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CORRECTION

Correction to: An Integral Pharmacokinetic Analysis of Piperacillin and Tazobactam in Plasma and Urine in Critically Ill Patients

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Correction to: Clinical Pharmacokinetics (2022) 61:907–918
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This is a corrigendum to Clin Pharmacokinet. 2022 Apr 4 An Integral Pharmacokinetic Analysis of Piperacillin and Tazobactam in Plasma and Urine in Critically Ill Patients concerning a correction in the simulations of piperacillin and tazobactam concentrations with the developed pharmacokinetic model. In the original simulation dataset, by accident double doses were entered. The exposure of both piperacillin and tazobactam based on the new corrected simulations is 50% of the exposure presented in the original publication. This applies to the following sections of the article: abstract, results, discussion, conclusion, Figs. 3, 4, 5 and Tables 3 and 4. Therefore, all simulated piperacillin and tazobactam concentrations in the original manuscript should be divided by 2. The published model does not contain any errors, as the error concerns only the performed simulations. Although the main conclusion of the article remains intact, some parts of the results and discussion are subject to reinterpretation.

In the results section it is mentioned that the target concentration for tazobactam (2.86 mg/L) was predicted to be reached in 100% of the population when tazobactam in a dose of ≥ 2 g/ 24 h was administered and in 99.0% and 99.4% of the population with doses of 1 and 1.5 g/24 h, respectively. Based on the new simulations the target was predicted to be reached in 99.0% of the population when a dose of ≥ 2 g/24 h was administered, and in 76.1% and 94.1% of the population with doses of 1 and 1.5 g/24 h, respectively.

In the results it is mentioned that piperacillin dosed at 12 g/24 h is predicted to be sufficient to attain a target of 100% $fT_{>1\times MIC}$ (MIC ≤ 16 mg/L), even for patients with a creatinine clearance of up to 200 mL/min. Based on the correct simulations a dose of 12 g/24 h is sufficient for patients with creatinine clearances < 150 mL/min. Patients with a creatinine clearance of 150-200 mL/min should be administered a dose of 16 g/24 h.

In the results it is also mentioned that in case a target of 100% $fT_{>5\times MIC}$ is desired, a piperacillin dose of 20 g/24 h is predicted to be sufficient for patients with creatinine clearances of 10-60 mL/min. Based on the correct simulations a dose of 20 g/24 h is inadequate to reach a target of 100% $fT_{>5\times MIC}$ for patients with creatinine clearances of 10-60 mL/min.

Concerning the piperacillin toxicity, it is mentioned in the results section that a limited fraction of 8.0% of the population is predicted to reach the putative toxicity threshold of 157 mg/L at a dose of 8 g/24 h and in 19.6% with a dose of 12 g/24 h, in 33.3% with a dose of 16 g/24 h, and in 47.8% with a dose of 20 g/24 h. Based on the corrected simulations the predicted fraction of the population reaching an exposure of 157 mg/L is 0.9% at a dose of 8 g/24 h, 3.7% with a dose of 12 g/24 h, 8.1% with a dose of 16 g/24 h, and 13.8% with a dose of 20 g/24 h.

The corrected Figs. 3, 4, 5 and Tables 3, 4 are enclosed.

The original article can be found online at https://doi.org/10.1007/s40262-022-01113-6.

