International Journal of Medical and Health Research
ISSN: 2454-9142; Impact Factor: RJIF 5.54
Received: 27-05-2019; Accepted: 29-06-2019
www.medicalsciencejournal.com
Volume 5; Issue 8; August 2019; Page No. 193-196

A Pressing Need To Consider Colistin For Empirical Therapy In The Treatment Of Blood Stream Infections: Indian Scenario

Mohd Shahid[1], Hiba Sami[2], Shariq Ahmed[3], Fatima Khan[4], Asfia Sultan[5], Haris M Khan[6]

[1, 3-6] Department of Microbiology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

[2] Assistant professor, Department of Microbiology, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

Abstract

Introduction: The increasing prevalence of the multidrug-resistant Gram-negative bacteria and the lack of new antibiotics to combat them have led to rekindled interest in colistin, a bactericidal antibiotic that was used in the 1960s for treatment of infections caused by Gram-negative bacilli. Colistin is used as a salvage therapy for multidrug-resistant and extremely drug-resistant Gram-negative bacterial infections. We suggest that early use of colistin as empirical therapy would decrease mortality rate in paediatric ICU patients.

Materials and methods: This study was conducted in the Department of Microbiology, JNMCH, Aligarh over a period of 6 months. All samples from paediatric ICU (PICU) submitted to Bacteriology lab for blood culture were screened. All isolates were identified by standard biochemical techniques and antimicrobial sensitivity was determined by Kirby Bauer disc diffusion method as per CLSI guidelines. Few of the representative samples were confirmed by VITEK 2 system.

Results: A total of 103 (39.01%) blood culture were positive out of total of 264 blood culture received from PICU over a 6 month period. 30 (29.1%) of these were Burkholderia spp, 10(9.7%) were identified as Klebsiella pneumonae, 9 (8.7%) were Pseudomonas species,12 (11.6%) were Acinetobacter species and one was identified as Enterococcus species. While the other antibiotics showed a sensitivity of less that 50% for Gram negative isolates, polymyxin B and colistin showed a sensitivity of 100%. Most of the ESBL producing strains were isolated from inpatients.

Conclusion: Multi-drug resistant Gram negative isolates have emerged as important nosocomial pathogen. Antibiotic susceptibility testing is critical in the treatment of infections caused by these pathogens, particularly in those with inadequate response to antibiotic therapy. Colistin can be considered as an emperical therapy in paediatric ICU to reduce the mortality rate in these patients.

Keywords: Colistin, blood stream infections

1. Introduction

1.1 Multidrug-resistant Gram-negative bacteria are known to cause neonatal sepsis in different parts of the world [1, 2]. They are a major threat to neonatal care, carrying a high rate of morbidity and mortality [3, 4]. The increasing prevalence of the multidrug-resistant Gram-negative bacteria and the lack of new antibiotics to combat them have led to rekindled interest in colistin, a bactericidal antibiotic that was used in the 1960s for treatment of infections caused by Gram-negative bacilli.

1.2 Colistin is an antibiotic of the polymyxin family and it is produced by Bacillus colistinus. It has been available since 1959 for the treatment of infections caused by Gram-negative bacteria [5]. Its main mechanism of action is by altering the cell wall permeability producing bacterial lysis [6]. *In vitro* colistin has a broad spectrum of action against Gram-negative bacteria, including those resistant to penicillins, carbapenems, aminoglycosides and fluoroquinolones. However, Proteus mirabilis, Providencia spp., Serratia spp., Burkholderia cepacia and Stenotrophomonas maltophilia are naturally nonsusceptible to colistin [7]. Nephrotoxicity and neurotoxicity are the main adverse effects that have been reported which led to the discontinuation of parenteral use of this drug in the 1970s [7, 8].

1.3 Acquisition of resistance to colistin is uncommon; it has been described in cystic fibrosis patients chronically treated with nebulised colistin for tracheal colonisation with MDR P. aeruginosa. Sodium colistin methanesulphonate is the commercially available form for i.v. use [9]. Colistin is used as a salvage therapy for multidrug-resistant and extremely drug-resistant Gram-negative bacterial infections. We suggest that the early use of colistin as empirical therapy would decrease the mortality rate in paediatric ICU patients.

