Transfusion and Apheresis Science 54 (2016) 373–376

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Prophylactic low dose continuous calcium infusion during peripheral blood stem cell (PBSC) collections to reduce citrate related toxicity

Vikas Hegde *, Rasika Setia, Shivkumar Soni, Anil Handoo, Sanjeev Kumar Sharma, Dharma Chaudhary, Meenu Kapoor

BLK Superspeciality Hospitals, Pusa Road, Rajendra Place, New Delhi 110006, India

ARTICLE INFO

Article history:
Received 1 August 2015
Received in revised form 9 October 2015
Accepted 5 November 2015

Keywords:
Calcium
Bolus
Continuous infusion
Apheresis
ACD

ABSTRACT

Background: Citrate toxicity is one of the most frequent complications of apheresis procedures. It is caused by the infusion of the acid citrate dextrose (ACD), which chelates the calcium ions.
Aims: The aim of this study is to assess the effectiveness of prophylactic continuous infusion of calcium gluconate over intermittent bolus infusion to reduce citrate toxicity during large volume peripheral blood stem cell collection.
Materials and Methods: We retrospectively analysed the records of PBSC collection procedures performed from March 2010 to December 2013. Donors were selected as per the set guidelines. Machine used to perform the procedures was Cobe spectra. The study population was divided into 2 groups. One composed of intermittent intravenous bolus infusion at the onset of hypocalcaemic symptoms, the other composed of calcium gluconate administration as continuous infusion throughout the procedure.
Result: The most common reported hypocalcaemic symptoms were mild perioral paresthesia followed by digital numbness. Of the 50 individuals who were injected with bolus calcium 40 (80%) individuals suffered from symptoms of hypocalcaemia, whereas 23 of 66 individuals (34.8%) suffered from hypocalcaemia in the continuous infusion group. This difference was significant ($P < 0.001$). Both groups were compared with respect to age, gender ratio, weight of the individuals, total blood volume processed, ACD used, calcium gluconate dose used, time taken for the procedure, the product volume. Significant difference was noticed only with respect to the product volume. This implies that the groups were comparable with respect to parameters such as age, gender ratio, weight of the individuals, total blood volume processed, ACD used, calcium gluconate dose used, and the time taken for the procedure. Also that significantly more products (244 v/s 204 ml) was collected in the continuous infusion group.
Conclusions: Our results show that prophylactic continuous IV administration of low dose calcium-gluconate throughout the PBSC harvesting procedure reduced the incidence as well as the severity of citrate related toxicity. This increases his/her tolerance to withstand longer durations of the procedure and collect more volume of the product, hence may reduce the number of sittings of the procedure.

1. Introduction

Citrate toxicity is one of the most frequent complications of apheresis procedures. It is caused by the infusion of the acid citrate dextrose (ACD), which chelates the calcium

* Corresponding author. BLK Superspeciality Hospitals, Pusa Road, Rajendra Place, New Delhi 110006, India. Tel.: +91 8004987393.
E-mail address: drvikashegde@gmail.com (V. Hegde).

http://dx.doi.org/10.1016/j.transci.2015.11.015
1473-0502/

ions. ACD is used to prevent the coagulation of blood in the tubings of the apheresis kit. Chelation of calcium causes a wide range of symptoms and signs can be graded into 3 categories. Citrate-related hypocalcaemia commonly causes symptoms of tingling around the mouth and nose, more rarely tingling in the fingers (Grade I). More severe toxicity may cause nausea or vomiting (Grade II) or – much more rarely – tetany, hypotension and/or cardiac dysrrhythmia (Grade III) [1].

