Results: One hundred and thirty-four patients were analyzed (59 for allograft and 75 for autograft). Thirty-eight bacterial isolates from blood of 34 patients (25.3%; 20 patients for allograft and 14 for autograft) were reported. Patients with allogenic HSCT had more frequent BSI (odds ratio 2.23, $p = 0.047$) compared to those with autologous HSCT. BSI of autologous HSCT were reported earlier compared to those of allogenic HSCT (mean 12.1±3.4 vs. 26.5±18.5 days, $p = 0.007$). HSCT in patients with AML ($p = 0.029$), no use of antibiotics from conditioning ($p < 0.001$), and elevated CRP ($p = 0.001$) were independently associated with higher incidence of BSI in whole patient population. Among 59 patients with allogenic HSCT, HSCT > 180 days after diagnosis ($p = 0.035$), elevated CRP ($p = 0.018$), lower serum albumin ($p = 0.033$), and acute GVHD ≥ G2 ($p = 0.015$) showed relation to BSI in multivariate analysis. As for 75 patients with autologous HCT, only no antibiotics use ($p = 0.007$) and elevated CRP ($p = 0.031$) were independent risk factors of BSI. BSIs after allograft was more fatal: 7 of 20 patients with allograft (35%) died of BSI whereas only 1 of 14 patients who underwent autologous HSCT expired.
Conclusion: Except pre-transplant serum CRP elevation, allogenic and autologous HSCT have different risk factors. BSI with autologous HSCT occurred earlier and showed better clinical outcomes compared to BSI with allograft. Distinctive natures of bacterial infection after HSCT between allogenic and autologous HST should be considered to establish the best defense strategy against BSI.

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Persistently High Gam Levels Are Associated with Nonrelapse Mortality in HCT Recipients Irrespective of Invasive Aspergillosis: A Prospective Cohort Study

Sarita Jaiswal [1], Ujjwayini Ray [2], Basudevi Mishra [3], Suparno Chakrabarti [4]. [1] Blood and Marrow Transplantation, Apollo Gleneagles Cancer Hospital, Kolkata, India; [2] Microbiology, Apollo Gleneagles Hospital, Kolkata, India; [3] Blood and Marrow Transplantation, Apollo GLENEAGLES Cancer Hospital; [4] Manashi Chakrabarti Foundation, Kolkata, India

Detection of galactomannan (GAM) antigen in the serum has been found to strongly correlate with Invasive Aspergillosis (IA) in patients undergoing HCT. We prospectively evaluated the significance of serial GAM measurements in 11 patients undergoing HCT(cohort1) and compared this with 16 patients (cohort2) receiving non-HCT treatment for haematological disorders. GAM values were measured in all patients on admission and weekly thereafter until discharge. A CT scan of the chest was done for all patients with two serial GAM values above 0.5. A throat swab for fungal culture was sent for all patients at diagnosis and weekly thereafter. The median age of the entire group was 38 years (range 6 – 74 years). The cohorts did not differ significantly in age, gender or disease distributions. All patients received antifungal prophylaxis with fluconazole in cohort 2 and mould active azoles in cohort1. The GAM values on admission were not significantly different among two cohorts; however subsequent GAM values (1.32 vs 0.77, $P = .03$) were significantly higher in cohort 1. The mean, maximum and minimum values of GAM (GAMmean, GAMmax, GAMmin) were significantly higher in cohort1($P < .05$). Two patients in cohort1 and one patient in cohort2 developed proven IA. GAM cutoff of 0.5 didnot correlate with mycological or radiological evidence of IA in either cohort. However a higher GAMmean (1.92 vs 0.81, $P = .03$) and GAMmax (3.17 vs 2.69 $P = .08$) were associated with proven IA. Higher GAM values on admission (1.23 vs 0.54, $P = .04$) and higher GAMmean (1.54 vs 0.76, $P = .009$) correlated with higher mortality irrespective of evidence of IA. In multivariate analysis, only GAMmean was associated with higher mortality, particularly in cohort 1. In conclusion, a cut-off value of 0.5 did not correlate with development of IA in our population, however a persistently high GAM value in HCT recipients was an adverse prognostic factor for nonrelapse mortality irrespective of evidence of IA.

