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Letter to the Editor

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Experience With Pre-Dialysis Administration of Tobramycin in the Outpatient Setting

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The optimal dosing regimen for aminoglycoside in hemodialysis patients is not well defined. Traditionally, aminoglycosides have been given 1 to 2 mg/kg post-hemodialysis thrice a week in outpatients. Pharmacokinetic (PK)/pharmacodynamic (PD) parameters of aminoglycosides are not optimal when using that dosing regimen.[1-3] In adults with normal renal function, a target peak of 8 to 10 times the minimal inhibitory concentration (MIC) has been suggested. A prior study among hemodialysis patients showed that to achieve a peak of 7 to 10 mg/L with the traditional post-hemodialysis dosing, a trough concentration of 3.5 to 5.0 mg/L would be needed.[4] Such a target would increase the risk of toxicity. We and other investigators have previously published encouraging PK results by administrating the aminoglycoside before or at the beginning of the hemodialysis treatment.[5-7] These regimens have a higher probability of attaining PK/PD targets, such as peaks >8 mg/mL, while limiting exposure (area under the curve [AUC]). In this letter, we report our 2-year experience of administrating tobramycin in the first 30 minutes of the hemodialysis treatment among outpatients.

Tobramycin was used in 16 courses of treatment for 14 patients. Every patient received 5 mg/kg at the beginning of each hemodialysis session. Dose was reduced at the next hemodialysis if the trough was more than 2.0 mg/L. For each course, the mean number of tobramycin doses was 2.88 (SD = 1.54). In all treatments where tobramycin was administrated, the patient completed the prescribed dialysis duration (4 hours for 13 patients and 3.5 hours for 1 patient). Tobramycin was used for the following reasons: antimicrobial resistance, allergy, therapeutic failure with other antibiotics, or drug-drug interactions. We aimed to measure serum concentration of tobramycin (trough) at the beginning of every hemodialysis session. As expected, the trough could only be used for dose adjustment at the next administration. The highest trough we measured was 3.5 mg/L, and only 2 patients had a trough above 3.0 mg/L (Table 1). Clinical success (defined as resolution of symptoms without a second course of antibiotics) was obtained in 14 out of 16 treatment courses, and no adverse effects were reported. The obtained troughs were higher than what we measured in our previous study. This could be explained by the fact that some patients had a body mass index (BMI) above 40 kg/m^2 (they were excluded in our prior study), that dialysis vintage was higher (mean of 3.9 ± 3.0 years compared to 2.3 ± 1.85 years in our prior study), and that most patients received more than 1 dose of tobramycin. Indeed, among the patients with the highest troughs, one had a high BMI (37 kg/m^2) and another was on hemodialysis for more than 10 years. According to these data, aiming at a trough below 3 mg/L seems more realistic than 2.0 mg/L. To our knowledge, this is the first report of administration of multiple doses of tobramycin in the first 30 minutes of the hemodialysis treatment in an outpatient setting. This regimen appeared to be feasible, safe, and potentially more efficacious.

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Table 1. Patient Characteristics and Trough Values.

Age	BMI	Years on dialysis	Indication	Number of doses	Trough >2.0 per-treatment	Highest trough
76	23	>10 years	COPD exacerbation in multiresistant *Serratia*-colonized patient	4	Yes	3.5
68	25	9 years	Urinary tract infection	1	Yes	3.2
79	37	3 years	Polymicrobial infected chronic wound	5	Yes	3.0
57	21	1 year	Pseudomonas infected chronic wound	5	Yes	2.9
71	26	7 years	Catheter-related sepsis *Serratia* resistant to ciprofloxacin	3	Yes	2.9
87	34	6 months	Urosepsis with extended-spectrum beta-lactamases producing bacteria resistant to ciprofloxacin	3	Yes	2.3
70	49	3 years	Persistent urinary tract infection resistant to ciprofloxacin	2	No	2.0
64	33	2 years	Persistent urinary tract infection (failure to ciprofloxacin and fosfomycin)	3	No	2.0
64	44	5 months	Pyelonephritis	4	No	2.0
85	28	2.5 years	Urinary tract infection nonresponsive resistant to ciprofloxacin	1	No	1.4
83	16	7 years	Exit site access infection	1	No	1.3
85	25	2 years	Urinary tract infection in patient taking oral anticoagulant	2	No	1.3
74	23	5 years	Urinary tract infection	2	No	1.1
47	25	8 months	Enterobacter catheter-related sepsis	6	No	0.9
70	31	7 years	Persistent urinary tract infection without response to ciprofloxacin and amoxicillin allergy	2	No	0.7
70	49	3 years	Repetitive urinary tract infection resistant to ciprofloxacin	2	N/A	N/A

Note. Tobramycin dosage was prescribed before each dialysis (N/A: dosage not available). BMI = body mass index; COPD = chronic obstructive pulmonary disease.

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