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Laxative Use in the Setting of Positive Testing for *Clostridium difficile* Infection

To the Editor—*Clostridium difficile* infection (CDI) is the most common healthcare-associated infection in the United States.¹ In 2011, almost half a million infections and ~29,000 deaths were estimated to be associated with *C. difficile*.² Timely testing and treatment is critical for improving outcomes and reducing transmission.³ Given the high rate of asymptomatic *C. difficile* carriage, appropriate testing is also essential.⁴ In healthcare settings, *C. difficile* colonization is reportedly 5 to 10 times more common than CDI and other noninfectious causes of diarrhea.^{5,6}

Unformed stools due to laxative use are often submitted for CDI testing, although these specimens are not appropriate for CDI diagnosis. Recent laxative use has been reported in up to 44% of CDI tested specimens.^{3,7,8} Interventions to reduce the testing of inappropriate specimens, including those due to laxative use, have led to a reduction of CDI rates and treatment.⁹ We further examined the relationship between laxative use and patients who tested positive for CDI.

A retrospective study was conducted at a 537-bed teaching community hospital and included hospitalized patients who tested positive for CDI in 2014 and 2015. Testing for CDI comprised an enzyme immunoassay (EIA) for glutamate dehydrogenase (GDH) and an EIA for detection of toxin A/B (*C. diff* Quik Check Complete, Alere, Waltham, MA). If the GDH test was positive and the EIA for the toxin A/B was negative, a confirmatory polymerase chain reaction (PCR) assay (Xpert *C. difficile*, Cepheid, Sunnyvale, CA) was performed. *Clostridium difficile* infection was diagnosed using either GDH-positive and toxin-positive or PCR-positive laboratory results.

Patients who received laxatives up to 24 hours prior to positive CDI testing were identified. Laxatives included docusate sodium, senna, polyethylene glycol, bisacodyl, milk of magnesia, sodium polystyrene sulfonate, and lactulose. Sodium polystyrene and lactulose were considered laxatives if the indications for use were neither hyperkalemia nor hepatic

TABLE 1. Demographic and Clinical Characteristics of Hospitalized Patients with Laxative Use Within 24 Hours of Positive Testing for *Clostridium difficile*

| Demographic and Clinical Characteristics, n = 29 | No. (%) ^a |
|--------------------------------------------------|----------------------|
| Age, mean y (range) | 68 (26–95) |
| Gender | |
| Female | 9 (31) |
| Male | 20 (69) |
| Race | |
| Black | 6 (21) |
| White | 23 (79) |
| Toxin EIA+ | 11 (38) |
| Toxin EIA–/PCR+ | 18 (62) |
| Ordering hospital service | |
| Medicine | 15 (52) |
| Surgery | 6 (21) |
| Intensive care unit (medical and cardiac) | 8 (28) |
| Proton pump inhibitor use | 19 (66) |
| H2 receptor blocker use | 15 (52) |
| Corticosteroid use | 13 (45) |

NOTE. EIA, enzyme immunoassay; PCR, polymerase chain reaction.

^aUnless units are otherwise specified.

encephalopathy, respectively. Physician and nursing notes were reviewed to determine whether diarrhea (≥ 3 unformed stools over 24 hours) resolved within 24 hours of positive CDI testing. The medication administration record was reviewed to determine whether laxatives were administered for greater than 24 hours after positive testing. Validation procedures were conducted for >10% of the study population to ensure reviewer consistency.

A total of 211 patients with CDI were included in the study. Overall, 82 patients (39%) had received laxatives within 7 days prior to positive CDI testing. Of these, 29 (14%) had received laxatives in the 24 hours prior to positive testing (Table 1). In the 24 hours prior to positive testing, 11 patients (38%) received 1 laxative; 12 patients (41%) received 2 laxatives; 4 patients (14%) received 3 laxatives; and 2 patients (7%) received 4 laxatives. The most commonly administered laxatives were docusate sodium (72%), polyethylene glycol (41%), senna (38%), and bisacodyl (17%). Furthermore, 15 patients (52%) continued to receive laxatives for >24 hours after positive CDI testing.

Of the 29 patients, 12 (41%) had resolution of diarrhea within 48 hours of positive CDI testing, including 9 (31%) who had resolution within 24 hours. Of the 9 patients who had resolution of diarrhea within 24 hours, 2 patients (22%; both toxin EIA–/PCR+) did not receive CDI treatment, and 7 patients (78%; 3 toxin EIA+, 4 toxin EIA–/PCR+) received CDI treatment.

Other studies have reported the association of laxative administration with testing for CDI.^{3,7,8,9} We reviewed this association for those patients who tested positive for CDI. Surprisingly, 82 patients (39%) received laxatives within 1 week of CDI diagnosis; 29 (14%) received laxatives (usually ≥ 2) within 24 hours of positive testing. Despite positive results for CDI, 15 patients (52%) continued to receive laxatives for >24 hours after diagnosis.

