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Proficiency testing for meropenem and piperacillin therapeutic drug monitoring: preliminary results from the SBIMC/BVIKM PK-PD working group

Mieke Carlier[1], Alexandre Athanasopoulos[2], Danielle Borrey[3], Pieter Colin[4], Frédéric Cotton[5], Raphael Denooz[6], Hugo Neels[7], Isabel Spriet[8], Timothy Ghys[9], Veronique Stove[1]

[1] Ghent University Hospital; [2] University Hospital of Charleroi; [3] AZ Sint Jan Brugge, [4] Faculty of Pharmaceutical Sciences, Ghent University
[5] Erasme Hospital, Brussels; [6] University Hospital Liège; [7] Ziekenhuisnetwerk Antwerpen; [8] University Hospital Leuven; [9] AZ Sint Lucas Gent

Background

Therapeutic drug monitoring of β–lactam antibiotics is gaining importance as a way to optimize dosing in difficult to treat patients. However, currently all used assays are in house developed and no commercial control samples are available. It is known that in house methods lack standardization.

Objectives

The purpose of this study was to evaluate the variability in reported concentrations for piperacillin and meropenem.

Materials and methods

Two sets of 8 meropenem and two sets of 8 piperacillin samples were sent on dry ice to 9 participating laboratories in Belgium. Each set contained spiked blank samples with known concentration, further called quality control (QC) samples, in a low, medium and high concentration, and patient pool samples (low, medium, high) from patients treated with the antibiotic.

The laboratories were asked to run the sets on different occasions.

Results given as less than a specific concentration e.g. <1.5 mg/L were not included in the statistics,

The consensus mean was calculated as specified by guidelines from the International Federation of Clinical Chemistry (IFCC).

Centers which had a bias (determined as the mean percentage difference from the true concentration) of more than 50% for at least 2 QC samples were excluded from calculation of the consensus mean of the patient samples. For the remaining samples, the mean concentration and standard score (the number of standard deviations the observation is above the mean) was calculated. Values with a standard score ≥2 were excluded and a new mean concentration and a new standard score were calculated. This process was repeated until all remaining values have a z score <2. This mean value was then used as the consensus mean.A standard score using the consensus mean and consensus standard deviation was calculated for each sample for each lab. A z-score >2 was considered not acceptable.

Bias and precision were calculated for each sample set for each lab and a report was sent.

Results

Nine laboratories analyzed the meropenem samples and 6 for piperacillin. Three out of 9 laboratories who reported on meropenem used LC-MS, 6 used LC-UV. For piperacillin, 2 out of 6 used LC-MS and 4 used LC-UV. The reported concentrations varied widely between labs.

Table 1 : Sample characteristics meropenem

	PP1	*PP2*	*PP3*	*QCL*	*QCM*	*QCH*
Target	Pool	Pool	Pool	1,11	5,53	55,30
Consensus mean	2,68	11,74	49,90	1,22	6,51	61,21
SD	0,26	0,54	5,47	0,18	1,55	8,05
CV	9,8%	4,6%	11,0%	15,1%	23,8%	13,2%
Matrix	Patient plasma	Patient plasma	Patient plasma	Bovine serum	Bovine serum	Bovine serum
interference	Lipemic	None	None	None	None	None
Aliquots	4	3	3	2	2	2
Number of results	34/36	25/27	26/27	15/18	17/18	17/18
% of samples between 80-120 %	59 %	60%	69%	60%	41%	59%
% samples > 120 %	38%	28%	23%	33%	41%	41%
% samples < 80%	3%	12%	8%	7%	18%	0%
% of samples with z-value between -2 and 2	59 %	52%	73%	73%	88%	76%
% of samples with z value >2	38%	32%	19%	27%	12%	24%
% of samples with z value <-2	3%	16%	8%	0%	0%	0

PP1 : patient pool 1 ; PP2 : patient pool 2; PP3: patient pool 3; QCL : quality control low ; QCM : quality control medium, QCH : quality control high

