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Use of aminoglycosides for peritoneal dialysis-associated peritonitis does not affect residual renal function

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Abstract

Background. Aminoglycosides offer several potential benefits in their treatment of peritoneal dialysis (PD)-associated peritonitis, including low cost, activity against Gram-negative organisms (including *Pseudomonas aeruginosa*), synergistic bactericidal activity against some Gram-positive organisms (such as *Staphylococci*) and relatively low propensity to promote antimicrobial resistance. However, there is limited conflicting evidence that aminoglycosides may accelerate loss of residual renal function (RRF) in PD patients. The aim of this study was to study the effect of aminoglycoside use on slope of decline in RRF.

Methods. The study included 2715 Australian patients receiving PD between October 2003 and December 2007 in whom at least two measurements of renal creatinine clearance were available. Patients were divided according to tertiles of slope of RRF decline (rapid, intermediate and slow). The primary outcome was the slope of RRF over time in patients who received aminoglycosides for PD peritonitis versus those who did not.

Results. A total of 1412 patients (52%) experienced at least one episode of PD peritonitis. An aminoglycoside was used as the initial empiric antibiotic in 1075 patients. The slopes of RRF decline were similar in patients treated and not treated with at least one course of aminoglycoside (median [interquartile range] −0.26 [−1.17 to 0.04] mL/min/1.73 m^2/month versus −0.22 [−1.11 to 0.01] mL/min/1.73 m^2/month, P = 0.9). The slopes of RRF decline were also similar in patients receiving repeated courses of aminoglycoside.

Conclusions. Empiric treatment with aminoglycoside for peritonitis was not associated with an adverse effect on RRF in PD patients.

Keywords: aminoglycosides; end-stage kidney disease; peritonitis; peritoneal dialysis; residual renal function

Introduction

Peritonitis is a common complication of peritoneal dialysis (PD) and can lead to increased risk of death, permanent transfer to haemodialysis and peritoneal membrane failure [1]. The 2010 update of the International Society for Peritoneal Dialysis (ISPD) PD-related Infections Guidelines recommends prompt diagnosis and initiation of empiric antibiotics to cover both Gram-positive and Gram-negative organisms [2]. For Gram-negative coverage, the ISPD Guidelines recommend use of either an extended spectrum cephalosporin or an aminoglycoside, depending on 'centre-specific' factors, such as antimicrobial sensitivities.

Aminoglycosides are favoured by many clinicians because they are inexpensive, have excellent activity against *Pseudomonas aeruginosa* [3, 4], confer synergistic bactericidal activity in the treatment of staphylococcal, streptococcal and enterococcal infections [5], exhibit post-antibiotic actions against both staphylococci and Gram-negative bacilli [6, 7] and are less likely to induce antimicrobial resistance than extended spectrum cephalosporins, such as ceftazidime [8]. Moreover, the alternative use of third or fourth generation cephalosporins has been linked to the emergence of vancomycin-resistant enterococci [9] and extended-spectrum beta lactamase producing enterobacteriaceae [10]. Consequently, between 2003 and 2008, aminoglycosides were selected for the initial empiric antibiotic treatment of 70% of episodes of PD-associated peritonitis in Australia [11].

However, aminoglycosides can also be associated with significant adverse effects, such as ototoxicity and nephrotoxicity [5, 12]. One report by Shemin *et al.* [13] observed that PD patients treated with aminoglycosides during peritonitis episodes experienced more rapid residual renal function (RRF) decline than those who had not received aminoglycosides. On the basis of this finding and the recognized association of RRF with improved PD patient survival [14–18], the 2000 update of the ISPD Peritonitis

Guidelines recommended that extended spectrum cephalosporins be used in preference to aminoglycosides for the treatment of PD peritonitis [19]. Subsequently, three small studies [20–22] have reported conflicting results with one investigation observing that higher use of aminoglycosides in PD patients was a significant independent predictor of more rapid RRF decline [22], while two other studies found no such relationship [20, 21]. These variable findings led to a relaxation of the ISPD warnings against aminoglycoside therapy for PD peritonitis [2, 23]. However, all these studies were limited by small sample size and single-centre design, thereby reducing their statistical power to detect a clinically important effect of aminoglycosides on RRF and decreasing the applicability of their findings to other PD centres.

The aim of the current study was to examine the effect of aminoglycoside use for the treatment of PD peritonitis on RRF in all Australian PD patients involving all 72 PD centres.