2. Materials and methods

The study was conducted in the Department of Microbiology, JNMCH, AMU, Aligarh from September 2107 to March 2018. Samples were received for blood culture in brain heart infusion broth. Repeated subcultures were done on 5% sheep Blood agar and Mac-Conkeys agar after 24 hours, 48 hours and 5 days of incubation at 37°C. Cultures showing growth were identified by standard biochemical procedures [10].

Antimicrobial susceptibility testing was done on Mueller Hinton agar by Kirby Bauer disc diffusion method as per the Clinical and Laboratory Standards Institute (CLSI) guidelines (CLSI, 2017) [11].

2.1. For Oxidase-negative Gram-negative isolates, following antibiotics were tested

Cephalosporins (ceftazidime, cefepime and ceftriaxone); β-lactam/ β-lactamase inhibitor (piperacillin/ tazobactam); carbapenems (meropenem); fluoroquinolones (levofloxacin); aminoglycosides (amikacin and gentamycin); tetracyclines (minocycline and tigecycline); cotrimoxazole and polymyxins (polymyxin B and colistin).

2.2. For Pseudomonas Isolates, following antibiotics were tested

Cephalosporins (ceftazidime and cefepime); β-lactam/β-lactamase inhibitor (piperacillin/tazobactam); carbapenems (meropenem); fluoroquinolones (levofloxacin); aminoglycosides (amikacin, Tobramycin and Gentamycin); and polymyxins (polymyxin B and colistin).

2.3. For Burkholderia cepacia Isolates, following antibiotics were tested

Cephalosporins (ceftazidime); carbapenems (meropenem); cotrimoxazole; chloramphenicol; tetracyclines (Minocycline). Few of the strains that were resistant to first line drugs were retested by Vitek 2.

3. Results

Out of 264 blood culture samples, 103 (39%) were culture positive. Among the isolated strains, 93 (90.2%) were Gram-negative bacilli, 6 (5.8%) were Candida species, 4 (3.9%) were Gram Positive species as seen in Figure 1.

Table 1: Distribution of various Blood Culture pathogens (n=103)

Organism Name	Number	%
Acinetobacter species	12	11.6
Burkholderia cepecia complex	30	29.1
Budding yeast like cells	6	5.8
Citrobacter species	27	26.2
Escherichia coli	4	3.9
Enterococcus faecalis	1	1
Klebsiella species	10	9.7
Pseudomonas species	9	8.7
Coagulase negative Staphylococcus species	2	2
Staphylococcus aureus	1	1
Unidentified GNR	1	1

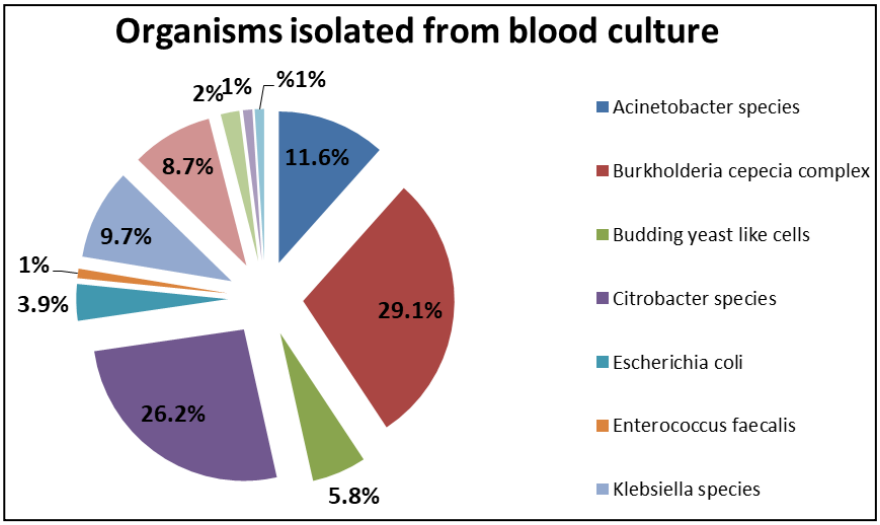

Fig 1: Prevalence of different organism in blood culture

3.1 Among the Gram negative pathogens, Most common was Burkholderia cepecia complex 30(29.1%) followed by Citrobacter species 27 (26.2%), Acinetobacter species 12 (11.6%), Klebsiella species 10 (9.7%), Pseudomonas species 9 (8.7%) and E.coli 4 (3.9%) as shown in Table 1.

