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Brief report

Laboratory-based strategy using a new marketed polymerase chain reaction assay to manage diarrheic episodes among patients from rehabilitation and long-term care facilities

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Management of *Norovirus* and *Clostridium difficile* gastroenteritis is challenging for rehabilitation and long-term care facilities. We evaluated the contribution of a 2-step laboratory-based strategy, including a new ready-to-use *Norovirus* polymerase chain reaction assay to promote isolation precautions. *C difficile* and *Norovirus* were successively identified from 17% and 23% of 52 episodes of diarrhea, respectively, during the winter season, leading to 100% adequate isolation measures. In patient populations with numerous risk factors for diarrhea, a combined laboratory-based approach could improve infection control.

Gastroenteritis is a major cause of hospital-acquired infections, involving primarily *Clostridium difficile* (Cd) or *Norovirus* (Nv).[1,2] These agents require prompt and specific infection control measures to prevent secondary cases among patients and, for Nv, health care professionals and visitors.[1,3] In rehabilitation care facilities (RCFs) and long-term care facilities (LTCFs) outbreaks are difficult to manage because of the dependency of patients, low health care professional to patient ratio, and single room scarcity.[3-6] Product and process innovations are essential to improve Nv and Cd detection. In the present pilot study we prospectively evaluate the contribution of a new 2-step, laboratory-triggered strategy based on the successive polymerase chain reaction (PCR) detection of Cd and Nv.

MATERIALS AND METHODS

Population sampling and study period

The Emile Roux facility has 397 RCF beds and 387 LTCF beds, with half of the rooms being single-bed rooms. The study period was February-April 2015.

Microbiologic testing

We compared 2 different approaches during the study period. The first approach was a standard approach that was historically implemented and included Nv or Cd testing only at the request of clinicians or infection control practitioners using an immunochromatographic test (ICT) (RidaQuick Norovirus; R-Biopharm, Darmstadt, Germany) or a PCR assay (Xpert *C. difficile*; Cepheid, Sunnyvale, CA) within a 1-hour turnaround time (TAT).

The second approach was a new 2-step laboratory-based approach using PCR assays: Nv were tested on the initiative of the laboratory on each Cd negative stool specimen using a new PCR assay according to the manufacturer's recommendations. This new molecular assay (Xpert Norovirus; Cepheid) detects the 2 main human genogroups (GI and GII) over 90 minutes.

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These 2 approaches were tested simultaneously during the same period to limit confounding factors. The result of each test was immediately transmitted to the infection control team to verify the implementation of precautions measures. Only 1 episode per patient was included. Patients were informed, and consent was obtained.

Data collection

The following data were collected from patient files: history of antibiotic, acid-suppressive, or laxative consumption; Cd infection; active chronic bowel inflammatory disease; immunosuppression (including active malignancy or transplantation); chronic renal failure; mobility; cognitive impairment; and dependency. Regarding the present diarrheic episode, the date of the first clinical sign, stool specimen collection, and contact precaution implementation were collected.

RESULTS

During the study 52 episodes of diarrhea were analyzed. Patients' characteristics were reported in Table 1: most patients were older adults, dependent, mobile, and disoriented. Positive Cd PCR was obtained for 9 of the 52 patients (17%). The Nv PCR performed for all of the Cd-negative specimens was positive in 10 of 43 (23%) patients (all GII). Considering the former standard approach, only 19 out of 43 Cd-negative specimens were tested for Nv, yielding 3 positive ICT (GII) and 1 uninformative result. In addition to the 3 ICT-positive patients, the study protocol allowed the identification of 7 additional Nv-positive cases. No false-negative ICT result was detected. Therefore, the improved performance of the new approach was caused by the laboratory-triggered Nv testing on Cd-negative specimens rather than the PCR detection of ICT false-negative specimens: only the uninformative ICT result tested positive using the new Nv PCR assay, whereas no ICT-negative specimen tested positive using this PCR-based approach. Considering the new PCR combined strategy, an infectious agent was identified in 19 of the 52 (37%) patients.

At the time of specimen collection, 5 of the 52 patients were under contact precautions, with 2 patients being PCR positive for Cd and 1 patient being PCR positive for Nv. Once the PCR results were transmitted, all of the Cd- or Nv-positive patients were placed under contact precautions.

DISCUSSION

Cd and Nv are the 2 main agents responsible for extensive gastroenteritis outbreaks in RCFs and LTCFs.[3-6] As expected, our study population accumulated risk factors for Cd infection.[5] Laxative medications promote Cd infections and mime infectious diarrhea. This confounding condition (36/52 patients) could explain the deleterious delay between the onset of symptoms and stool testing. In our study, physicians widely prescribed specific Cd testing but not preemptive contact isolation that meets with its psychosocial deleterious consequence and the decreasing compliance rate with increasing burden of isolation.[1,7] Rapid diagnostic tests are recommended to support clinical decision, but stool testing practices vary across facilities.[8] In the present instance the availability of a rapid and sensitive nucleic acid amplification test could limit the risk of cross-transmission.