Materials and methods

Study population

The study included all Australian adult patients from the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) who were receiving PD between 1 October 2003 (when detailed peritonitis data started to be collected) and 31 December 2007. The primary outcome of the study was the slope of RRF over time in patients who received aminoglycosides for PD peritonitis versus those who did not. RRF was recorded as the measured urinary creatinine clearance normalized to 1.73 m^2 body surface area at the end of each survey period (every 6 months for the first year of the study then every 12 months thereafter). The slope of RRF decline over time was then determined by linear regression analysis of serial urinary creatinine measurements for each patient. Patients were excluded if they were anuric or had less than two measurements of urinary creatinine clearance.

Other data collected included demographic data, cause of primary renal disease, co-morbidities at the start of dialysis (coronary artery disease, peripheral vascular disease, cerebrovascular disease, chronic lung disease, diabetes and smoking status), body mass index, late referral (defined as commencement of dialysis within 3 months of referral to a nephrologists), estimated glomerular filtration rate (eGFR) at the time of dialysis commencement [calculated according to the 4-variable Modification of Diet in Renal Disease (MDRD) formula] [24], smoking status, baseline dialysate:plasma creatinine ratio (D:P Cr, 4 h) determined by peritoneal equilibration test [25], peritonitis episodes, initial and subsequent antibiotic treatment regimens, proportion of PD time spent on automated peritoneal dialysis and centre size. Diagnosis of peritonitis was made based on a PD effluent white cell count >100/μL, with >50% polymorphonuclear leucocytes. In cases of polymicrobial peritonitis, non-Pseudomonas Gram-negative (NPGN) peritonitis was recorded if an NPGN species was at least one of the isolated organisms. Centre size was categorized according to quartiles of the numbers of patients cared for by individual units over the duration of the study: small (<5 patients), small-medium (5–33 patients), medium-large (34–121 patients) and large (>121 patients).

Statistical analysis

Results were expressed as frequencies and percentages for categorical variables, mean ± SD for continuous variables and median and interquartile [IQR] range for non-parametric data. Patients were divided according to tertiles of slope of RRF decline (rapid, intermediate and slow decline) as well as by history of aminoglycoside treatment. Differences between groups of patients were analysed by χ^2 test for categorical data; *t*-test or one-way analysis of variance for continuous variables if data were normally distributed and Mann–Whitney *U*-test or Kruskal–Wallis test for non-normally distributed data. Predictors of rapid RRF decline versus combined tertiles of intermediate and slow RRF decline were determined by the multivariate ordinal logistic regression. Data on the slopes of monthly decline in RRF were not normally distributed (skewness −5.9, kurtosis 87.6, $P < 0.001$) and could not be satisfactorily transformed to improve normality. Therefore, predictors of slope of RRF decline were not able to be determined by linear regression. Data were analysed using the software packages SPSS for Windows release 17.0 (SPSS Inc., North Sydney, Australia) and Stata/SE 11.1 (College Station, TX). P-values <0.05 were considered statistically significant.

Results

Baseline characteristics

A total of 6024 patients received PD in Australia during the study period (1 October 2003 to 31 December 2007). Of these, 3309 patients were excluded because they were either anuric or had less than two RRF measurements. The remaining 2715 patients were included in the analysis and were followed for 4916 patient-years on PD. A comparison of the characteristics of patients who were and were not included in the study is provided in the Supplementary. Patients who were included in the study were significantly more likely to have experienced PD peritonitis, received aminoglycosides for PD peritonitis, undergone assessment of peritoneal membrane transport status, received treatment in a larger centre as well as have a lower eGFR at dialysis commencement.

A median number [IQR] of 3 [2–4] RRF measurements were recorded per patient. The median monthly decline in RRF was −0.24 [−1.14 to −0.03] mL/min/1.73 m^2. Baseline characteristics of the study population according to tertiles of RRF decline are described in Table 1. Compared to patients with slow RRF decline, those with rapid RRF decline were significantly less likely to be of Australian aboriginal or Torres Strait Islander racial origin and more likely to be Caucasian, obese and diagnosed with coronary artery disease. All other variables were comparable between the groups. Compared to patients who did not receive aminoglycosides for peritonitis, those treated with aminoglycosides were significantly less likely to have undergone assessment of peritoneal membrane transport status and more likely to be older, have high or high-average peritoneal membrane transport status and have received treatment in a larger centre (Table 2). On the multivariate ordinal logistic regression, the only variable associated with rapid RRF decline versus combined slow and intermediate RRF decline was Australian aboriginal or Torres Strait Islander racial origin (odds ratio 0.64, 95% confidence interval 0.47–0.86, $P = 0.003$ compared to Caucasians) (Table 3).

