Journal of Pharmaceutical Care
jpc.tums.ac.ir

Antibiotic Resistance Pattern of Pathogens Isolated from Clinical Specimens of a Hematology-Oncology Hospital, Ahvaz, 2016-17

Ali Aminasnafi[1],Mandana Ghorbani Kalkhajeh[2],Setareh Razooghi[3],Kaveh Eslami[4],Leila Kouti[4*]

[1]Health Research Institute, Research Center of Thalassemia & Hemoglobinopathy,Ahvaz Jundishapur University of Medical Sciences,Ahvaz, Iran.
[2]Student Research Committee,Ahvaz Jundishapur University of Medical Sciences,Ahvaz, Iran.
[3]School of Pharmacy,Ahvaz Jundishapur University of Medical Sciences,Ahvaz, Iran.
[4]Department of Clinical Pharmacy, School of pharmacy,Ahvaz Jundishapur University of Medical Sciences,Ahvaz, Iran.
Received: 2017-07-23, Revised: 2017-09-12,Accept: 2017-10-27, Published: 2017-12-01.

ARTICLE INFO

Article type:
Original article

Keywords:
Anti-BacterialAgents
Antibacterial Drug Resistance
Cancer
Neutropenia

ABSTRACT

Background: Resistance to antibiotics exists around the world. In patients with various types of cancer and also in patients undergoing bone marrow transplantation, infections and febrile neutropenia can be very dangerous.Administration of intravenous ceftazidime alone or in combination with other antibiotics is one of the first empirical treatment regimens. The present study was carried out to determine the resistance pattern of various gram negative and gram positive microorganisms to different antibiotics of Hematology-Oncology (Shafa) hospital in Ahvaz.
Methods:This retrospective descriptive cross-sectional study was conducted for a period of one year including all referral clinical specimens from patients with malignancies to Shafa Hospital's Microbiology Laboratory. Isolated bacteria were tested for sensitive antibiotics used in clinics, especially ceftazidime, using a disc diffusion method.
***Results*:** After reviewing the records of all patients with malignancies admitted to Shafa hospital from July 2016 to July 2017, 310 patients had a recorded culture result (438 culturesintotal).Thepatientswerebetween1-85yearsold(mean±SD:29.9±24.6years). 50.6% of the patients were male, mostly admitted to emergency pediatric hematology ward (25.8%). The most common type of malignancy was acute lymphoblastic leukemia (27.1%). Pseudomonas aeruginosa was the most common isolated pathogen (34.1 %). Only 63 positive cultures containing pseudomonas were tested for antimicrobial resistance, and among these cultures, 55.5% were resistant and 42.8% were sensitive to ceftazidime. Among 9 isolated E.coli cultures, 66.6% were resistant and 33.3% were sensitive to ceftazidime. For Acinetobacter and Staphylococcus epidermidis species, only one positive culture (out of 33 and 34 respectively) was tested, and in both cases was resistant to ceftazidime.
Conclusion: Pseudomonas was the most common pathogen among isolated pathogens and about 56% of positive cultures were resistant or had intermediate sensitivity. It seems that ceftazidime empiric therapy of infections in patients with malignancies at Hematology-Oncology hospital might face high resistance.

J Pharm Care 2017; 5(3-4): 56-60.

► Please cite this paper as:
AminasnafiA, Ghorbani Kalkhajeh M, Razooghi S, Eslami K, Kouti L.Antibiotic Resistance Pattern of Pathogens Isolated from Clinical Specimens of a Hematology-Oncology Hospital,Ahvaz, 2016-17. J Pharm Care 2017; 5(3-4): 56-60.

* *CorrespondingAuthor*: Dr Leila Kouti
Address: Department of Clinical Pharmacy, School of Pharmacy,Ahvaz Jundishapur University of Medical Sciences, Golestan blvd.,Ahvaz 61357-33184, Iran.Tel: +986113738378, Fax: +986113738381.
Email: lkouti.pharmacotherapy@gmail.com

Introduction

Function of the immune system in determining the nature of the infection, the rate of its recurrence, and the overall response to treatment is an important factor. But in patients with malignancies, due to the nature of the disease and medications used, have some degrees of immune deficiencies and in risk of different infections. Empirical antibiotic therapy is often needed for inpatient individuals with malignancy (1).