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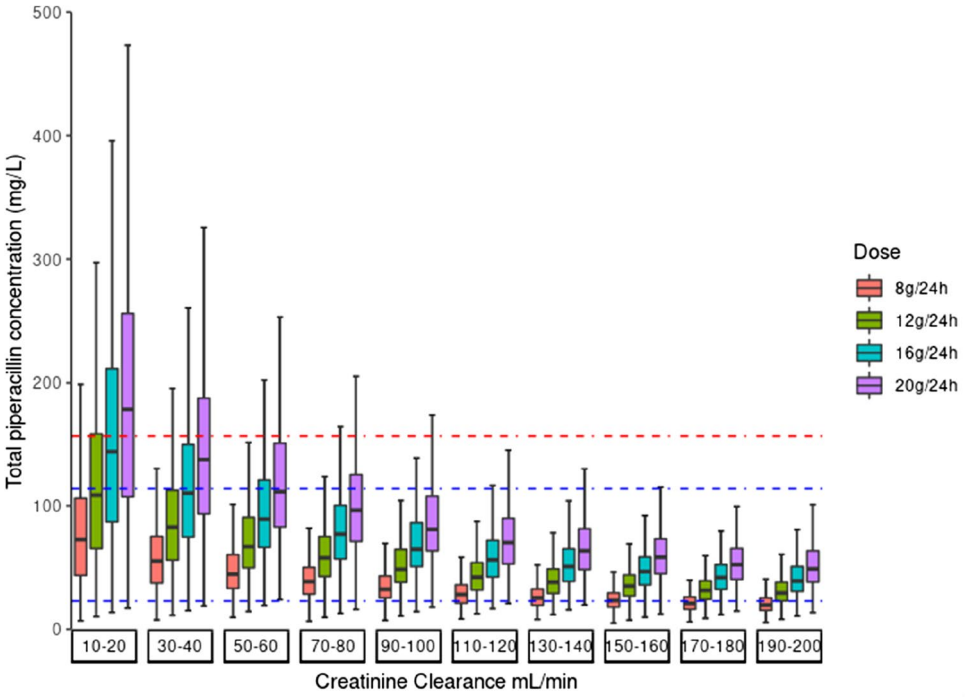

Fig. 3 Simulated piperacillin concentrations for different dosing regimens versus creatinine clearance. The blue horizontal lines represents a target of 100% fT>1xMIC (22.9 mg/L) and 100% fT>5xMIC (114 mg/L), assuming an MIC of 16 mg/L. The red horizontal line represents the upper limit of toxicity (157 mg/L). Simulations were performed in 20 groups of creatinine clearance between 10-200 mL/min, with 10 mL/min increments. In this table pairs of two groups have been combined

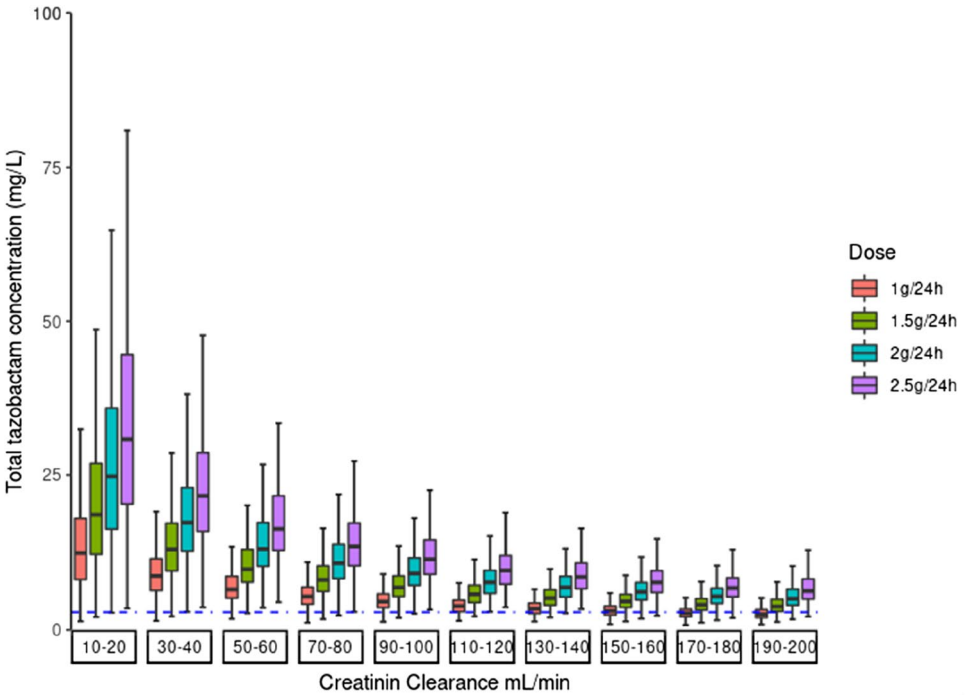

Fig. 4 Simulated tazobactam concentrations for different dosing regimens versus creatinine clearance. The blue horizontal line represents a target of 2.86 mg/L. Simulations were performed in 20 groups of creatinine clearance between 10-200 mL/min, with 10 mL/min increments. In this table pairs of two groups have been combined