Early detection of sporadic NV cases during the seasonal period cost-effectively prevents outbreaks.[2,3] The diagnosis of Nv would benefit from easy-to-use and more sensitive methods.[2] Neither ICT with a poor sensitivity (17%-92%) nor conventional PCR with inadequate availability and TAT encouraged clinicians to prescribe specific Nv testing.[2] A recent report from English hospitals underlined the weak percentage of stools testing with a targeted pathogen demand (20.2%) and the better infection control practices when the infectious status of diarrhea was confirmed.[8] These data supported the implementation of a laboratory-based nucleic acid amplification test strategy. Our PCR assays are based on a user-friendly platform allowing a random-access PCR-based diagnosis of numerous infectious agents without technical skills requirement. Because of its analytical performance, this PCR assay could facilitate Nv diagnosis.[9] To our knowledge, our work reports for the first time the implementation of this test in a prospective clinical study, focusing on its putative contribution in infection control. Within a maximum TAT of 3 hours, our approach could accurately identify the 2 main infectious agents responsible for gastroenteritis outbreaks. Our work cannot be reduced to a simple

Table 1
Characteristics of the patients suffering from diarrhea, including results from Cd and Nv PCR testing

Characteristic	Total (N = 52)	Cd positive (n = 9)	Cd negative, Nv positive (n = 10)
Mean age (range), y	87 (75-103)	88 (84-92)	90 (82-103)
Sex ratio, M/F	0.31	0.44	0.11
History of antibiotic consumption in the previous month	39 (75.0)	9	6
History of acid-suppressive consumption in the previous month	27 (51.9)	7	2
History of laxative consumption			
In the previous month	36 (69.2)	8	7
In the previous week	33 (63.5)	8	4
History of Cd infection in the previous year	4 (7.7)	2	0
Chronic bowel inflammatory disease	3 (5.7)	0	0
Chronic renal insufficiency	10 (19.2)	0	2
Immunosuppression	5 (9.6)	3	1
Dependency	35 (67.3)	7	6
Cognitive impairment	32 (61.5)	5	5
Mobility	42 (80.8)	6	9
At the time of the episode of diarrhea, presence of			
Fever (>38.5°C)	4 (7.7)	1	2
Vomiting or nausea	23 (44.2)	5	8
Average delay between the onset of the symptoms and the specimen collection (range), d	3.3 (0-32)	3.1 (0-32)	3.6 (0-19)
Average delay between admission and specimen collection (range), d	201 (0-3,925)	163 (0-732)	16 (0-5)

NOTE. Values are listed as n (%), n, or as otherwise indicated.
Cd, *Clostridium difficile*; *F*, female; *M*, male; *Nv*, *Norovirus*; *PCR*, polymerase chain reaction.

comparison between the ICT and PCR detection of Nv: this issue has been widely addressed in the literature and supported the implementation of a PCR-based assay.[2] However, in our study we did not identify any false-negative ICT result: this could be explained by the low number of ICT-tested specimens or the performance of the marketed ICT assay that ranked first in a recent comparative study.[10] We focused on the putative pivotal role of the laboratory that could be the mainspring of the testing strategy to detect the 2 main agents responsible for gastroenteritis among patients from RCFs and LTCFs. Our 2-step laboratory-based strategy seems to be economical and efficient: the 37% positive rate was similar to the 37.8% of tests identifying a single infectious agent in a recent large European study.[11] In the near future this strategy will be challenged by syndromic PCR panels, including bacteria, virus, and parasites, that could be of great interest for infection control purposes.[11,12] Nevertheless their cost and the debating infection control relevance of some of the targeted microorganisms could limit their implementation. Our pilot study has several limitations: we could not prove that our strategy prevents outbreaks of Nv: the study lacks a control arm and does not count secondary cases. Our approach missed Nv and Cd coinfections that were recently reported in LTCFs.[13] However, the contact precautions that were recommended for Cd infection could prevent Nv contamination, except for viral airborne transmission.[2] Additionally, we performed our study during the seasonal peak of Nv, among a mobile population presenting numerous confounding and risk factors for infectious and noninfectious diarrhea, in a context of limited availability of single rooms and low preemptive isolation measures. These conditions could have maximized the contribution of our proactive laboratory-based strategy.

To conclude, this study underlines the significant contribution of a laboratory-based strategy, including a new ready-to-use Nv PCR assay, to adequately implement isolation precautions for diarrheic patients from RCFs and LTCFs.

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