One of the important indications of empirical antibiotic therapy is febrile neutropenia (FN). Common guidelines recommend the use of cefepime, ceftazidime, imipenem or meropenem as the only beta-lactam with or without vancomycin (2).

Ceftazidime has a broad-spectrum effect against Gram-negative bacteria (2). Ceftazidime is widely used in the therapy of infectious complications in neutropenic patients (3). It is the most used antibiotic as monotherapy and a number of clinical trials have confirmed the safety and efficacy of it. The logic of the use of ceftazidime as monotherapy is based on wide range of its anti-microbial effect including its effectiveness against Pseudomonas aeruginosa and low coverage against gram-positive organisms as well as bactericidal effect (rather than a bacteriostatic effect) and its ability to reach the maximum serum levels in the body (4).

But if antimicrobial resistance is not examined, poor infection control will result (5). The present study was carriedouttodeterminetheresistancepatternofvarious gram negative and gram positive microorganisms to different antibiotics at Hematology-Oncology (Shafa) hospital in Ahvaz.

Methods

This study retrospectively investigated the microbial resistance to ceftazidime in patients with malignancy during 2016 and 2017 in Shafa hospital inAhvaz.After obtaining a code of ethics from the Ahvaz Jundishapur University of Medical Sciences.All types of specimens were included. Then by HIS system, the age of patients and the type of their malignancies were recorded.

Results

During the time of this study, 435 episodes of blood dyscrasia ofWBCs were evaluated among 310 patients. The patients were between 1 and 85 years old (mean ± SD: 29.9±24.6 years). 50.6% of the patients were male and 49.3% female.

In this study, out of 438 positive cultures, 77.2% (338) of isolated pathogens were gram negative and 22.8% (100) were gram positive. Pseudomonas aeruginosa was the most common (34.1%) gram negative isolated pathogen and enterobactericeae was in the second place (10.1%) also Staphylococcus epidermidis was the most common isolated pathogen in gram positive group (7.8%). Microbial resistance to Ceftazidime was 58.9% of all the tested cases of this antibiotic (46/78).Only 63 positive cultures containing pseudomonas were tested for antimicrobial resistance, and among these cultures, 55.5% were resistant and 42.8% were sensitive to ceftazidime.Among 9 isolated E.coli cultures, 66.6% were resistant and 33.3% were sensitive to ceftazidime. For Acinetobacter and Staphylococcus epidermidis, only one positive culture (out of 33 and 34 respectively) was tested, and in both cases was resistant to ceftazidime.

Microbial resistance to imipenem was 32.4% (117/361) and to meropenem was 36.3%(119/328) of all the tested cases of these antibiotics.

Among 27 isolated Staphylococcus aureus, 7 cases were tested to methicillin and all of them were resistant to methicillin also among 149 isolated pseudomonas species only 7 cases were tested to cotrimoxazole and all of them were resistant to cotrimoxazole. Table 1 and 2 show the results of this study.

Discussion

Determination of microbial resistance pattern especially in patients with malignancy is very important. Infection is a major cause of life-threatening complication in this group of patients and lack of correct and rapid treatment can be fatal (1).

In the study of Castagnola et al., with aim to evaluate the proportion of Gram-negative rods isolated in bloodstream infections in children with cancer resistant to antibiotics recommended for this indication, 263 strains were evaluated: 27% were resistant to piperacillin-tazobactam, 23% to ceftazidime, 12% to meropenem and 13% to amikacin. Concomitant resistance to β-lactam and amikacin was detected in 6% of strains for piperacillin-tazobactam, 5% for ceftazidime and 5% for meropenem. During the study period there was a non significant increase in the proportions of strains resistant to β-lactams indicated for mono-therapy, and also increase in the resistance to combined therapies (21).

