Laxative Use and Testing Delays May Overestimate the True Burden of C. difficile

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Abstract
Background: With increasing use of molecular diagnostic methods for C. difficile toxin testing and greater recognition of asymptomatic colonization, the true burden of hospital-onset C. difficile (HO-CDT) is uncertain, resulting in overreporting of CDT. Laxative use and lack of diarrheal symptoms may indicate a lower likelihood of CDT. The study objective was to estimate the likelihood of HO-CDT in patients receiving laxatives or delayed testing, and to determine factors associated with CDT cases.

Methods: All CDT tests were reviewed within hospital CDT clinics between September 2013 and December 2014. Cases were classified by CDC definition which was a positive CDT result on an inpatient on hospital day 3 or later. Characteristics of HO-CDT cases for laxative use and delayed testing led to a sensitivity of 94% and 75% for true CDI. A total of 3,234 CDT tests were run on 2,543 unique patients of which 234 (9.2%) were on laxatives ≥24 hours, of which 30 (13.3%) were classified HO-CDT. Among 203 CDT stool tests collected <24 hours following the time of onset of diarrhea, sensitivity for HO-CDT was 94% and 48%, respectively. Among all patients in laxative use and those with delayed testing, sensitivity of HO-CDT cases reported the true burden of HO-CDT cases by 20% or more.

Conclusions: Positive HO-CDT results arising from testing delays and laxative use may suggest an overestimation of true HO-CDT cases as suggested by low pretest probability and low EIA sensitivity. Additional clinical studies should be done to validate these results.

Keywords: Laxative use, asymptomatic colonization, C. difficile colonization, EIA, PCR

Results
A total of 3,234 CDT tests were run on 2,543 unique patients of which 287 (8.9%) were positive; 145 (4.6%) were classified as HO-CDT. Prevalence was slightly higher (15.5%) in patients on laxatives ≥24h. Of 167/387 stool samples collected ≥24h, 13% were classified HO-CDT. Sensitivity of EIA testing among all CDT cases was 16% and 40%, respectively, among patients in laxative use and those with delayed testing. Sensitivity of EIA testing among all CDT cases was 16% and 40%, respectively, among patients in laxative use and those with delayed testing. Sensitivity of EIA testing among all CDT cases was 16% and 40%, respectively, among patients in laxative use and those with delayed testing.

Table. Comparison of EIA sensitivity among all CDT positive cases and HO-CDT cases, by laxative use or delayed testing

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EIA Sensitivity (%)</th>
<th>No. EIA Positive / No. positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>All CDT cases</td>
<td>43</td>
<td>66/149</td>
</tr>
<tr>
<td>HO CDT cases</td>
<td>44</td>
<td>66/149</td>
</tr>
<tr>
<td>on laxatives</td>
<td>48</td>
<td>49/126</td>
</tr>
<tr>
<td>delayed ≥24h</td>
<td>61%</td>
<td>61/100</td>
</tr>
</tbody>
</table>

Discussion
• Heightened awareness of CDI may lead to overtesting of CDT, and sensitive PCR assays will lead to overdiagnosis of CDT given a significant number of asymptomatic patients with CDT.
• Lower EIA sensitivity of patients on laxatives or delayed testing suggests overestimation of patients with true CDI, assuming every such case represented asymptomatic colonization, this would result in an overestimation of HO-CDT cases by 20%.
• In a scenario where the above cases were excluded from HO-CDT reporting, the sensitivity of remaining cases would still be only 50%, suggesting additional factors leading to overtesting at play. Expected EIA sensitivity is low for true CDI.

Limitations
• This was a retrospective study, and chart review was not done to corroborate results.
• Lower EIA sensitivity of patients on laxatives or delayed testing suggests overestimation of patients with true CDI, assuming every such case represented asymptomatic colonization, this would result in an overestimation of HO-CDT cases by 20%.
• In a scenario where the above cases were excluded from HO-CDT reporting, the sensitivity of remaining cases would still be only 50%, suggesting additional factors leading to overtesting at play. Expected EIA sensitivity is low for true CDI.

Conclusion
We conclude that laxative use or delayed testing in patients for CDT could potentially overestimate the true burden of HO-CDT by over 20%.

Next steps for validation include clinical correlation and/or analysis of a larger data set.
We suggest that a process be put in place (e.g. an electronic alert) to remind providers about laxative use or other alternative explanations for diarrhea when CDT is being ordered, and to discontinute a test order if no loose stool can be provided for testing after a period of time.

References