CASE REPORT

Emergence of *Burkholderia cepacia* in ICU Setting

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Abstract

Background: *B. cepacia* is metabolically versatile organism which is not only resistant to many antibiotics but also disinfectants. This makes their survival easy even in restricted areas like intensive care unit (ICU) and management difficult.

Aims and objectives: To describe sudden emergence of *Burkholderia* at a tertiary care centre ICU setting in milieu of colistin usage

Materials and methods: Cases were patients with culture proven *B.cepacia.* They were picked up as non-lactose fermenting, oxidase positive, motile, gram-negative bacilli which was resistant to colistin and aminoglycosides and sensitive to cotrimoxazole. These isolates were further confirmed by both VITEK-2 compact system (Biomerieux, France) and standard bacterial techniques.

Colistin consumption data were retrospectively collected from medical store records of hospitals and individual ICU pharmacy records from January 2016 to June 2016, and were expressed as total dialy doses in a month per 1000 patient days (DDD/1000PD)

Results: An increase was observed in *B. cepacia* infection linked to increased consumption of colistin in ICU**.**

Conclusion: Based on these results an increase was observed in *B.cepacia* infection which correlated with increased consumption of colistin in ICU. We speculate that extensive use of colistin may lead to selection of intrinsically resistant *B. cepacia* and may facilitate their spread as nosocomial pathogens.

Keywords: *Burkholderia cepacia*, Colistin, ICU

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Introduction

Burkholderia cepacia is widely distributed in the natural environment and has been isolated from water, soil, fruits, and vegetables.[1] It is an aerobic, motile, glucose-nonfermenting, multidrug resistant gram-negative bacillus that is also resistant to many disinfectants.[2] These bacteria exhibit an extraordinary metabolic versatility, allowing their adaptation to a wide range of environments. Over the last 2 decades, *B. cepacia* complex has emerged as a serious human pathogen. It can cause fatal necrotizing pneumonia and bacteremia, especially in patients with cystic fibrosis or chronic granulomatous diseases.[3–5] It is an opportunistic pathogen that causes disease in immunocompromised individuals and has been associated with outbreaks in intensive care unit (ICU) settings.[6] However, *Burkholderia cepacia* detection from clinical samples is very infrequent in All India Institute of Medical Sceinces, Delhi. But, an upsurge of pneumonia caused by this organism which is intrinsically resistant to colistin, was observed for last six months from January 2016 to June 2016 at a tertiary care referral hospital in various ICU. Unfortunately in this context increased use of colistin as a last line therapeutic drug for patients infected with multidrug resistant (MDR) gram-negative bacteria has led to the recent emergence of colistin-resistant bacteria (CRB) among bacterial species.[7] The present study endeavours to describe sudden emergence of Burkholderia at a tertiary care centre ICU setting in milieu of colistin usage.

Material and Methods

Our center is a tertiary care referral hospital in northern India. We isolated and identified *B. cepacia* isolates from clinical samples, such as endotracheal (ET) aspirate, bronchoalveolar lavag (BAL), blood, drain fluid and blood who were admitted between January 2016 and June 2016

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Cases were patients with culture proven *B.cepacia*. The patients' records were reviewed with respect to age, gender, clinical features, antimicrobial treatment, outcome. Sites of infection were established based on history and examination findings in the medical notes together with investigation reports and procedure notes.

Microbiological Investigations

The samples were cultured in blood, chocolate, and MacConkey agars. The antibiotic sensitivity pattern was determined using Muller Hilton agar by Kirby–Bauer disk diffusion method as per Central laboratory standards institute (CLSI) 2016 guidelines.[8] *B. cepacia* was picked up as non-lactose fermenting, oxidase positive, motile, gram-negative bacilli which was resistant to colistin and Aminoglycosides and sensitive to cotrimoxazole. These isolates were further confirmed by VITEK-2 compact system (Biomerieux, France). Since automated systems are not infallible the identification of the isolates was confirmed by conventional biochemical testing and only the isolates positive by both methods were taken for the study. Conventional tests included triple sugar iron agar, lead acetate paper strip for hydrogen sulphide production,

decarboxylases, aerobic low-peptone basal medium containing glucose.[9]

Colistin Consumption

Colistin consumption data were retrospectively collected from medical store records of hospitals and individual ICU pharmacy records from January 2016 to June 2016, and were expressed as total dialy doses in a month per 1000 patient days (DDD/1000PD).