In another study, Trecarichi and colleagues, examine the recent trends in epidemiology and antimicrobial resistance in Gram-negatives recovered from neutropenic cancer patients, with particular emphasis on the impact of antimicrobial resistance on the clinical outcome of severe infections caused by such microorganisms. In result Overall, from 2007 to date of study, the rate of Gram-negative bacteria recovery ranged from 24.7 to 75.8% (mean 51.3%) in cancer patient cohorts. Escherichia coli represented the most common species (mean frequency of isolation 32.1%) among the Gram-negatives, followed by Pseudomonas aeruginosa (mean frequency of isolation

Table 1. Characteristics of patients admitted for WBC dyscrasia (N=130).

Wards (Percent of patients admitted)	Type of blood dyscrasia (Percent of patients diagnosed)	Pathogens identified from clinical specimens (Percent of patients)
Pediatric Hematology Emergency (39.3%)	ALL (27.1%) AML (10.3%)	Pseudomonas (32.9%) Enterobacteriaceae (10%)
Adult Hematology Emergency (15.5%)	Non Hodgkin lymphoma (5.8%) Aplastic anemia (4.8%)	Staphylococcus epidermidis (8.7%) Acinetobacter (7.4%)
ICU(14.2%)	MM (4.5%) Osteosarcoma (4.2%)	E.coli (6.4%) Klebsiella (5.8%)
Men's adult hematology (12.9%)	Hodgkin lymphoma (4.2%) Malignant breast cancer (2.9%)	Staphylococcus aureus (4.5%) Moraxella (3.2%)
Women's adult hematology (12.6%)	ITP (2.6%) Nephroblastoma (1.9%)	Staphylococcus coagulase negative (2.9%) Shigella (2.6%)
Transplant (3.5%)	Neoplastic malignant colon (1.6%) Sickle-cell anemia with crisis (1.3%)	Staphylococcus spp. (1.9%) Klebsiella pneumonia (1.6%)
Thalassemia (1.9%)	Other diagnosis less than 1%	Other pathogens less than 1.5%

ALL:Acute lymphoblastic leukemia,AML:Acute myeloid leukemia, ITP; Idiopathic thrombocytopenic purpura , MM: Multiple myeloma.

20.1%). An increasing frequency of Acinetobacter spp. and Stenotrophomonas maltophilia was also reported. Increased rates of multidrug-resistant Gram-negative strains have been highlighted among Enterobacteriaceae and non fermenting Gram-negative rods, despite discontinuation of fluoroquinolone-based antibacterial prophylaxis for neutropenic patients. In addition, antimicrobial resistance and/or the inadequacy of empirical antibiotic treatment have been frequently linked to a worse outcome in cancer patients with bloodstream infections caused by Gram-negative isolates (22).

The aim of Ozdemir et al., study was determine the causative microorganisms, infection focus and antibiotic treatment success in febrile neutropenic children with leukemia. In result, Among 136 febrile neutropenic episodes, 68 (50%) episodes were microbiologically documented. Methicillin sensitive coagulase negative Staphylococcus aureus were the most common isolates from hem culture (20.5%) (23).

In study of Sirkhazi, with aim to evaluate the Bacterial Spectrum, isolation sites and susceptibility patterns of pathogens in adult febrile neutropenic cancer patients at a specialist hospital in Saudi Arabia. A total of 138 bacterial isolates were identified. The overall prevalence of gram-negative bacteria was 65.9% (91/138) and for gram-positive bacteria was 34.1% (47/138).The most predominant pathogen was Escherichia coli 30.4% (42/138) (24).

The aim of Lakshmaiah et al., study was to evaluate febrile neutropenia in hematological malignancies. Majority of the patients with febrile neutropenia episodes had acute myeloid leukemia. Overall culture positivity was 29.6%. The most common organisms isolated were Gram-negative bacilli (63.6%), with Escherichia coli being the most frequent pathogen. All Gram-negative organisms were sensitive to imipenem, whereas sensitivity pattern to other antibiotics were as follows: 85.7%, 78.3%, 69.52%, 63.6%, 41.6% and 47.1% for pipercillin-tazoactum, meropenem, cefoperazone-sulbactum, amikacin, ceftazidime, ciprofloxacin respectively (25).

