Use of a Rapid Antigen Test, C. DIFF QUIK CHEK®, as a Screening Test for C. difficile Disease

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ABSTRACT: C. DIFF QUIK CHEK® (TECHLAB®) is a rapid test for detection of glutamate dehydrogenase (GDH) in fecal specimens. GDH is produced by all strains of Clostridium difficile, which causes nosocomial and community-acquired infections, most often following antibiotic therapy. Some C. difficile strains are nontoxicogenic while toxigenic strains cause gastrointestinal problems ranging from diarrhea to colitis through the production of toxin A, an enterotoxin, and toxin B, a cytotoxin. Diagnosis of C. difficile disease relies on patient symptoms and toxin detection. Tissue culture, which is highly sensitive and specific for toxin detection, requires special equipment and 48 hours before a specimen can be reported as negative. ELISA toxin tests are more rapid but not as sensitive. Screening with C. DIFF QUIK CHEK® would allow samples negative for GDH, and therefore C. difficile, to be reported out immediately. Positive samples could then be confirmed for toxin by additional testing.

RESULTS: Compared to tissue culture, C. DIFF QUIK CHEK® had a sensitivity, specificity, predictive negative value, and correlation of 95%, 78%, 98%, and 82%, respectively. Compared to C. DIFF CHEK-60™, the sensitivity, specificity, and correlation were each 94%. The predictive negative value was 98%.

ANALYSIS OF THE C. DIFF QUIK CHEK® VERSUS TISSUE CULTURE

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<th>(N=200)</th>
<th>TISSUE CULT</th>
<th>Pos</th>
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<tr>
<td>C. DIFF QUIK CHEK® *-pos</td>
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<tr>
<td>C. DIFF QUIK CHEK® *-neg</td>
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Sensitivity 95% (95% CI 83% - 99%)
Specificity 76% (95% CI 70% - 84%)
Pred Neg Val 97% (95% CI 94% - 100%)
Correlation 82% (95% CI 77% - 86%)

NOTE: The Predictive Positive Value was not determined because the C. DIFF QUIK CHEK® detects the presence of both toxigenic and nontoxigenic strains whereas the tissue culture assay detects only toxigenic strains. Thus, PPV is not an accurate indication of test performance.

BACKGROUND: C. DIFF QUIK CHEK® (TECHLAB®) is a rapid test for detection of glutamate dehydrogenase (GDH) in fecal specimens. GDH is produced by all strains of Clostridium difficile, which causes nosocomial and community-acquired infections, most often following antibiotic therapy. Some C. difficile strains are nontoxicogenic while toxigenic strains cause gastrointestinal problems ranging from diarrhea to colitis through the production of toxin A, an enterotoxin, and toxin B, a cytotoxin. Diagnosis of C. difficile disease relies on patient symptoms and toxin detection. Tissue culture, which is highly sensitive and specific for toxin detection, requires special equipment and 48 hours before a specimen can be reported as negative. ELISA toxin tests are more rapid but not as sensitive. Screening with C. DIFF QUIK CHEK® would allow samples negative for GDH, and therefore C. difficile, to be reported out immediately. Positive samples could then be confirmed for toxin by additional testing.

METHODS: With C. DIFF QUIK CHEK®, the specimen, diluent, and conjugate are mixed, added to a cassette containing immobilized anti-GDH antibodies, and incubated for 15 minutes. The membrane is washed and substrate is added. Reaction development occurs during a subsequent 15-minute incubation. 200 fresh fecal specimens were tested using C. DIFF QUIK CHEK®, C. DIFF CHEK-60™, and tissue culture TOX-B TEST.

ANALYSIS OF THE C. DIFF QUIK CHEK® VERSUS C. DIFF CHEK-60™

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<tr>
<td>C. DIFF QUIK CHEK® *-neg</td>
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Sensitivity 94% (95% CI 86% - 98%)
Specificity 94% (95% CI 88% - 97%)
Pred Pos Val 89% (95% CI 80% - 95%)
Pred Neg Val 97% (95% CI 91% - 99%)
Correlation 94% (95% CI 92% - 95%)

NOTE: The Predictive Positive Value was not determined because the C. DIFF QUIK CHEK® detects the presence of both toxigenic and nontoxigenic strains whereas the tissue culture assay detects only toxigenic strains. Thus, PPV is not an accurate indication of test performance.

DISCUSSION: Our study was undertaken to evaluate a new rapid antigen screen for C. difficile, the C. DIFF QUIK CHEK®. Our results showed the following:

- The test exhibited a high predictive negative value (>98%) for the detection of stool specimens that were negative for C. difficile toxin. This screen allows laboratories that use the tissue culture assay to focus on performing this more complicated test only on specimens that are antigen-positive. In our study involving 200 specimens, 159 specimens (ca. 80%) would not have required further testing, although 2 would have been missed upon initial testing.

- The test provided results in less than 30 minutes. This rapid turn-around time allows the physician to know quickly whether the patient is infected with C. difficile. This information allows the necessary precautions to be implemented rapidly and efficiently.

- The performance of the test, which uses a new membrane format, correlated closely (94%) with an ELISA format (the C. DIFF CHEK-60™) that is specific for glutamate dehydrogenase.

- A limitation of the test is that it does not distinguish between toxigenic and nontoxigenic strains. In our study, 54% of the C. DIFF QUIK CHEK®-positive specimens were positive by tissue culture assay. We did not determine whether antigen-positive, tissue culture-negative specimens represented true nontoxicogenic strains or contained levels of toxin that were too low to be detected by tissue culture assay. Our results show, however, that GDH, which is expressed constitutively by all strains of C. difficile, is an excellent marker for determining the presence of the organism.

CONCLUSIONS: The C. DIFF QUIK CHEK® is a rapid test that is simple to use with a quick (<30 minutes) turn-around time for reporting samples as negative when no GDH is detected. C. DIFF QUIK CHEK® correlates well with the ELISA antigen test, C. DIFF CHEK-60™. With high sensitivity and high predictive negative values compared to tissue culture, it is an effective way to screen samples and reduce the workload and cost of diagnosing C. difficile without sacrificing patient care.