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Stress Testing Prior to Allogeneic Hematopoietic Stem Cell Transplantation

Anthony Pham [1], Daniel Amoruso [2], Susanna Nguy [3], Elizabeth E. Stillwell [4], Jeffrey D. Wessler [5], Brian J. Rebolledo [6], Richard M. Steingart [4], Ann A. Jakubowski [7], Wendy L. Schaffer [4]. [1] Weill Cornell University Medical College, New York, NY; [2] New York Presbyterian-Cornell, New York, NY; [3] City College of New York, New York, NY; [4] Cardiology, Memorial Sloan-Kettering Cancer Center, New York, NY; [5] New York Presbyterian-Columbia, New York, NY; [6] Hospital for Special Surgery, New York, NY; [7] Department of Medicine, Adult Bone Marrow Transplant Service, Memorial Sloan-Kettering Cancer Center, New York, NY

Hematopoietic stem cell transplantation (HSCT) exposes patients to significant physiologic stress. Risk stratification prior to HSCT is routine. Despite limited data supporting the prognostic benefit, assessment of left ventricular systolic function and cardiac stress testing are often performed. A retrospective analysis of 284 allogeneic HSCT performed from 1999-2000 in 260 patients, all of whom had a pre-HSCT stress test, is presented. Stress echos, 170, and stress MUGAs, 114, were performed at Memorial Sloan-Kettering or with outside physicians. Patients who underwent supine bicycle exercise multiple gated cardiac blood pool imaging (stress MUGA) or treadmill exercise echo were included, allowing for assessment of augmentation in left ventricular ejection fraction with exercise and functional capacity. Stress tests used standardized exercise protocols (Bruce, modified Bruce for stress echo or WHO for supine exercise bicycle). Stress tests were in reasonable temporal proximity to HSCT, 46±61 days prior for stress echo and 36±66 days prior for stress MUGA (not significantly different). Average age at transplant was approximately 55 years and was not statistically different for patients who had stress echo or stress MUGA, but was significantly older when compared patients who were transplanted over the same period and for whom only a rest echo could be identified in the medical record (54±8yrs vs 52±7yrs, $P = .01$). Coronary artery disease or at least one major cardiac risk was identified in 69% of patients who underwent stress testing. Two thirds of patients who had stress tests had leukemia and one third lymphoma. As measured with stress echo, percent maximum predicted heart rate (%MPHR), workload (measured in METS), and percent augmentation in LVEF with exercise did not correlate with ICU admission, in-hospital death or death within one year. Decreased exercise time and decreased rest LVEF both correlated significantly with in-hospital death (ET 6±3min vs 7±2min, $P = .01$ and rest LVEF 57±7% vs 62±7%, $P = .01$), but neither correlated with ICU admission or death at one year. Correlation with stress MUGA was weaker with decreased workload (measured in WATTs) correlating with in-hospital death (59±25WATTs vs 76±30WATTs, $P = .03$), but without correlation with ICU admission or death at one year. Other stress MUGA parameters (%MPHR, rest LVEF, percent augmentation in LVEF, exercise time) had no significant

correlation with ICU admission, in-hospital death or death within one year of transplant. Most stress test parameters correlate poorly with outcomes of HSCT. Routine stress testing is unlikely to be of significant prognostic value. Stress echocardiogram is of somewhat more value than stress MUGA given that rest LVEF and exercise time correlate with in-hospital death, but a standardized evaluation of exercise capacity in the clinic and rest echo may be adequate substitutes.

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Population Pharmacokinetic Study of a Test Dose Busulfan Patients Undergoing Hematopoietic Stem Cell Transplantation

Iracema Esteves Nogueira [1], Juliana Fernandes [2,3], Eduardo K. Sugawara [4], Jose Salvador de Oliveira [5], Roseane Gouveia [6], Morgani Rodrigues [7], Daniele Porto Barros [8], Mariane Pereira Diniz [9], Fabio P. de Souza Santos [4], Andreza Feitosa Ribeiro [7], Jairo J.N. Sobrinho [4], Sandra Saemi Nakashima [4], Marcos de Lima [10], Nelson Hamerschlak [4], Fabio R. Kerbauy [4,5]. [1] UNIFESP (Universidade Federal de São Paulo), Brazil; [2] Onco-Hematology Unit, Instituto da Criança - HC - FMUSP, Sao Paulo, Brazil; [3] Hospital Israelita Albert Einstein, Brazil; [4] Hematology and Bone Marrow Transplantation Dept, Hospital Israelita Albert Einstein, Brazil; [5] Hematology and Bone Marrow Transplantation Dept, UNIFESP (Universidade Federal de Sao Paulo), Brazil; [6] Pediatric Bone Marrow Transplantation Center, Instituto de Oncologia Pediatrica, São Paulo, Brazil; [7] Hematology and Bone Marrow Transplantation Dept, Hospital Israelita Albert Einstein, Sao Paulo, Brazil; [8] Instituto de Oncologia Pediátrica, São Paulo, Brazil; [9] Clinical Research Center, Instituto de Oncologia Pediátrica, São Paulo, Brazil; [10] Department of Medicine - Bone Marrow Transplant Program, Case Western Reserve University, Cleveland

