Clinical Risk Factors for Infection and Antibiotic Resistance in BMT Patients

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Infection is a Leading Cause of Mortality and Morbidity in Blood and Marrow Transplantation (BMT) Patients

• Incidence of bacteremia, bacterial isolates in the blood, ranges from 20-62% in BMT patients, often with a higher incidence during the first 30 days when most patients are neutropenic (absolute neutrophil count, ANC <500/uL)1-2
• Many of the overall risks BMT patients face occur within these first 30 days post-transplant and are a consequence of the patient’s decreased immune defense ability
• Mortality rates for infection differ significantly by institution and bacterial organism, emphasizing the importance of hospital conditions and antibiotic selection
• Gram positive organisms account for the majority of infection, with coagulase negative Staphylococcus (CNS) being the most frequently isolated organism
• However, infection by gram negative organisms is associated with a higher case fatality rate and more serious clinical consequences and complications such as sepsis, pneumonia, and shock3
• There are some reports of a reemergence in infection by gram negative organisms that is associated with multi-drug resistance (MDR)4

Study Goal

• The relative importance of clinical features on the incidence and timing of post-transplant bacterial infections is uncertain, but a detailed analysis could provide guidance and therapy
• This study also examined the antibiotic sensitivity profiles of the BMT patients and the contemporaneous hospital-wide microbiology laboratory antibiotic sensitivity profiles to describe the bacterial isolate susceptibility changes in the BMT population compared to the general hospital population

Patients and Management of Infection

• We retrospectively analyzed 834 adult patients who received a BMT at the University of Minnesota between January 2005 and October 2010
• All patients with at least one positive bacterial blood culture within the first 100 days post-transplant were considered to have bacteremia
• BMT patients without bacteremia during the six year period were defined as controls
• All patients received the broad spectrum quinolone, levofloxacin for prophylaxis (500mg/day). If allergic, patients were given penicillin or a related beta-lactam antibiotic
• Empiric antibiotic regimens started at the onset of fever include cefazidime, vancomycin, and tobramycin with a modification after the identification of the bacterial organism

Antibiotic Sensitivity Testing of BMT and Hospital Bacterial Isolates

• Antibiotic sensitivities were done on the first positive blood culture taken from the BMT patient, and all relevant hospital blood isolate data was obtained from the microbiology laboratory at University of Minnesota Medical Center-Fairview (UMMC)
• Antibiotic sensitivities were determined using the Vittek Automated Microbiology System or a microdilution minimum inhibitory concentration (MIC) procedure
• The sensitivities from BMT patients were compared with hospital wide sensitivities that are analyzed yearly at UMMC

Results

Infection by antibiotic resistant gram negative bacteria is more frequent in BMT patients compared to the general hospital population

Table 1. The sensitivity of P. aeruginosa, E. coli, and K. pneumoniae blood isolates from hospital wide and BMT patients between 2005 and 2010. A) Cefazidime and gentamicin alone are not sufficient empiric therapy treatment for infections by P. aeruginosa for both BMT and hospital patients. B) Ampicillin is not effective for use against E. coli for both BMT and hospital patients. Resistance to cefazidime and piperacillin/tazobactam increases in BMT patients in latter four years. C) Cefazidime and ceftriaxone alone are not sufficient empiric therapy treatment for infections by K. pneumoniae in BMT patients. Piperacillin/tazobactam and tobramycin remain effective for K. pneumoniae for both BMT and hospital wide patients.

Conclusions

• Allogeneic transplants and patients receiving myeloablative conditioning regimens have a substantially higher risk of developing infection compared to autologous transplant recipients and those receiving RIC
• The development of acute GVHD grade III IV was a significant risk factor for all bacteremia overall (0-100 days post-transplant)
• Further, infection risk is similar for allogeneic transplants from a sibling, non-sibling related donor, or unrelated donor
• Resistance to levofloxacin is more frequent in BMT patients
• For the three most frequent gram negative organisms (E. coli, P. aeruginosa, K. pneumoniae), ampicillin, cefazidime, gentamicin, or ceftriaxone alone are insufficient empiric therapy treatments
• Thus, prescription of tobramycin or other aminoglycosides may be necessary for initial empiric therapy

References


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Figure 2. The sensitivity of E. coli, P. aeruginosa, K. pneumoniae, and Coag Neg Staph (CNS) blood isolates to levofloxacin from hospital wide and BMT patients between 2005 and 2010.

Figure 3. Allogeneic transplant recipients have a significantly higher incidence of bacteremia in each of the three infection groups compared to autologous transplant recipients (left). Among allogeneic infections, the incidence of bacteremia is similar in each infection group (right). There is no major difference between donor type in any of the groups.

Cumulative Incidence of Bacteremia by 100 Days Post-Transplant

Table 2. Multivariate Analysis for impact of clinical features on infection risk and timing. Allogeneic transplants have a significantly higher risk overall and independently in the first three months post-transplant for infection by all bacterial species and infection excluding CNS in comparison to autologous days post-transplant. The development of GVHD is also a significant risk factor for infection overall in both infection groups. B) Among allogeneic transplants, myeloablative conditioning is associated with a significantly higher risk of bacteremia by an bacterial species overall and in the first 30 days post transplant. Development of acute GVHD III-IV is also a significant risk factor overall for bacteremia by any bacterial species.

Clinical Features of Patients

Table 3. Cumulative Incidence of bacteremia by 100 days post-transplant. There is no difference in incidence between the two conditioning groups.