It seems that the cause of difference between results of above studies is different locations of studies which show microbial resistance pattern in each country, city or hospital is exclusive. This subject indicates the need to determine microbial resistance pattern in each hospital and updated analyses of the local epidemiology are mandatory to support appropriate empirical therapy.

Acknowledgement

This study was the Pharm D thesis of Ms. Mandana Ghorbani Kalkhajeh, and was funded by Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Table 2. Results of antibiograms.

Antimicrobial agents	Resistant %	Intermediate %	Sensitive %	Not tested %
Ceftazidime	11.3%	0.6%	6.3%	81.9%
Amikacin	22.2%	3.8%	37.4%	36.4%
Cotrimoxazole	12.2%	0%	16.4%	71.3%
Ceftriaxone	40.9%	2.9%	15.2%	40.9%
Ciprofloxacin	12.9%	1.6%	47.4%	38.1%
Penicillin	5.5%	0.3%	1.2%	92.6%
Tobramycin	0%	0%	0%	100%
Imipenem	25.4%	1.9%	54.8%	17.7%
Vancomycin	6.3%	1.9%	15.8%	6.2%
Meropenem	27.7%	1.6%	45.8%	24.8%
Ofloxacin	6.4%	0.6%	14.2%	78.7%
Azithromycin	0%	0%	0%	100%
Methicillin	0%	0%	0%	100%
Tetracycline	2.2%	0.3%	1.3%	96.2%
Cephalothin	0.6%	0%	0%	99.3%
Nitrofurantoin	0.3%	0%	0.9%	98.7%
Cefazolin	11.3%	0.6%	3.9%	84.2%
Rifampin	2.2%	0%	5.5%	92.2%
Levofloxacin	3.2%	0.6%	15.8%	80.3%
Cefepime	15.8%	1.3%	3.5%	79.3%
Ceftizoxime	12.5%	1.6%	1.9%	83.9%
Teicoplanin	0.6%	0%	0.6%	9.7%
Cefoxitin	0.6%	0%	0.9%	98.4%
Clindamycin	28.4%	0.6%	3.9%	67.1%
Gentamicin	8.4%	0%	9.1%	82.6%
Cefixime	0.3%	0%	0%	99.7%

