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Nosocomial outbreak of Burkholderia cepacia bacteremia in Pediatric Cardiothoracic Intensive Care Unit due to contaminated deionized water

Microbiology

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ABSTRACT

We report an ICU outbreak of Burkholderia cepacia bacteremia, root cause analysis and risk factor assessment. A cluster of 8 cases of Burkholderia bacteremia with similar antimicrobial susceptibility pattern were observed within 45 days in PCTICU, suggesting an outbreak. Environmental samples (n=21) from all potential reservoirs were taken & processed according to standard microbiological procedures. B.cepacia with similar susceptibility pattern was isolated from deionized water (outside supply), used in humidifier reservoirs for delivery of low-flow oxygen therapy. With immediate effect, in-house reverse osmosis water was put to use. Risk factors were previous hospitalizations; co-morbidities; antimicrobial administration and duration of mechanical ventilation. Implementing best practices in respiratory therapy, administration of I.V. fluids and parenteral nutrition, play an indispensible role in preventing outbreaks due to environmental contaminants. Surveillance cultures of fluids administered to patients is a critical element of Hospital Infection Control practices.

KEYWORDS:

Nosocomial, Outbreak, Deionized water, Surveillance

Introduction:

This is a report of an ICU outbreak of Burkholderia cepacia (B.cepacia) bacteremia in a tertiary care hospital with root cause analysis, risk factor assessment and outcome. B.cepacia is a multi-resistant & nutritionally adaptive Gram-negative bacillus. It has both beneficial and destructive effects.(1) To list a few, the beneficial effects include production of antimicrobial compounds (which prevent damping off disease of seedlings and moulding of fruit), nitrogen fixation by colonization of plant roots, degradation of groundwater contaminants by utilizing a wide variety of carbon compounds etc. However, as a pathogen, it can cause disease in plants (Sour skin onion rot) and humans (Septicemia, Pneumonia). Recently, its emergence as a potentially fatal nosocomial pathogen is of concern. (2)

Clinically important Non-fermentative Gram negative bacilli which are rarely associated with nosocomial outbreaks include Burkholderia cepacia, Stenotrophomonas maltophilia, Ralstonia picketti and Sphingomonas paucimobilis.(3) Some of these non-fermenters have minimal nutritional requirements and can tolerate a variety of physical conditions and are therefore well adapted for survival in water systems. Major risk factor for these infections is a breach in the immunity. The first report of nosocomial infections caused by intrinsically contaminated povidone-iodine with B.cepacia was reported in 1981. (4)

Species of Burkholderia belong to Burkholderiaceae family which is rRNA Group II as classified by Palleroni based on rRNA-DNA homology studies. (5) These organisms have been referred to in the past as Pseudomallei group. Though many species are included in this group, only a few are human pathogens, namely B.mallei, B.pseudomallei, B.cepacia Complex and B.gladioli. According to recent taxonomy, B.cepacia is a cluster of at least 18 closely related genomic species now called the B.cepacia complex. (6)

Primarily a respiratory pathogen in Cystic Fibrosis patients, B.cepacia can also cause hospital outbreaks. Because of its unique ability to fix CO2 from air, it can grow in distilled water with a nitrogen source. Clinical infections include pneumonia and pneumonitis in patients receiving contaminated anesthetics, urinary tract infection in patients receiving contaminated irrigation fluids following catheterization or cystoscopy, septicemia following heart surgery, endocarditis caused by contaminated heart valves, conjunctivitis and septic arthritis. (7)

Hospital outbreaks of B.cepacia are usually due to a single contaminated source such as anaesthetics, (8) disinfectants, (9, 10) distilled water, (11) intravenous solutions, (12) nebulizer solutions, (13, 14, 15) mouthwash, (16) and medical devices.

The present study aimed to perform an environmental surveillance to identify the source & route of infection of Burkholderia outbreak in a dedicated Pediatric cardiothoracic surgical ICU (PCTICU) of a tertiary care hospital. It aimed to control the prevailing outbreak using Hospital Infection Control practices and to formulate a protocol to prevent further such outbreaks.

Methods:

A trend analysis of various isolates from PCTICU revealed unusual clustering of eight cases within a short span of 45 days (July – September 2015), which raised the suspicion of an outbreak.