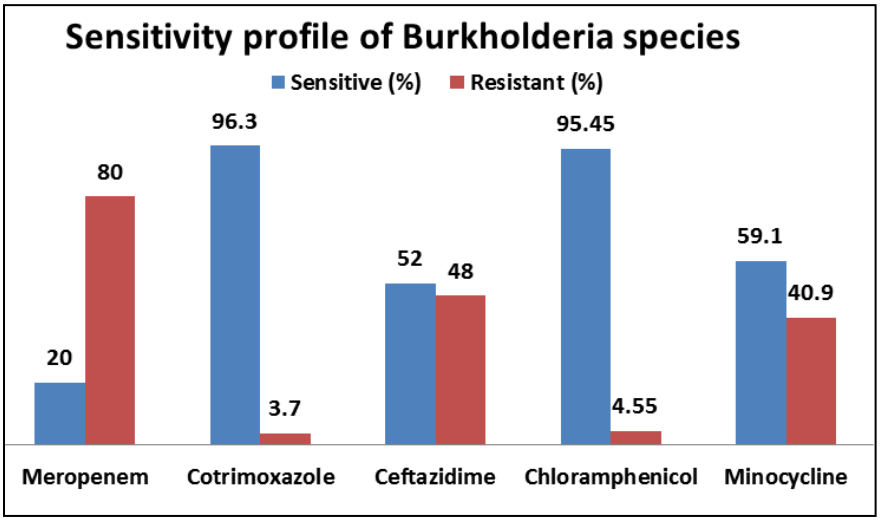

Fig 2: Antimicrobial susceptibility pattern of Burkholderia species isolated from blood culture

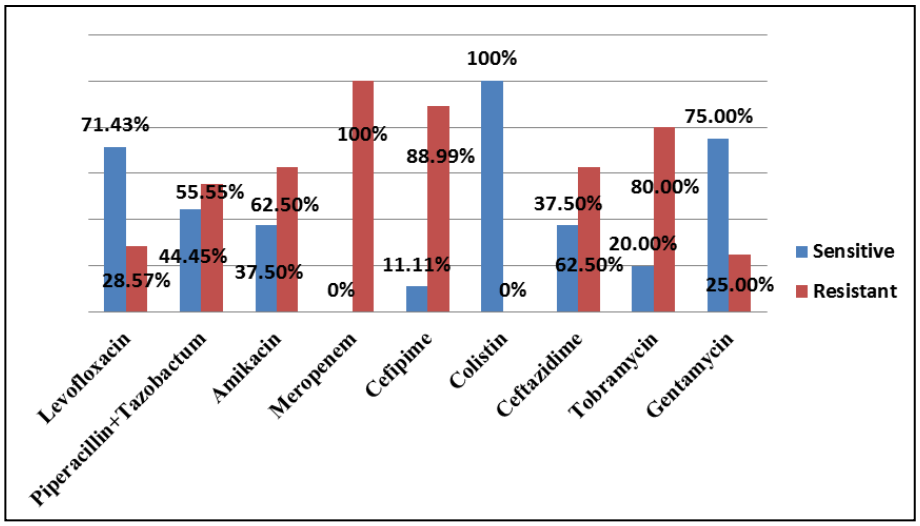

Fig 3: Antimicrobial susceptibility pattern of Pseudomonas species isolated from blood culture

