27th ECCMID Vienna, Austria 22 – 25 April 2017
The congress of ESCMID

Session: P017 Challenges in diagnostic bacteriology

Category: 4b. Diagnostic bacteriology – non-culture based, including molecular and MALDI-TOF

22 April 2017, 15:30 - 16:30
P0338

Screening for relevant bacteriuria by flow cytometry: evaluation of more than 44,000 urine samples analyzed by the UX-2000 flow cytometer and microbiological culture

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Background: Diagnosis of urinary tract infections (UTI) usually requires the presence of symptoms and bacteriuria defined by conventional microbiological culture. Bacterial and leucocyte counts in the urine determined by flow cytometry promise to be a time and resource saving screening method for relevant bacteriuria, but cut-off values are a matter of debate. This study addresses those uncertainties by an analysis of a combined microbiological culture and urine flow cytometry dataset.

Material/methods: Species identification and colony-forming unit (CFU/ml) quantification from microbiological cultures of blood-agar and non-selective CHROMagar were matched to corresponding cellular (leucocytes/erythrocytes/epithelial cells) and bacterial counts per µl urine obtained from an UX-2000 flow cytometer (Sysmex, Kobe, Japan). Results comprise all samples that were sent to the diagnostic laboratories of the University Hospital of Basel between 2013 and 2015 and for which bacterial culture and flow cytometry data were available (local standard of practice). A positive microbiological culture was defined with more than 100,000 CFU/ml on any positive culture plate.

Results: Matching the microbiological reference standard with flow cytometry data resulted in a set of 44,986 urine samples (34.4% of which had relevant bacteriuria) of 25,196 patients. Prediction of a positive microbiological culture by bacterial counts measured by flow cytometry was most accurate and was a better predictor than leucocyte counts independent of the source of the urine (area under the receiver operator curve (AUC) of 92.8% and 78.6%, respectively). Table 1 summarizes cut-off values of 20, 100 and 200 bacteria/µl for different material categories.

Conclusions: The results emphasize the possibility of using bacterial counts from flow cytometry to predict relevant bacteriuria, yielding clinically relevant information that is usually available within a few hours after sampling. The data was obtained from routine laboratory results from a diverse set of patients over three years and underlines the robustness of these findings. 20 bacteria/µl as lower "rule-out" and 200 bacteria/µl as upper "rule-in" cut-off concentration appear to be pragmatic values for bacteriuria with sufficient sensitivity and specificity of > 95% and ~ 90%, respectively. Surprisingly, when contaminated samples with ≥ 10 epithelial cells (absolute) were omitted from the analysis, sensitivity decreased while specificity increased for all observed cut-off values but resulted in a high number of samples that had to be rejected (29.8%). This data therefore suggests that bacterial counts can still be used to exclude relevant bacteriuria even in contaminated samples.

Table 1: Sensitivity and specificity to predict bacterial growth of at least 100,000 CFU/mL for different urine sources and cut-off values.

Cut-off		20 bacteria/µl		100 bacteria/µl		200 bacteria/µl	
Material category	n	Specificity	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity
Midstream urine	29,491	58.7%	95.7%	82.4%	84.9%	89.1%	77.6%
One-time catheter	4,218	65.8%	98.2%	86.5%	95.3%	91.1%	93.7%
Indwelling catheter	7,275	54.8%	96.1%	84.6%	89.8%	91.2%	85.5%
Other sources[1]	4,002	58.1%	95.6%	84.9%	86.1%	90.6%	77.9%
Total	44,986	58.7%	96.0%	83.4%	86.9%	89.7%	80.5%
Total (not contaminated[2])	31,569	67.7%	94.6%	88.6%	85.0%	93.8%	79.0%

1: Suprapubic catheter, not-specified, unknown, before/after manual stimulation of prostate and others.
2: Defined as samples with <10 epithelial cells in total.