Peritonitis and aminoglycosides use

A total of 1412 patients (52%) experienced at least one episode of PD peritonitis (Tables 4 and 5). Of these, 687 patients (49%) had multiple episodes (two or more) of PD peritonitis. An aminoglycoside was used as the initial empiric antibiotic in 1075 patients (76% of all PD peritonitis episodes or 40% of all patients). Four hundred and fifty-nine patients received two or more courses of aminoglycosides for multiple episodes of PD peritonitis. Of these, 253

Table 1. Baseline characteristics of the study population as a whole and according to tertiles of RRF decline

Characteristic	Total population ($n = 2715$)	RRF decline tertile			P-value
		Rapid ($n = 905$)	Intermediate ($n = 905$)	Slow ($n = 905$)	
RRF decline (mL/min/1.73 m^2)	−0.24 (−1.14, 0.03)	−1.68 (−2.73, −1.14)	−0.24 (−0.45, −0.10)	0.22 (0.03, 0.96)	<0.001
Age (years)	57.8 ± 17.0	58.5 ± 16.9	58.1 ± 16.8	56.7 ± 17.4	0.06
Women	1237 (46%)	405 (45%)	402 (44%)	430 (48%)	0.3
Racial origin					
Caucasian	2088 (77%)	721 (80%)	680 (75%)	687 (76%)	0.04
Aboriginal/Torres Strait Islander	211 (8%)	52 (6%)	77 (8%)	82 (9%)	
Maori/Pacific Islander	60 (2%)	22 (2%)	23 (3%)	15 (2%)	
Asian	266 (10%)	78 (9%)	102 (11%)	86 (9%)	
Other	90 (3%)	32 (3%)	23 (3%)	35 (4%)	
BMI (kg/m^2)	25.7 ± 5.2	26.0 ± 5.2	25.5 ± 5.2	25.5 ± 5.2	0.07
BMI					
Underweight (<20 kg/m^2)	312 (12%)	77 (9%)	116 (13%)	119 (13%)	0.04
Normal (20–24.9 kg/m^2)	1,002 (37%)	346 (39%)	332 (37%)	324 (36%)	
Overweight (25–29.9 kg/m^2)	893 (33%)	297 (33%)	296 (33%)	300 (34%)	
Obese (≥30 kg/m^2)	473 (18%)	171 (19%)	150 (17%)	152 (17%)	
eGFR at dialysis start (mL/min/1.73 m^2)	6.1 (4.6–8.3)	6.3 (4.7–8.4)	6.0 (4.6–8.5)	6.1 (4.5–8.1)	0.2
Late referral	626 (23%)	189 (21%)	214 (24%)	223 (25%)	0.1
ESRF cause					
Chronic glomerulonephritis	780 (29%)	231 (25%)	286 (32%)	263 (29%)	0.1
Diabetic nephropathy	748 (28%)	272 (30%)	242 (27%)	234 (26%)	
Renovascular disease	361 (13%)	126 (14%)	125 (14%)	110 (12%)	
Polycystic kidneys	145 (5%)	51 (6%)	48 (5%)	46 (5%)	
Reflux nephropathy	115 (4%)	36 (4%)	32 (3%)	47 (5%)	
Other	385 (14%)	127 (14%)	112 (12%)	146 (16%)	
Unknown	181 (7%)	62 (7%)	60 (7%)	59 (7%)	
Smoking status					
Current	333 (12%)	105 (12%)	110 (12%)	118 (13%)	0.9
Former	1029 (38%)	343 (38%)	348 (39%)	338 (37%)	
Never	1353 (50%)	457 (50%)	447 (49%)	449 (50%)	
Chronic lung disease	348 (13%)	104 (12%)	121 (13%)	123 (14%)	0.3
Coronary artery disease	965 (36%)	343 (38%)	328 (36%)	294 (33%)	0.04
Peripheral vascular disease	619 (23%)	220 (24%)	208 (23%)	191 (21%)	0.3
Cerebrovascular disease	351 (13%)	136 (15%)	107 (12%)	108 (12%)	0.07
Diabetes mellitus	965 (36%)	340 (38%)	320 (35%)	305 (34%)	0.2
D:P Cr, 4 h	0.69 ± 0.12	0.69 ± 0.12	0.68 ± 0.12	0.69 ± 0.12	0.7
Peritoneal transport status					
High	307 (11%)	101 (11%)	103 (11%)	103 (11%)	0.6
High average	1050 (39%)	356 (39%)	355 (39%)	339 (38%)	
Low average	670 (25%)	211 (23%)	238 (26%)	221 (24%)	
Low	122 (4%)	37 (4%)	43 (5%)	42 (5%)	
Unknown/not specified	566 (21%)	200 (22%)	166 (18%)	200 (22%)	
Treatment with APD					
Never	1212 (45%)	400 (44%)	412 (46%)	400 (44%)	0.8
Ever	1503 (55%)	505 (56%)	493 (54%)	505 (56%)	
Centre size (no. PD patients)					
Small (≤10)	11 (<1%)	3 (<1%)	5 (1%)	3 (<1%)	0.1
Small-med (11–38)	146 (5%)	44 (5%)	41 (5%)	61 (7%)	
Med-large (39–98)	629 (23%)	205 (23%)	233 (26%)	191 (21%)	
Large (≥99)	1929 (71%)	653 (72%)	626 (69%)	650 (72%)	