Results

From Jan 2016 to May 2016, a total of 15 patients had cultures positive for *B. cepacia*. Four of the positive cultures came from tracheal aspirates, 9 from bronchoalveolar lavage (BAL), 1 from blood 1 from chest drain fluid. There was no accumulation of *B. cepacia* infection according to occurrence time and wards or ICU during the study period. Infections caused by *B. cepacia* included pneumonia ($n = 14$) and bacteremia ($n = 3$). Two patients had both bacteremia and pneumonia. One isolate was obtained from chest drain fluid of one patient who also had concurrent pneumonia.

All the isolates were from various ICUs of the institution. Most of the infections were hospital acquired due to various risk factors like tracheostomy and intravenous line. *Burkholderia* being a contaminant was considered infectious agent only when it was repeatedly isolated and correlated with clinical features. The demographic and clinical characteristics of the patients are given in Table 1.

The correlation between colistin consumption and prevalence of *B.cepacia* infection is shown in Figure 1. A scatter plot was also plotted to show association between colistin usage and emergence of *B. cepacia* in Figure 2.

By disk diffusion method all the isolates were susceptible to cefoperazone/sulbactam (100%),

Piperacillin/tazobactam (100%), levofloxacin (100%). Maximum resistance was observed against ceftazidime (93%) followed by meropenam (53%).

Discussion

As stated previously *Burkholderia cepacia* is ubiquitously present in environment, has been isolated from water, soil. It is frequently recovered from hospital water sources.[1,10] Moreover it can survive in the presence of certain disinfectants.[2,11] It is non-pathogenic in healthy hosts and is commonly associated with colonization and pulmonary infection, especially in cystic fibrosis patients.[12] However, it is increasingly being recognised as a newly nonfermenting gram-negative bacteria causing nosocomial infections in hospital setting. It is associated with a wide variety of infections, including pneumonia, bacteremia, skin and soft tissue infection, genitourinary tract infection secondary to urethral instrumentation. Outbreaks have occured through exposure to contaminated solutions such as antiseptics, disinfectants, nebulizer solution, and dextrose solution in hospitalized patients.[13] After January 2016 number of patients with *B. cepacia* infections increased, which correlated well with increased consumption of colistin. However, all the cases were sporadic and there was no accumulation according to occurrence time and location. Moreover, regular periodic environmental sampling of all the ICU could not isolate *B. cepacia*

Table1: Demographic and clinical characteristics of 15 patients with *Burkholderia* cepacia infection

Characteristic	*Value*
Total no. *B. cepacia*	15
Patient distribution in intensive care unit	
Medical ICU	4
Surgery ICU	2
Neurosurgery ICU	3
AB8 ICU	6
Demographic and clinical characteristics	
Male/female	8/7
Age mean	51.8
Duration of hospitalization	47.2
No. of patients who died	5/15(33.3%)
Tracheostomy	7/15
Hematological malignancy	1/15
Diabetes mellitus	2/15
Pneumonia	14/15

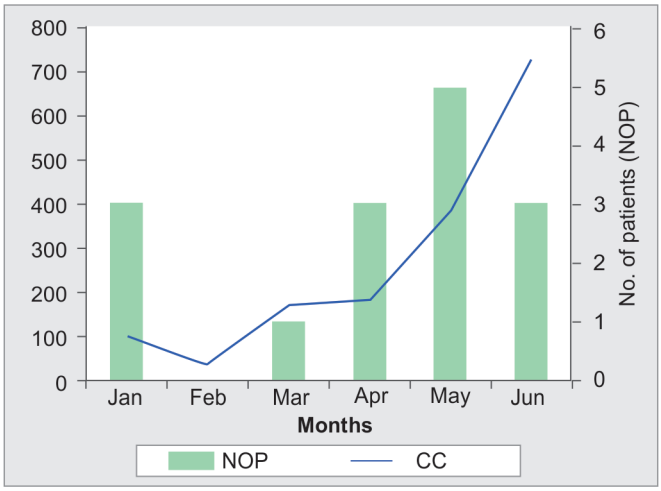

Fig. 1: Correlation between colistin consumption (DDD/1000PD) and no. of patients infected with *B. cepacia*

