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A set of environmental measures to control a *Fusarium* outbreak in an oncohematologic ward: An interrupted time series study

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Fungal infections in immunocompromised patients constitute a challenge.[1] *Fusarium* spp are widely distributed in the environment.[2] In oncologic and hematologic patients, especially those with prolonged periods of neutropenia, *Fusarium* spp can disseminate, causing invasive fusariosis with mortality rates of up to 75%.[3] Previous studies assessing *Fusarium* outbreaks have identified environmental sources.[1,3] Here, we describe an outbreak in our institution and the bundle we implemented to contain it.

Materials and methods

Study design and setting

We conducted an interrupted time series study from December 2018 to June 2019 at Hospital Universitario Austral. The institution is a 209-bed private tertiary-care teaching hospital in Buenos Aires, Argentina. The bone marrow transplant (BMT) ward has 8 individual rooms with an antechamber, high-efficiency particulate air (HEPA) filters, and positive pressure airflow, and the hematology ward has 8 private rooms. The rooms have bathrooms with showers, and a window, which does not open to the exterior. Plants are not allowed in the premises. Floors and surfaces are cleaned twice daily with a quaternary ammonium compound solution (Surfanios, Laboratories Anios, France), or 10% bleach in rooms with patients with *C. difficile* infection.

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Patients with invasive fusariosis were included. Positive cultures for *Fusarium* spp were obtained from a usually sterile site plus clinical and/or radiologic alterations compatible with fungal infection).

Once the outbreak was identified, the infection control department led the creation of a working team, with representatives from general services, internal medicine, haematology, infectious diseases, microbiology, security and hygiene, nursing staff and maintenance services. An inspection of the hospital's infrastructure was conducted. Cleaning and disinfection policies, as well as the patient hygiene policy, were revised. Surveillance for new cases was initiated.

Environmental sampling

One-liter water samples were collected from taps, showers, and the central reservoirs in accordance with the protocol of the National Institute of Farming Technology, ISO 7954. Air IDEAL 3P Traceability (bioMèrieux, Marcy-l'Étoile, France) was placed at 1.5 m above the floor for 10 minutes (volume, 1,000 m^3) using agar Sabouraud dextrose 2% medium plastic strips. The interior surfaces of faucets and the drains of sinks, showers, bidets, and toilets were swabbed. Other samples included stains from walls and floors. Specimens were obtained with sterile swabs presoaked in distilled water.

Culture and identification

Samples were seeded in Sabouraud dextrose agar culture plates and tubes and incubated at 28°C and 37°C. After 3 days, the culture plates were evaluated. If negative, incubation was maintained for

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Table 1. Characteristics of the Cohort (n=5)

Characteristic	No. (%)
Sex, male	3 (60)
Age, median y (range)	35 (19–56)
Time to invasive fusariosis diagnosis, median d (range)[a]	34 (8–112)
Diagnosis	
Acute lymphoblastic leukaemia	2 (40)
Hodgkin's lymphoma	1 (20)
Acute myeloid leukaemia	2 (40)
Phase of treatment	
Relapse	2 (40)
Induction	1 (20)
Consolidation	1 (20)
Allogenic hematopoietic stem cell transplantation	1 (20)
Portal of entry	4 (80)
Profound neutropenia (<500 neutrophiles/mm^3)	5 (100)
Clinical manifestation	
Skin and soft tissue	5 (100)
Lung	1 (20)
Outcome	
Discharge	3 (60)
Death	2 (40)

[a]From the first registry of neutropenia.

15 days. Plates with positive results were studied macroscopically and microscopically. Colonies from the genus *Fusarium* spp were isolated in potato dextrose agar for identification of the species complex.

Results

Case analysis

The characteristics of the patients are described in Table 1.

Outbreak investigation

Clinical data

Overall, 5 five cases of infection by *Fusarium solani* species complex were identified from June 2018 to January 2019. The incidence of invasive fusariosis increased from 0.56 in the second semester of 2018 to 5.3 per 1,000 oncohematologic patient days during the first trimester of 2019. Patients presented neutropenia, fever, and erythematous subcutaneous nodules, and 80% had a portal of entry. All patients received liposomal amphotericin and voriconazole. Mortality due to invasive fusariosis was 40% (2 of 5).

Infrastructure investigation

Overall, 72% of the rooms in the BMT unit had visible fungi on bathroom walls and faucets. Structural deficits halted the drainage of water in the showers. A renovation was conducted to achieve clean and washable surfaces. Also, the personal hygiene of patients was modified to chlorhexidine and chamomile wipes. Air and water samples were negative. Shower and sink surface samples (n = 75) were positive for *Fusarium* spp. Cleaning and disinfection policies were modified in the bone marrow transplant and hematology wards to daily application of sodium dichloroisocyanurate (NaDCC) and biweekly use of a 20% quaternary ammonium compound (Surfanios). Furthermore, sink lids were uncoupled and cleaned twice each year with hyperchlorination and 20% quaternary ammonium compound. Finally, a disposable water filter (Pall-Aquasafe, Pall, Port Washington, NY) was installed in one of the BMT rooms. Since the outbreak, prospective surveillance for new cases has been maintained, including periodical environmental sampling.

Evolution of the outbreak

Only 1 case has been identified since the intervention. The reported incidence since the implementation of the bundle in February 2019 through September 30, 2019, was 0.63 per 1,000 oncohematologic patient days.

