Evaluation of Sex on RBC Storage Hemolysis: Considerations for Transfusion Medicine

RBC transfusion is the most common inpatient medical procedure, offering life-saving therapy to ∼5 million Americans every year. Storage within the blood bank is a logistic necessity to enable blood transfusion as a commodity. However, it comes at the cost of the progressive accumulation of a series of biochemical and morphological alterations to the stored erythrocyte. These alterations are collectively referred to as the “storage lesion”. Clinically, the storage lesion has been implicated with increased risk of pulmonary complications such as transfusion-related acute lung injury (TRALI), multi-organ failure (MOF), and mortality 1-2. The progression and severity of the storage lesion is impacted by several donor-specific biological factors such as age, ethnicity, and sex3-4. Most notably, the male hormone testosterone was identified as an etiological mechanistic contributor to the storage lesion3,4. Testosterone has been shown to increase store RBCs propensity to hemolyze creating heterogeneity of regularly issued blood products3-4. However, despite this recent evidence, little is known about the mechanism by which donor sex and testosterone levels affect RBC propensity to hemolyze. To investigate potential mechanisms mediated by testosterone, omics-based technology was employed to determine systemic and red cell-specific metabolic signatures of testosterone. These signatures were later validated and compared to subjects with sub and supra-physiological levels of testosterone. Metabolites of the arginine pathway, as well as acylcarnitines and fatty acids, were found to be mediated by testosterone. However, further investigation is still needed to identify how testosterone mediation directly affects these pathways and ultimately RBC hemolyze.

References: