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711.CELL COLLECTION AND PROCESSING

Cryopreservation Impacts Allogenic Stem Cell Engraftment: Relation between Graft Quality Control and Post-Transplant Clinical Outcome

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Introduction: Freezing hematopoietic stem cells (HSC) has been a standard procedure in cellular therapy, either for allogenic, autologous, or cord blood transplantation. While cryopreservation is generally reported in the literature as a safe procedure with little impact on graft quality, some reports suggest significant effects of cryopreserved HSC as compared to fresh cells in the outcome of Hematopoietic Stem Cell Transplantation (HSCT). Recently, the COVID-19 pandemic enforced cryopreservation of HSC to secure allograft transplantation from related and unrelated donors. Modifying our standard practices was a unique opportunity to analyze the impact of this additional procedure on cell quality and HSC engraftment.
Method: This study compared the HSCT engraftment from fresh versus cryopreserved allogeneic HSC performed in Necker Hospital (n = 236) between January 2020 to December 2022. We retrospectively collected clinical data on patients from our unicentric PROMISE database and extracted the graft characteristics (cell phenotypes, viability, and clonogenicity) from the quality assurance database. Delayed platelets or neutrophils recoveries, early graft loss, and the need for CD34+ selected stem cell boost were used to define post-transplant graft dysfunctions.
Results: 107 pediatric patients with a median age of 3.9 years old and 129 Adult patients underwent primary HSCT in our center during the COVID-19 pandemic. Indications were hematological malignancies (n= 97: Acute leukemia, myelodysplastic syndrome, lymphoma, plasma cell disorders), inborn error diseases (n= 131: primary immune deficiency, hemoglobin disorder, histiocytic disorder), and bone marrow failure (n= 8). Sixty six (28.0%) graft of hematopoietic stem cells were cryopreserved from Bone Marrow (BM) (n = 18, 14.8%) and Peripheral Blood Stem Cells (PBSC) (n = 48, 42.1%). Cryopreservation significantly affects the viability (98.2% fresh vs. 84.4% cryopreserved HSC, $p<0.0001$) and the clonogenicity (18.7% fresh vs. 8.75% cryopreserved HSC, $p<0.0001$), whatever the source of stem cells. While cell viability and clonogenicity complied with the international standard before graft infusion, graft dysfunctions were a significant concern for cryopreserved allogeneic transplant (n= 22; 33.3%). Graft dysfunctions in cryopreserved HSC groups occurred with both bone marrow and PBSC. Significantly, dysfunctions increased to 38.5% for cryopreserved BM despite a higher median dose of CD34+/kg infused 15.5 (range, 10.2-20.7). No quality control parameter was predictive of engraftment dysfunction.
Discussion conclusion: Cryopreservation of HSC was critical during the SARS-CoV-2 pandemic; however, in our experience, the procedure could impact graft function. Considering the development and worldwide distribution of cell therapy drug products, accurately evaluating the pretransplant graft quality is an issue in predicting the engraftment of HSC.

Disclosures No relevant conflicts of interest to declare.

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