Autologous Stem Cell Mobilization and Collection

Yen-Michael S. Hsu, MD, PhD[a,*], Melissa M. Cushing, MD[b,*]

KEYWORDS

• G-CSF • Plerixafor • Mobilization • Collection • Transplantation • Stem cell • Hematopoiesis • Laboratory

KEY POINTS

- The clinical use of mobilization agents is effective to achieve peripheral collection of stem cells.
- Stem cell sources, mobilization strategies, and collection methods may impact graft quality and transplantation outcomes.
- Monitoring and predicting mobilization are critical to coordinate between the various clinical services involved in stem cell transplantation.
- Apheresis-based peripheral blood stem cell collection is safe but requires many periprocedural preparations.

INTRODUCTION

Autologous stem cell transplant can be a curative therapy to restore normal hematopoiesis after myeloablative treatments in patients with lymphocytic malignancies, such as multiple myeloma (MM), non-Hodgkin lymphoma (NHL), Hodgkin lymphoma, and other malignancies. Mobilized hematopoietic stem/progenitor cells (HSPCs) collected by apheresis are the predominant source of stem cells for autologous and allogeneic transplant because of their higher yield and the decreased procedural risk compared with bone marrow (BM) harvest. Patients who have had many cycles of high-dose chemotherapy and/or radiation may have a significantly reduced BM reserve and a poor autologous yield after attempted stem cell mobilization and collection. Owing to the toxicity of prolonged chemotherapy exposure, alternative mobilization agents, and algorithms have been explored continuously for improvement.

[a] Pathology and Laboratory Medicine, Transfusion Medicine and Cellular Therapy, Weill Cornell Medical College, 525 East 68th Street, Box 251, New York, NY 10065, USA; [b] Transfusion Medicine and Cellular Therapy, Weill Cornell Medical College, 525 East 68th Street, Box 251, M09, New York, NY 10065, USA
* Corresponding authors.
E-mail addresses: ysh9001@med.cornell.edu; mec2013@med.cornell.edu

Hematol Oncol Clin N Am 30 (2016) 573–589
http://dx.doi.org/10.1016/j.hoc.2016.01.004 **hemonc.theclinics.com**
0889-8588/16/$ – see front matter

The clinical practice of HSPC mobilization and collection requires real-time and frequent communication between the clinical transplant team, the apheresis service, and the cellular therapy/stem cell laboratory. These optimized interactions are essential to the success of graft collection for patients who await hematopoietic rescue. There have been several published review articles addressing various aspects of HSPC mobilization. However, very few integrate solutions to the logistical and communication issues between the different services that allow for optimal patient management.

In this article, we review the safety, efficacy, and cost, as well as recent improvements in HSPC mobilization and collection. Finally, we address some of the practical concerns during the coordination of care between the clinical transplant team, the apheresis service and the cellular therapy laboratory. Although the practice continues to evolve, HSPC mobilization for allogeneic donors tends to have less mobilization failure given the allogeneic donor's healthier status and BM reserve compared with diseased autologous donors. There have been several reviews published on the topic of allogeneic mobilization,[1,2] and this review focuses on adult autologous donors, with an occasional reference to allogeneic donors when appropriate.

DISCOVERY OF THE HEMATOPOIETIC STEM CELL NICHE AND CLINICAL TRANSLATION

Since hematopoietic transplantation was established in the 1960s, the intricate cellular mechanisms and interactions of HSPCs and their BM microenvironment or "niche" have been investigated extensively.[3] Studies have shown that the BM niche plays an essential role in determining the ultimate fate of the HSPCs, including cellular trafficking, differentiation, and self-renewal. The main cell types comprising the niche are mesenchymal stem cells, osteoblasts, perivascular stromal cells, and endothelial cells. Various ligands expressed on the surface of or secreted from the niche cells dynamically interact with their cognate receptors on the HSPCs. This highly organized, direct cellular engagement is mediated by a sophisticated lipid raft formation that permits the proximity of signaling molecules to transduce intracellular signals (**Fig. 1**).[4,5] The formation and disassembly of the lipid raft result in HSPC BM retention and mobilization, respectively. Molecular analyses of these interactions have translated into the rapid development of drugs that are used clinically to mobilize BM HSPCs into peripheral circulation, which allows collections by apheresis.

CLINICAL HEMATOPOIETIC STEM/PROGENITOR CELL MOBILIZATION

Quiescent repopulating HSPCs are often tethered to osteoblasts, other stromal cells, and the extracellular matrix in the stem cell niche through a variety of adhesive molecule interactions. Disruption of niche interactions using cytotoxic agents, hematopoietic growth factors, small-molecule chemokine analogs, or even recombinant monoclonal antibodies can lead to release of HSPCs from the BM into the PB.[6] In 2010, Sheppard and colleagues[7] published a systematic review on 28 published randomized, controlled trials evaluating HSPC mobilization/collection strategies. The consensus was that mobilization improvement often comes with increased toxicity; therefore, the selection of a mobilization regimen should be considered and determined based on clinical resources and patient-specific factors. Since 2010, additional published algorithms have addressed some of those considerations (**Table 1**).[8–14]

Chemotherapy Mobilization

It was discovered in the early 1990s that HSPC concentration increased 5- to 15-fold during the postcyclophosphamide (CY) recovery period and that the increase is