneal equilibration test at our PD center from December 1, 2016 to March 6, 2018 were enrolled. Inclusion criteria for participants were PD duration ≥ 1 month and stable clinical condition. All the patients used lactate-glucose (GLU) peritoneal dialysate (from Baxter Healthcare, Guangzhou, China; GLU 1.5% or 2.5%, Mg^{2+} 0.25 mmol/L, Ca^{2+} 1.25 mmol/L or 1.75 mmol/L, Na^+ 132 mmol/L, and Cl^- 96 mmol/L).

Data Collection

Demographic information, clinical characteristics, and laboratory data were collected for all enrolled patients.

Data included age, gender, primary renal disease, PD duration, PD modality (continuous ambulatory PD [CAPD] or daytime ambulatory PD [DAPD]), body mass index, body surface area, normalized residual renal creatinine clearance rate (R-Ccr), normalized PD creatinine clearance rate (PD-Ccr), serum Mg, phosphorus (P), calcium (Ca), potassium (K), sodium (Na), GLU, creatinine (Cr), urea nitrogen, albumin (Alb), prealbumin (Pre-A), intact parathyroid hormone, 25-hydroxyvitamin D, C-reactive protein, peritoneal dialysate Mg (PD-Mg) concentrations, peritoneal dialysate phosphorus concentrations, peritoneal dialysate potassium concentration, peritoneal dialysate protein concentrations, daily peritoneal protein loss, urine protein concentrations, daily urine protein, and so on. Biochemical parameters were determined using a BECKMAN AU5800 automatic biochemical analyzer.

Twenty-four-hour peritoneal Mg clearance (mg/24 h) = (PD-Mg [mmol/L] $\times$ the daily dialysate outflow volume [L] - 0.25 [mmol/L] $\times$ the daily dialysate outflow volume [L]) $\times$ 24 (mg/mmol).

The normalized peritoneal Mg clearance rate (L/day/1.73 m²) = (PD-Mg [mmol/L] $\times$ the daily dialysate outflow volume [L] - 0.25 [mmol/L] $\times$ the daily dialysate outflow volume [L]) $\times$ 1.73 m²/(serum Mg [mmol/L] $\times$ body surface area [m²]).

The corrected serum Mg (cS-Mg, mmol/L) = experimentally determined Mg concentration (mmol/L) + (40 - Alb [g/L]) $\times$ 0.005 mmol/L [5].

The corrected serum calcium (mmol/L) = experimentally determined calcium concentration (mmol/L) - 0.025 $\times$ Alb (g/L) + 1 mmol/L.

According to the cS-Mg concentration, patients were divided into 3 groups, hypomagnesemia ($Mg^{2+} < 0.77$ mmol/L, group A), normal serum Mg concentration ($0.77 \text{ mmol/L} \leq Mg^{2+} \leq 1.03$ mmol/L, group B), and hypermagnesemia ($Mg^{2+} > 1.03$ mmol/L, group C).

Statistical Methods

We performed statistics with SPSS package. The measurement data of normal distribution are expressed as mean $\pm$ SD, measurement data of non-normal distribution are expressed as median and interquartile range, and categorical data are expressed as frequencies and percentages. Student-Newman-Keuls test was used for pairwise comparison between 3 serum Mg groups. Rate, proportion, and categorical data were analyzed using the chi-square test. Simple linear correlation among variables was performed by Pearson product moment correlation coefficient. A *p* value of less than 0.05 was considered significant.

Results

Demographic and Clinical Characteristics

Table 1 lists demographic and clinical characteristics of the 115 patients included in the study with 71 men and 44 women. The mean age was 46.03 ± 14.51 years old and the median PD duration was 16 months (range 6–37 months). The mean body mass index of patients was 22.36 ± 3.60 kg/m². And mean cS-Mg was 0.95 ± 0.16 mmol/L. The mean PD-Mg was 0.53 ± 0.10 mmol/L. The mean 24-h peritoneal Mg clearance was 39.75 ± 17.42 mg. And mean normalized peritoneal Mg clearance rate was 1.82 ± 0.82 L/day/1.73 m². The leading cause of end-stage renal disease was glomerulonephritis ($n = 93$, 80.87%), followed by chronic tubule interstitial nephropathy ($n = 3$, 2.61%), diabetic nephropathy ($n = 8$, 6.96%), lupus nephritis ($n = 2$, 1.74%), and others ($n = 9$, 7.83%). CAPD was used in 54 patients (46.96%) and DAPD was used in 61 patients (53.04%).

