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CLINICAL BRIEF

Burkholderia cepacia Sepsis Among Neonates

Saikat Patra · Ramesh Bhat Y · Leslie Edward Lewis · Jayashree Purakayastha · V. Vamsi Sivaramaraju · Vandana Kalwaje E · Swathi Mishra

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Abstract *Burkholderia cepacia* is a rare cause of sepsis in newborns and its transmission involves human contact with heavily contaminated medical devices and disinfectants. The authors aimed to determine epidemiology, clinical features, antibiotic sensitivity pattern, complications and outcome of blood culture proven *B. cepacia* infections in 12 neonates. All neonates were outborn, 5 preterm and 7 term. *B. cepacia* was isolated from blood in all and concurrently from CSF in three neonates. Lethargy and respiratory distress (41.7 %) were major presenting features. Five newborns (41.7 %) required mechanical ventilation for 3–7 d. Highest bacterial susceptibility was observed for meropenem (100 %), followed by cefoperazone-sulbactam, piperacillin-tazobactam, sulfamethoxazole-trimethoprim (all 83 %), ceftazidime (75 %) and ciprofloxacin (42 %). Piperacillin-tazobactam, ciprofloxacin and cotrimoxazole either singly or in combination led to complete recovery of 11 (91.7 %) newborns; one developed hydrocephalus. Eight of nine infants who completed 6 mo follow up were normal. Prompt recognition and appropriate antibiotic therapy for *B. cepacia* infection results in complete recovery in majority.

Keywords *Burkholderia cepacia* · Neonates · Sepsis

S. Patra (✉) · R. Bhat Y · L. E. Lewis · J. Purakayastha · V. V. Sivaramaraju
Department of Pediatrics, Kasturba Medical College, Manipal University, Manipal 576104, Udupi District, Karnataka, India
e-mail: dr.saikatpatra@gmail.com

V. Kalwaje E
Department of Microbiology, Kasturba Medical College, Manipal University, Manipal, Udupi District, Karnataka, India

S. Mishra
Kasturba Medical College, Manipal University, Manipal, Udupi District, Karnataka, India

Introduction

Burkholderia cepacia is an aerobic, glucose non-fermenting gram negative bacillus (NFGNB) which is not considered as part of normal human flora [1]. They are commonly found in moist environments such as intravenous fluids, nebuliser solutions, contaminated disinfectants, medical devices [1, 2] as well as skin of health care workers. In recent years, *B. cepacia* infections have increased due to indiscriminate use of antibiotics, longer duration of hospital stay and indwelling catheter related infections [1–5]. It rarely causes sepsis in neonates in the absence of predisposing factors [1, 2], but infections are usually severe [3]. The authors aimed to analyse the disease spectrum, source of infection, antibiotic sensitivity pattern, complications and outcome of *B. cepacia* infections in neonates.

Material and Methods

This retrospective study was conducted in a level III Neonatal intensive care unit of Kasturba Hospital, Manipal which is a tertiary care referral hospital. Blood culture proven *B. cepacia* infections between May 2011 and April 2012 were analysed by retrieving data from patient records and computerised database. The data included gestational age, birth weight, gender, presenting complaints, risk factors, source of infection, antibiotic sensitivity, response to antibiotics, complications and outcome. Neonatal sepsis was categorised as early onset (≤72 h after birth) or late onset (>72 h after birth).

BacT/ALERT PF Pediatric FAN (bioMérieux, France) bottles were used for blood culture. Blood samples for routine investigations and culture were obtained concurrently at admission. Oxidase positive, glucose NFGNB grown in blood cultures were further characterized by standard microbiological methods. Antimicrobial susceptibility was determined by

Table 1 Demographic characteristics, clinical features, risk factors and outcome of 12 neonates with *Burkholderia cepacia* infections

Case no.	GA (wk)	BW (g)	MOD	Age at adm (d)	Presenting features	Risk factors	TLC (cells/mm^3)	Platelets (cells/mm^3)	Sample from which organism isolated	Outcome at discharge	Outcome at 6 mo
1	33	1750	NVD	4	Apnea	Twin, LBW	2500	196000	Blood & CSF	Normal	Normal
2	33	1300	NVD	4	Lethargy	Twin,VLBW	1700	112000	Blood	Normal	Normal
3	41	2620	Forceps assisted	2	Tachypnea, hydrocephalus, lethargy	PROM 24 h, MV - 5 d	28300	166000	Blood & CSF	Seizures & Hydrocephalus	Seizures & Hydrocephalus
4	39	2600	LSCS	3	Seizures	-	14400	271000	Blood	Normal	Normal
5	34	1520	NVD	1	Poor feeding	-	7100	199000	Blood	Normal	Normal
6	39	2800	NVD	3	Tachypnea	CDH (S),UVC,MV - 3 d	21700	57000	Blood	Normal	Normal
7	38	2005	NVD	6	Lethargy, poor feeding	-	18300	80000	Blood	Normal	Lost to follow up
8	39	2745	NVD	2	Bleeding from mouth	-	18700	280000	Blood	Normal	Lost to follow up
9	40	2245	LSCS	1	Blood in stools	PROM 20 h	11500	253000	Blood	Normal	Lost to follow up
10	38	2715	NVD	15	Tachypnea, poor feeding	MV - 4 d	10000	369000	Blood	Normal	Normal
11	39	2800	NVD	3	Tachypnea, lethargy	MV - 3 d	19500	304000	Blood	Normal	Normal
12	29	1255	NVD	1	Tachypnea, lethargy	RDS,MV - 7 d, PICC	8500	208000	Blood & CSF	Normal	Normal