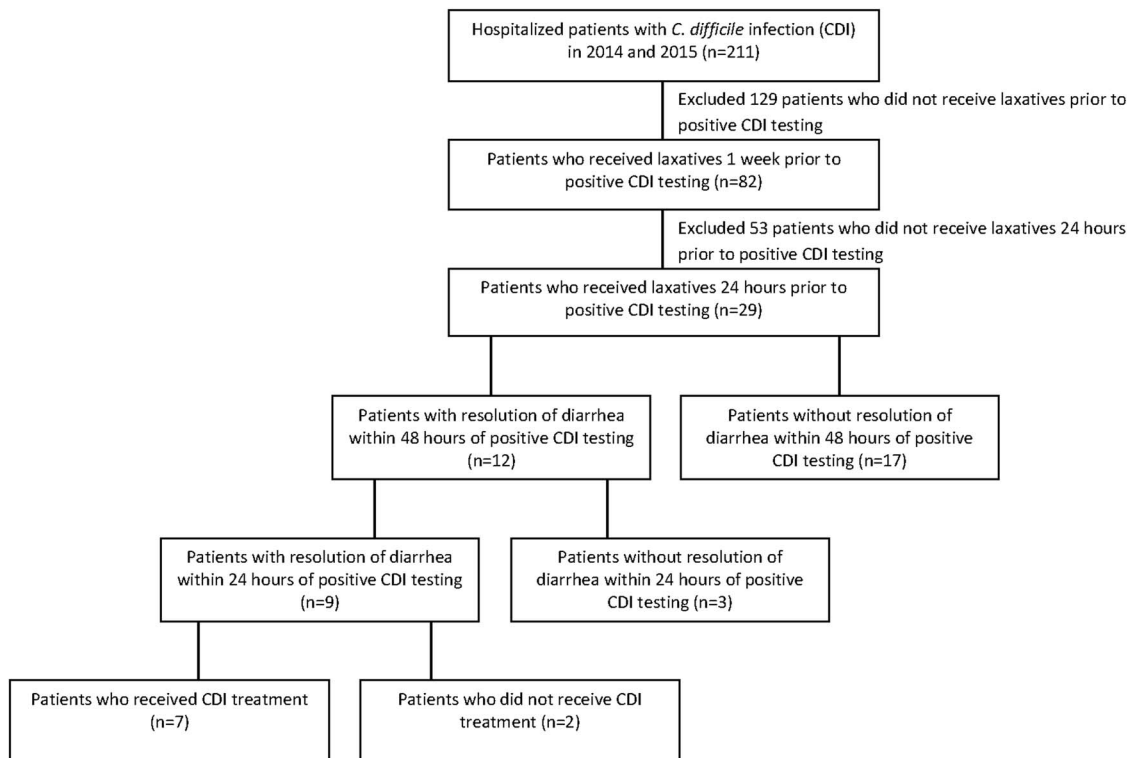


FIGURE 1. Laxative Use Among 211 Hospitalized Patients with Positive Testing for *Clostridium difficile*.

It is critical for clinicians to distinguish patients with clinically significant diarrhea from those with diarrhea due to laxatives. Of the 29 patients who received laxatives 24 hours prior to CDI diagnosis, 12 patients (41%) had resolution of diarrhea within 48 hours including 9 (31%) with resolution in 24 hours. These findings illustrate that diarrhea in the setting of laxative use and positive CDI testing may be of noninfectious etiology.¹⁰ As further supporting evidence, 2 patients (7%) had resolution of diarrhea without any CDI treatment.

Asymptomatic colonization among hospitalized patients with *C. difficile* may be as high as 21%.⁴ Appropriate testing for CDI is critical given the inability of current testing to distinguish between asymptomatic carrier and disease state. Truong et al⁹ recently reported a significant decrease in *C. difficile* test utilization from 208.8 to 143 tests per 10,000 patient days and a decrease in healthcare facility-onset CDI of >25% (ie, from 13.0 to 9.7 cases per 10,000 patient days) using real-time electronic data to enforce laboratory testing criteria, which they defined as the presence of diarrhea and absence of laxative use in the prior 48 hours.⁹

In addition to improving testing cascades for CDI by limiting specimens from patients receiving laxatives, education must also engage the nursing staff. Nurses are integral in the stewardship of specimen collection for CDI because they are likely more aware of when laxatives are administered, especially since laxatives are often ordered as needed and through order sets.

Further interventions are urgently needed to improve testing stewardship for CDI, as restricting collection to patients not on

laxatives represent potential opportunities for significant impact. Furthermore, providers must also consider receipt of other agents (eg, tube feeds, oral contrast) that may cause non-infectious diarrhea when considering testing for CDI.

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