Transfusion Medicine Reviews 28 (2014) 198–204

Contents lists available at ScienceDirect

Transfusion Medicine Reviews

journal homepage: www.tmreviews.com

Use of Laboratory Tests to Guide Initiation of Autologous Hematopoietic Progenitor Cell Collection by Apheresis: Results From the Multicenter Hematopoietic Progenitor Cell Collection by Apheresis Laboratory Trigger Survey

Robert S. Makar [a,*], Anand Padmanabhan [b], Haewon C. Kim [c], Christina Anderson [d], Michele W. Sugrue [e], Michael Linenberger [f]

[a] Department of Pathology, Massachusetts General Hospital, Harvard Medical School, Boston, MA
[b] Medical Sciences Institute, Blood Center of Wisconsin, Milwaukee, WI
[c] Apheresis Service, Department of Pediatrics, Children's Hospital of Philadelphia, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA
[d] Clinical Apheresis Services, Carter BloodCare, Dallas, TX
[e] Department of Medicine, University of Florida College of Medicine, Gainesville, FL
[f] Department of Medicine, Division of Hematology, University of Washington, Seattle, WA

ARTICLE INFO

Available online 27 August 2014

Keywords:
HPC(A) collection
PB CD34+ cell count
Trigger
Mobilization

ABSTRACT

Limited literature describes the value of laboratory "triggers" to guide collection of peripheral blood (PB) hematopoietic progenitor cells (HPCs) by apheresis [HPC(A)]. We used a web-based survey to determine which parameters are used to initiate autologous HPC(A) collection in adult and pediatric patients and to identify common practice patterns. Members of the AABB Cellular Therapy Product Collection and Clinical Practices Subsection and the American Society for Apheresis HPC Donor Subcommittee drafted and developed relevant survey questions. A web link to the survey was distributed by electronic newsletter or email. Responses from 67 programs that perform autologous HPC(A) collections, including academic medical centers (n = 46), blood centers (n = 10), community hospitals (n = 5), and a variety of other medical institutions (n = 6), were analyzed. Ninety-three percent (62/67) of programs used a laboratory parameter to initiate HPC(A) collection. In both adult (40/54, 74%) and pediatric (29/38, 76%) patients, the PB CD34+ cell count was the most common parameter used to initiate HPC(A) collection. The median PB CD34+ trigger value was 10/μL for both patient populations. Among centers routinely using the PB CD34+ cell count to initiate apheresis, 51% (22/43) first sent the test before the patient presented for collection. Although more than 90% of centers used a laboratory test to trigger apheresis in cytokine-mobilized (44/48) or chemomobilized patients (50/53), only 57% (30/53) used a laboratory trigger if the patient was mobilized with granulocyte colony-stimulating factor plus plerixafor. Forty-two percent (21/50) of programs that routinely measured the PB CD34+ count before collection and discontinued further HPC(A) collection based on product CD34+ cell yield also stopped if the PB CD34+ value before apheresis was considered too low to proceed. Most programs use the PB CD34+ cell count to trigger autologous HPC(A) collection. Some centers also use this parameter to stop further collections. Laboratory tests are used less frequently to initiate apheresis when patients are mobilized with plerixafor. These data reveal ongoing diversity in clinical practices and suggest that consensus guidelines on use of laboratory parameters may further optimize HPC(A) collection.

Collection of peripheral blood (PB) hematopoietic progenitor cells (HPCs) by apheresis [HPC(A)] is the standard technique to obtain CD34+ stem cells to reconstitute hematopoiesis after autologous stem cell transplantation [1-3]. A number of recently published guidelines and consensus recommendations have addressed the options and approaches to improve the efficacy and safety of HPC mobilization and collection [2-4]. Common regimens to mobilize CD34+ HPCs into the blood of autologous patients include the use of hematopoietic growth factors, particularly filgrastim (granulocyte colony-stimulating factor [G-CSF]), either alone, after chemotherapy or, more recently, in combination with plerixafor [1-4]. Optimal collection of CD34+ stem cells requires initiating apheresis when HPCs are at their highest concentration in the PB. Mobilization with

Conflict of interest: The authors have no relevant conflicts of interest to declare.

* Corresponding author: Dr. Robert S. Makar, MD, PhD, Massachusetts General Hospital, Blood Transfusion Service, 55 Fruit St, GRJ-2-206C, Boston, MA 02114-2696.
E-mail address: rmakar@partners.org (R.S. Makar).

http://dx.doi.org/10.1016/j.tmrv.2014.08.002
0887-7963/

daily G-CSF alone results in a predictable peak in PB CD34+ cell counts after 4 to 5 days [5,6]; therefore, initiating HPC(A) collection 4 to 5 days after starting G-CSF usually results in sufficient CD34+ cell yields for transplantation of autologous patients [4-7] and allogeneic recipients [4,8,9]. By comparison, the kinetics of PB CD34+ cell counts are relatively unpredictable among patients who undergo mobilization using chemotherapy followed by growth factor (chemomobilization) [10-12]. Therefore, for chemomobilized patients, the optimal time to initiate apheresis must be guided by measuring PB either for CD34+ cells or a surrogate marker of CD34+ cell yield in the apheresis product.