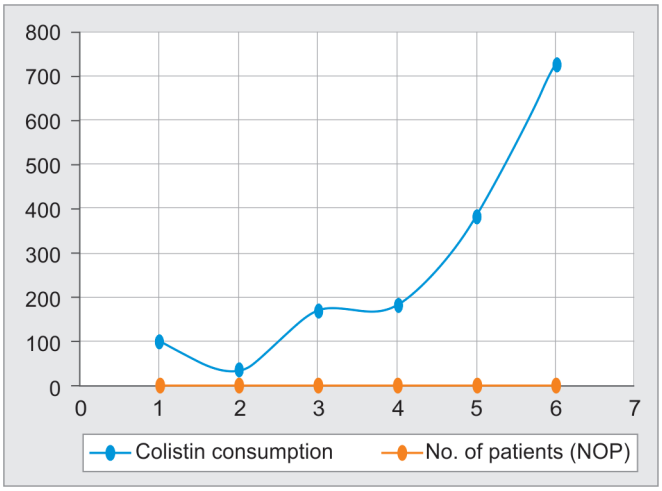

Fig. 2: Scatter plot depicting association between colistin usage and emergence *B. cepacia*

B. cepacia complex has intrinsic resistance to many antimicrobials. It has been well documented to have intrinsic resistance to aminoglycosides, first- and second-generation cephalosporins, traditional antipseudomonal penicillins and polymixins. The multiple antibiotic resistance of *Burkholderia* has been ascribed to an impermeable selective outer membrane, efflux pump mechanism and/or production of an inducible chromosomal beta-lactamase.[14] In our study also, isolates were resistant to amoxicillin-clavulanic acid (100%) and ceftazidime (100%). It is possible that it may potentially survive well in the environment if there is frequent exposure to broad spectrum antibiotics. Increased use of colistin may cause collatereal damage and incresesd healthcare associated *B. Cepacia* infections. The most active antimicrobial agent against *B. cepacia* isolates were piperacillin-tazobactam and cefoperazone-sulbactam.

Based on these results an increase was observed in *B. cepacia* infection linked to increased consumption of colistin in ICU. Resistance to carbapenem compounds is now endemic in several countries worldwide and has led to an increased use of colistin. This result can be further explained by the fact that colistin has been extensively used as a treatment of last resort for patients of ventilator associated pneumonia due to carbapenamase producing bacteria mainly in *Pseudomonas aeruginosa, Acinetobacter baumannii* and *K. pneumonia*. We speculate that extensive use of colistin may lead to selection of intrinsically resistant *B. cepacia* and may facilitate their spread as nosocomial pathogens. This phenomenon has been previously observed in cystic fibrosis where colistin use by aerosols occasionally has led to the selection of intrinsic CRB (colistin resistant bacteria) including *Inquilinus limosus, Brevundimonas diminuta, Ochrobactrum anthropi, Pandoraea spp., Chryseobacterium indologenes* and *Burkholderia* spp.[15–17]

Nosocomial pneumonia (n = 12) accounted for most of the *B. cepacia* infections and 75% (n = 9) were under mechanical ventillation. All the patients were admitted in various ICU (Table 1). Several predisposing factors have been suggested as the major determinants for developing pneumonia. These include permanence in ICU, having undergone major surgery, and having an intravascular catheter.[18] It is difficult to point out at a predisposing factor in this short study with small number of isolates. So far during the study period crude mortality rate was 33.3% (n = 5). But patients were already admitted in ICU for severe underlying condition.

Our study had several limitations. Firstly, it was a retrospective short duration study where smaple size was small so risk factor analysis could not be done. Secondly, *Burkholderia* isolates were picked up on the basis of antibiotic susceptibility. So, isolates which were cotrimoxazole resistant could have been missed. Lastly, simulataneous emergence of other colistin resistant bacteria (CRB) of genera *Proteus, Providencia, Morganella* and *Serratia* was not looked for. Nevertheless, this short report does highlight emergence of *B. cepacia* in era of increased usage of colistin as last resort for multidrug resistant bacteria (MDR) gram-negative bacteria. However, other factors could have been responsible for the same which could not be identified in this study.

Use of colistin, also known as the 'antibiotic of last resort' should be restricted. Clinicians should avoid using it as initial empirical therapy. It may be used in combination with other antibiotics to increase antibacterial efficacy and to maintain usefulness against MDR gram-negative infections.

Conclusion

Use of colistin as last resort for MDR organisms is acting as grounds for emergence of CRB like *B. cepacia*. Colistin should definitely not be used empirically rather in combination with other antibiotics as per the antibiotic policy. It is in this context that hospital should update its antibiogram and make it readily available to clinicians managing patients in such setting.

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