Differences in Demographic and Clinical Characteristics among Groups A, B, and C

One hundred and fifteen patients were enrolled. Nine patients (7.82%) were affected by hypomagnesemia and 27 patients (23.48%) were affected by hypermagnesemia, and in 79 patients (68.70%), serum Mg concentration was normal. By comparing groups A, B, and C, we found that PD-Mg of group A was significantly lower than that of groups B and C (0.44 ± 0.06 vs. 0.52 ± 0.10 and 0.56 ± 0.08 , $p < 0.01$). Twenty-four-hour peritoneal Mg clearance of group A was significantly lower than that of group C (29.60 ± 13.13 vs. 43.08 ± 10.46 , $p < 0.05$; Table 2).

Table 1. Patient general condition

Characteristics	Results
Number of patients, <i>n</i>	115
Age, years, $\bar{x} \pm SD$	46.03±14.51
Gender, male: female, <i>n</i>	71: 44
PD duration, months, median, IQR	16, 31
Primary renal diseases, <i>n</i> (%)	
Glomerulonephritis	93 (80.87)
Chronic tubule interstitial nephropathy	3 (2.61)
Diabetic nephropathy	8 (6.96)
Lupus nephritis	2 (1.74)
Others	9 (7.83)
Height, m, $\bar{x} \pm SD$	1.67±0.08
Weight, kg, $\bar{x} \pm SD$	62.36±12.68
BMI, kg/m ² , $\bar{x} \pm SD$	22.36±3.60
Dialysis modality, <i>n</i> (%)	
CAPD: DAPD	54 (46.96): 61 (53.04)
Serum Mg, mmol/L	0.95±0.16
cS-Mg, mmol/L	0.95±0.16
PD-Mg, mmol/L	0.53±0.10
24 h-peritoneal Mg clearance, mg/24 h	39.75±17.42
Normalized peritoneal Mg clearance rate, L/day/1.73 m ²	1.82±0.82

Mg, magnesium; PD, peritoneal dialysis; BMI, body mass index; CAPD, continuous ambulatory PD; DAPD, daytime ambulatory PD; cS-Mg, corrected serum Mg; PD-Mg, peritoneal dialysate Mg.

Linear Correlation

Correlation Analysis for Serum Mg Concentration and Variables

As shown in Table 3, cS-Mg was positively correlated with PD-Mg ($r = 0.256$, $p = 0.006$). cS-Mg was also negatively correlated with normalized peritoneal Mg clearance rate ($r = -0.186$, $p = 0.048$).

Correlation Analysis for Twenty-Four-Hour Peritoneal Mg Clearance and Variables

As shown in Table 4, 24-h peritoneal Mg clearance was positively correlated with serum Cr ($r = 0.456$, $p = 0.000$), Pre-A ($r = 0.302$, $p = 0.006$), daily peritoneal protein loss ($r = 0.332$, $p = 0.000$), and the normalized PD-Ccr ($r = 0.590$, $p = 0.000$). And 24-h peritoneal Mg clearance was negatively correlated with the normalized R-Ccr ($r = -0.384$, $p = 0.000$).

Correlation Analysis for Normalized Peritoneal Mg Clearance Rate and Variables

As shown in Table 4, normalized peritoneal Mg clearance rate was positively correlated with serum Cr ($r =$

0.362 , $p = 0.000$), Pre-A ($r = 0.225$, $p = 0.045$), daily peritoneal protein loss ($r = 0.335$, $p = 0.000$), and the normalized PD-Ccr ($r = 0.668$, $p = 0.000$). The normalized peritoneal Mg clearance rate was also negatively correlated with the normalized R-Ccr ($r = -0.362$, $p = 0.000$).

Comparison of Clinical Characteristics between Different Dialysis Modality

cS-Mg of patients with CAPD was significantly lower than that of patients with DAPD (0.92 ± 0.12 vs. 0.99 ± 0.18 , $p = 0.009$). Twenty-four-hour peritoneal Mg clearance of patients with CAPD was significantly higher than that of patients with DAPD (46.63 ± 13.66 vs. 33.56 ± 18.20 , $p = 0.000$). The normalized peritoneal Mg clearance rate of patients with CAPD was also significantly higher than that of patients with DAPD (2.16 ± 0.58 vs. 1.51 ± 0.88 , $p = 0.000$; Table 5).