patients received two courses and the remaining 203 patients received three or more courses of aminoglycosides. The predominant aminoglycoside prescribed for peritonitis was gentamicin (99% of occasions), while use of other aminoglycosides was infrequent (amikacin 0.6%, netilmicin 0%, tobramycin 0.4%).

The median [IQR] slope of RRF decline in patients who did not experience any peritonitis (−0.26 [−1.19 to 0.04] mL/min/1.73 m^2/month) was similar to those who experienced single (−0.22 [−1.13 to 0.01] mL/min/1.73 m^2/month) or multiple (−0.23 [−1.10 to 0.03] mL/min/1.73 m^2/month; P = 0.9) episodes of peritonitis. The number of peritonitis episodes was not a predictor of rapid RRF decline on the multivariate ordinal logistic regression (Table 3).

Aminoglycoside use and RRF

The slope of RRF decline in patients treated with aminoglycosides (−0.26 [−1.17 to 0.04] mL/min/1.73 m^2 per month) was similar to those who did not receive aminoglycosides (−0.22 [−1.11 to 0.01] mL/min/1.73 m^2 per month, P = 0.9) (Table 4). There was no statistically significant difference in the slope of RRF decline when analysed

Table 2. Baseline characteristics of the study population as a whole and according to aminoglycoside treatment

Characteristic	No aminoglycosides group	Aminoglycosides group	P-value
Number of patients	1640	1075	
Age (years)	57.1 ± 17.6	58.7 ± 16.1	0.014
Women	727 (44%)	510 (47%)	0.1
Racial origin			
Caucasian	1281 (78%)	807 (75%)	0.07
Aboriginal/Torres Strait Islander	128 (8%)	83 (8%)	
Maori/Pacific Islander	40 (2%)	20 (2%)	
Asian	144 (9%)	122 (11%)	
Other	47 (3%)	43 (4%)	
BMI (kg/m^2)	25.7 ± 5.3	25.7 ± 5	0.9
BMI			
Underweight (<20 kg/m^2)	199 (12%)	113 (11%)	0.6
Normal (20–24.9 kg/m^2)	596 (37%)	406 (38%)	
Overweight (25–29.9 kg/m^2)	537 (33%)	356 (34%)	
Obese (≥30 kg/m^2)	287 (18%)	186 (17%)	
eGFR at dialysis start (mL/min/1.73 m^2)	6.2 (4.6–8.3)	6.1 (4.6–8.4)	0.9
Late referral	368 (22%)	258 (24%)	0.3
ESRF cause			
Chronic glomerulonephritis	478 (29%)	302 (28%)	0.2
Diabetic nephropathy	437 (27%)	311 (29%)	
Renovascular disease	218 (13%)	143 (13%)	
Polycystic kidneys	76 (5%)	69 (6%)	
Reflux nephropathy	75 (5%)	40 (4%)	
Other	238 (14%)	147 (14%)	
Unknown	118 (7%)	63 (6%)	
Smoking status			
Current	197 (12%)	136 (13%)	0.9
Former	622 (38%)	407 (38%)	
Never	821 (50%)	532 (50%)	
Chronic lung disease	212 (13%)	136 (13%)	0.8
Coronary artery disease	573 (35%)	392 (36%)	0.4
Peripheral vascular disease	382 (23%)	237 (22%)	0.4
Cerebrovascular disease	206 (13%)	145 (13%)	0.8
Diabetes mellitus	562 (34%)	403 (37%)	0.08
D:P Cr, 4 h	0.68 ± 0.13	0.69 ± 0.12	0.5
Peritoneal transport status			
High	170 (10%)	137 (13%)	<0.001
High average	612 (37%)	438 (41%)	
Low average	375 (23%)	295 (27%)	
Low	79 (5%)	43 (4%)	
Unknown/not specified	404 (25%)	162 (15%)	
Treatment with APD			
Never	717 (44%)	495 (46%)	0.2
Ever	923 (56%)	580 (54%)	
Centre size (no. PD patients)			
Small (≤10)	6 (0%)	5 (0%)	<0.001
Small-med (11–38)	113 (7%)	33 (3%)	
Med-large (39–98)	375 (23%)	254 (24%)	
Large (≥99)	1146 (70%)	783 (73%)	