Introduction: Busulfan (bu) is one of the most used chemotherapy in conditioning regimens for patients submitted to hematopoietic cell transplantation (HCT). As Bu pharmacokinetic (PK) is widely variable, dose adjustment according to patient PK has been shown to minimize toxicities improving clinical outcome. Usually, PK is calculated from blood samples collected after the first Bu dose, guiding adjustment of following doses. Although this method has shown to be reliable, it can be difficult to perform PK in an optimal time frame. Therefore, using a test dose before HCT can optimize this method, potentially given more accurate dose adjustment. Bu test dose has been used with Bu iv formulation, but little is known with oral Bu. In countries like Brazil where oral Bu is still been used because of cost issues an optimal drug administration should be developed.
Objectives: To validate the use of oral Bu test dose by comparing PK from dose test and first conditioning regimen dose.
Methods: 19 patientes were enrolled. Median age was 28 year (range, 4-56). 4 (21%) patients received autologous HCT while 19 (79%) allogeneic grafts from MRD or MUD donors. As conditioning regimens, 1 patient recieved Bu(16)/Flu(160), 9 Bu(16)/Cy(120), 3 Bu(16)Mel(140), 2 Bu(12)/Cy(120)/Mel(140) and 4 Bu(12)/Cy(120)/Etoposide(1200). After oral test dose (1mg/kg) 72 hours before conditioning regimen, blood samples were collected at 8 time points. Samples were also collected after the first Bu dose (1mg/kg) during conditioning regimen. Bu concentrations were measured by HPLC. PK parameters were estimated by using nonlinear mixed effects model computer program. No Bu dose adjustment was performed based on test dose.
Results: PK parameters were comparable between test dose and first conditioning dose: median Bu Clearance (microMol/min) was 10115,9 (range: 333,43-18270,4) and 11866,1 (range: 4520,3-15589,2) respectively ($P = 0,738$); median concentration steady state (mcg/L) was 0,80 (range: 0,55-1,59) and 0,76 (range: 0,59-1,23) respectively ($P = 0,672$); half life (hours) was 2,85 (range: 1,65-5,61) and 2,65 (range: 1,71-6,09) respectively ($P = 0,172$). Area under the curve (AUC) (mcgMol.min) was also comparable showing a median of 1174 (range: 799-2328) and 1110 (range: 857-1795) respectively ($P = 0,679$). Toxicities was comparable to literature data: 14 (88%) and 5 (12%) patients developed grades 1 to 3 and grade 4 mucositis respectively; 2 (10%) patients developed sinuisodal obstruction syndrome (SOS) both received Bu/Cy/Etoposide protocol. All patients achieved full donor chimerism. Incidence of grade II-IV acute and extensive chronic GVHD was 55% and 31% respectively. With a median follow-up of 82 days (range: 18-321) 17 patients were alive.
Conclusions: A population PK model for oral Bu could be developed, showing efficacy and safety of oral Bu test dose.

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Catheter-Related Complications in Acute Myeloid Leukemia Patients After Hematopoietic Stem Cell Transplant

Mohammad O. Khalil [1], Namali Pierson [2], George Selby [1], Mohamad Cherry [1], Jennifer Holter [1]. [1] Department of Internal Medicine, Section of Hematology and Oncology, University of Oklahoma Health Sciences Center, Oklahoma City, OK; [2] Department of Internal Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK

Background: Intravenous catheters are widely used in hematopoietic stem cell transplant (HSCT) patients. Complications associated with these catheters are frequently encountered and contribute to morbidity, mortality, and increased cost of treatment. Studies exploring such complications in this unique patient population are lacking. We retrospectively studied infectious and thrombotic catheter-related complications in acute myeloid leukemia (AML) patients after undergoing HSCT at the largest tertiary referral center in Oklahoma.
Methods: AML patients above the age of 18 who had HSCT at The University of Oklahoma Health Sciences Center between January, 2000 and June, 2012 were identified and medical records were reviewed. Patients were stratified according to age, first HSCT type and type of catheter(s) present at or after the first HSCT (Hickman, peripherally inserted central catheter (PICC) or infusion port (IP)). First blood stream infection (BSI) and deep venous thrombosis (DVT) events after the first HSCT were reported (subsequent events were not included). Statistical analysis was performed using SAS 9.2 software (SAS Institute Inc.). Fisher's exact test was used to compare patients in the different groups.
Results: 62 patients were included. Median age at diagnosis was 44 years. 42 (68%) were males and 20 (32%) were females. 53 (87%) were White, 4 (7%) Native American and 3 (5%) African American. 26 (43%) had sibling (SIB), 22 (36%) unrelated donor (URD) and 13 (21%) double cord blood (DCB) transplant. 56 (93%) had Hickman, 30 (50%) PICC and 7 (12%) IP. 28 patients had one catheter type only (24 Hickman and 4 PICC). BSI occurred in 37% of all cases. BSI rates according to the presence or absence of a particular catheter type were 38% vs. 33% for Hickman, 37% vs. 38% for PICC and 43% vs. 36% for IP. In patients with only one catheter type, BSI rates were 38% for Hickman vs. 50% for PICC ($P = .9$). BSI occurred in 40%