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Analysis of norovirus outbreaks reveals the need for timely and extended microbiological testing

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SUMMARY

Background: Norovirus outbreaks in hospitals remain a substantial threat despite many recommendations for prevention published recently.
Aim: To analyse the factors contributing to onset of a norovirus outbreak in hospitals in order to identify new prevention options.
Methods: Data from 71 norovirus outbreaks occurring in five German hospitals between 2002 and 2012 were analysed focusing on the start conditions: the weekday of outbreak, the time span between the first symptomatic cases and the outbreak onset date, the timing of a positive norovirus test result in an outbreak, and presence of concomitant *Clostridium difficile* infections.
Findings: In 68 (96%) outbreaks index cases were identifiable. In 30 of 44 (68%) outbreaks the index case patient acquired norovirus infection in hospital. In 20% of all outbreaks, the index case was a staff member. Nine outbreaks were caused by not isolating contact patients during the incubation time after their exposure to a symptomatic case. Case numbers in norovirus outbreaks were lower when the norovirus test results were available before the outbreak onset ($P = 0.028$). In 30 of 46 (64%) norovirus outbreaks, *C. difficile* toxin tests were positive in up to ten patients. Co-infection or subsequent infection with norovirus and *C. difficile* in single patients occurred in nine (20%) outbreaks.
Conclusion: Future prevention strategies should focus not only on patients but also on staff. Constant surveillance for new cases of diarrhoea and vomiting and timely adherence to contact precautions for all exposed persons is crucial in outbreak control, as is the need for extended microbiological testing.

Introduction

Though the awareness and the availability of evidence-based guidelines on the prevention of norovirus outbreaks are increasing, the number of hospital outbreaks does not seem to decline.[1–5] Moreover, the clinical impact of norovirus infection in the vulnerable population of hospitalized, elderly, or immunosuppressed patients may even be more severe and prolonged than formerly suspected.[6–10] Even in otherwise

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healthy individuals norovirus infection may lead to post-infectious irritable bowel syndrome.[11] Norovirus infection in hospitals may be missed despite routine laboratory testing and this diagnostic failure results in costly abdominal imaging and potential nosocomial outbreaks.[12] Furthermore, these norovirus outbreaks lead to additional costs due to extended length of stay and to staff shortages.[13,14] A recent systematic review of control measures targeting norovirus transmission revealed that control measures taken during ongoing norovirus outbreaks might not reduce the magnitude or duration of a nosocomial outbreak.[15] Thus, the most promising approach to reducing the number of norovirus outbreaks appears to prevent the transmission from the very first (index) case. To characterize triggers for a nosocomial norovirus outbreak, we analysed the beginning of 71 norovirus outbreaks on ward level in five German hospitals regarding the identification of an index case, the time span between the first symptoms in the index case and the onset of the outbreak, and we documented breaches of adherence to appropriate isolation precautions and the timing of positive norovirus test results. We also analysed the occurrence of *C. difficile* infection (CDI) during norovirus outbreaks.

Methods

Data were collected in three university hospitals (nos. 1, 3 and 5) and two teaching tertiary care hospitals (nos. 2 and 4) in Germany (Table I). Local infection control personnel of the respective hospitals collected the data by checking all patients' charts and staff schedules for persons with diarrhoea and vomiting. Data capture included the date of onset for every patient, contact persons, and staff members; admission and discharge dates; and the date of norovirus test result. Data collection continued during the ongoing outbreak and included additional information such as transfers between wards, events of vomiting in the corridor, and whether isolation precautions were applied.

Onset of a norovirus outbreak was defined clinically (gastrointestinal symptoms) as the occurrence of at least two additional nosocomial symptomatic individuals after the first case on the same ward and at least one of the cases tested positive for norovirus. The first norovirus outbreak in 2002 was based only on the clinical definition as specific norovirus tests were not available. Patients who became symptomatic more than 48 h after admission were defined as having nosocomially acquired disease. The first person detected with diarrhoea or vomiting was regarded as the index case of the respective outbreak. If symptoms started in more than one person at the same time, all were defined as index cases. All consecutive nosocomial norovirus outbreaks occurring in 2002/2003 (hospitals 1 and 2) and from 2007 to 2012 (hospitals 3 to 5) in the indicated hospitals were included. One outbreak at hospital 4 was excluded due to insufficient data collection. The outbreak size was defined as the total number of nosocomial cases per outbreak. Multiplex microbiologic testing for norovirus and *C. difficile* toxin and since 2010 also for *Campylobacter* spp., rotavirus and adenovirus in some of the hospitals allowed analysis of a subset of outbreak data on norovirus and *C. difficile* infection.

For statistical analysis, Pearson's chi-square test was performed for weekday analysis using R-software.[18] Values were

Table I
Description of outbreak data used for different data analysis

Hospital	No. of beds	Region	Study period	Routinely performed norovirus diagnostic method	No. of outbreaks used for descriptive index case analysis	No. of outbreaks used for specific norovirus diagnostic analysis	No. of outbreaks used for *C. difficile* infection involvement analysis	Staff members involved	Patients involved
1	1400	Central Germany	2002–2003	PCR[16]	5	–	–	46	84
2	800	Northern Germany	2002–2003	PCR[16]	13	–	–	83	299
3	1200	Northern Germany	2007–2009	ELISA[31]	24	24	18	129[a]	313
4	500	Western Germany	2010–2012	ELISA,[31] PCR[17]	11	11	10	36	145
5	700	Western Germany	2010–2012	ELISA,[31] PCR[17]	18	18	18	54	243
Sum	4600				71	53	46	348	1084

PCR, polymerase chain reaction; ELISA, enzyme-linked immunosorbent assay.
[a] In one outbreak the involvement of staff members was not recorded.