Use of Leukocyte Esterase-Nitrate Activity as Predictive Assays of Significant Bacteriuria

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The present study evaluated the usefulness of the 1-min leukocyte esterase-nitrite tests in a tertiary-care hospital as a screening procedure to detect significant bacteriuria and correlated the findings with culture results. A total of 531 urine samples were reviewed, of which 484 were evaluated. Of the evaluated samples, 113 positive cultures (23.4%) were found, of which 93 (82.3%) were detected by leukocyte esterase-nitrate tests. In addition, 365 of 371 (98.4%) urine samples with negative bacterial cultures were negative in leukocyte esterase and nitrite tests.

During the past several years, a number of techniques have been reported as rapid methods for the detection of significant bacteriuria. Although the procedures have been successfully used, each has been found to be either time consuming or costly or to have pH interference or other technical problems. Recently, the nitrite test was evaluated and found to lack specificity and sensitivity (2) when used alone as a screening test for bacteriuria. Another procedure evaluated was the 15 min leukocyte esterase test (LE), the results of which were compared with those for Gram-stained specimens (3). The LE test in males was less specific than the Gram stain but equally sensitive and thus an excellent predictor of negative cultures (3). Since this study, a new 1-min test strip for LE has been developed, which we assessed in conjunction with the nitrite test as a rapid screen for bacteriuria.

A total of 531 randomly collected urine samples were obtained by clean midstream catch or catherization and processed in this study. Urine specimens were plated within 2 h of collection with .01-ml calibrated platinum loop. The specimens were inoculated onto sheep blood agar and MacConkey agar plates for quantitative culture (1), and then the plates were placed at 35°C for 18 h in an incubator under atmospheric conditions. Colony counts were done by visually examining the blood agar plates, and bacterial isolates were identified by the MicroScan procedure (American MicroScan, Sacramento, Calif.).

Significant bacteriuria was defined as ≥10^5 CFU of one clearly predominant organism per ml. Secondary organisms were accepted also if they occurred in concentrations of <10^4. All cultures with three or more organisms were considered contaminated and were excluded from the evaluation.

LE activity was determined by dipping a Chemstrip 9 (Biodynamics, Div. of Boehringer Mannheim Corp., Indianapolis, Ind.) for 1 s into urine. The strip was then withdrawn over the specimen cup rim to remove excess fluid, followed by incubation at room temperature for 30 s for nitrite and 1 min for LE. Color reactions on the LE and nitrite pads were compared with a color chart, and the results were immediately recorded. The LE-nitrite results were retrospectively compared with corresponding culture results.

Of the 531 urine specimens tested, 113 had colony counts indicative of significant bacteriuria. Isolates from urine samples showing significant bacteriuria are shown in Table 1. Of the 531 specimens, 41 were contaminated by three or more organisms. Six specimens had discoloration that interfered in the interpretation of the LE-nitrite tests and were excluded. Subsequently, 484 specimens were evaluated, of which 371 had either no growth or less than 10^5 CFU/ml. Of the 113 specimens (23.4%) that showed significant bacteriuria, 93 were positive by either LE or nitrite or both, 89 were positive by LE, and 4 were positive by nitrite only. Of the 89 specimens positive by LE, 43 also were positive by nitrite. Twenty specimens that showed significant bacteriuria had LE- and nitrite-negative results. The correlation of LE, nitrite, and culture results is shown in Table 2. The sensitivity, specificity, and predictive values for predicting significant bacteriuria are shown in Table 3. Cultures with ≥10^3 and ≥10^4 CFU/ml were also evaluated; however, only one culture with ≥10^5
TABLE 1. Predominant clinical isolates found in significant bacteriuria

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>37 (32.7)</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>8 (7.1)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>6 (5.3)</td>
</tr>
<tr>
<td>Enterobacter aerogenes</td>
<td>6 (5.3)</td>
</tr>
<tr>
<td>Serratia spp.</td>
<td>4 (3.5)</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>3 (2.7)</td>
</tr>
<tr>
<td>Morganella morgani</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Other</td>
<td>47 (41.6)</td>
</tr>
</tbody>
</table>

CFU/ml was considered clinically significant, and only two cultures with ≥10⁴ CFU/ml were considered clinically significant. In all three cases, the LE and nitrite tests were positive.

As expected, Escherichia coli was the predominant clinical isolate, followed by Klebsiella, Pseudomonas, and Enterobacter spp. (Table 1). The results are similar to those found by Wenk et al. (6). The LE-nitrite screen was positive for either LE or nitrite in 93 (82.3%) of the 113 positive cultures. The LE-nitrite screen correlated extremely well with negative results and negative cultures (specificity, 98.4%). Six specimens were positive by LE and nitrite but had negative cultures (Table 2). This phenomenon was possibly due to the presence of antimicrobial agents preventing bacterial growth or other interfering factors that are yet to be defined.

The predictive indices of the LE-nitrite screening procedure are shown in Table 3. Sensitivity and specificity were 82.3 and 98.4%, respectively, and the predictive positive index was 93.9%, which was much better than previously reported (3, 6). The predictive negative index in the present study was 94.8% and was comparable to that found in previous studies (3, 6). The rate of positivity (23.4%) in our tertiary-care facility is higher than that of other health care settings, such as Health Maintenance Organization laboratories, which have a low rate of positivity (12.5%) (K. S. Wise, G. L. Grammens, and L. A. Sagert, Abstr. Annu. Meet. Am. Soc. Microbiol. 1983, C12, p. 313). Therefore, the predictive indices may change from one setting to another.

In a tertiary-care institution such as ours, which includes nephrology, endocrinology, oncology, cardiology, transplant (renal and liver), and medical-surgical services, the combination of the LE and nitrite tests as a screen has proven to be quite useful in predicting the outcome of urine cultures. Preliminary reporting has been well accepted by the medical staff in our institution. The LE test has been shown to be specific for leukocytes and thus indicative of pyuria (4, 5). Although the sensitivity is only 82.3%, the specificity of 98.4% suggests that LE- and nitrite-negative specimens could be eliminated from further testing (e.g., culture and Gram staining). The use of these tests as a screen to eliminate further testing or as a preliminary report needs further evaluation in various patient populations. It should also be pointed out that the quality of the specimen should be considered, as it poses a problem in screening just as it does in culture analysis. In the present study, 41 specimens (7.8%) were not evaluated, owing to contamination, thus suggesting that improved sterile collection may improve the statistical evaluation of LE-nitrite screening.

LITERATURE CITED