Comparison of Clinical Characteristics among Different Peritoneal Transport Characteristics

As shown in Table 6, among the patients with different peritoneal transport characteristics of peritoneal equilibration test, PD-Mg of high average (HA) transport patients was significantly higher than that of patients with low transport (L) and high transport (H; 0.58 ± 0.11 vs. 0.47 ± 0.08 and 0.48 ± 0.09 , $p < 0.05$). Twenty-four-hour peritoneal Mg clearance of HA transport patients was significantly higher than that of patients with low transport, low average (LA) transport, and high transport (52.15 ± 19.77 vs. 28.24 ± 13.51 and 38.84 ± 13.18 and 30.55 ± 14.50 , $p < 0.05$). The normalized peritoneal Mg clearance rate of HA transport patients was significantly higher than that of patients with low transport, LA transport, and high transport (2.46 ± 1.01 vs. 1.34 ± 0.57 and 1.74 ± 0.58 and 1.57 ± 0.81 , $p < 0.05$).

Discussion

PD is an effective alternative to end-stage renal disease. It uses peritoneum as a semi-permeable membrane to eliminate excess fluid, waste products, and toxins. There were few studies about the peritoneal Mg clearance. Delmez et al. [6] found that 24-h peritoneal Mg clearance was 31.2 ± 15.5 mg. Our study found that serum Mg could be partly cleared by PD. The mean PD-Mg was 0.53 ± 0.10 mmol/L. The mean 24-h peritoneal Mg clearance was 39.75 ± 17.42 mg and mean normalized peritoneal Mg clearance rate was 1.82 ± 0.82 L/day/1.73

Table 2. Comparisons of demographic and clinical characteristics in patients among groups A, B, and C

Variable	Corrected serum Mg concentration, mmol/L			<i>p</i> value
	group A <0.77	group B 0.77 ≤ Mg ≤ 1.03	group C >1.03	
Number of patients, <i>n</i> (%)	9 (7.82)	79 (68.70)	27 (23.48)	
Gender, male: female, <i>n</i>	6:3	48:31	17:10	>0.05
Dialysis modality (CAPD:DAPD), <i>n</i>	7:2	39:40	8:19	<0.05
Age, years	46.78±15.17	45.80±14.55	46.44±14.74	>0.05
PD duration, months, median, IQR	6.00, 31.00	13.00, 23.00	27.00, 45.00	>0.05
BMI, kg/m ²	22.57±3.03	22.35±3.72	22.33±3.54	>0.05
S-Mg, mmol/L	0.71±0.03	0.90±0.07	1.15±0.16	
cS-Mg, mmol/L	0.72±0.04	0.91±0.06	1.16±0.15	
PD-Mg, mmol/L	0.44±0.06	0.52±0.10*	0.56±0.08*	<0.05
PD-P, mmol/L	0.82±0.57	1.08±1.36	0.96±0.80	>0.05
PD-K, mmol/L	3.17±0.59	3.48±0.82	3.37±0.61	>0.05
24-h peritoneal Mg clearance, mg/24 h	29.60±13.13	39.92±19.28	43.08±10.46*	<0.05
Normalized peritoneal Mg clearance rate, L/day/1.73 m ²	1.73±0.59	1.90±0.91	1.61±0.50	>0.05

* Represents that “*p* < 0.05” compared with group A.

Mg, magnesium; PD, peritoneal dialysis; BMI, body mass index; CAPD, continuous ambulatory PD; DAPD, daytime ambulatory PD; cS-Mg, corrected serum Mg; PD-Mg, peritoneal dialysate Mg.

Table 3. Correlation analysis for serum Mg concentration and variables

Variable	Corrected serum Mg, mmol/L	
	<i>r</i>	<i>p</i> value
PD-Mg, mmol/L	0.256	0.006
PD-P, mmol/L	−0.021	0.827
PD-K, mmol/L	−0.030	0.753
PD-PR, g/L	−0.085	0.382
24-h peritoneal Mg clearance, mg/24 h	0.122	0.195
Normalized peritoneal Mg clearance rate, L/day/1.73 m ²	−0.186	0.048
Mg, magnesium; PD-Mg, peritoneal dialysate Mg.		

m². Our results are consistent with those of the study conducted by Delmez et al. [6].