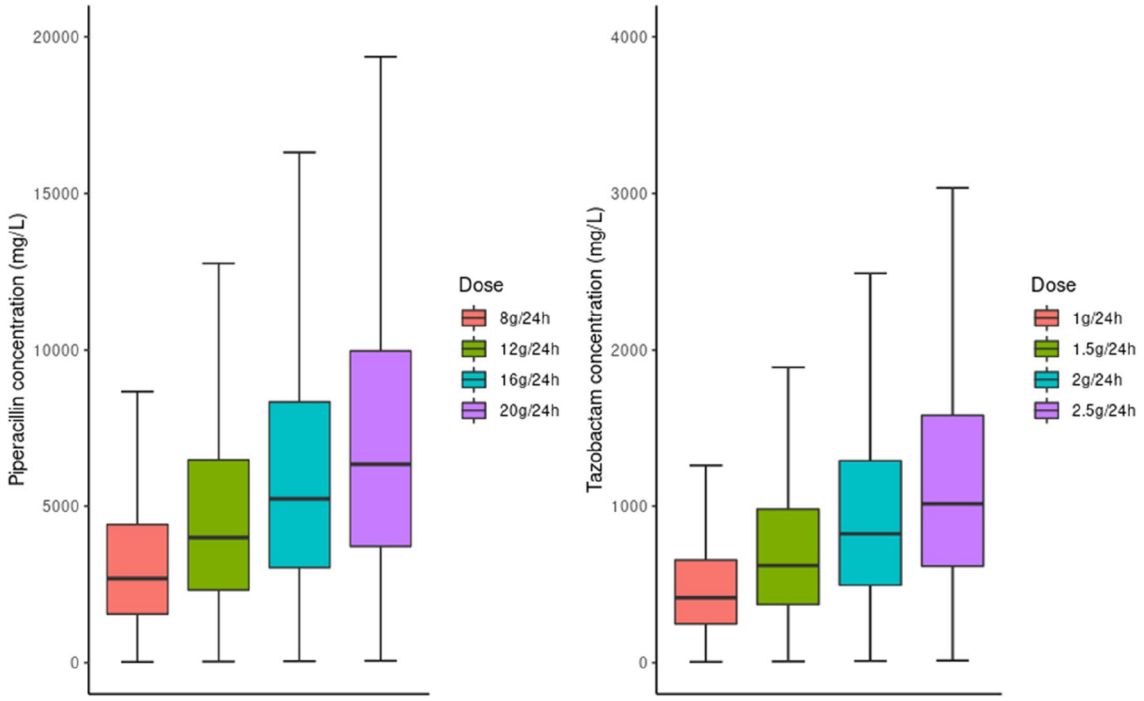

Fig. 5 Piperacillin (left) and tazobactam (right) concentrations in urine

Table 3 Probability of target attainment for MIC=16 mg/L (ECOFF *P. aeruginosa*), and probability of reaching the potential toxicity level of 157 mg/L for different doses of piperacillin and different classes of creatinine clearance