according to the number of courses of aminoglycoside patients received (−0.24 [−1.14 to 0.03] mL/min/1.73 m^2/month, −0.22 [−1.13 to 0.01] mL/min/1.73 m^2/month, −0.18 [−0.92 to 0.00] mL/min/1.73 m^2/month, and −0.30 [−1.14 to 0.02] mL/min/1.73 m^2/month for patients receiving none, 1, 2, and ≥ 3 aminoglycoside courses, respectively, P = 0.9) (Table 5).

The proportion of patients receiving at least one course of aminoglycoside treatment was comparable in all tertiles of slope of RRF decline (40, 41 and 38% in rapid, intermediate and slow decline, respectively, P = 0.6). Similar results were observed when the analysis was performed according to the number of aminoglycoside courses (Table 6). The number of aminoglycoside courses was not a significant predictor of rapid RRF decline on the multivariate ordinal logistic regression.

The median cumulative exposure to aminoglycoside treatment was 14 days (1–28 days). There was no statistically significant difference in the slope of RRF decline when analysed according to the tertiles of the cumulative exposure to aminoglycoside treatment (Tertile 1: median [IQR] 0 [0–2] days, slope −0.25[−1.18 to 0.05] mL/min/1.73 m^2/month; Tertile 2: median [IQR] 15 [12–19] days, slope −0.22 [−0.99 to 0.01] mL/min/1.73 m^2/month; Tertile 3: median [IQR] 41 [30–56] days, slope −0.21 [−1.13 to 0.02] mL/min/1.73 m^2/month, P = 0.97).

Table 3. Ordinal logistic regression showing odds ratio for rapid RRF decline versus combined slow and intermediate RRF decline

Variable	Odds ratio	95% Confidence interval	P
Women	0.98	0.84–1.15	0.82
Age	1.00	0.99–1.00	0.6
Racial origin			
Caucasian	Reference		
Aboriginal/Torres Strait Islander	0.64	0.47–0.86	<0.01
Maori/Pacific Islander	1.19	0.73–1.95	0.49
Asian	0.87	0.67–1.12	0.29
Other	0.88	0.67–1.12	0.56
BMI			
Underweight (<20 kg/m^2)	0.81	0.62–1.05	0.11
Normal (20–24.9 kg/m^2)	1.00	0.81–1.23	0.2
Overweight (25–29.9 kg/m^2)	0.89	0.75–1.06	0.2
Obese (≥30 kg/m^2)	1.00	0.81–1.21	0.97
Log of eGFR at dialysis start	1.02	0.86–1.21	0.81
Late referral	0.85	0.71–1.02	0.08
ESRF Cause			
Chronic glomerulonephritis	Reference		
Diabetic nephropathy	1.26	0.93–1.72	0.14
Renovascular disease	1.12	0.87–1.44	0.39
Polycystic kidneys	1.09	0.78–1.54	0.62
Reflux nephropathy	0.82	0.55–1.23	0.35
Other	1.04	0.81–1.57	0.35
Unknown	1.14	0.83–1.57	0.77
Smoking status			
Current	0.93	0.73–1.19	0.56
Former	0.93	0.79–1.10	0.56
Never	Reference		
Chronic lung disease	0.80	0.64–1.00	0.56
Coronary artery disease	1.14	0.95–1.6	0.16
Peripheral vascular disease	1.00	0.81–1.22	0.96
Cerebrovascular disease	1.16	0.92–1.47	0.2
Diabetes mellitus	0.97	0.74–1.27	0.82
Peritoneal Transport Status			
High	0.95	0.74–1.21	0.65
High average	Reference		
Low average	0.95	0.79–1.21	0.65
Low	0.87	0.61–1.24	0.43
Unknown/not specified	1.01	0.82–1.24	0.95
Treatment with APD			
Never	Reference		
Ever	1.01	0.87–1.17	0.94
Centre size (no. PD patients)			
Small (≤10)	0.71	0.22–2.34	0.58
Small-med (11–38)	0.75	0.49–1.16	0.19
Med-large (39–98)	1.06	0.89–1.26	0.53
Large (≥99)	Reference		
Aminoglycoside treatment			
Never	Reference		
Single course	1.03	0.79–1.34	0.82
Two courses	1.12	0.78–1.61	0.53
Three or more courses	1.25	0.86–1.83	0.25
Peritonitis			
No episodes	Reference		
Single episode	1.00	0.77–1.29	0.99
Multiple episodes	0.86	0.64–1.16	0.31