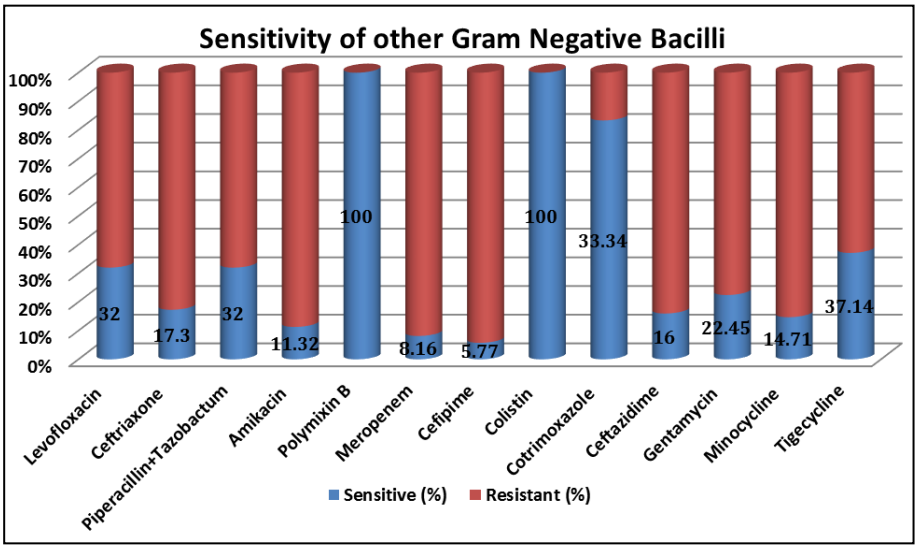

Fig 4: Antimicrobial susceptibility profile of Gram-negative Oxidase Negative isolates from blood culture

3.2 Twelve of the isolates that were resistant to first line drugs were again tested by Vitek 2 for identification and antimicrobial sensitivity with the ID-GNB card of the VITEK 2 system, results of which were in 91.7% agreement with those of disc diffusion method.

Table 2: Isolates Identified by Vitek 2 (N=12)

Isolate	Number
Klebsiella pneumoniae	8
Acenetobacter baumanii complex	2
Burkholderia Species	2

12 (9.8%) of the patients were followed up in which mortality rate was 30%.

4. Discussion

4.1 This study was conducted to evaluate the potential of colistin in the treatment of Blood stream infection (BSI) in PICU patients especially against MDR pathogens.

Multidrug resistant Gram-negative bacilli are frequently associated with infections in the patients admitted to intensive care units of hospitals. Klebsiella pneumoniae has been identified as one of the most frequent causes of outbreaks reported in neonatal intensive care units (NICUs) [12, 13]. Nosocomial infection due to multidrug-resistant Gram-negative pathogens in intensive care units is a challenge for clinicians and microbiologists, and has led to resurgence of parenteral colistin use in the last decade [14].

4.2 In this study the most common isolated microorganism was Burkholderia cepacia complex in 30 (29.1%) cultures, followed by Citrobacter in 27 (26.2%). Other isolates were Acinetobacter in 12 (11.6%), Klebsiella sp. in 10 (9.7%), P. aeruginosa in 9 (8.7%) and Escherichia coli in 4 (3.9%).

On antimicrobial susceptibility testing of the Gram-negative isolates for different group of drugs it was noted that amongst the various antimicrobial group tested Cephalosporins (ceftazidime, cefepime and ceftriaxone); β-lactam/β-lactamase inhibitor (piperacillin/tazobactam), carbapenems (meropenem), fluoroquinolones (levofloxacin), aminoglycosides (amikacin and Gentamycin), tetracyclines (minocycline and tigecycline) and cotrimoxazole showed sensitivity below 50%. Polymyxin B and colistin showed a sensitivity of 100% in our isolates except Burkholderia species in which the drug was not tested because of its intrinsic resistance.

4.3 A study from Jordan [15], have demonstrated 91% clinical efficacy of Colistin in treating neonatal sepsis, thus decreasing the mortality and morbidity in this vital age group. The clinical characteristics and treatment outcomes

of 36 patients with BSIs due to carbapenem-resistant Enterobacteriaceae (CRE) were investigated in a cohort study by Balkan *et al*. [16] The microbiological and clinical responses within the first 7 days of the treatment were the major determinant of 28-day mortality. Colistin-based dual combinations and preferably triple combinations were associated with significantly better outcomes when compared to noncolistin based regimens [16].

Ideally empirical regimens for life-threatening infections should cover all likely pathogens. If this is not possible by giving one drug, combination therapy can be used but should be streamlined to specific monotherapy as soon as the microbiology reports are available.