The PB CD34+ cell count is the best parameter to use to initiate apheresis collection because it most accurately predicts the CD34+ cell yield in the HPC(A) product [12-18]. However, accurately quantitating the PB CD34+ cell number is expensive and time consuming and requires technical expertise and access to a flow cytometer. As an alternative, investigators have described the use of several other PB surrogate markers to guide apheresis collection, including white blood cell (WBC) count [10,12], WBC and platelet count [19,20], reticulocyte fraction [21], and the number of circulating immature myeloid cells quantitated either by May-Giemsa stain of PB smears [22,23] or by a proprietary methodology (referred to as the "HPC parameter") that identifies these cells by their differential sensitivity to in vitro lysis [24-28]. Except for the HPC parameter, which closely approximates the PB CD34+ cell concentration within certain HPC ranges [24-28], these surrogate methodologies are inferior predictors of CD34+ cell yields in HPC(A) collection products.

No data are currently available describing the diversity of clinical practice related to the initiation of HPC(A) collections among apheresis centers serving autologous transplant programs. Understanding current practices may identify important limitations in knowledge, resources, or institutional polices that affect the quality of HPC(A) collection and that could benefit from educational initiatives and consensus guidelines recommending best practices. With this goal in mind, the Cellular Therapy (CT) Product Collection and Clinical Practices Subsection of the CT Section of AABB in collaboration with members of the American Society for Apheresis (ASFA) HPC Donor Subcommittee developed a survey tool to investigate the use of PB laboratory parameters as triggers to initiate HPC(A) collections from patients undergoing autologous transplantation. The objectives were to identify those tests used most commonly, determine how those test results informed decision making around apheresis, and assess the extent to which "real-world" practice patterns agree with published literature describing optimal approaches and consensus recommendations.

Methods

Questions for the HPC(A) Laboratory Trigger Survey (see the Supplementary Appendix) were developed, compiled, and reviewed by a subgroup of members of the AABB CT Product Collection and Clinical Practices Subsection in collaboration with representative members of the ASFA HPC Donor Subcommittee. The questions were designed to collect demographic, organizational, and operational information from the responding apheresis facilities and the annual numbers of collection procedures for adult and/or pediatric transplantations as well as specific data pertaining to clinical practices and decision making around the use of laboratory information to initiate apheresis to collect HPC(A) products. The survey questions were compiled into a commercially available web-based tool, SurveyMonkey (Palo Alto, CA). Skip logic (conditional branching) was incorporated in the survey design so that the questions a respondent was asked were appropriate given their responses to prior questions (eg, selecting PB CD34+ cell count as the test of choice led to a question about the value of the PB CD34+ cell count trigger, not the WBC count trigger). To facilitate data analysis, multiple-choice responses as opposed to free-text entries were used for most questions. To ensure that only a single survey response was received for any given apheresis facility, respondents were asked to supply the name and location of the institution to which the captured responses applied. We also requested permission to contact respondents for further information regarding their program's collection practices as necessary. Because the survey was designed to be web based, the IP address of the computer used to respond to the survey as well as the date and time the survey was taken was also collected. Upon completion of survey design, all questions were reviewed by the membership of the CT Product Collection and Clinical Practices Subsection and vetted for clinical relevance and clarity. Finally, the web link and web-based survey tool were beta tested by limited release to a select group of programs to ensure that they functioned as anticipated and that we were able to capture appropriate data. Feedback received from beta-testing sites was used to improve the clarity of some survey questions to capture the intended information.

The web link to the survey was released to general membership of AABB and ASFA via electronic newsletters. An invitation to participate in the survey and the survey web link was subsequently sent by email to select members of the AABB CT Product Collection and Clinical Practices Subsection who had not completed the survey. Survey data were captured in an Excel (Microsoft Corporation, Redmond, WA) database and validated by one of the authors (RM) to verify that responses from each participant were internally consistent and that there was only a single response for each medical facility represented in the database, either by using the identifying information provided by the respondent or the IP address used to fill out the survey. When present, multiple responses from any single institution were reviewed for discrepancies before selecting a single response for inclusion in the database. Whenever possible, any discrepancy in the data was clarified by contacting either the survey respondent or the physician overseeing the institution's HPC(A) collection program. Responses with internal inconsistencies (ie, mutually contradictory responses to survey questions) or unclear data (ie, numerical values without units) that could not be resolved by email communication with the respondent were excluded from analysis. Data are reported as the number of respondents giving a particular response or the percentage of all respondents who answered the question and provided a particular response.

Results

Ninety-five individual respondents representing different medical institutions or organizations completed at least a portion of the web-based HPC(A) Laboratory Trigger Survey between May 2012 and July 2013. Eighty-five of these participating sites indicated that they collected autologous HPC(A), which was the focus of the survey. Responses from 18 of these sites were excluded from analysis either because of inconsistent or uninterpretable answers to study questions (7 responses) or because less than 5 of the survey questions, including question 5 (does your facility routinely [ie, as part of a standard procedure for a group of patients] use a defined laboratory parameter [ie, a lab test value] to initiate autologous HPC(A) collection?), were answered (11 responses). This left 67 responses that were included in this analysis (Fig). Within this group, 84% (56/67) of respondents answered all the questions in the survey, and 91% (61/67) completed more than 95% of survey questions. Most of these respondents were from academic medical centers, whereas roughly one-third represented blood centers, community hospitals, and a variety of other medical facilities (Table 1). Of 67 respondents, 57 (85%) provided contact information and identified their role within their institution's HPC(A) collection program (Table 2). Most of these survey respondents were medical directors or physicians (22/57, 39%) and laboratory directors or supervisors (11/57, 19%). Of 57 respondents, 48 (84%) were from the United States, but responses were also