Our study showed that serum Mg was positively correlated with PD-Mg. It suggested that peritoneal Mg clearance was related to serum Mg concentration, which was concentration-dependent. And our study also found that daily peritoneal Mg clearance increased with serum Mg. Moreover, PD-Ccr was positively correlated with daily peritoneal Mg clearance and peritoneal Mg clear-

ance rate. All these findings showed that the clearance of serum Mg by peritoneum was similar to the clearance of serum GLU, urea nitrogen, and other small molecular solutes by peritoneum.

Peritoneal transport characteristics were closely related to PD-Mg, 24 h-peritoneal Mg clearance, and peritoneal Mg clearance rate in our study. PD-Mg of HA transport patients was significantly higher than that of those with low transport and high transport. Twenty-four-hour peritoneal Mg clearance and normalized peritoneal Mg clearance rate of HA transport patients were significantly higher than those of patients with low transport, LA transport, and high transport respectively. It suggested peritoneal Mg clearance increased with the transport ability of peritoneum to small molecular substances. However, it was unclear that these clinical indicators of high transport were lower than those of HA transport. It might be that the sample size of high transport is too small, resulting in a large sampling error.

In our study, the serum Mg of patients with CAPD was significantly lower than that of patients with DAPD. Furthermore, 24-h peritoneal Mg clearance and normalized peritoneal Mg clearance rate of patients with CAPD were significantly higher than those of patients with DAPD. It suggested that compared with DAPD, the CAPD was more effective in removing Mg. It was probably due to the fact that patients with CAPD had a longer

Table 4. Correlation analysis for 24-h peritoneal Mg clearance, normalized peritoneal Mg clearance rate and variables

Variable	24-h peritoneal Mg clearance, mg/24 h		Normalized peritoneal Mg clearance rate, L/day/1.73 m ²	
	<i>r</i>	<i>p</i> value	<i>r</i>	<i>p</i> value
S-P, mmol/L	0.050	0.598	-0.052	0.584
cS-Ca, mmol/L	0.132	0.162	0.165	0.080
S-K, mmol/L	-0.105	0.266	-0.179	0.057
S-Na, mmol/L	-0.060	0.527	-0.054	0.566
S-GLU, mmol/L	-0.010	0.918	-0.013	0.894
S-Cr, μ mol/L	0.456	0.000	0.362	0.000
S-BUN, mmol/L	-0.006	0.948	-0.142	0.133
iPTH, pg/mL	0.016	0.871	0.006	0.950
25(OH)D, nmol/L	-0.028	0.790	-0.003	0.978
Alb, g/L	-0.093	0.323	-0.135	0.153
Pre-A, g/L	0.302	0.006	0.225	0.045
CRP, mg/L	-0.186	0.196	-0.123	0.394
Urine protein concentrations, g/L	0.025	0.799	-0.004	0.965
PD-PR, g/L	0.061	0.528	0.088	0.363
Daily peritoneal protein loss, g/24 h	0.332	0.000	0.335	0.000
Normalized R-Ccr, mL/week/1.73 m ²	-0.384	0.000	-0.362	0.000
Normalized PD-Ccr, mL/week/1.73 m ²	0.590	0.000	0.668	0.000

Mg, magnesium; iPTH, intact parathyroid hormone.

Table 5. Patient clinical characteristics according to PD modality

Variable	Dialysis modality		<i>p</i> value
	CAPD	DAPD	
cS-Mg, mmol/L	0.92±0.12	0.99±0.18	0.009
PD-Mg, mmol/L	0.53±0.08	0.52±0.11	0.503
24-h peritoneal Mg clearance, mg/24 h	46.63±13.66	33.56±18.20	0.000
Normalized peritoneal Mg clearance rat, L/day/1.73 m ²	2.16±0.58	1.51±0.88	0.000
Daily dialysis time, h	24.00±0.00	11.38±2.57	0.000
Daily dialysis dose, mL/24 h	7,777.78±1,268.88	5,800.00±1,459.05	0.000

Mg, magnesium; PD, peritoneal dialysis; CAPD, continuous ambulatory PD; DAPD, daytime ambulatory PD; cS-Mg, corrected serum Mg; PD-Mg, peritoneal dialysate Mg.

dwelling time of peritoneal dialysate and a larger dialysis dose.

