Utility of Perirectal Swab Specimens for Diagnosis of Clostridium difficile Infection

Sirisha Kundrapu,1 Venkata C. K. Sunkesula,1 Lucy A. Jury,2 Ajay K. Sethi,3 and Curtis J. Donskey1,2

1Department of Medicine, Infectious Diseases Division, Case Western Reserve University School of Medicine; 2Geriatric Research, Education, and Clinical Center, Cleveland Veterans Affairs Medical Center, Cleveland, Ohio; and 3Department of Population Health Sciences, University of Wisconsin School of Medicine Public Health, Madison

For 139 patients tested for Clostridium difficile infection by polymerase chain reaction, the sensitivity, specificity, positive predictive value, and negative predictive value of testing perirectal swabs vs stool specimens were 95.7%, 100%, 99.1%, and 99.9%, respectively. For selected patients, perirectal swabs provide an accurate toxigenic C. difficile detection strategy.

Accurate and efficient strategies to diagnose Clostridium difficile infection (CDI) are essential to guide management and prevent transmission. Currently, nearly all CDI testing is accomplished through collection of stool specimens from patients with diarrhea that are analyzed for the presence of toxin or toxin-producing strains of C. difficile. One limitation of the reliance on stool specimens for diagnosis is that patients with severe CDI complicated by ileus may be unable to produce specimens for testing. Moreover, factors such as altered patient mental status or frequent absences from the ward may result in delayed collection of stool specimens. Several studies have reported that delays from onset of diarrhea to collection of stool specimens for testing are common. Because perirectal swabs have been shown to be equivalent to stool specimens for detection of other healthcare-associated pathogens, we hypothesized that collection of perirectal swabs might provide an accurate and efficient strategy for detection of toxigenic C. difficile in stool of patients with suspected CDI.

MATERIALS AND METHODS

The Cleveland Veterans Affairs Medical Center includes a 215-bed hospital and 165-bed long-term care facility. During the study, clinical testing for CDI was performed on stool specimens using an enzyme immunoassay for glutamate dehydrogenase (Wampole C. diff Chek-60, Inverness Medical, Princeton, New Jersey) as an initial screen with positive tests being confirmed with a commercial polymerase chain reaction (PCR) assay (Xpert C. difficile, Cepheid, Sunnyvale, California). The laboratory rejected formed stool specimens. The hospital’s institutional review board approved the study protocol.

We conducted a 4-month prospective study of inpatients being tested for CDI. Medical record review was performed to obtain information regarding demographics and laboratory tests. Patients were interviewed regarding the consistency and frequency of stools. For patients who were unable to provide information, nursing staff and/or family members were interviewed. Patients were excluded if they did not have at least 1 unformed stool. A diagnosis of CDI required a positive PCR test and diarrhea, defined as ≥3 unformed bowel movements in a 24-hour period. Severe CDI was defined as a case associated with leukocytosis with white blood cell count of ≥15 000 cells/µL or a serum creatinine level ≥1.5-fold above the pre-morbid value.

Perirectal swabs were collected using BD BBL CultureSwab (Becton Dickinson, Cockeysville, Maryland) and were considered adequate if fecal staining was visible. For all swabs, 1 prong was tested by PCR (Xpert C. difficile, Cepheid) according to the manufacturer’s protocol and the other was directly plated onto selective media for culture of toxigenic C. difficile as previously described. For the final 50 consecutive patients, a second swab was collected and tested by enzyme immunoassay for glutamate dehydrogenase (Wampole C. diff Chek-60); the assay was performed according to the manufacturer’s instructions except that, rather than adding 25 µL of stool suspension, the swabs were vortexed for 10 seconds in the diluent. Swabs were processed within 3 hours of collection.

The timing from test order to test results for perirectal swabs was compared with the timing from test order to test results for stool specimens. The sensitivity, specificity, positive
predictive value, negative predictive value, and time to diagnosis of CDI (ie, from order to lab result) were determined in comparison with standard testing of stool specimens. Data were analyzed using SPSS statistical software, version 10.0 (SPSS Inc, Chicago, Illinois) and Stata 11 (StataCorp, College Station, Texas).

RESULTS

Figure 1 provides a flow diagram of the study participants. Of 186 inpatients with orders for CDI testing, 17 (9%) were excluded, including 6 who declined to participate, 6 who did not have unformed stool, and 5 not available for enrollment. For the 169 patients who had perirectal swabs collected, the mean age was 66 years (range, 43–94 years) and 12 (7%) were long-term care facility residents. Of 30 patients who did not have stool specimens tested by the microbiology laboratory, 23 were diagnosed with CDI on the basis of positive PCR results from stool specimens and diarrhea, including 2 (9%) with severe CDI. Overall, 142 of 169 (84%) study patients and 26 of 27 (96%) patients with positive perirectal PCR results met clinical criteria for CDI testing based on ≥3 unformed stools in a 24-hour period.

