NEUTROPENIC SEPSIS AND CHALLENGES TO COMBAT

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Neutropenic sepsis (NS) is a common and predictable complication of bone marrow disorders and cytotoxic chemotherapy. After intensive chemotherapy, the incidence of NS is about 70–100% during the neutropenic phase. Patients with neutropenia are vulnerable to invasive infections, which can be rapidly overwhelming, causing septic shock and death. The epidemiology of sepsis in industrialized countries is mainly influenced by the age of the population and the increasing prevalence of comorbidities, such as chronic organ dysfunctions, non-cancer-related immunosuppressive diseases, or cancer itself. Patients with cancer are at more than 10 times higher risk for sepsis than the general population, with some variability according to the cancer types. There is frequent frustration among physicians caring for patients with neutropenic sepsis. Infections are a frequent complication in leukopenic patients, affecting an estimated 24% of patients after chemotherapy for hematologic diseases or solid organ tumors. Bloodstream infections (BSIs) are the most frequent infection in febrile neutropenic, onco-hematological patients, with incidence rates spanning from 10% to 38%. Septic shock is the most severe clinical presentation form of such infections. This is becoming a cause for growing concern due to several factors. Rates of Gram-negative bacilli (GNB) in onco-hematological patients are progressively increasing. It is shown that ~50% of bacteremia in cancer patients was caused by GNB, among which almost 14% were MDR GNB. This could impact a greater percentage of patients presenting with septic shock. The widespread emergence and dissemination of multidrug-resistant Gram-negative bacilli, which are a common cause of infection and sepsis in patients with cancer, is of great concern. Several investigators have reported high rates of bacteremia due to extended-spectrum â-lactamase (ESBL)-producing Enterobacterales, MDR Pseudomonas aeruginosa (MDR-PA), and carbapenem-resistant Enterobacterales. Additionally, empirical antibiotic therapy is challenging in the era of emerging multidrug-resistant (MDR) GNB. Indeed, inappropriate empirical antibiotic therapy (IEAT) has been associated with increased mortality in patients with febrile neutropenia and BSI. Neutropenic sepsis is a medical emergency in which broad-spectrum antibiotics must be given without delay. Delaying treatment in neutropenic sepsis may increase the risk of death. â-Lactam/â-lactamase inhibitors (BL/BLIs) and carbapenems are often considered for the treatment of sepsis when the main suspected pathogens are Gram-negative bacteria, because of their broad spectrum of coverage. Ceftazidime avibactam is a new molecule available against these bugs. It is a novel combination of ceftazidime (third-generation cephalosporin) and avibactam (novel, non-â-lactam â-lactamase inhibitor) which covers ESBL isolates like E Coli & K. Pneumoniae, MDR Pseudomonas aeruginosa, and CRE. Ceftazidime and avibactam are now playing a crucial role in combating MDR gram-negative infections in sepsis patients. Many international guidelines recommend using early ceftazidime and avibactam in sepsis patients to achieve better outcomes and reduce volatility.

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