5. Conclusions

Multi-drug resistant Gram negative isolates have emerged as important nosocomial pathogen. Antibiotic susceptibility testing is critical in the treatment of infections caused by these pathogens, particularly in those with inadequate response to antibiotic therapy. Colistin can be considered as an emperical therapy in paediatric ICU to reduce the mortality rate in these patients.

6. References

1. Al-lawama M, Badran E, Khuri-Bulos N. Neonatal Gram-negative sepsis in a tertiary hospital in Jordan: when fever means multidrug resistance. Pediat Therapeut. 2014; 4:212.
2. Mavroidi A, Liakopoulos A, Gounaris A, Goudesidou M, Gaitana K, Miriagou V, *et al*. Successful control of a neonatal outbreak caused mainly by ST20multidrug-resistant SHV-5-producing Klebsiella pneumoniae, Greece. BMC Pediatr. 2014; 17(14):105.
3. Thatrimontrichai A, Apisarnthanarak A, Chanvitan P, Janjindamai W, Dissaneevate S, Maneenil G. Risk factors and outcomes of carbapenem-resistant Acinetobacter baumannii bacteremia in neonatal intensive care unit: a case-case-control study. Pediatr Infect Dis J. 2013; 32(2):140-145.
4. Tsai MH, Chu SM, Hsu JF, Lien R, Huang HR, Chiang MC, *et al*. Risk factors and outcomes for multidrug-resistant Gram-negative bacteremia in the NICU. Pediatrics. 2014; 133(2):e322-e329.
5. Ross S, Puig JR, Zaremba EA. Colistin: some preliminary laboratory and clinical observations in specific gastroenteritis in infants and children. Antibiot Annu. 1959-1960; 7:89-100.
6. Polimixina-Colistina. [Polymyxin-Colistin.] In: Bergoglio RM, ed. Antibióticos [Antibiotics.]. Buenos Aires, Editorial Médica Panamericana, 1993, 254-259.
7. Catchpole CR, Andrews JM, Brenwald N, Wise R. A reassessment of the *in vitro* activity of colistin sulphomethate sodium. J Antimicrob Chemother. 1997; 39:255-260.
8. Levin AS, Barone AA, Penco J, *et al*. Intravenous colistin as therapy for nosocomial infections caused by multidrug-resistant Pseudomonas aeruginosa and Acinetobacter baumannii. Clin Infect Dis. 1999; 28:1008-1011.
9. Rios FG, Luna CM, Maskin B, Saenz A, Valiente M, Lloria S, *et al*. Apezteguia. Ventilator-associated pneumonia due to colistin susceptible-only microorganisms. European Respiratory Journal Aug 2007; 30 (2):307-313
10. Collee JG, Fraser AG, Marmion BP, Simmons A. Tests for the identification of bacteria. In: Collee JG, Miles RS, Watt B, editors. Mackey and McCartney Practical Medical Microbiology. 14th Ed. New Delhi, India: Elsevier, 2006: 131-49.
11. CLSI. Performance standards for antimicrobial susceptibility testing, 27th ed CLSI document M100-S27 CLSI, Wayne, PA, 2017.
12. Viswanathan R, Singh AK, Mukherjee S, Mukherjee R, Das P, Basu S. An outbreak of neonatal sepsis presenting with exanthematous rash caused by Klebsiella pneumoniae. Epidemiol. Infect. 2011; 139:226-228.
13. Rastogi V, Nirwan PS, Jain S, Kapil A. Nosocomial outbreak of septicaemia in neonatal intensive care unit due to extended spectrum βlactamase producing Klebsiella pneumoniae showing multiple mechanisms of drug resistance. Indian J Med. Microbiol. 2010; 28:380-384.
14. Jajoo M, Kumar V, Jain M, Kumari S, Manchanda V. Intravenous Colistin Administration in Neonates. The Pediatric Infectious Disease Journal. 2011; 30(3):218-221.
15. Al‑lawama, *et al*. Intravenous Colistin in the treatment of multidrug-resistant Acinetobacter in neonates. Ann Clin Microbiol Antimicrob. 2016; 15:8.
16. Balkan II, Aygün G, Aydin S, Mutcali SI, Kara Z, Kuskucu M, *et al*. Blood stream infections due to OXA-48-like carbapenemase-producing Enterobacteriaceae: Treatment and survival. Int J Infect Dis. 2014; 26:51-6.