The kidney has a vital role in Mg homeostasis. In individuals with normal renal function, about 70–80% of serum Mg is filtered by the kidneys, and 95% of the filtered Mg can be reabsorbed by the renal tubule with 5% excreted in urine. For patients with chronic kidney disease, patients with Cr clearance > 30 mL/min can generally compensate for the loss of renal function by in-

creases in the fractional excretion of Mg such that serum Mg are maintained within the normal range. When Cr clearance < 30 mL/min, this compensatory mechanism becomes inadequate. And patients with Cr clearance < 10 mL/min are likely to be with hypermagnesemia [7]. Our study showed that 24-h peritoneal Mg clearance and normalized peritoneal Mg clearance rate were negatively correlated with the normalized R-Ccr. On the one hand, the kidney still played an important

Table 6. Comparison of clinical characteristics among different peritoneal transport characteristics

Variable	PET				<i>p</i> value
	L	LA	HA	H	
Number of patients, <i>n</i> (%)	24 (26.97)	37 (41.57)	24 (26.97)	4 (4.49)	
Gender, male:female, <i>n</i>	11:13	21:16	18:6	2:2	>0.05
Age, years	47.58±15.90	45.38±14.45	46.20±14.73	43.50±9.33	>0.05
PD duration, months, median, IQR	12.00, 43.75	13.00, 37.00	15.00, 24.75	9.00, 31.50	>0.05
BMI, kg/m ²	20.88±2.92	22.37±3.62	22.95±3.34	23.65±2.83	>0.05
cS-Mg, mmol/L	0.95±0.15	0.97±0.16	0.91±0.11	0.86±0.13	>0.05
PD-Mg, mmol/L	0.47±0.08	0.52±0.08	0.58±0.11*	0.48±0.09 [#]	<0.05
24-h peritoneal Mg clearance, mg/24 h	28.24±13.51	38.84±13.18	52.15±19.77*, ^Δ	30.55±14.50 [#]	<0.05
Normalized peritoneal Mg Clearance rate, L/day/1.73 m ²	1.34±0.57	1.74±0.58	2.46±1.01*, ^Δ	1.57±0.81 [#]	<0.05

* Represents that “*p* < 0.05” compared with L.

^Δ Represents that “*p* < 0.05” compared with LA.

[#] Represents that “*p* < 0.05” compared with HA.

Mg, magnesium; PD, peritoneal dialysis; BMI, body mass index; CAPD, continuous ambulatory PD; DAPD, daytime ambulatory PD; cS-Mg, corrected serum Mg; PD-Mg, peritoneal dialysate Mg; LA, low average; HA, high average; PET, peritoneal equilibration test.

role in removing serum Mg for patients with residual renal function, so the clearance of serum Mg by PD was relatively weak. On the other hand, with the loss of residual renal function, serum Mg concentration increased. Moreover, peritoneal Mg clearance might be concentration dependent, so that the peritoneal Mg clearance might be higher with higher serum Mg concentration.

Serum Mg is categorized into 3 fractions, including ionized, bound to protein, or complexed with anions. Ionized Mg and complexed Mg together form the ultra-filterable fraction of Mg, which can be removed by kidneys or through the process of dialysis. Our study also found that 24-h peritoneal Mg clearance and normalized peritoneal Mg clearance rate were positively correlated with daily peritoneal protein loss. It was speculated that because the increased peritoneal protein loss decreased serum protein, further leading to the decrease of proteins binding to serum Mg, ionized Mg and complexed Mg increased in the serum, and peritoneal Mg clearance also increased. On the other hand, as peritoneal protein loss increased, the loss of proteins binding to Mg in peritoneal dialysate also increased, so peritoneal Mg clearance increased. Pre-A was an important indicator of evaluating the nutritional status, which had a half-life of 1.9 days. Twenty-four-hour peritoneal Mg clearance and normalized peritoneal Mg clearance rate were positively correlated with Pre-A in our study. It might be related to the level of nutrition intake in PD

patients. Due to better nutrient intake, patients who were well-nourished also had a relatively higher intake of Mg, leading to the increase of peritoneal Mg clearance.

In conclusion, serum Mg could be partly cleared by PD. Mean 24-h peritoneal Mg clearance was 39.75 ± 17.42 mg and mean normalized peritoneal Mg clearance rate was 1.82 ± 0.82 L/day/1.73 m². The peritoneal Mg clearance was related with serum Mg concentration, which was concentration dependent. Furthermore, peritoneal Mg clearance was negatively correlated with the residual renal function, while it was positively correlated with nutritional status and daily peritoneal protein loss. Peritoneal Mg clearance was higher in patients with high transport characteristics or CAPD patients.

Ethics Statement

This study protocol had been approved by the local Ethics Committee, who stated that informed consent was not necessary because data analyzed were all from previous clinical cases as a retrospective study.

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.

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