Application of Laser Light Scattering Technology in Rapid Diagnosis of Urinary Tract Infections and Antimicrobial Susceptibility Testing in a Tertiary Children’s Hospital

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Background
UTIs are one of the most common infections that require healthcare visits. Traditional urine culture can take up to 2 days before identification (ID) and AST results are available.

Timely and accurate microbiology testing is crucial in the diagnosis and management of urinary tract infections (UTIs). The ability to rapidly screen for potential UTIs can lead to early rule out and judicious use of antimicrobial therapy. This study examines the application of laser scattering for bacterial detection and antimicrobial susceptibility testing (AST) directly from urine.

BacterioScan™ Technology
BacterioScan platforms use laser scattering technology to rapidly differentiate bacterial growth vs no growth directly from clinical specimens (Figure 1). 216x UTI assay detects potential UTIs in about 3 h with a limit of detection of 10,000 CFU/ml of uropathogens.

216x UTI assay provides susceptibility testing directly from urine samples after 3 h of growth.

When paired with an ID system, the BacterioScan system has the potential to provide ID and AST within 24 h.

METHODS
Clinical Specimens:
- 237 urine samples collected within 24 h were de-identified and enrolled in the study.
- Residual urine samples collected for routine culture were tested using the BacterioScan 216x™ UTI System and 216x™ AST System.

216x UTI System:
- 2.5 mL of tryptic soy broth + 360 μL urine was added to the 216x UTI cartridge.
- Continuous collection of light refraction pattern generated growth curves that were used to determine if the samples were likely positive or negative for bacteria.
- Growth curves of “likely positive” were further analyzed for suitability and dilution factor for AST using the 216x AST assay.

For ID, 1 mL of all “likely positive” samples were centrifuged at 13,000 rpm for 2 min. The pellet was spotted on a MALDI-TOF MS (Bruker Corporation) target plate using a wooden stick.

216x AST System:
- Urine from 216x UTI assay was diluted in 2.5 mL Mueller-Hinton broth.
- AST for ampicillin, cefazolin, ceftriaxone, and ciprofloxacin was performed concurrently on the instrument. Samples were incubated for up to 16 hours with results available as early as 2 hours.

RESULTS
- Samples included 120 (50.6%) midstream, 83 (35.0%) catheter, 4 (1.7%) surgical, and 30 (12.7%) unknown urine.
- 84/237 (35.4%) and 153/237 (64.6%) urine were positive and negative by 216x UTI, respectively (Figure 2).
- 94.1% (144) 216x UTI negative showed either no growth or mixed flora by culture. The remaining 9 (5.9%) were catheter (5) or surgical (4) samples that grew >10K CFU/ml organisms. 3 grew >10K CFU/ml non-typical uropathogens (Table 1).
- Direct MALDI-TOF MS was performed on 67/84 (79.8%) positive and provided ID for 25 (37.3%) and no ID for 42 (62.7%) samples (Figure 3). MALDI was not performed on 17 (20.2%) due to insufficient volume.
- 216x AST was done on 42/84 (50.0%) likely positive. MALDI was performed on 32/42 (76.2%), 25 (78.1%) of which had MALDI results (Figure 4, Table 2, Figure 3).
- The other 38 (45.5%) likely positive showed no significant growth by culture. 2 (2.6%) grew Candida, which the 216x UTI was not designed to detect and 2 (2.4%) midstream urine grew >10K CFU/ml Pseudomonas aeruginosa. These 42 likely positive yielded “no peaks” by MALDI.

Table 1. Comparing 216x UTI to Culture

<table>
<thead>
<tr>
<th>Culture results</th>
<th>216x UTI Neg (%)</th>
<th>216x UTI Pos (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No growth</td>
<td>102 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>Mixed flora</td>
<td>42 (27.5%)</td>
<td></td>
</tr>
<tr>
<td>+10K CFU/mL</td>
<td>6 (3.9%)</td>
<td></td>
</tr>
<tr>
<td>Not uropathogens</td>
<td>3 (2.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Comparing Susceptibility Results

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Culture</th>
<th>216x AST</th>
<th>No. of Isolates (%)</th>
<th>Categorical Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>S</td>
<td>R</td>
<td>16 (50%)</td>
<td>100%</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>S</td>
<td>R</td>
<td>25 (78.1%)</td>
<td>100%</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>S</td>
<td>R</td>
<td>25 (78.1%)</td>
<td>100%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>S</td>
<td>R</td>
<td>1 (3.3%)</td>
<td>100%</td>
</tr>
</tbody>
</table>

Conclusions
- The 216x UTI System could be utilized as a screening platform to rule out UTIs within 3 hours with AST available after an additional 2-6 hours for suspect UTI positive samples. This could potentially prevent unnecessary antimicrobial therapy. Preliminary data are promising but testing of additional clinical samples is warranted.