American Journal of Infection Control 41 (2013) 1038-42

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Multi-institutional outbreak of *Burkholderia cepacia* complex associated with contaminated mannitol solution prepared in compounding pharmacy

Maria Beatriz Souza Dias MD, PhD [a,*], Larissa G. T. Cavassin RN [a], Valeska Stempliuk RN, PhD [a], Luciene S. Xavier RN [a], Renata D. Lobo RN, MSc [a], Jorge L. M. Sampaio MD, PhD [b], Antonio Carlos Pignatari MD, PhD [c], Vera L. Borrasca RN, MSc [a], Ana Luiza Bierrenbach MD, PhD [d,e], Cristiana M. Toscano MD, PhD [d,e,f]

[a] *Infection Control Department, Hospital Sírio Libanês, São Paulo, Brazil*
[b] *Fleury Medicina e Saúde, São Paulo, Brazil*
[c] *Hospital 9 de Julho, São Paulo, Brazil*
[d] *Teaching Research Institute (IEP), Hospital Sírio Libanês, São Paulo, Brazil*
[e] *Sanas Epidemiology and Research, São Paulo, Brazil*
[f] *Department of Community Health, Institute of Tropical Pathology and Public Health, Federal University of Goiás, Goiânia, Brazil*

Key Words:
Outbreak investigation
Extrinisic contamination
Health care-associated infection
Endoscopic urological surgery

Background: *Burkholderia cepacia* complex (BCC) has been described as a cause of nosocomial outbreaks. We describe an outbreak of and identify risk factors for nosocomial BCC infections associated with intrinsically contaminated mannitol 3% solution.

Methods: Urinary and bloodstream infection caused by BCC were identified in hospitalized patients who underwent urologic surgery and received intraoperative irrigation of 3% mannitol solution in February 2009. The investigation included retrospective chart review, case control study, procedural review, and culture of mannitol solution.

Results: Seven BCC infections were identified. BCC isolates were recovered from blood and/or urine from patients and lots of mannitol in use during the outbreak period. Mannitol solution was produced by a compounding pharmacy. Receipt of larger volumes of contaminated solution was identified as a significant risk factor for infection (odds ratio, 1.5; P value $< .05$). BCC was also cultured in lots of mannitol in use in other hospitals.

Conclusion: Manipulated mannitol solution is a potential source of infection. Contamination with paraben-degrading organisms can occur at the time of manufacture. Our findings suggest that contamination of mannitol at a compounding pharmacy occurred. Prompt communication to other hospitals and implementation of infection control measures were effective in avoiding further cases of infection.

Species pertaining to the *Burkholderia cepacia* complex (BCC) are ubiquitous in water, soil, and plants and comprise 17 species including *B cepacia*. Patients with cystic fibrosis, chronic lung disease, chronic granulomatous disease, sickle cell disease, and burn and oncology patients are at high risk for infection.[1]

Various outbreaks of BCC infection have been recently described in the literature, usually associated to contaminated substances and technology for patient care in the hospital setting. Identification of the outbreak source and its control represents a challenge. To date, there is no report in the literature of BCC infection outbreak in patients undergoing endoscopic urologic surgery.

In January 2009, identification of urinary tract infection caused by BCC—an unusual cause of infection—in patients submitted to endoscopic urologic surgery, prompted active search of additional cases and identification of a *B cepacia* outbreak. We describe the outbreak, risk factors for BCC infection, and the measures required to control the outbreak. Furthermore, we describe risk communication measures implemented and their impact on avoiding further

* Address correspondence to Maria Beatriz Souza Dias, MD, PhD, CCIH-Hospital Sírio Libanês, Rua Dona Adma Jafet 91, São Paulo, SP 01308-050, Brazil.
E-mail address: maria.beatriz@hsl.org.br (M.B. Souza Dias).

Partially presented at 12th Brazilian Conference of Hospital Infection Control. September 1-4, 2010; Recife, Brazil.

Current affiliations: Cristiana M. Toscano: Federal University of Goiás, Goiânia, Brazil. Valeska Stempliuk: Pan-American Health Organization, Washington, DC.

Conflicts of interest: None to report.

0196-6553/$36.00 - Copyright © 2013 by the Association for Professionals in Infection Control and Epidemiology, Inc. Published by Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.ajic.2013.01.033

cases of infection in other large, private, tertiary care hospitals in the city.

PATIENTS AND METHODS

Setting

The outbreak occurred in patients submitted to urologic surgery at a 350-bed, private, tertiary care hospital (hospital A) in São Paulo, Brazil. The outbreak period was January to February 2009.

Case ascertainment

After reports from medical staff about the occurrence of 2 cases of urinary tract infection caused by an unusual agent (BCC) following elective endoscopic urologic surgeries, the hospital infection control searched through laboratory reports and infection control logs for positive BCC cultures. To enhance case identification, active surveillance was performed from January 16 to March 1, 2009.