Peripheral blood has become an alternative to bone marrow as a source of stem cells (peripheral blood stem cells (PBSC)) for transplantation. It has been preferred over marrow harvests due to ease and less invasive nature of the procedure. For successful engraftment, the infusion of at least 2×10^6 CD-34+ cells per kg are required, which can be achieved by processing at least 3–4 times the blood volume of the donor/patient. Anticoagulation in the extracorporal circuit is performed by means of the citrate solution, usually ACD-A. In general, the leukapheresis is well tolerated and apheresis related adverse reaction is mostly restricted to symptoms of citrate toxicity. Large volume leukapheresis procedures will inevitably result in a larger volume of infused citrate [2–4]. Citrate related complications have been reported to occur in 48% of patients undergoing large volume leukapheresis during peripheral blood progenitor cell collection [2]. To reduce the incidence of citrate related complications, different measures are utilized, like, reducing the whole blood flow rate thus allowing less citrate into the system, pausing the procedure for a while, administrating chewable calcium tablets, altering the whole blood: ACD flow ratio [5,6] and combining heparin administration with citrate infusion [7,8]. Citrate toxicity can be prevented using continuous or bolus infusion of calcium into the return line during the leukapheresis procedure [9–11]. Prophylactic (before the onset of symptoms) calcium therapy is not routinely recommended in apheresis procedures, however in procedures which take long duration such as therapeutic plasma exchange, PBSC etc prophylactic continuous calcium infusions preferred by some.

We report our comparison between of prophylactic continuous IV administration of calcium-gluconate throughout the PBSC harvesting procedure and intermittent bolus infusion.

2. Aims and objectives

The aim of this study is to assess the effectiveness of prophylactic continuous infusion of calcium gluconate over intermittent bolus infusion to reduce citrate toxicity during large volume peripheral blood stem cell collection.

3. Materials and methods

We retrospectively analysed the records of PBSC collection procedures performed from March 2010 to December 2013 at BLK Super specialty hospital, New Delhi. Both autologous and allogeneic donors who successfully donated PBSC product at the blood bank were included in the study. Donors with incomplete data, those who underwent more than one procedure or those who switched the calcium infusion groups (bolus/continuous) were excluded from the study.

Donors were selected on the following criteria: 1) HLA matched (at least haploid match), 2) G-CSF mobilization (at least 4 days) prior to the procedure, 3) CD34+ count >10/μl prior to the procedure, 4) fitness to donate [Those who did not have histories of malignant tumour, collagen vascular diseases, cardiovascular diseases, convulsive disorders, infectious diseases such as HIV, Hepatitis B/C, malaria and syphilis. Systolic blood pressure ranged from 90 mmHg to 160 mmHg and diastolic blood pressure of 100 mmHg or less]. Autologous donors had certain ease with respect to physical fitness criteria based on the blood bank consultant's discretion.

Machine used to perform the procedures was Cobe spectra with version 7.0 software program (Terumo, Inc, Lakewood, CO). The machine was used on default parameters. The ACD: blood ratio was 1:12 and the anticoagulant infusion rate was 1.1 ml/min/litre total body volume. The Collection Concentration Monitor (CCM) was set between 2–4%. Blood flow rate was maintained average at 60 ml per minute (Range 30 to 80).

3.1. Study model

The study population was divided into 2 groups. Group I composed of procedures during which 10% calcium gluconate was administered by intravenous bolus infusion (5 ml to 10 ml) over 10–15 minutes at the onset of hypocalcaemic symptoms intermittently. Group II composed of procedures during which 10% calcium gluconate was administered as continuous infusion throughout the procedure. Prophylactic calcium gluconate infusion started at the start of procedure and was administered via return line. Calcium was administered at 0.5 mg of calcium ion per ml of ACD-A.

3.2. Statistical methodology

All the data was analysed using SPSS (version 20) software for windows. Unpaired sample t-test applied to compare the various parameters of the groups with respect to age, gender ratio, autologous–allogeneic donor ratio, weight of the individuals, total blood volume processed, TNC count, CD34+ count and number of individuals reacted. Chi-squared test was used to compare the severity of citrate toxicity between the groups. A P value <0.05 was considered significant.

4. Results

One hundred sixteen subjects (51 patients for autologous and 65 donors for allogeneic (Table 1)) underwent 116 peripheral blood stem cell harvesting procedures after standard mobilization regimens when the CD34+ count increased to 10 cells/μl to obtain a target of $>2 \times 10^6$ CD34+ cells/kg for transplantation after taking informed consent of the possible risks of the leukapheresis procedure. All subjects had normal hepatic and renal function. Of the 116 patients, 39 had acute leukaemias, 21 had multiple myelomas, 17 had aplastic anaemia, 5 had thalassaemia major, 15 had relapsed Hodgkin's lymphoma, 10 had non-Hodgkin's