Figure 1 : reported concentrations for meropenem

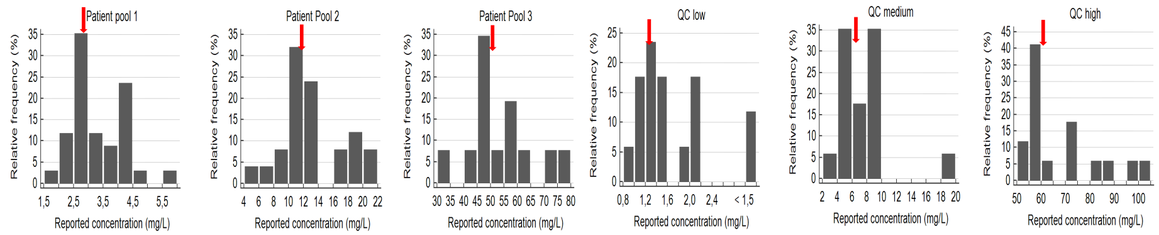


Table 1 : Sample characteristics piperacillin

	PP1	*PP2*	*PP3*	*QCL*	*QCM*	*QCH*
Target	Pool	Pool	Pool	1,63	8,15	114,00
Consensus mean	2,51	42,13	129,90	1,43	8,17	100,40
SD	0,49	4,98	16,40	0,10	1,97	10,74
CV	19,5%	11,8%	12,6%	7,0%	24,1%	10,7%
Matrix	Patient plasma	Patient plasma	Patient plasma	Bovine serum	Bovine serum	Bovine serum
interference	Lipemic	None	None	none	None	None
Aliquots	4	3	3	2	2	2
Number of results	18/24	18/18	18/18	10/12	12/12	12/12
% of samples between 80-120	69	78	78	60	50	92
% samples > 120 %	13	6	6	30	17	0
% samples < 80%	19	17	17	10	33	8
% of samples with z-value between -2 and 2	100	83	83	60	83	92
% of samples with z value >2	0	6	0	30	8	0
% of samples with z value <-2	0	11	17	10	8	8

Figure 2 : reported concentrations for piperacillin

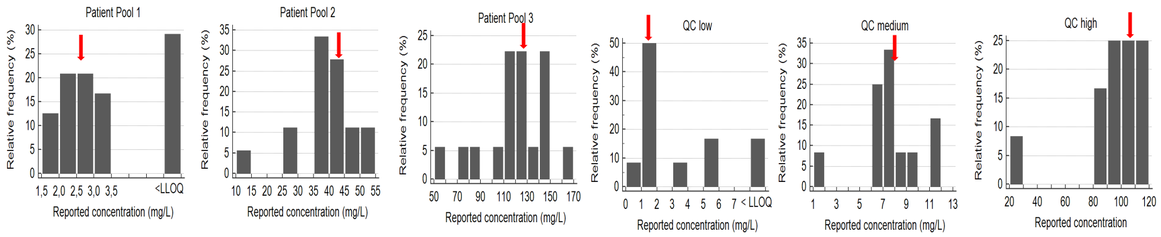
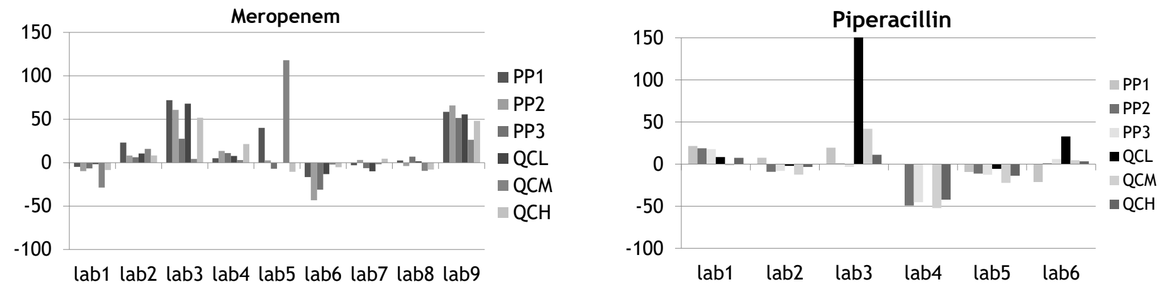


Figure 3 : bias per lab



Conclusion

There is a wide variability between the reported concentrations. The causes for the reported differences are further investigated. There is a need for external quality assessment of these methods.