GA Gestational age; *BW* Birth weight; *MOD* Mode of delivery; *NVD* Normal vaginal delivery; *LSCS* Lower segment cesarian section; *adm* admission; *MV* Mechanical ventilation; *CDH*(*S*) Congenital diaphragmatic hernia (Post surgery); *UVC* Umbilical vein catheter; *RDS* Respiratory distress syndrome; *CSF* Cerebrospinal fluid; *TLC* Total leucocyte count; *PICC* Peripherally inserted central venous catheter; *PROM* Premature rupture of membrane

disc diffusion method according to CLSI guidelines [6]. Cerebrospinal fluid (CSF) analysis and culture were performed in all.

Results

Of 594 neonates suspected of sepsis, 61 (10.3 %) were blood culture positive, 12 were identified with *B. cepacia*. In these 12 patients, *B. cepacia* was the sole organism isolated. All 12 neonates were outborn referrals with male to female ratio of 2:1. Gestation ranged from 29–41 wk. Four neonates had low birth weight and two had very low birth weight. Early onset sepsis (EOS) was observed in 8 and late onset sepsis in 4. Major presenting complaints were lethargy (41.7 %) and tachypnea (41.7 %) followed by refusal of feeds (25 %). Bleeding from gut, seizures and apnea were the other complaints (Table 1). Five (41.7 %) newborns required mechanical ventilation for 3–7 d. *B. cepacia* was simultaneously isolated from CSF in three neonates. The antibiotic sensitivity pattern is shown in Fig. 1. Neonates were treated with piperacillin-tazobactam, ciprofloxacin and cotrimoxazole either singly or in combination for 14–21 d depending on associated meningitis. Repeat blood cultures were sterile in all. Average duration of nursery stay was 21.2 (range, 5–60) d.

Normal outcome until discharge was observed in 11 (91.7 %) neonates. One neonate developed hydrocephalus and had multiple seizures. He needed multiple anticonvulsants and ventriculoperitoneal shunt. Hearing evaluation in 3 neonates with meningitis was normal. There was no mortality. At 6 mo follow up visit 8 infants were neurologically normal and 1 had hydrocephalus. Three infants were lost to follow up.

Discussion

B. cepacia is a bacillus of low virulence but can cause serious infection in people with weakened immune system and chronic lung disease [1, 2]. *B. cepacia* most commonly presents with respiratory tract, urinary tract and blood stream infections [1, 2]. In the present study, neonates with relatively weaker immune system had infections with respiratory distress (41.67 %) and poor feeding (25 %) as common presentations. About 66.7 % neonates had EOS which agrees with reports by Sundaram et al. [5]. They observed 75 % of NFGNB neonatal infections as EOS.

B. cepacia are usually multidrug resistant organisms [1]. Resistance is common to aminoglycosides, polymyxins B and colistin [7–9]. Jacquier et al. reported 100 % resistance to colistin-a "last resort antibiotic" [10]. Co-trimoxazole has been reported as a drug of choice [2, 9] but intravenous cotrimoxazole is not available in most places of India. Avgeri et al. reported ceftazidime, meropenem and piperacillin, either alone or in combination as an effective alternative [9]. The authors used piperacillin-tazobactam, ciprofloxacin or cotrimoxazole either singly or in combination depending on the sensitivity reports, with good results. All *B. cepacia* isolates were resistant to ampicillin, amikacin and colistin.

B. cepacia can survive in moist environment including disinfectants and frequently colonise various medical solutions. Direct person-to-person spread is also known. In an attempt to find out the source, the authors cultured tap water, humidifier water, nebuliser solution, disinfectants at both their hospital and referring hospital but found negative results.

The most dreaded complication of *B. cepacia* infection is meningitis, leading to mortality and long term sequelae. Complete recovery was observed in most of the case with no mortality.