Discussion

During the outbreak, 5 cases of invasive fusariosis were identified. These patients had profound and prolonged neutropenia and developed subcutaneous nodules; they were placed under combined antifungal therapy, and 2 of these patients died.

Water samples were negative. However, samples from showers and sinks held positive results for *Fusarium* spp, supporting the hypothesis of water as the source of the outbreak.

Previous studies assessing *Fusarium* outbreaks have addressed methods to control them, yet this was not their focus. We demonstrate the effectiveness of a comprehensive package of measures to control a *Fusarium* spp outbreak in a tertiary-care teaching hospital. Key components included changes in hospital cleaning/disinfection policies, patients' hygiene policy, and renovation of rooms.

This study has several limitations. First, we assumed that the source of the outbreak was the water, although water samples were negative. We based our assumption on the fact that all of the samples drawn from taps and faucets were positive. Second, monetary limitations precluded us from performing genetic compatibility studies between fungi isolated from the environment and those isolated from patients.

In conclusion, we present an interrupted time series of immunocompromised patients with invasive fusariosis in a tertiary-care teaching hospital. A comprehensive package of measures was effective in controlling the outbreak. Further studies are needed to determine whether the bundle is applicable to other microorganisms and institutions.

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Larger endotracheal tube size in women increase the risk for ventilator-associated events

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Even though endotracheal tube (ETT) size selection is often the result of clinical judgement, factors such as age, gender, height, body mass index (BMI), and anticipated bronchoscopies are often considered before insertion.[1–3] The objective of this study was to explore whether gender differences exist in ventilator-associated event (VAE) development based on larger ETT selection. The surveillance paradigms for VAEs are established by the Centers for Disease Control and Prevention.[4] They denote 3 categories of increasing progression in mechanically ventilated patients from a ventilator-associated condition (VAC), to an infection-related ventilator-associated complication (IVAC), and finally to possible ventilator-associated pneumonia (PVAP). Our a priori hypothesis for this study was that an 8.0-mm ETT is associated with less risk of VAEs because a larger diameter is optimal for pulmonary hygiene.

Methods

The study was approved by our university's biomedical institutional review board (protocol no. 200301R002). After approval, VAEs records were gathered from May 2013 to December 2017 and were collected by the infection prevention department as part of daily VAE surveillence. Using both our clinical database and retrospective chart review, we gathered specific patient characteristics, medication administration, and ventilator data. Controls consisted of patients intubated for ≥3 ventilator days and matched 1:1 based on age, gender, and unit while intubated during the hospital encounter, use of vasopressors during intubation, and total ventilator days. Patients with chronic tracheostomies were removed from the analysis.

To determine the association between ETT size and VAEs, Pearson χ^2 tests were conducted, and odds ratios (ORs) with 95% confidence intervals (CIs) were reported for each gender. We conducted a post hoc analysis using a *t* test or the Mann-Whitney U test where appropriate. All analyses were performed using R version 3.6.1 software (R Foundation for Statistical Computing, Vienna, Austria) with an α level of 0.05.

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Results

Within both the male and female populations, the results of the χ^2 tests indicated a statistically significant relationship between ETT and VAE development, $\chi^2 = 20.05$ ($P = .000$) and $\chi^2 = 10.17$ ($P = .001$), respectively. Among male patients, 64 of 160 VAEs and 104 of 160 controls were intubated with 8.0-mm ETTs (OR, 0.39; 95% CI, 0.22–0.58). Conversely, among female patients, 34 of 89 VAES and 15 of 89 controls were intubated with 8.0-mm ETTs (OR, 3.03; 95% CI, 1.44–6.62). According to these preliminary results, male patients intubated with 8.0-mm ETTs were less likely to develop VAEs, and female patients intubated with the same size were at greater risk.

In our post hoc analysis, we did not find any widespread indications among female patients that warranted a larger ETT size, such as aggressive airway clearance, hemorrhage, or bronchiectasis. Likewise, we did not detect any statistical differences between female height and BMI between ETT size groups or within female patients intubated with 8.0-mm ETTs only (Table 1). Given the mean biometric values, we assumed that most 8.0-mm ETTs were inappropriately selected by BMI and placed in smaller airways. Also, we determined from this analysis that female patients in the VAE group were not taller, which might have justified a larger diameter ETT.

Discussion

Our findings are difficult to explain, but we propose some potential mechanisms for higher rates of VAE development among female patients intubated with 8.0-mm ETTs. When endotracheal cuffs are inflated, channels are created that allow the leakage of fluids. Larger diameter tubes tend to have more longitudinal folds than smaller sized tubes,[5] which could increase the likelihood of microaspiration. Furthermore, larger-diameter ETTs tend to be longer (up to 2 cm) and could present problems for patients with shorter airways.[6] For example, tubes that are inserted too distally (ie, <4 cm above the carina) and need to be repositioned multiple times may intensify the cuff folds.[7] Another consideration is that malposition of the ETT, which in 1 study was more frequent in female patients,[8] might be exacerbated by movement (eg, head flexion) if not corrected and allowed to reside too close to the carina. Additionally, the suboptimal depth of the ETT may introduce a larger surface area of biofilm deeper into the patient's airway.[9] Lastly, carinal impingement or endobronchial migration

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