The preoutbreak period was defined as January 2007 through December 2008. The postoutbreak period was defined as March 2009 through December 2010. A colonized patient was defined as any patient in which BCC had been isolated from any body site and for which the attending physician did not institute antimicrobial therapy. An infected patient was defined as any patient with a positive BCC culture from a sterile fluid (blood, urine, cerebrospinal fluid), with signs and symptoms of infection and who received antimicrobial therapy for BCC treatment.

Trends in rates

Monthly BCC colonization and infection rates were calculated by dividing the number of patients with positive cultures for BCC from any body site or the number of patients with BCC infection, respectively, by the total number of patient-days in the hospital during each month and multiplying by 1,000. BCC infection rates in the pre-epidemic and epidemic periods were compared, to confirm the existence of an outbreak. After control measures were implemented, BCC infection and colonization rates in the outbreak and postoutbreak periods were compared, to confirm decline in rates and outbreak control.

Procedural review

A review of medical procedures performed, medications received, and equipment used in colonized and infected patients was conducted to identify potential common source of the infection.

Microbiologic studies

Clinical specimens for culture were collected based on clinical criteria established by hospital medical staff. For blood cultures, 20 mL were drawn after skin antisepsis with alcoholic chlorhexidine solution and inoculated into both aerobic and anaerobic Bactec Plus vials and incubated in a Bactec 9240 (BD Diagnostic Systems, Sparks, MD) instrument until positivity. Positive cultures were subcultured on sheep blood and chocolate agar and incubated in 5% CO_2 at 35°C for 18 to 24 hours. Urine samples were plated on cystine lactose electrolyte deficient medium and MacConkey agar and incubated in ambient air at 35°C for maximum of 48 hours.[2] Approximately 250 mL from each batch of ready to use 3% mannitol solution were filtered in a 0.22-μm filter Stericup (Millipore, Billerica, MA) unit. The filter was aseptically cut with a disposable sterile blade, transferred to a sheep blood agar plate, and incubated in ambient air at 35°C for up to 7 days. Cultures were obtained from samples of all lots of mannitol 3% distributed in the hospital during the outbreak period, except for one, which was no longer available. In addition, lots of mannitol 3% from the same manufacturer used in other hospital (hospital B) during the outbreak period were also collected and assessed. Bacterial identification was performed using the gram-negative card and the Vitek2 system (bioMérieux, Crappone, France). Antimicrobial susceptibility tests were performed using the Kirby-Bauer method as described previously.[3,4]

Case-control study

A case-control study was conducted to identify risk factors for BCC infection among the patients who received manipulated mannitol solution at 3% during the outbreak period. A case of BCC bloodstream infection was defined as any patient with a positive BCC culture isolated from blood with signs and symptoms of infection and who received antimicrobial therapy. A case of BCC urinary tract infection was defined as any patient with a positive BCC culture isolated from urine who received antimicrobial therapy and who received mannitol 3%. Controls were all patients who had received mannitol 3% solution during the outbreak period. Potential risk factors assessed included the following: type of surgical procedure, duration of surgical procedure, age, gender, underlying illness, volume of mannitol 3% received, length of surgery in hours, and American Society of Anesthesiologists physical status classification presurgical scores. Outcomes assessed included length of stay in the hospital and death. Information was obtained from patient medical and surgical records, as well as nursing and billing records.

Statistical analysis

All data were collected on standardized forms, entered into a computerized database, and analyzed. BCC colonization and infection rates during preoutbreak, outbreak, and postoutbreak periods were compared, and *P* value for mean difference in incidence density was calculated. Categorical variables were compared using the χ^2 or Fisher exact test. Continuous variables were compared using the Mann-Whitney test. Odds ratios and 95% confidence intervals were calculated. For all variables with *P* value $< .1$ in the univariate analyses, regression analysis was performed. Statistical analyses were performed using STATA (STATA Corp, College Station, TX).

RESULTS

Outbreak description and trends in rates

During the outbreak period, 7 cases of BCC infection were identified, of which 4 were bloodstream infections and 3 urinary tract infections. One patient with bloodstream infection also had positive urine cultures (Table 1).

BCC infection rates increased significantly from the preoutbreak to the outbreak period (preoutbreak, 0.06/1,000 vs outbreak, 0.49/1,000 patient-days, *P* value $< .01$). After implementation of control measures, BCC infection rates decreased significantly (outbreak, 0.49/1,000 vs postoutbreak, 0.09/1,000 patient-days, *P* value $< .01$). BCC colonization rates in the postoutbreak levels did not differ significantly from preoutbreak levels (postoutbreak, 0.07/1,000 vs preoutbreak, 0.03/1,000 patient-days, *P* value $< .07$) (Fig 1).