References

1. Amiri P, Pournajaf A, Shavalipour A, Tayebi Z, Goudarzi H, Eslami G, et al. Evaluation of Antimicrobial Resistance in the Beta-lactamase Producing Escherichia Coli Isolated from Urinary Tract Infection in the Patients Referring to Taleghani Hospital of Tehran. Tabari Journal of Preventive Medicine. 2015;1(2):11-9.
2. Berliner N. Approach to the adult with unexplained neutropenia. UpToDate. Waltham,MA: UpToDate; 2017.
3. Coates TD. Overview of neutropenia in children and adolescents. In: E Richard Stiehm WCM, editor. UpToDate. Waltham,MA: UpToDate; 2017.
4. Eric Bow JRW. Overview of neutropenic fever syndromes. In: Marr KA, editor. UpToDate. Waltham,MA2017.
5. Koda-Kimble M YB. Prevention and Treatment of infections in Neutropenic Cancer Patients. In: Drew RH, editor.Applied Therapeutics. 10 ed. philadelphia(USA): Lippincott Williams and Wilkins; (2013). pp. 1675
6. Wingard JR. Treatment of neutropenic fever syndromes in adults with hematologic malignancies and hematopoietic cell transplant recipients(high-risk patients). In: Marr KA, editor. UpToDate. Waltham,MA: UpToDate; 2017.
7. BowE.Treatmentandpreventionofneutropenicfeversyndromesinadult cancer patients at low risk complications. In: Marr KA, editor. UpToDate. Waltham,MA:UpToDate;2017.
8. Terzah M Horton CPS. Overview of the presentation and diagnosis of acute lymphoblastic leukemia inchildren and adolescents. In: Park JR, editor. UpToDate. Waltham,MA: UpToDate; 2017.
9. Terzah M Horton CPS. Overview of the treatment of acute lymphoblastic leukemia in children and adolescents. In: Park JR, editor. UpToDate. Waltham,MA: UpToDate; 2017..
10. Charles A Schiffer JA. Clinical manifestations,pathologic features,and diagnosis of acute myeloid leukemia. In: Larson RA, editor. UpToDate. Waltham,MA: UpToDate; 2017.
11. Rains CP, Bryson HM, Peters DH. Ceftazidime. Drugs. 1995;49(4):577-617.
12. Kathy Moscou KS. Treatment Of Bacterial Infection. Pharmacology for pharmacy technicians. 2 ed: Elsevier Mosby; (2012). p. 605.
13. Ceftazidime: Drug information. UpToDate. Waltham,MA: UpToDate; 2017.
14. Davies J, Davies D. Origins and evolution of antibiotic resistance. Microbiol Mol Biol Rev. 2010;74(3):417-33.
15. HarbarthS.microbialresistancetoantibiotics.In:FelissaR.LashleyJDD, editor.EmergingInfectiousDiseases2.ed.NewYork:springerPublishing Company,LLC;(2007).pp.25-47.
16. Hess DR. Retrospective studies and chart reviews. Res Care. 2004;49(10):1171-4.
17. J.G.R.Howie. Doing Research. Research In General Practice. 2ed. Great Britain: Chapman and Hall; 1989. pp. 67.
18. Beyar-Katz O, Dickstein Y, Borok S, Vidal L, Leibovici L, Paul M. Empirical antibiotics targeting gram-positive bacteria for the treatment of febrile neutropenic patients with cancer. Cochrane Database Syst Rev. 2014;(1):CD003914.
19. Özdemir ZC, Koç A, Ayçiçek A. Microorganisms isolated from cultures and infection focus and antibiotic treatments in febrile neutropenic children from Şanlıurfa, Turkey. Turk J Pediatr 2016;58(1):47-53.
20. Moghnieh R, Estaitieh N, Mugharbil A, et al. Third generation cephalosporin resistant Enterobacteriaceae and multidrug resistant gram-negative bacteria causing bacteremia in febrile neutropenia adult cancer patients in Lebanon, broad spectrum antibiotics use as a major risk factor, and correlation with poor prognosis. Front Cell Infect Microbiol 2015;5:11.
21. Castagnola E, Caviglia I, Pescetto L, Bagnasco F, Haupt R, Bandettini R. Antibiotic susceptibility of Gram-negatives isolated from bacteremia in children with cancer. Implications for empirical therapy of febrile neutropenia. Future Microbiol 2015;10(3):357-65.
22. Trecarichi EM, Tumbarello M. Antimicrobial-resistant Gram-negative bacteria in febrile neutropenic patients with cancer: current epidemiology and clinical impact. Curr Opin Infect Dis 2014;27(2):200-10.
23. Özdemir ZC, Koç A, Ayçiçek A. Microorganisms isolated from cultures and infection focus and antibiotic treatments in febrile neutropenic children from Şanlıurfa, Turkey. Turk J Pediatr 2016;58(1):47-53.
24. Sirkhazi M, Sarriff A, Aziz NA, Almana F, Arafat O, Shorman M. Bacterial Spectrum, Isolation Sites and Susceptibility Patterns of Pathogens in Adult Febrile Neutropenic Cancer Patients at a Specialist Hospital in Saudi Arabia. World J Oncol 2014;5(5):196-203
25. Lakshmaiah KC, Malabagi AS, Govindbabu RS, Sinha M, Jayashree RS. Febrile neutropenia in hematological malignancies: clinical and microbiologicalprofileandoutcomeinhighriskpatients.JLabPhysicians 2015;7(2):116-120.