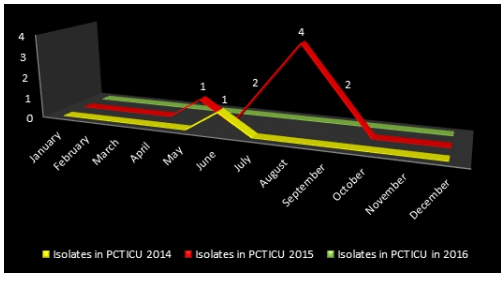

Figure 1: Trend of isolation of Burkholderia cepacia in PCTICU during 2014, 2015 and 2016

Active surveillance was undertaken to identify any ongoing case. A cohort study was initiated assessing the risk factors for the bacteremia in all babies treated during the same period in the same ICU. A retrospective case review revealed that all these children had a common significant clinical history.

1. They were operated for different cardiac anomalies
2. They were intubated for 48 hours post-surgery
3. They were given supplemental oxygen
4. They were ventilated mechanically
5. They all developed post-operative fever spikes (<5 days)
6. All of them had positive paired blood cultures for Burkholderia cepacia

Methodology of processing blood samples:

The blood samples of babies received were inoculated in a pair of BacT/Alert PF plus aerobic pediatric bottles (bioMerieux) and incubated in automated machine for a period of 7 days. All the culture bottles flagged positive were sub cultured onto Blood agar and MacConkey agar, incubated at 37℃ for a period of 48 hours. Colonies

obtained were identified using colony characteristics, Gram staining, biochemical reactions and Vitek 2 (automated identification system). Burkholderia isolates were confirmed by performing supplemental biochemical tests, which included Oxidase, Catalase, Oxidation-Fermentation test of glucose (OF test), Lysine decarboxylase (LDC), Malonate utilization & Resistance to colistin. (7) Antibiotic susceptibility testing was done by using Vitek 2 compact (bioMerieux) and manually using Kirby-Bauer disc diffusion method and interpreted according to Clinical Laboratory Standards Institute guidelines.

Methodology of processing endotracheal secretion & Central line tip: These were processed in a similar way to blood except that the samples were directly inoculated onto agar plates following standard microbiological procedures. Gram smear was prepared from the sample and examined.

All the isolates had similar antimicrobial susceptibility pattern. They were uniformly susceptible to Ceftazidime, Cefoperazone Sulbactam, Meropenem, Levofloxacin, Minocycline and Cotrimoxazole. All isolates (except one) were resistant to Ticarcillin-Clavulanic acid.

Table 1: Clinical and outcome details of babies with positive cultures during outbreak

S. No	Child age	Diagnosis	Surgery done	Culture positive sample	Antibiotic used	Outcome
1.	1 year	Large perimembranous VSD + COA	Repair of VSD + Repair of COA	Blood	Cefoperazone + Sulbactam	Discharged
2.	10 months	TOF	TOF repair	Blood	Ceftazidime	Discharged
3.	11 months	Multiple VSD with severe PAH	Repair of multiple VSD	Blood	Ceftazidime	Expired
4.	5 months	ALCAPA with severe LV dysfunction	Repair	Blood	Ceftazidime	Discharged
5.	1 month	TGA with large VSD & PAH	Arterial switch + VSD closure	Blood	Cefoperazone + sulbactam	Discharged
6.	1 month	Large VSD with severe PAH & CHF	VSD closure	Blood, ET, CLT	Ceftazidime	Discharged
7.	4 months	Large VSD with PAH	VSD closure	Blood	Ceftazidime	Discharged
8.	9 months	TOF	TOF repair	Blood	Ceftazidime	Discharged

Abbreviations: VSD – Ventricular Septal Defect; COA – Coarctation of Aorta; TOF – Tetralogy of Fallot; PAH – Pulmonary Arterial Hypertension; ALCAPA – Anomalous Left Coronary Artery from Pulmonary Artery; LV – Left Ventricular; TGA – Transposition of Great Arteries; CHF – Congestive Heart Failure; ET – Endotracheal Secretion; CLT – Central Line Tip

Epidemiological Investigation workup:
Environmental sampling was done as it is indicated in the investigation of an outbreak when environmental reservoirs or fomites are implicated epidemiologically in disease transmission.

Manual sampling was done using universal sterile sample containers (wherever applicable).

Environmental samples (n=21) taken randomly from pre-operative ward, operation theatres, ICU and post-operative ward of Pediatric unit included

- Disinfectant solutions
- Intravenous fluids
- Duolin (Ipratropium bromide, Salbutamol) respules
- Humidifier water
- Swabs from oxygen ports

Water samples, disinfectant solutions, Duolin solutions and surface swabs were inoculated on Mueller-Hinton agar, Blood agar and Mac Conkey agar plates and incubated at 37°C for 72 hours. Intravenous fluid solutions collected were inoculated in blood culture bottles (FA plus aerobic bottles; bioMerieux) and placed in an automated apparatus for 7 days (BacT/Alert system; bioMerieux). B. cepacia isolates were identified on the basis of colony morphology and biochemical characteristics, supplemented by VITEK 2 compact (bioMerieux) as previously described.
Sampling and processing of deionized water from other ICUs (n=9) followed to detect any contamination.

