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Paper Poster Session
PK/PD of agents against Gram-negatives

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

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Background: Therapeutic drug monitoring of beta 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. The purpose of this study was to evaluate the variability in reported concentrations for piperacillin and meropenem.

Material/methods: Two sets of 8 meropenem and two sets of 8 piperacillin samples were sent on dry ice to the participating laboratories in Belgium. Each set contained 3 spiked blank samples at 3 different concentrations, further called quality control (QC) samples (low, medium, high), and 5 samples from patient pools at 3 different concentrations (low, medium, high). The laboratories were asked to run the sets on different occasions. Results given as less than a specific concentration e.g. < 1.5 were not included in the statistics. The consensus mean was calculated as specified by guidelines from the International Federation of Clinical Chemistry. A standard score (the number of standard deviations an observation is deviated from the mean) was calculated for each sample for each lab. A z-score up to 2 was considered acceptable performance. Inaccuracy was evaluated for each sample group for each lab.

Results: Eight laboratories analyzed the meropenem samples, with three laboratories using LC-MS and 5 using LC-UV. For piperacillin, 5 laboratories joined this proficiency testing, of which 2 used LC-MS and 3 used LC-UV. The reported concentrations varied widely between labs as shown in table 1. For meropenem, only 2 labs had a z-score of ≤2 for all samples. Two labs had a z score >2 for 1 sample, one lab for 2 samples, one lab for 5 , and two labs for more than 10 samples. For piperacillin, 2 out of 5 centers had a z-score ≤2 for all samples, two labs had a z-score >2 for 2 samples, and one

lab for 8 samples. For meropenem, inaccuracy ranged from -53% to 243%, and for piperacillin from -52% to 299%.

	Meropenem Median (range) mg/L	Piperacillin Median (range) mg/L
QC low	1.4 (0.9-2.1)	1.5 (0.8-5.0)
QC medium	6.7 (3.9-19.0)	7.3 (1.4-11.7)
QC high	59.1 (53.3-103.1)	99 (25.4-115.0)
Patient pool low	3.0 (1.9-5.6)	2.5 (1.6-3.1)
Patient pool medium	11.9 (5.4-20.4)	40.6 (12.9-51.0)
Patient pool high	52.1 (30.7-76.7)	122.8 (52.3-160.3)

Conclusions: In this Belgian pilot study, we obeserved a wide variability between the reported meropenem and piperacillin concentrations from the different participating laboratories. The causes for the reported differences are further investigated. However, this study demonstrates that there is a need for external quality assessment of these methods.