Creatinine clearance (mL/min)[a]	Dose piperacillin/tazobactam (g)	100% $fT_{>1xMIC}$	100% $fT_{>5xMIC}$	Toxicity level >157 mg/L
10–20	8/1	93	**21**	8.2
	12/1.5	97.4	**47.8**	26.2
	16/2	99.4	**63.2**	45.2
	20/2.5	99.8	**73.2**	58.4
30–40	8/1	92.6	**5.4**	0.6
	12/1.5	98	**24.2**	8.4
	16/2	98.6	**47.4**	22.6
	20/2.5	99.2	**63.8**	40.4
50–60	8/1	91.2	**1.2**	0
	12/1.5	97.6	**9.6**	1.8
	16/2	99.4	**29.8**	8
	20/2.5	100	**46.8**	22.2
70–80	8/1	**87.2**	**0.4**	0
	12/1.5	97.2	**4.2**	0.6
	16/2	99.2	**16.4**	3.6
	20/2.5	99.6	**31.6**	10.6
90–100	8/1	**81.2**	**0**	0
	12/1.5	95	**1.4**	0
	16/2	98.2	**7.6**	1
	20/2.5	98.8	**22.4**	4.2
110–120	8/1	**70**	**0**	0
	12/1.5	90.8	**0**	0
	16/2	97.4	**2.6**	0
	20/2.5	99.6	**10.6**	1.2
130–140	8/1	**60.8**	**0**	0
	12/1.5	90.4	**0.2**	0.2
	16/2	96.6	**1**	0.2
	20/2.5	99.2	**5.8**	0.8
150–160	8/1	**51.6**	**0**	0
	12/1.5	**84.6**	**0**	0
	16/2	95.6	**0.2**	0
	20/2.5	99.2	**2.2**	0
170–180	8/1	**40.6**	**0**	0
	12/1.5	**79.2**	**0**	0
	16/2	94.8	**0**	0
	20/2.5	99.4	**1.2**	0
190–200	8/1	**37**	**0**	0
	12/1.5	**75.6**	**0**	0
	16/2	93.4	**0**	0
	20/2.5	98	**0.8**	0

[a]Simulations were performed in 20 groups of creatinine clearance between 10 and 200 mL/min, with 10 mL/min increments. In this table pairs of two groups have been combined

Table 4 Cumulative fraction of response

Creatinine clearance (mL/min)[a]	Dose piperacillin/tazobactam (g)	*E. coli*		*K. pneumoniae*	
		100% $fT_{>1xMIC}$	100% $fT_{>5xMIC}$	100% $fT_{>1xMIC}$	100% $fT_{>5xMIC}$
10–20	8/1	100	96.0	100	93.0
	12/1.5	100	99.0	100	97.6
	16/2	100	99.0	100	98.6
	20/2.5	100	100	100	98.4
30–40	8/1	100	95.6	99.8	90.4
	12/1.5	100	97.4	100	96.0
	16/2	100	99.0	100	98.2
	20/2.5	100	99.0	100	99.0
50–60	8/1	100	95.8	99.8	**88.6**
	12/1.5	100	97.6	100	93.4
	16/2	100	100	100	98.2
	20/2.5	100	100	100	98.2
70–80	8/1	99.8	92.2	99.8	**82.6**
	12/1.5	100	96.8	100	94.2
	16/2	100	99.4	100	96.8
	20/2.5	100	99.6	100	99.0
90–100	8/1	100	**89.8**	99.8	**79.6**
	12/1.5	100	95.0	100	**88.8**
	16/2	100	98.8	100	95.2
	20/2.5	100	98.4	100	96.8
110–120	8/1	100	**86.8**	98.8	**70.2**
	12/1.5	100	94.0	100	**89.0**
	16/2	100	97.4	100	91.8
	20/2.5	100	98.8	100	96.2
130–140	8/1	99.8	**86.6**	99.6	**68.4**
	12/1.5	100	93.8	100	**83.0**
	16/2	100	96.8	100	92.0
	20/2.5	100	97.8	100	96.0
150–160	8/1	99.8	**82.6**	99.4	**63.6**
	12/1.5	100	93.0	100	**82.2**
	16/2	100	96.2	100	**89.2**
	20/2.5	100	97.0	100	93.6
170–180	8/1	99.6	**80.0**	100	**63.0**
	12/1.5	100	**89.4**	100	**79.4**
	16/2	100	94.0	100	**83.8**
	20/2.5	100	96.6	100	91.0
190–200	8/1	99.8	**79.0**	99.4	**55.8**
	12/1.5	100	91.2	99.6	**74.0**
	16/2	100	96.2	100	**85.6**
	20/2.5	100	96.6	100	**89.2**

[a]Simulations were performed in 20 groups of creatinine clearance between 10 and 200 mL/min, with 10 mL/min increments. In this table pairs of two groups have been combined