Table 1 shows the sensitivity, specificity, and positive and negative predictive values of perirectal swab PCR testing for the 139 patients who also had stool test results and for the 50 subjects who had glutamate dehydrogenase testing. The median time from CDI test order to PCR or glutamate dehydrogenase test result was 0.5 days (interquartile range [IQR], 0–1 days) for perirectal swab specimens vs 1.2 days (IQR, 1.2–2.1) for stool specimen results \( P < .0001 \). All of the patients with positive PCR and/or glutamate dehydrogenase results from perirectal swabs also had positive perirectal cultures for toxigenic \( C. \) difficile. For the 1 patient with positive stool test results but negative perirectal PCR, glutamate dehydrogenase,
DISCUSSION

Our findings demonstrate that testing of perirectal swabs is an accurate and efficient method to detect toxigenic *C. difficile* in the stool of symptomatic patients being tested for CDI. This technique for detection of toxigenic *C. difficile* could provide clinicians with a useful alternative testing strategy in settings where it is impossible or impractical to collect stool specimens. Patients with ileus may be unable to produce stool specimens, and confused patients may have difficulty cooperating with collection procedures. In outpatient settings, collection of stool specimens may be an inconvenience for patients who take stool collection supplies home or wait in the clinic to produce a specimen. Collection of stool specimens may also result in contamination of shared clinic bathroom facilities. When severe infection is suspected, it is impractical to delay CDI treatment for long periods. In this setting, delays in testing may result in prescription of empirical therapy for patients whose testing is ultimately negative. Thus, the use of perirectal swabs to assist in rapid detection of toxigenic *C. difficile* in patients meeting clinical criteria for testing could be used to ensure timely treatment of severe CDI while minimizing overuse of empirical therapy and guiding clinicians to pursue prompt evaluation for alternative illnesses when testing is negative.

Prevention of *C. difficile* transmission is dependent on rapid and accurate identification of infected patients [1]. Our results suggest that use of perirectal swabs for some CDI testing could enhance infection control efforts by significantly reducing the time to diagnosis. In healthcare facilities where patients being tested for CDI are not put in isolation until results are finalized, testing of selected patients using perirectal swabs could reduce the risk for transmission by minimizing the time that undiagnosed patients are not isolated. Alternatively, if patients being tested are placed in contact precautions, expediting testing may reduce the time that they are kept in contact precautions. Placement of patients in contact precautions may have adverse effects, including preventing them from receiving rehabilitation therapy [9].

Perirectal swabs could also potentially be used to detect asymptomatic carriers of toxigenic *C. difficile* if such carriers were to be isolated as an infection control strategy. However, further studies will be needed to evaluate the effectiveness of perirectal swab testing for detection of asymptomatic carriers. The patients in the current study had at least 1 unformed stool and a majority had ≥3 unformed stools within 24 hours. In a previous study, the mean density of *C. difficile* in stool of asymptomatic carriers was 100-fold lower than for CDI patients (3.6 vs 5.6 log_{10} colony-forming units [CFU]/g of stool, respectively) [10]. Although the commercial PCR assay used in this study has a reported limit of detection of 23–460 CFU of *C. difficile* (Xpert *C. difficile* package insert, Cepheid), data regarding detection of asymptomatic carriers has not been reported. Another commercial PCR assay had a limit of detection of approximately 4 log_{10} CFU in laboratory studies vs 1 CFU when a broth preamplification step was included [11].

Our study has some limitations. The patient population included mostly men and the current epidemic strain accounts for a majority of *C. difficile* isolates. None of the patients had ileus and outpatients were not included. Therefore, additional studies are needed in other settings. Routine collection of perirectal swabs for testing could contribute to inappropriate testing if patients without diarrhea are tested (ie, rejection of formed stool specimens provides one mechanism to reduce such inappropriate testing). We recommend that perirectal specimen testing for

### Table 1. Performance of Perirectal Swab Testing for Diagnosis of *Clostridium difficile* Infection in Comparison With Testing of Stool Specimens Collected by the Clinical Nursing Staff

<table>
<thead>
<tr>
<th>Testing Method</th>
<th>No. Perirectal Stool Positive</th>
<th>No. Perirectal Negative</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR (n = 139)</td>
<td>22/23&lt;sup&gt;c&lt;/sup&gt;</td>
<td>116/116</td>
<td>95.7 (76.0–99.8)</td>
<td>100 (96.0–100)</td>
<td>100 (81.5–100)</td>
<td>99.1 (94.6–100)</td>
</tr>
<tr>
<td>Glutamate dehydrogenase (n = 50)</td>
<td>7/8</td>
<td>42/42</td>
<td>87.5 (46.7–99.3)</td>
<td>100 (89.6–100)</td>
<td>100 (56.1–100)</td>
<td>97.7 (86.2–99.9)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; NPV, negative predictive value; PCR, polymerase chain reaction; PPV, positive predictive value.

<sup>a</sup> Stool specimens were collected on average 1.3 days after perirectal swabs (range, 0.1–9.6 days).

<sup>b</sup> All of the patients with positive PCR and/or glutamate dehydrogenase results from perirectal swabs also had positive perirectal cultures for toxigenic *C. difficile*.

<sup>c</sup> The 1 patient with positive stool but negative perirectal swab PCR and glutamate dehydrogenase test results also had negative culture results from the perirectal swab. The stool specimen was collected 2 days after the perirectal swab; it was not possible to assess whether the discordant results were related to the timing of sampling because the patient was discharged at the time the stool result became available and an additional perirectal swab could not be collected.
CDI be restricted to patients with ≥3 unformed stools within 24 hours or with ileus suspected to be due to CDI. Finally, appropriate collection of perirectal swab specimens is needed because collection of swabs could be prone to variability in sampling technique. Requiring visible fecal soiling on swabs may be useful to ensure adequate specimen collection.

Notes

Financial support. This work was supported by a Merit Review grant from the Department of Veterans Affairs to C. J. D.

Potential conflicts of interest. C. J. D. is a consultant for ViroPharma, Optimer, and GOJO and has received research grants from ViroPharma, Pfizer, and Merck. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References


