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Hematopoietic Stem Cell Transplantation in Pediatric Oncology: Successes and Challenges

Lures Axim*
Li Ki Sheng Knowledge Institute, St. Michael's Hospital, Canada

Abstract

Hematopoietic stem cell transplantation (HSCT) has revolutionized the treatment of high-risk and relapsed pediatric malignancies, offering a potential cure for conditions such as leukemia, lymphoma, and certain solid tumors. Over the years, advancements in donor selection, conditioning regimens, and graft-versus-host disease (GVHD) management have improved survival outcomes and reduced complications. However, challenges remain, including transplant-related toxicities, immune reconstitution delays, and the risk of GVHD. Innovations in haploidentical transplantation, reduced-intensity conditioning, and post-transplant immune modulation are shaping the future of HSCT in pediatric oncology. This review discusses the successes, ongoing challenges, and emerging strategies in optimizing HSCT outcomes for children with cancer.

Keywords: Hematopoietic stem cell transplantation; Pediatric oncology; Leukemia; Lymphoma; Graft-versus-host disease; Donor selection

Introduction

Hematopoietic stem cell transplantation (HSCT) has become a cornerstone of treatment for pediatric patients with high-risk or relapsed malignancies, offering a potentially curative option for leukemia, lymphoma, and certain solid tumors [1]. The procedure involves the replacement of diseased or damaged hematopoietic cells with healthy stem cells from either autologous (self), allogeneic (donor), or haploidentical (partially matched donor) sources. Over the past few decades, significant advancements in donor selection, conditioning regimens, and post-transplant care have led to improved survival rates and reduced complications in pediatric HSCT recipients [2].

Despite these successes, HSCT presents several challenges, including transplant-related toxicities, delayed immune reconstitution, and the risk of graft-versus-host disease (GVHD), particularly in allogeneic transplants. These complications can impact both short-term recovery and long-term health outcomes, necessitating ongoing research and innovation to enhance the safety and efficacy of the procedure [3]. Additionally, disparities in donor availability, the need for better conditioning strategies, and improvements in post-transplant immune modulation remain key areas of focus in pediatric oncology. This paper explores the current state of HSCT in pediatric oncology, highlighting its successes, the persistent challenges, and emerging strategies aimed at optimizing outcomes. Innovations such as reduced-intensity conditioning, haploidentical transplantation, and targeted immune therapies are shaping the future of HSCT, offering hope for improved survival and quality of life in children undergoing this life-saving procedure [4].

Discussion

Hematopoietic stem cell transplantation (HSCT) has significantly improved outcomes for pediatric patients with high-risk and relapsed malignancies. Advances in donor selection, conditioning regimens, and supportive care have enhanced survival rates, yet several challenges remain in optimizing safety and efficacy [5].

One of the key successes in HSCT is the expansion of donor options. While matched sibling donors (MSDs) remain the gold standard, advancements in haploidentical transplantation and umbilical cord blood transplantation (UCBT) have increased donor availability for children without MSDs [6]. Improved graft manipulation techniques, such as T-cell depletion and post-transplant cyclophosphamide (PTCy), have helped mitigate the risk of graft-versus-host disease (GVHD) while preserving graft-versus-leukemia (GVL) effects. Conditioning regimens have also evolved to balance efficacy and toxicity. Traditional myeloablative conditioning (MAC) remains standard for many pediatric cancers but is associated with severe toxicities, including organ damage and infertility. Reduced-intensity conditioning (RIC) has emerged as an alternative, particularly for patients with comorbidities, offering lower toxicity at the potential cost of higher relapse rates. Research into targeted conditioning strategies, such as antibody-based conditioning, aims to improve safety and long-term outcomes [7].

Despite these advances, GVHD remains a major post-transplant complication, affecting both morbidity and mortality. Acute and chronic GVHD can lead to severe organ dysfunction, infections, and impaired quality of life. Novel immunosuppressive approaches, including regulatory T-cell therapy, JAK inhibitors, and microbiome-targeted interventions, are being explored to reduce GVHD incidence while maintaining immune reconstitution.

Immune reconstitution following HSCT is another critical concern, as delayed recovery increases the risk of infections and relapse. Strategies such as adoptive T-cell therapy, cytokine-based immune modulation, and prophylactic antiviral therapies are being developed to accelerate immune recovery and enhance post-transplant surveillance [8].

Transplant-related toxicities, including veno-occlusive disease (VOD), pulmonary complications, and metabolic disorders, continue

***Corresponding author:** Lures Axim, Li Ki Sheng Knowledge Institute, St. Michael's Hospital, Canada, E- mail: luresaxim@gmail.com

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to pose risks for pediatric patients. Advances in supportive care, such as defibrotide for VOD and novel antifungal and antiviral prophylaxis, have improved management but require further refinement. Personalized risk stratification and biomarker-based toxicity prediction models may help tailor transplant strategies to individual patients, reducing complications and improving outcomes [9]. Looking ahead, precision medicine approaches, including genetic and immune profiling, may enable more individualized HSCT strategies. The integration of novel cellular therapies, such as chimeric antigen receptor (CAR) T-cell therapy in post-transplant settings, may further improve disease control while reducing reliance on conventional chemotherapy and radiation-based conditioning. While HSCT remains a curative option for many pediatric cancer patients, continued research is essential to address its remaining challenges. Multidisciplinary collaboration and advancements in transplantation biology, immunotherapy, and supportive care will be critical in optimizing outcomes, reducing toxicity, and improving the quality of life for pediatric HSCT recipients [10].

Conclusion

Hematopoietic stem cell transplantation (HSCT) has revolutionized the treatment of high-risk and relapsed pediatric malignancies, offering a potential cure for many patients. Advances in donor selection, conditioning regimens, and post-transplant immune modulation have significantly improved survival outcomes. The expansion of haploidentical transplantation, reduced-intensity conditioning, and novel graft manipulation techniques have enhanced the accessibility and safety of HSCT for children without matched sibling donors. Despite these advancements, challenges such as graft-versus-host disease (GVHD), delayed immune reconstitution, and transplant-related toxicities remain significant barriers to optimal outcomes. Continued research into targeted conditioning strategies, immunomodulatory therapies, and precision medicine approaches will be essential to further reduce complications and improve long-term survival. Moving forward, integrating innovative cellular therapies, predictive biomarkers, and personalized transplant strategies will play a crucial role in optimizing HSCT for pediatric oncology. Through ongoing advancements and multidisciplinary collaboration, HSCT will continue to evolve, offering improved survival and quality of life for children battling cancer.

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