Pharmacokinetics of Polymyxin B in a Patient With Renal Insufficiency: A Case Report

To the Editor—The pharmacokinetics of polymyxin B, especially with regard to the renal insufficiency cohort, are extremely lacking despite the increasing clinical use of this agent [1]. We described the pharmacokinetics of polymyxin B in a patient with renal insufficiency who was not undergoing dialysis.

The patient, a 50-year-old Chinese man, underwent surgical resection to remove retroperitoneal sarcoma. He developed postsurgical intra-abdominal and wound infections. Multidrug-resistant *Acinetobacter baumannii* (which was susceptible to polymyxin B alone) was isolated from both the retroperitoneal hematoma drainage site and wound cultures. The patient weighed 50 kg and had a baseline serum creatinine level of 3.5 mg/dL (estimated creatinine clearance, 18 mL/min). Polymyxin B sulfate (USP) was given as intermittent intravenous infusions; a single dose of 50 mg was initially given over a 60-min period, followed by 75 mg over 90-min periods every 24 h. The patient died on day 4 of therapy; his serum creatinine level had been >2.8 mg/dL throughout the treatment course. Three blood samples were obtained serially after administration of the second dose. The serum samples were assayed in duplicate for polymyxin B concentrations using a validated liquid chromatography tandem mass-spectroscopy method [2], which was modified to detect various major polymyxin B components concurrently [3]. On the basis of our previous findings, the proportions of polymyxin B1 and isoleucine polymyxin B1 in polymyxin B (USP) were assumed to be 73.5% and 8.6%, respectively [4]. A 1-compartment linear model was fit to the concentration-time profiles to derive the best-fit pharmacokinetic parameters. All model fittings were performed with the ADAPT II program [5].

Both polymyxin B1 and isoleucine polymyxin B1 (>80% of total polymyxin B content) were satisfactorily detected in the serum samples. The overall model fits to the data were satisfactory ($R^2 \geqslant 0.98$), and the best-fit pharmacokinetic parameters are as shown in Table 1.

Table 1. Pharmacokinetic Parameters of Polymyxin B1 and Isoleucine Polymyxin B1

	Polymyxin B1	Isoleucine polymyxin B1
Ke, h^{-1}	0.060	0.038
$T_{1/2}$, h	11.5	18.4
V, L	55.47	40.78
Cl, L/h	3.35	1.54
AUC_{24}, mg.h/L	16.5	4.2
Model fit (R^2)	0.99	0.98

NOTE. The proportions of polymyxin B1 and isoleucine polymyxin B1 in polymyxin B (USP) were assumed to be 73.5% and 8.6%, respectively [4]. AUC_{24}, area under the concentration-time curve over 24 hours; Cl, clearance; Ke, elimination rate constant; $T_{1/2}$, elimination half-life; V, volume of distribution.

To our knowledge, this is the first report to date of the pharmacokinetics of polymyxin B in a patient with renal insufficiency. Polymyxin B1 is the major component of polymyxin B (USP). The serum elimination half-life of polymyxin B1 in renal insufficiency was 11.5 h, which was similar to data previously observed in patients with normal renal function [2]. The anticipated peak and trough concentrations were less than the polymyxin B susceptibility breakpoint (2 μg/mL) throughout the entire dosing interval. This finding is important, because it is widely believed that dosing of polymyxin B should be adjusted in the event of renal insufficiency [1]. It was reported previously that the half-lives with renal insufficiency were 48–72 h and that 60% of the dose was excreted in urine [6], but details of the original study could not be retrieved. Recently, it has been suggested that polymyxin B undergoes nonrenal clearance and that total body clearance appears to be relatively insensitive to renal function, because minimal polymyxin B was detected in urine [7].

Our data provided further direct evidence that intravenous polymyxin B dose and/or frequency need not be adjusted in the event of renal insufficiency. However, more studies are warranted to validate our findings. Investigations are ongoing addressing to the pharmacological relevance of various polymyxin B components.

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