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Research Article

AN OUTBREAK OF *Burkholderia cepacia* BACTERAEMIA IN A TERTIARY CARE CENTRE, DHAKA DUE TO CONTAMINATED NEBULIZER SOLUTION

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ABSTRACT

Burkholderia cepacia complex (BCC) is an opportunistic bacteria causing infection in immunocompromised patients and well distributed in the hospital environment. Nosocomial outbreaks of BCC are due to contaminated solutions and medical devices. However, in Bangladesh there have been no nosocomial outbreaks of BCC reported in the past. We report here an outbreak of *Burkholderia cepacia* bacteraemia in a Tertiary Care Centre, Dhaka, due to contaminated nebulizer solution during the period of 7th January 2020 to 5th February 2020. That was an extensive investigation traced to a contaminated nebulizer solution of a particular brand of ipratropium bromide. The blood culture isolates from the patients with bacteraemia and from the particular nebulizer solution were found to be identical and confirmed as BCC. Our observation was reported officially to the relevant authorities of the hospital and an alternative agent for the use of nebulization was strongly recommended to prevent further cases immediately.

INTRODUCTION

The *Burkholderia cepacia* and 17 other genomospecies comprise the *B. cepacia* complex (BCC). The classification of these bacteria is complex; the specific identification is difficult. These are environmental organisms able to grow in water, soil, plants, animals and decaying vegetables materials. In hospitals, members of BCC have been isolated from a variety of environmental sources from which they can be transmitted to patients. People with cystic fibrosis (CF) and those patients with chronic granulomatous disease are particularly vulnerable to infection with BCC. It is likely that BCC can be transmitted from one CF patient to another by close contact. They may have asymptomatic carriage, progressive deterioration over a period of months or rapidly progressive deterioration with necrotizing pneumonia and bacteremia[1].

B. cepacia grows on most media used in culturing specimens for gram negative bacteria. They are oxidase positive and lysine decarboxylase positive and produce acid from glucose, but differentiating *B. cepacia* from other pseudomonads, including *Stenotrophomonas multopholia*, requires a battery of biochemicaltests and can be difficult. Submission of isolates to reference laboratories is recommended because of the prognostic implications of colonization in CF patients. Susceptibility tests should be done on BCC isolates recovered from CF patients are often multidrug resistant. Trimethoprim-sulphamethoxazole, meropenem and ciprofloxacin or alternatively minocycline, are effective treatments[1].

Nosocomial outbreaks associated with BCC are known to be due to contaminated disinfectants, nebulizer solutions, mouth wash, medical devices and intravenous solutions[2]. It can be also due to contaminated fresh frozen plasma (FFP) and cryoprecipitate due to thawing in water baths[3].
During the period between 7th January and 5th February2020, we observed a steep increase in the isolation of BCC from blood cultures of patients from several intensive care units (ICU), high dependency units (HDU) and oncology wards of the hospital with the isolates having mostly same antibiotic susceptibility profile. This unexpected finding led to a detailed investigation for a possible common source, as finding the source was essential to control the outbreak.

METHODS AND MATERIALS

This observational study on *Burkholderia cepacia* complex infection was carried out on Combined Military Hospital, Dhaka. For this study we analyzed 132 blood culture positive

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isolates for a short duration of 7th January to 5th February 2020. Among them total 53 cases were due to BCC infection. Eight of these patients expired because of possibly BCC septicaemia and other co-morbidities. Others were treated with appropriate antibiotic therapy and improved clinically. This unexplained increase in isolation of BCC in blood cultures initiated an outbreak investigation to find the possible common source which caused the outbreak. Medical devices and solutions were tested for bacterial contamination to identify the possible source. The devices tested were different sizes of syringes, IV cannulae and burette sets. Other solutions tested were opened and unopened ipratropium bromide nebulizer solutions, salbutamol nebulizer solutions, working and stock solutions of disinfectants, 5% dextrose solutions and normal saline solutions.

Sterile water was aspirated under aseptic conditions into sterile syringes, cannulae and burette sets, decanted into sterile tubes and centrifuged. The deposit was used for culture. Five ml of all liquid samples were directly inoculated onto the culture media. Blood agar, chocolate agar and MacConkey agar were inoculated and incubated overnight at 37 ºC. Samples were subcultured into MacConkey agar after overnight incubation. The final identification and antibiotic susceptibility testing (AST) of the isolates were done by the BD Phoenix M50 automated identification and susceptibility testing system.

RESULTS

Total isolates of BCC from blood culture were 53(40%) among 132 positive blood cultures during the period of 7th January to 5th February 2020. All the blood culture isolates were identified as *Burkholderia cepacia* complex and AST were almost same.