Results & Discussion:Deionized water sampled from PCTICU and one of the Medical ICUs showed confluent growth of Burkholderia cepacia. Biotyping and resistotyping of the isolate matched well with the patient isolates. All other samples tested were sterile after respective periods of incubation. Even though the water sample taken from MICU showed growth, no clinical cases were reported with Burkholderia bacteremia during the same period. Deionized water (outside supply) was being used in humidifier reservoirs for delivery of low-flow oxygen therapy in the hospital. The deionized water was supplied as five liter sterile cans and water from single can was used for more than one patient. With immediate effect, "Reverse Osmosis" water from the in-house RO plant was used in place of deionized water. Appropriate antibiotic therapy was started. The supplier of deionized water was promptly informed and appropriate administrative action was taken.

Burkholderia is one of the less commonly encountered microorganisms as a cause of water borne infection in healthcare facilities. Earlier reports implicated contaminated distilled water, solutions and disinfectants, dialysis machines, nebulizers, water bath, ventilator temperature probes etc. as causes for such outbreaks due to B. cepacia. Contamination of medical devices and supplies can be broadly categorized to be intrinsic (that occur during manufacture) and extrinsic (entry other than during manufacture). Cause of outbreak could be intrinsically contaminated deionized water in our case. However, extrinsic contamination could not be ruled out.

Risk factor analysis:
Though many babies were exposed to the bacteria, only a few manifested the infection because of the associated risk factors as detailed in table 2.

Table 2: Risk factor comparison of babies with and without Burkholderia bacteremia during the outbreak

S. No	Variable (Risk factor)	Average for babies who did not develop bacteremia	Average for babies who developed bacteremia
1.	Mean hospital stay (days)	10.4	21
2.	Antimicrobial administration (days)	5.8	8.5
3.	Mechanical ventilation (days)	2.3	5.5
4.	Supplemental O2 therapy (days)	4.7	11.2
5.	Average weight to age	69%	65%
6.	Heart surgery	Done for all	Done for all
7.	Prior health status	History of recurrent respiratory tract infections	History of recurrent respiratory tract infections

Surveillance:
The active surveillance initiated as a part of case finding continued. Timely intervention with appropriate antibiotics prevented progression to septicemia in 7 cases. One baby who developed septicemia was successfully treated. Repeat blood cultures were sent and found to be negative in all children except the one who succumbed. The death was due to surgical complications and not directly related to Burkholderia infection. Continuous monitoring of all patients for development of infection as a part of comprehensive surveillance, combining patient and lab based elements was undertaken. Surveillance cultures from intubated patients continued and contact precautions for all patients with Burkholderia cepacia bacteremia were followed. Once the explanation for outbreak was made, and there was occurrence of no more cases, surveillance cultures were stopped. In the

post-outbreak surveillance period (6 months), no baby had Burkholderia bacteremia in PCTICU.

Modes of Transmission of Waterborne diseases:

According to CDC, there are 5 principal ways of transmission.(2) They are direct contact (Ex: hydrotherapy), ingestion of water, in-direct contact transmission (Ex: improperly reprocessed medical device), inhalation of aerosols dispersed from water sources or aspiration of contaminated water. The first three routes are commonly associated with infections due to Gram-negative bacilli. However, we propose the fourth route to be the cause for outbreak in our institution.

Policy:

Our institutional Infection Control Committee team has decided to conduct surveillance cultures in any ICU reporting "more than 3 positive cultures" of Burkholderia or other rare nosocomial pathogen in a month.

Fortnightly sterility checking of in-house RO water was implemented. Training sessions were conducted for health care staff. Hand hygiene, barrier nursing, use of personal protective equipment, disinfection of medical equipment and other infection control practices were emphasized.

Limitations of the study:

Molecular typing of strains was not done. Sampling from manufacturing unit to demonstrate the causal association of contamination could not be done.

Conclusion:

Outbreaks of bacteremia due to environmental contaminants are rare, but still possible. Epidemiological investigations are imperative to find out source and route of infection. Implementation of best practices in respiratory therapy, administration of I.V. fluids and parenteral nutrition play an indispensible role in preventing these outbreaks. Ways to achieve this is by training health care workers & having a vigilant Infection Control Team. However, contamination occurring at the production point and during transport is always a possibility. The present study highlights the importance of surveillance cultures of fluids administered to patients. An institutional policy can be devised as an alerting tool of an impending outbreak in critical care areas with vulnerable population.

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