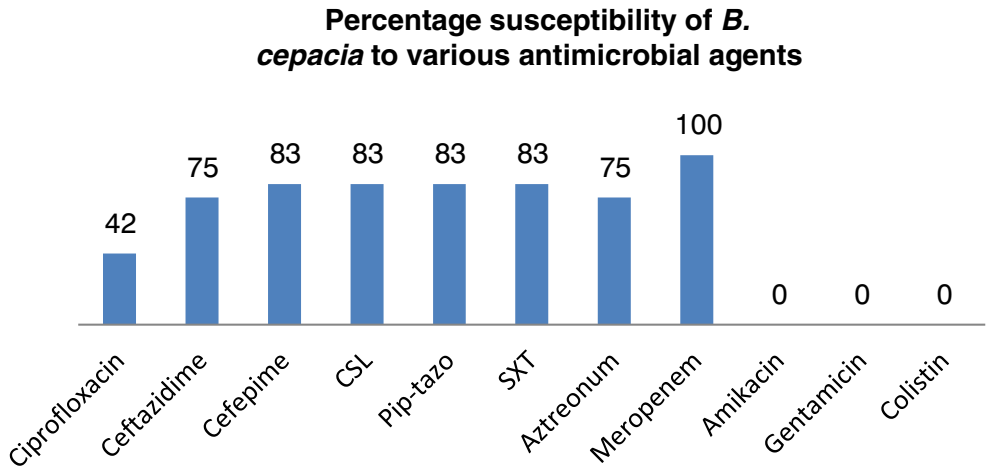

Fig. 1 Antimicrobial susceptibility pattern of *B. cepacia* isolates
CSL Cefoperazone-sulbactam; *Pip-tazo* Piperacillin-tazobactam; *SXT* Sulfamethoxazole-trimethoprim

Conclusions

B. cepacia is an upcoming pathogen causing neonatal sepsis. Intrinsic resistance to aminoglycosides and colistin is a potential problem to effective therapy and demands a relook into aminoglycoside containing regimen for empirical therapy. Appropriate infection control measures in high risk neonatal care areas are needed to prevent this infection.

Contributions SP: Involved in data collection and preparation of the manuscript; RBY and LEL: Involved in patient treatment, supervision of data collection and critical approval of the manuscript; JP and VVS: Involved in helping manuscript preparation; VKE: Provided expert microbiological inputs; SM: Involved in data collection. LEL will act as guarantor for this paper.

Conflict of Interest None.

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References

1. Forbes BA, Sahm DF, Weissfeld AS. Pseudomonas, Burkholderia and similar organisms. In: Forbes BA, Sahm DF, Weissfeld AS, editors. Bailey and Scott's diagnostic microbiology. 12th ed. St. Louis: Elsevier; 2007. p. 340–50.
2. Winn Jr WC, Allen SD, Janda WM, Koneman E, Procorp G, Schreckenberger P, et al. The nonfermentative Gram-Negative bacilli. In: Winn Jr WC, Allen SD, Janda WM, Koneman E, Procorp G, Schreckenberger P, Woods GL, editors. Koneman's Color atlas and textbook of diagnostic microbiology. 6th ed. Philadelphia: Lippincott Williams and Wilkins; 2006. p. 326–8.
3. Kuzumoto K, Kubota N, Ishii K, Yumoto K, Ogiso Y, Nakamura T, et al. Successful cessation of transmitting healthcare associated infections due to Burkholderia cepacia complex in a neonatal intensive care unit in a Japanese children's hospital. Eur J Med Res. 2011;16: 537–42.
4. Viswanathan R, Singh AK, Ghosh C, Dasgupta S, Mukherjee S, Basu S. Profile of neonatal septicaemia at a district-level sick newborn care unit. J Health Popul Nutr. 2012;30:41–8.
5. Sundaram V, Kumar P, Dutta S, Mukhopadhyay K, Ray P, Gautam V, et al. Blood culture confirmed bacterial sepsis in neonates in a North Indian tertiary care centre: changes over the last decade. Jpn J Infect Dis. 2009;62:46–50.
6. Clinical Laboratory Standards Institute. 2006. Performance standards for antimicrobial disk susceptibility tests; Approved standard-9th ed. CLSI document M2-A9.26:1, Clinical Laboratory Standards Institute, Wayne, PA.
7. Hancock RE. Resistance mechanism in Pseudomonas aeruginosa and other nonfermentative gram-negative bacteria. Clin Infect Dis. 1998;27:93–9.
8. Gautam V, Singhal L, Ray P. Burkholderia cepacia complex: beyond pseudomonas and acinetobacter. Indian J Med Microbiol. 2011;29:4–12.
9. Avgeri SG, Matthaiou DK, Dimopoulos G, Grammatikos AP, Falagas ME. Therapeutic options for Burkholderia cepacia infections beyond co-trimoxazole: a systematic review of the clinical evidence. Int J Antimicrobial Agents. 2009;33:394–404.
10. Jacquier H, Monnier AL, Carbonnelle E, Corvec S, Illiaquer M, Bille E, et al. In vitro antimicrobial activity of "last resort" antibiotics against unusual non fermenting gram negative bacilli clinical isolates. Microb Drug Resist. 2012;18:396–401.