The Brazilian Journal of
INFECTIOUS DISEASES
www.elsevier.com/locate/bjid

Original article

Autologous transplant: microbial contamination of hematopoietic stem cell products

Igor Dullius Almeida[a], *Tissiana Schmalfuss*[b], *Liane Marise Röhsig*[b], *Luciano Zubaran Goldani*[c,*]

[a] *Hemotherapy Section, Hospital de Clínicas de Porto Alegre, Brazil*
[b] *Cryobiology Unit of Blood Umbilical Cord and Placental Bank, Hospital de Clínicas de Porto Alegre, Brazil*
[c] *Universidade Federal do Rio Grande do Sul, Infectious Diseases Section, Hospital de Clínicas de Porto Alegre, Brazil*

ARTICLE INFO

Article history:
Received 19 December 2011
Accepted 18 March 2012

Keywords:
Autologous transplant
Hematopoietic stem cell products
Microbial contamination
Quality control
Bacterial contamination

ABSTRACT

Hematopoietic progenitor cells from peripheral blood (HPCPB) are commonly used for autologous and allogenic transplants in patients with most various onco-hematological diseases, and despite the utilization of sterile techniques during collection and processing of these products, bacterial contamination can occur. This study aimed to investigate the microbial contamination of HPCPB products. Microbial cultures of 837 HPCPB products between the year 2000 and 2009 were retrospectively analyzed to determine the incidence of culture positivity and identify the main organisms that cause contamination. The microbiological studies were performed with an automated system (BacT/Alert® bioMérieux Corporate). Thirty-six (4.3%) of 837 microbial cultures were contaminated. Coagulase-negative *Staphylococcus* was the most frequent bacteria isolated from HPCPB products (20 [56%] of the 36 positive microbial cultures). Considering the 36 contaminated samples, 22 HPCPB products were infused and 14 discarded. Pre- and post-infusion antibiotic therapy of the patients transfused with contaminated products was established based on the isolated microorganism and its antibiogram. Microbial contamination rate of HPCPB products was low. Clinically significant outcomes after infusion of contaminated HPCPB products were not observed.

Introduction

Hematopoietic progenitor cells from peripheral blood (HPCPB) are commonly used for autologous and allogenic transplants in patients with various onco-hematological diseases. The progenitor hematopoietic cells are capable of self-renewal and differentiation in all blood cells lineages. Bone marrow is the traditional source for obtaining HPCPB, collected by multiple punctures and aspirations of the posterior iliac crests. The aspirated material contains red blood cells, leukocytes, platelets, mast cells, plasma, and pluripotent hematopoietic progenitor cells. In recent years, the collection of HPCPB via apheresis has been increasingly used. The combination of

* *Corresponding author at*: Hospital de Clínicas de Porto Alegre, Section of Infectious Diseases, Rua Ramiro Barcelos, 2350, Porto Alegre, RS, 90035-003, Brazil.
E-mail address: lgoldani@ufrgs.br (L. Zubaran Goldani).
1413-8670
http://dx.doi.org/10.1016/j.bjid.2012.06.012

Table 1 – Management considerations of HPCPB products with positive microbial cultures.

Administer the product	Discard the product
Slow growing organism*	Rapidly growing organism
Skin or environmental contaminant	Enteric or pathogenic organism
Donor or patient is not available for recollection	Product can easily be replaced
New product requires remobilization or central line placement	Patient can tolerate delay and recollection
Product contains majority of total cell dose	Product contains small percentage of total cell dose

HPCPB, hematopoietic progenitor cells from peripheral blood.
* Culture positivity beyond 30 hours of incubation.

high doses of chemotherapy with subsequent transplantation of these cells constitutes the standard treatment for many onco-hematological diseases.

