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Extended Abstract

Prevalence of MDR-and XDR Gram-negative pathogens isolated from febrile neutropenic cancer patients with bloodstream infections in Egypt and new synergistic antibiotic combinations

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Introduction:

Blood stream infections (BSIs) are defined as positive isolate(s) of blood culture and associated with clinical findings.Cancer patients are among the key candidates for this type of infections due to the methods of treatment they have, such as invasive surgery, chemotherapy, radiotherapy, immunosuppressive agents, or administration of anticancer drugs during hospital stay. Cancer patients sustaining BSI also have higher morbidity and mortality rates. Therefore, speedy identification of isolates, clinical diagnosis, and effective treatment of BSIs decrease the risk of mortality among cancer patients with BSI.Infection with multidrug-resistant (MDR) pathogens including extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae are particularly prevalent among cancer patients.Enterobacteriaceae cause approximately 65%–80% of documented Gram-negative infections in these patients. However, Pseudomonas aeruginosa is also associated with significant morbidity and mortality in immunocompromised hosts.Resistance to the β-lactams is mediated primarily through the production of a variety of β-lactamases including Ambler class C β-lactamases and ESBLs. ESBLs are derived from earlier, plasmid-mediated hydrolyzing enzymes, primarily the TEM and SHV types (both are ESBL enzymes). Other antibiotic resistance coding genes (i.e., to fluoroquinolones [FQs], aminoglycosides, macrolides, carbapenems, etc.) on the same plasmid can confer a MDR phenotype in a subset of these pathogens.Colistin resistance in Gram-negative bacteria (GNB) could be mainly attributed to excessive use of colistin in treating carbapenem-resistant bacteria.Clinical studies strongly suggest that combination therapy is superior to monotherapy for carbapenemase-producing Enterobacte-riacea. To improve potential survival among patients with high risk risk of death, combination therapy is recommended.However,, a combination of two or more active drugs (i.e., colistin, tigecycline, or fosfomycin) with carbapenem is join with a better outcome. A lot antimicrobial guidelines have addressed empirical treatment for such serious infections; however, the rapid treatment of such infections has become a significant problem worldwide. Therefore, in this study, we aimed at evaluating the genetic bases of antimicrobial resistance of MDR GNB in cancer patients against the most commonly used antimicrobial agents used for the treatment of such infections. In extension some antibiotic combinations have been calculate for use against the clinically relevant MDR GNB pathogens recovered in our study.

Materials and methods :

Specimen collections :

Opening from November 2015 to October 2016, a total of 529 blood specimens were collected from 529 cancer patients with absolute neutrophils count <500/mm3 and oral temperature >38°C over at least 1 hour from National Cancer Institute (NCI) Cairo University, Cairo, Egypt. The NCI is the biggest tertiary cancer hospital in Egypt, drawing patients nationwide. The study was approved by the NCI Ethics Committee and Faculty of Pharmacy Ethical Committee Nr. 173, and written informed consent was obtained from either patients or parents of patients after explaining the study purpose. The collected blood was straight add into Bactec® (Becton Dickinson, Franklin Lakes, NJ, USA) culture vials and incubated in the Bactec 9050® (Becton Dickinson) incubator. Positive blood culture specimens were directly streaked on blood agar, chocolate agar, and MacConkey agar (Oxoid, Cheshire, England) plates.

Identification of the recovered bacterial isolates:

The reborn clinical isolates were categorized according to their Gram stain. Several biochemical tests were performed to identify different bacterial species. The biochemical tests recycled comprised triple sugar iron test, oxidase test, citrate utilization test, urease test, methyl red test, Voges–Proskauer test, and eosin methylene blue agar test; all said test media were produced by Oxoid. Identification was confirmed using Microscan® WalkAway-96 Plus auto identification system (Beckman Coulter, Miami, FL, USA)

Antimicrobial susceptibility testing :

Antimicrobial susceptibility testing was carried out by both Kirby-Bauer disc diffusion method using commercial discs (Oxoid) on Muller Hinton agar (Oxoid) at 37°C for 18 hours and minimum inhibitory concentration (MIC) which is defined as the lowest

HIV and AIDS Research Journal

concentration of an antimicrobial that will inhibit the visible growth of a microorganism after overnight incubation. MIC was carried out in triplicate and average MIC was calculated, as recommended by the Clinical and Laboratory Standards Institute (CLSI).Isolates resistant to three or more classes of antimicrobials were considered as MDR isolates.The tested agents used in Kirby-Bauer disc (µL/disc) diffusion method belonged to five different classes of antimicrobials: the aminoglycosides (amikacin 30 µg, gentamicin 10 µg, and tobramycin 10 µg), β-lactams (ampicillin 10 µg, amoxicillin/clavulanic acid 20 µg/10 µg, aztreonam 30 µg, cefotaxime 30 µg, ceftazidime 30 µg, cefoxitin 30 µg, ceftriaxone 30 µg, cefepime 30 µg, ampicillin/sulbactam 20 µg/10 µg, piperacillin/tazobactam 100 µg/10 µg, imipenem 10 µg, ertapenem 10 µg, cefazolin 30 µg, and meropenem 10 µg), FQs (ciprofloxacin 5 µg and levofloxacin 5 µg), antimetabolites (sulfonamides/trimethoprim 1.25 µg/23.75 µg), and polypeptides (colistin 10 µg). The reference strain Escherichia coli ATCC® 25922™ was used for quality control.

Results:

Patient characteristics:

In the period from November 2015 to the end of October 2016, BSIs were detected in 102 of 529 (19.3%) febrile neutropenic patients. The patients' age ranged from 1 to 66 years, with a mean age of 16 years. There were 54 (54/102, 52.9%) males and 48 (48/102, 47%) females. Eighty-five (85/102, 83.3%) patients were analysed with hematological malignancies and 17 (17/102, 16.7%) with solid organ malignancies.

Antimicrobial susceptibility testing:

A total of 529 blood specimens were collected of which only 195 specimens showed positive bacterial growth. Out of the 195 positive culture specimens, a total of 102 (102/195, 52.3%) were Gram-negative and 93 (93/195, 47.7%) were Gram-positive. The antibiotic susceptibility patterns of the Gram-negative isolates are shown in Table 2A and andB.B. Out of the 102 GNB, 70 (70/102, 68.6%) isolates were resistant to three or more classes of antimicrobial agents and therefore considered MDR isolates.

Discussion:

BSI remains a major cause of life-threatening complications in patients with cancer23 and is directly associated with prolonged hospital stay, high health care costs, and increased risk of morbidity and mortality.24, 25 Bacteria are the most common cause of such infections.

Conclusion:

High prevalence of microbial resistance was detected among MDR GNB against penicillins; monobactams; third- and fourth-generation cephalosporins, particularly cefepime, which is described by several antimicrobial therapy guidelines for febrile neutropenic cancer patients.

Biography

Dr. Khaled Aboshanab is a Professor of Microbiology and Immunology, and Vice Dean for post graduate Studies and Scientific Research, Faculty of Pharmacy, Ain Shams University. Dr Khaled is a reporter of the Medical sector of the strategic research committee of Ain Shams University and a member of the permanent committee of the postgraduate studies and scientific Research. He supervised 14 PhD students and 22 Master students from Ain Shams and other universities, medial institutes and pharmaceutical industries in Egypt and published about 41 international, 10 national scientific and one of the international book