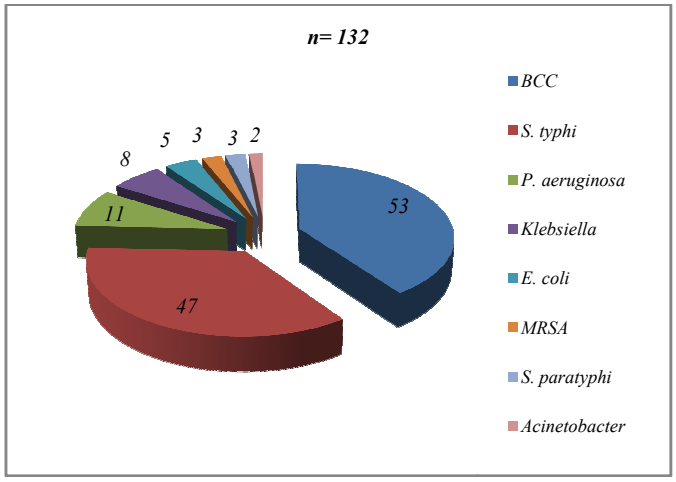

Fig 1 Pattern of isolation of various pathogens from positive blood cultures (n= 132)

Table 1 BCC isolates of blood cultures from different units of the Hospital

Units	Number of Isolates	Percentage (%)
Medical ICU	16	30
Surgical ICU	10	19
Medical HDU	07	13
Surgical HDU	05	9
Critical Care Centre	04	7
Geriatric HDU	04	8
BMT Ward	04	8
CVS ICU	01	2
Burn ICU	01	2
Oncology Ward	01	2
Total	**53**	**100**

All of the opened and multiple used ipratropium bromide nebulizer solutions tested were found to be positive for the same organism with an identical morphological pattern.

Cultures from other solutions and devices were negative. The colonies of the isolates were opaque, glistening and non pigmented on blood agar and on MacConkey agar, they were non lactose fermenting. They were catalase and oxidase positive. The isolates were confirmed by BD Phoenix M50 automated identification and susceptibility testing system as BCC. All the isolates had almost same antibiotic susceptibility pattern.

All the available stocks of different batches of opened and used ipratropium bromide nebulizer solutions of the particular brand in the hospital were then tested and became positive for BCC with the similar antibiogram.

Ultimately we found that the BCC isolates from the blood cultures and the isolates from the ipratropium bromide nebulizer solutions were mostly same in their antibiotic susceptibility profile. This suggested that the ipratropium bromide nebulizer solution was one of the common sources for the outbreak.

DISCUSSION

B. cepacia, formerly known as *Pseudomonas cepacia* was assigned to a new genus Burkholderia in 1992, in the honor of its discoverer[3]. BCC is a saprophyte commonly distributed in soil, water, fruits and vegetables as well as contaminants of pharmaceutical preparation and medical equipments[2]. In our case identical isolates of BCC obtained from ipratropium bromide nebulizer solutions, which were used with salbutamol solution for respiratory distressed patients.

According to the results of the extensive investigation, ipratropium bromide nebulizer solutions were the possible common source for the outbreak since the BCC isolates of blood cultures and the solution were similar in their antibiotic susceptibility. The patients who had positive blood cultures for BCC had been nebulized with the particular nebulizer solution during their stay in the hospital before their blood cultures became positive. Same results were observed by S. vathshalan *et al* of National Hospital, Sri Lanka. They found 27 BCC isolates over a period of one month from positive blood cultures and all of the opened and unopened ipratropium bromide nebulizer solutions were found to be positive for the same organism with an identical morphological pattern[5]. In fact this observation inspired us to evaluate the ipratroprium bromide nebulizer solutions.

The nosocomial outbreaks of BCC reported worldwide revealed that sources for outbreaks were contaminated disinfectants, nebulizer solutions, mouth wash, medical devices and intravenous solutions[3]. A study carried out in Saudi Arabia in 2006 found that the outbreak of BCC bacteraemia due to contaminated salbutamol nebulizer solution[6]. Studies done elsewhere have implicated contaminated nasal spray[7], contaminated rubber stopper of sealed multi dose amikacin vials[8], contamination of the gel applied to the ultrasound probe used to guide the insertion of a central venous catheter[9] and intravenous fentanyl[10].
In Bangladesh there is no available article and data regarding association of ipratroprium bromide with BCC, but study on HAI due to BCC was 15.4%[11].

Actions taken

Identifying the possible source of the outbreak enabled the outbreak from spreading further by informing the relevant authorities, i.e Commandant and Doctors in Charge of various ICU, with the recommendation for an alternative ipratropium bromide nebulizer solution and avoidance of using multi dose vials for several times.

Recommendations

We suggested to the hospital authorities to use an alternative solution for nebulization as there was evidence of bacterial contamination in the particular nebulizer solution.

Prevention of future outbreaks

Relevant standards should be maintained and monitored strictly and regularly regarding production of medical devices and solutions. Pre and post marketing surveillance of these products also have to be ensured for the safety of patients.

Limitation of the study

We could not able to identify the other sources of BCC, prevailing in the hospital environment.

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