Discussion

The present study represents the first comprehensive multicentre examination of the effect of aminoglycosides on RRF decline in PD patients and showed that empiric treatment with aminoglycosides for PD peritonitis was not associated with an adverse effect on RRF in 2715 Australian patients across 72 different PD centres. Even repeated courses of aminoglycoside for multiple episodes of peritonitis had no observable effect on RRF.

These results are in keeping with those of Baker *et al.* [20] who observed that the mean decline in RRF in 70 peritonitis episodes treated with aminoglycosides (-0.08 ± 0.50 mL/min/month) was not significantly different from that observed in 61 episodes treated without aminoglycosides (-0.17 ± 0.27 mL/min/month) or 74 control patients without peritonitis (-0.20 ± 0.39 mL/min/month). Similarly, in a randomized controlled trial of 102 PD patients with peritonitis treated with either intraperitoneal cephazolin plus netilmicin or cephazolin plus ceftazidime once daily in the long dwell for 14 days, Lui *et al.* [21] demonstrated in a subset of 36 patients with RRF >1 mL/min who achieved primary peritonitis cure with their antibiotic regimen that the reductions in RRF and daily urine volume did not differ significantly between patients treated with netilmicin and those treated with ceftazidime.

In contrast, Shemin *et al.* [13] observed in their single-centre retrospective observational cohort study that 17 PD patients with peritonitis who received aminoglycosides for at least 3 days had significantly higher rates of RRF decline than 26 patients with peritonitis who did not receive any aminoglycosides or 29 patients who did not experience any peritonitis (-0.66 ± 0.58 versus -0.21 ± 0.39 versus -0.07 ± 0.71 mL/min/month, respectively, $P < 0.01$). Similarly, Singhal *et al.* [22] found that higher use of aminoglycosides was independently associated with more rapid RRF decline in 242 PD patients at a single centre between 1994 and 1997. In this study, aminoglycoside antibiotics were administered to 103 patients.

These four prior studies, collectively involving only 208 PD patients exposed to aminoglycosides, were limited by small sample size and single-centre design, thereby reducing their statistical power to detect a clinically important effect of aminoglycosides on RRF, limiting their ability to adjust for potentially confounding variables and decreasing the applicability of their findings to other PD centres. In contrast, our study involved 2715 patients (including 1075 patients exposed to aminoglycosides) across 72 different PD centres. We involved a range of PD units with variable PD expertise and approaches to the treatment of PD peritonitis. This greatly enhanced the external validity of our findings.

Taken together, the available evidence does not support avoiding the use of aminoglycosides to treat PD peritonitis on the basis that these agents might hasten RRF decline. Furthermore, our study did not show rapid decline in RRF even with repeated courses of aminoglycosides. This finding does not support the current ISPD recommendation that repeated courses of aminoglycoside therapy are probably not advisable if an alternative approach (e.g. ceftazidime or cefepime) is possible [2].