Obtaining, processing, storing and transplantation of HPCPB involve many steps, which are normally performed in different environments and may result in microbial contamination. In fact, HPCPB manipulation during processing and pre- and post-cryopreservation are important sources of bacterial contamination of these cells.[1] The donor may be the source of microbial contamination of HPCPB. Donors with asymptomatic bacteremia or who are recovering from a bacterial infection may develop episodes of transient bacteremia, which can lead to product contamination. In addition, HPCPB collected by apheresis often requires the insertion of central venous catheters (CVC). Infections associated with CVCs are an important source of transient bacteremia and a possible cause of HPCPB contamination.[2]

Thus, in order to ensure a final product appropriate for transplant, it is essential to adhere to a quality control policy. Such controls should include CD34+cell count, cell viability assessment, and microbiological monitoring.[3]

The main objective of this study was to investigate the incidence of positive microbial cultures for HPCPB products from donors attending a tertiary care hospital in the period from 2000 to 2009. In parallel, the major bacteria contaminating HPCPB products and the pre- and post-infusion antibiotic therapy for the contaminated cells were also described. In addition, the blood culture results after thawing the bag containing HPCPB, which were infused or discarded according to medical decision, were also analyzed (Table 1).

Material and methods

Microbial cultures of 837 HPCPB products of donors attending a tertiary care hospital located in southern Brazil from 2000 to 2009 were retrospectively analyzed to determine the incidence of microbial culture positivity and identification of the main organisms causing contamination. In addition, the charts of the donors with positive HPCPB microbial cultures were reviewed.

For the sterility control of the HPCPB products, after the cryopreservation process and before freezing, 3 mL samples of the product were inoculated in pediatric blood culture bottles with 20 mL of activated charcoal (BacT/Alert® bioMérieux Corporate–Durham, USA). In addition, after blood bag thawing, samples were collected for microbial cultures at the moment of the infusion. Such action serves to verify a possible contamination at the time of water-bath defrosting. Cultures were sent to the microbiology department, where they were incubated for five days. When positive, microscopy and bacterial isolation were performed and identified through standard biochemical tests.

Data were organized and analyzed using the Microsoft Excel 2007® software, according to the distribution of frequency.

Microbiological surveys were performed with automated BacT/Alert® at 36 °C. The products were added into a class I laminar-flow cabinet with HEPA filters.

The study was approved by the local ethics committee, which is accredited by the National Committee of Ethics in Research of the National Health Department and the Office for Human Research Protection (OHRP) of the United States.

Results

A total of 837 HPCPB collections and microbial cultures were performed at the hemotherapy section from 2000 to 2009. The average volume drawn and time for collection and processing were 255 mL and 206 minutes respectively. The underlying diseases and the main characteristics of the patients that received HPCPB products are presented in Table 2. The main underlying diseases included multiple myeloma (n = 314), followed by Hodgkin lymphoma (n = 143), non-Hodgkin lymphoma (n = 132), acute myeloid leukemia (n = 63), neuroblastoma (n = 52), Wilms tumor (n = 28), medulloblastoma (n = 23), and Ewing sarcoma (n = 16).Thirty-six of the 837 collected samples (4.3%) yielded positive cultures for bacteria. Fig. 1 presents the annual contamination rate of the HPCPB products from 2000 to 2009. As shown in Fig. 2, the

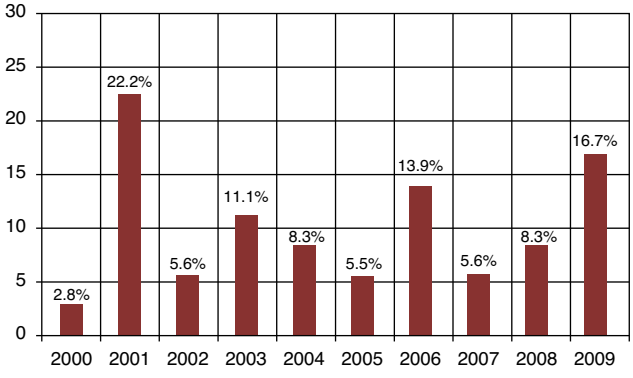

Fig. 1 – Annual rate of contamination in samples collected in the period from 2000 to 2009. Distribution of the 36 contaminated samples of total 837 made in this period.