Alerting Physicians during Electronic Order Entry Effectively Reduces Unnecessary Repeat PCR Testing for Clostridium difficile

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Hospital information systems (HIS) alerts restricting repeat Clostridium difficile PCR ordering by physicians in patients with a prior result within 7 days eliminated 91% of repeat tests, from 14.5% (282/1,949) repeats preintervention to 1.3% (135/10,285) postintervention. HIS alerting is an effective, targeted, patient-specific tool for improving the quality and utilization of C. difficile results.

Clostridium difficile is a major cause of diarrhea in hospitalized patients, particularly after antibiotic treatment, and can lead to colitis, toxic megacolon, and even death (1, 2). Although a variety of tests are used for the diagnosis of C. difficile infection (CDI), including enzyme immunoassays (EIAs) and lateral flow tests, PCR testing is growing in popularity (3–5). The high sensitivity of PCR has eliminated the need for multiple repeat tests, which was commonly done with EIAs, despite evidence suggesting that even repeating EIAs is of no value (3–6). Several studies, including one at our own institution, have demonstrated that repeat PCR testing, especially within the first 7 days of an initial negative test, does not change the test result for 97 to 99% of patients and leads to increased hospital costs and consequential false-positive results (6–10).

Based on these findings, our institution developed a policy for rejecting repeat PCR testing for CDI within 7 days of an initial test, except with the approval of the microbiology laboratory director, typically in cases where the initial diarrhea had resolved and was followed by a new bout of diarrhea and when there was high clinical suspicion for CDI. Tests with indeterminate results were automatically rejected. The rejection policy was enforced electronically through the hospital information systems (HIS), Epic Systems’ HIS (Verona, WI) and Cerner HIS (Kansas City, MO), at the level of physician order entry. When electronic orders were placed for C. difficile PCR, an HIS algorithm was triggered to search the patient’s orders and results to determine if the test had been collected (day 0) and/or resulted in the past 7 days. For repeat orders, a pop-up alert stated, “Order placed for the procedure in last 7 days.” The alert also displayed the date, time, and result of the last order. This provided the physician with the information needed to understand the current status of C. difficile testing when given the choice to cancel or continue placing the duplicate order. If the physician decided to continue with the order, a second alert stated, “C. difficile PCR is highly sensitive and should not be repeated within 7 days of a previous order. Consult to GI is recommended.” The alert also indicated that a message would be sent to the microbiology laboratory for review if the duplicate test was still ordered, which alerted the laboratory accessioning supervisor to intercept and manually reject duplicate C. difficile PCR orders that were not approved for repeat testing. The objective of the current study was to evaluate the impact of this HIS intervention on repeat PCR testing practices.

A retrospective cohort study was performed at the Stanford Medical Center clinical microbiology laboratory on all patients with Xpert C. difficile (Cepheid, Sunnyvale, CA) PCR results on stool samples from December 2010 to May 2013. Stool samples were accepted for PCR if they were loose and from patients above 1 year of age, although exceptions were made with approval from the laboratory director and pediatric infectious diseases in cases with high clinical suspicion for CDI. Testing intervals for each patient with more than one test were defined as days between two consecutive tests. Data from this study were compared using chi-squared testing to a published study on C. difficile testing in the same laboratory but using a lab-developed PCR, from July to December 2009, prior to restricting repeat PCR testing (7). In this previous study, 282 tests were repeated on patients within 7 days, representing 14.5% of 1,949 total tests, while 161 repeat tests were done 7 to 14 days after the initial test, accounting for 8.3% of total tests (7).

During the current study period, after restricting repeat PCR testing, 10,285 PCR tests were done on stool samples from 7,336 unique patients, meaning that there were 2,949 repeat tests. Patient ages ranged from 1 month to 105 years, with 88.3% being greater than 18 years of age. A total of 8,767 (85.2%) of the tests were negative, 1,501 (14.6%) were positive, and 17 (0.2%) remained indeterminate after a second test. Of all tests, 135 (1.3%) were repeat tests in patients that already had a positive or negative PCR result within the past 7 days. Of these 135 repeat tests, 122 (90.3%) were done in patients with a prior negative result and 13 (9.6%) were done in patients with a prior positive result. Of the 122 repeat tests with a prior negative result, 118 (96.7%) remained negative and only 4 turned positive, on days 2, 3, 5, and 6 (Fig. 1).

Upon further investigation, the patient that was positive on day 3 had multiple prior positive results and had recurrent colitis that did not clear despite a course of vancomycin, making it unclear what the meaning of the new positive was, as another positive PCR...
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could mean new infection, persistent infection, recurrent infection, colonization, or merely the presence of residual DNA. Excluding this patient, only 3 (2.5%) of 121 repeat tests with a prior negative result turned positive on repeat testing within 7 days.

To determine the reduction in C. difficile PCR repeat testing due to the HIS alert, we compared the proportion of repeat tests at our institution before and after the intervention. After the intervention, repeat testing within 7 days accounted for only 1.3% (135/10,285) of all tests, compared to 14.5% (282/1,949) of tests prior to the intervention, equating to a 91.0% reduction in the proportion of tests repeated within 7 days (P < 0.001). To ensure that physicians did not simply wait 7 days to order an additional repeat test, we also examined the proportion of tests done 7 to 14 days after the initial test in both the preintervention and postintervention periods. Of all tests after the intervention, 965 (9.4%) were repeat tests in patients that already had a positive or negative PCR result 7 to 14 days earlier. There was no significant difference in the proportion of tests done 7 to 14 days after the initial test before or after the intervention (8.3% preintervention versus 9.4% postintervention; P = 0.12).

To our knowledge, this study represents the first evaluation of an automated HIS intervention restricting repeat PCR testing for C. difficile within 1 week of an initial test result. This intervention significantly reduced repeat testing in the first 7 days by over 90%, from 14.5% to 1.3% of all tests. Additionally, the intervention did not appear to miss a significant number of true positives, since repeat testing within 7 days was still negative in nearly 98% of patients, even when clinicians had a high suspicion for CDI and advocated for a repeat test. The intervention also did not appear to simply shift repeat testing from the first 7 days to the subsequent 7 to 14 days, as the proportion of repeat tests 7 to 14 days after the initial result did not significantly differ before and after implementation of the intervention.

The percentage of positive tests within 7 days in patients with a prior negative result (2.5%) is still below the expected false-positive rate of 3 to 10%, based on reported specificities of the Xpert C. difficile PCR, suggesting that many if not all of these could be false positives (11–14). Although no further testing was done to evaluate for false positives, the low percentage of repeat tests which turned positive, even in patients with a high clinical suspicion for infection, suggests that very few, if any, positive results are missed by limiting repeat testing within 7 days.

In conclusion, implementation of an HIS algorithm to restrict repeat PCR testing for CDI within 7 days of an initial test result was highly effective in eliminating unnecessary testing. The intervention also reduces laboratory workload and hospital costs and empowers clinicians to accept negative results and avoid unnecessary antibiotic treatment and patient isolation without having to wait for the results of a repeat test. Although a formal cost analysis was not done, if the cost of each test is assumed to be approximately $40 based on values reported in the literature, the 91% reduction in repeat testing equates to a savings of 1,353 tests, or $54,120, in the postintervention period, not including the additional savings in labor, vancomycin usage, hospital isolation days, and other hospital-wide costs (15, 16). As institutions put limits on repeat testing for C. difficile PCR, ordering multiple tests to diagnose CDI may soon be relegated to the past. In addition to preventing unnecessary repeat testing, HIS alerts may prove useful in improving other aspects of C. difficile testing, such as enforcement of clinical criteria (14).

REFERENCES

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