The strengths of our study should be balanced against its limitations, which included the exclusion of just over half of the study population because of anuria or less than two recorded RRF measurements (such that a slope of RRF decline could not be drawn). This potentially introduced sampling bias since there were some differences in the characteristics of patients who were and were not included

Table 4. Peritonitis episodes and slope of monthly decline in RRF (mL/min/1.73 m^2) in median and interquartile range according to treatment with aminoglycosides

	Total population ($n = 2715$)	No aminoglycosides group ($n = 1640$)	Aminoglycosides group ($n = 1075$)	P-value
Peritonitis				
No episodes	1303 (48%)	1303 (79%)	0 (0%)	
Single episode	725 (27%)	213 (13%)	512 (48%)	
Multiple episodes	687 (25%)	124 (8%)	563 (52%)	
Slope of RRF decline (mL/min/1.73 m^2 per month)	−0.24 (−1.14, 0.03)	−0.26 (−1.17, 0.04)	−0.22 (−1.11, 0.01)	0.9

Table 5. Slope of monthly decline in RRF (mL/min/1.73 m^2) in median and interquartile range according to number of courses of aminoglycosides

	No aminoglycosides group ($n = 1640$)	Single course of aminoglycosides ($n = 616$)	Two courses of aminoglycosides ($n = 253$)	Three or more courses of aminoglycosides ($n = 206$)	P-value
Peritonitis					
No episodes	1303 (79%)	0 (0%)	0 (0%)	0 (0%)	
Single episode	213 (13%)	512 (83%)	0 (0%)	0 (0%)	
Multiple episodes	124 (8%)	104 (17%)	253 (100%)	206 (100%)	
Slope of RRF decline (mL/min/1.73 m^2 per month)	−0.24 (−1.14, 0.03)	−0.22 (−1.13, 0.01)	−0.18 (−0.92, 0.00)	−0.30 (−1.14, 0.02)	0.9

Table 6. Aminoglycoside treatment in study population as a whole and according to tertiles of RRF decline

		RRF decline tertile			
Characteristic	Total population ($n = 2715$)	Rapid ($n = 905$)	Intermediate ($n = 905$)	Slow ($n = 905$)	P-value
Peritonitis					
No episodes	1303 (48%)	439 (49%)	419 (46%)	415 (49%)	0.7
Single episode	725 (27%)	245 (27%)	243 (27%)	237 (26%)	
Multiple episodes	687 (25%)	220 (24%)	243 (27%)	224 (25%)	
Aminoglycoside treatment					
Never	1640 (60%)	546 (60%)	536 (59%)	558 (62%)	0.6
At least one course	1075 (40%)	359 (40%)	369 (41%)	347 (38%)	
Aminoglycoside treatment					
Never	1640 (60%)	546 (60%)	536 (59%)	558 (62%)	0.7
Single course	616 (23%)	209 (23%)	206 (23%)	201 (22%)	
Two courses	253 (9%)	76 (8%)	97 (11%)	80 (9%)	
Three or more courses	206 (8%)	74 (8%)	66 (7%)	66 (7%)	

in the study. The investigation was also constrained by limited depth of data collection. ANZDATA does not collect important information, such as patient compliance; individual unit management protocols, laboratory values (such as C-reactive protein and dialysate white cell counts); severity of co-morbidities; antibiotic dosages; serum aminoglycoside levels; routes of antibiotic administration; blood pressure control; proteinuria; hypotensive episodes; radiographic contrast medications or concomitant medications such as non-steroidal anti-inflammatory drugs, angiotensin converting enzymes inhibitors, angiotensin receptor blockers and diuretics and other aminoglycoside adverse effects such as ototoxicity. Even though we adjusted for a large number of patient characteristics, the possibility of residual confounding could not be excluded. In common with other Registries, ANZDATA is a voluntary Registry and there is no external audit of data accuracy, including the accuracy of urine collection and diagnosis of peritonitis. Since patients receiving aminoglycosides were more likely to be treated in the larger centres, resulting centre-bias cannot be ruled out. We did not perform time to event analyses (such as anuria or urine output <100 mL/day) as the required data were not collected.

In conclusion, empiric use of aminoglycosides for the treatment of PD peritonitis was not associated with an adverse effect on RRF in this large study using ANZDATA data. Our results do not support the ISPD recommendation of using extended spectrum cephalosporin as an appropriate alternative to aminoglycoside to preserve renal function.

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Supplementary data

Supplementary data is available online at http://ndt.oxfordjournals.org.

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