Beta-blocker use and hematopoietic stem cell transplant outcomes

Authors: Matthew A. Bergens, John T. Bokman, Ernaya Johnson, Yan Li, Amy Bush, Lauren Hill, Rebecca Fan, Sejal Kaushik, Paul E. Wischmeyer, and Anthony D. Sung

Background: While hematopoietic stem cell transplantation (HSCT) is an effective treatment for hematological malignancies, it is associated with several potential complications. Recent studies have associated beta-blocker (BB) use in critical care settings with improved survival outcomes, hypothesizing that blockade of the beta-adrengeric receptor (b-AR) is responsible for the improved outcomes. One specific complication of HSCT, acute graft versus host disease (aGVHD) is a severe complication of HSCT known to impact morbidity and mortality. Previous studies have also identified an intricate interaction between the immune system, inflammation, and b-AR signaling, which potentially offers a potential mechanism for BB to safely and specifically impacting aGVHD. Additionally, few studies have evaluated BB use and outcomes in the HSCT population. Our hypothesis evaluated the association between BB use and outcomes in HSCT patients.

Methods: We conducted a single center retrospective review of patients that received their first allogenic HSCT at Duke University Medical Center to assess the impact of BB use on overall survival (OS), non-relapse mortality (NRM), length of stay (LOS), aGVHD, and chronic GVHD (cGVHD). Demographic data including age, gender, transplant type, conditioning regimen, underlying hematological malignancy, and Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI) score before transplantation, were collected from the Duke ABMT database. Pre-transplant data was collected at D-10 and post-transplant data was collected at D+90. Outcomes such as GVHD occurrence and grade, LOS, NRM, OS, and cause of death, were collected from the Duke ABMT Database. All patients were chart reviewed to confirm their exposure to BB as well as record the specific BB administered. Comparisons of patient characteristics were performed using Chi-squared test or Fisher's exact test for categorical variables, and the analysis of variance or Wilcoxon Rank Sum test for continuous variables, respectively. The survival analyses were performed using the Kaplan-Meier method. The log-rank test was applied to detect overall group differences in outcome endpoints. Multivariate analysis (MVA) used the Cox proportional hazard model to evaluate the association of covariates and the aGVHD-free rates. The response variable of interest for the MVA is aGVHD, using all variables that had significant univariate analyses.

Results: We present over 10 years of data (January 2010 to May 2020) which included n=125 patients that were on a BB before transplant, with n=649 controls who did were not on a BB. We found that patients who received any BB had a lower incidence of acute GVHD on univariate analysis (55.2% vs. 66.1%, p=0.020); however, this significance disappeared on multivariate analysis (p=0.244). When categorized by BB mechanism, those who were on non-selective BB with alpha-adrenergic receptor antagonism (such as Carvedilol or Labetalol) had a shorter hospital length of stay (85 days) compared to those on a non-selective (97 days) or selective BB (92 days) (p=0.013). OS, NRM, and cGVHD were not significantly different between groups (all p>0.05).

Conclusion(s): While there is a growing body of literature suggesting BBs as an adjunctive therapy for patients receiving critical and cancer care, we found no evidence that they improve outcomes in HSCT patients. Namely, prior studies had attempted to connect BB usage with a reduction in GVHD; our findings do not support such a relationship. Therefore, we cannot recommend BBs as GVHD prophylaxis in patients receiving HSCT. However, we did identify a significant reduction in LOS for patients who were on non-selective BBs with alpha-adrenergic receptor antagonism, which we believe would be worth investigating further.