

## Technical reports

# Efficacy and safety of femoral vascular access for peripheral blood stem cell (PBSC) collection

M Moreiras-Plaza<sup>1</sup>, C Albo<sup>2</sup> and C Ares<sup>2</sup>

<sup>1</sup>Department of Nephrology, CH Xeral-Ciés Vigo, Spain; and <sup>2</sup>Department of Haematology, CH Xeral-Ciés Vigo, Spain

### Summary:

Central venous catheters are frequently used in leukapheresis to provide high flow rates. The most common locations are the subclavian or jugular vein, but insertion-related complications and inadequate flow are frequent problems. Experience using femoral venous access is limited, because this has been discouraged due to the high incidence of infectious or thromboembolic complications. We evaluated the safety and efficacy of 108 short-term femoral venous dialysis catheters used for the collection of peripheral blood stem cells (PBSCs). All catheters were placed by a member of the dialysis unit, and they remained *in situ* for the days needed to reach the target number of CD34+ cells. No prophylactic antibiotic or antithrombotic therapy was used. A total of 232 apheresis sessions was performed. The longest duration a catheter remained *in situ* was 5 days. Most of the patients finished the collection in one or two apheresis sessions. There were no thrombotic or infectious complications, and insertion-related complications or mechanical problems were minimal. Apheresis results were similar to those reported using subclavian or jugular venous access. The short-term use of femoral venous dialysis catheters appears safe and effective for PBSC collection, simplifying the procedure, improving patient comfort, and reducing cost.

*Bone Marrow Transplantation* (2004) 33, 347–350.  
doi:10.1038/sj.bmt.1704357

Published online 15 December 2003

**Keywords:** femoral vein; vascular access; PBSC collection; vascular catheter complications

economics. Carrying out of large-volume leukapheresis decreases the number of sessions required, by increasing the volume of blood treated during each session.<sup>1</sup> Good quality vascular access is thus necessary to allow the high flow rates required. However, most of the candidates for PBSC transplantation do not have adequate peripheral veins, and a central venous catheter (CVC) is therefore required.

Standard catheters are generally not adequate for apheresis procedures because they do not maintain constant high blood flow rates. The use of larger lumen and thicker walled catheters, such as those used for hemodialysis, is recommended for PBSC collection,<sup>2–6</sup> because they allow a high flow rate without collapse of the catheter.

Numerous methods of venous access have been attempted in patients undergoing PBSC. At present, experience with CVCs is mostly with the use of subclavian or jugular catheters, but tip occlusions or catheter obstruction are common problems experienced with their use. Other complications are those related to their insertion such as pneumothorax, hemothorax or nerve lesions.<sup>7</sup>

Femoral vein catheterization is an attractive method to obtain central venous access because it is associated with a low complication rate during insertion, but its use has traditionally been discouraged due to the high incidence of infection or thromboembolic complications.<sup>8–10</sup>

Although the femoral vein is a frequently used central access for hemodialysis, there are scant data in the setting of leukapheresis. We present our experience using short-term dialysis catheters placed in the femoral vein for venous access during PBSC collection.

### Patients and methods

This analysis includes the PBSC records from January 1998 to December 2002. The following data were reviewed: demographic characteristics of patients, details of each PBSC collection, dates and duration of each procedure, and any catheter-related complication until catheter removal.

### Patients

We reviewed 95 consecutive patients, whose diagnoses are shown in Table 1. The group consisted of 49 males and 46 females. In all, 13 patients had two different collections, and eight patients were healthy voluntary donors. For PBSC mobilization, patients received cyclophosphamide

Transplantation of autologous peripheral blood stem cells (PBSCs) is increasingly used in the treatment of certain haematological malignancies and solid tumours. Obtaining a sufficient number of progenitor cells for a successful transplant in as few apheresis sessions as possible is important with respect to both patient convenience and

Correspondence: Dr M Moreiras-Plaza, C/Padre don Rúa 17, Vigo 36203, Spain; E-mail: Mercedes.Moreiras.Plaza@sergas.es  
Received 17 April 2003; accepted 05 July 2003  
Published online 15 December 2003

**Table 1** Clinical characteristics of patients

Age in years (range)	Sex	Diagnosis	No
46.5 (12–69)	46f, 49m	Non-Hodgkin's lymphoma	25
		Hodgkin's lymphoma	16
		Multiple myeloma	23
		Acute leukaemia	13
		Chronic lymphatic leukaemia	5
		Breast cancer	3
		Healthy donors	8
		Others	2

(3 g per m<sup>2</sup>), followed by granulocyte-colony-stimulating factor (GCSF) 5 µg/kg/day s.c., or only GCSF (10–20 µg/kg per day for 5 days given subcutaneously). No apheresis session was initiated on any fixed day after chemotherapy: daily monitoring of the WBC count and CD34+ cell analysis was performed to determine the timing of the PBSC collection, and the presence of 5 × 10<sup>3</sup> CD34+ cells/ml was the target value for starting the collection. When the patients received only GCSF, monitoring of CD34+ was not performed, and the collection was always started on the fifth day. A total of 232 apheresis sessions were undertaken.

### Catheters

Vascular access was achieved through the femoral vein, using a short-term haemodialysis catheter (standard double-parallel-lumen silicon or polyurethane catheter, noncuffed, 11 Fr, 20–25 cm in length). In all, 108 femoral catheters were placed in these 95 patients by a member of the dialysis unit, the day before or just before starting collection. The femoral vein was cannulated according to the Seldinger technique, at the bedside, using a standard sterile technique. No prophylactic antibiotic was used. For those patients requiring more than one apheresis, the catheter remained in site, all sessions being performed on consecutive days. Heparin was added for washing and sealing both lumens, and the site of insertion was cleaned and covered with a sterile dressing after each manipulation. No antithrombotic therapy was used. Catheters were removed after completion of the apheresis when the target values had been met.

### PBSC collections

The COBE SPECTRA (COBE Laboratories, Lakewood, CO, USA) was used for all collections. The inlet flow rate was set at 90–100 ml/min. The reinfused blood was anti-coagulated using a median blood:ACD ratio of 15:1. Heparin was used for those patients with severe citrate intolerance. The absolute number of CD34+ cells was determined for each apheresis procedure, and the total number of CD34+ /kg of body weight (BW) collected was used to determine the need for further leukaphereses. We established a minimum target of 2 × 10<sup>6</sup> CD34+ /kg of BW for finishing the collection.

During each treatment, the adequacy of blood flow and any manipulation needed to improve blood flow or catheter function during session were documented. When the catheter failed to provide an adequate blood flow, the

following correcting manoeuvres were attempted progressively: changing the position of the patient, flushing each catheter limb with saline, reversing blood lines by connecting the arterial line to the venous limb of the catheter and *vice versa*, and partial removal of the catheter.

### Flow cytometry

We performed flow cytometry using two-colour direct immunofluorescence, and employing monoclonal antibodies labelled with fluorescein isothiocyanate-CD45- or phycoerythrin-CD34-. A concentration of 5 × 10<sup>6</sup> cells was incubated with 50 µl of antibodies for 10–15 min at room temperature. Lysing solution was added, and the sample was analysed within 1 h. A FACScan flow cytometer (Becton Dickinson, San José, CA, USA) was used to give an absolute CD43+ result.

*Progenitor cell assays* were performed on each apheresis product. Fresh viable peripheral blood cells (2 × 10<sup>6</sup>) were plated using a methylcellulose-based medium (Methocult™ H-4531®, Stem-cell Technologies, Vancouver, BC, Canada) in a 1:10 (v/v) ratio. After 12–14 days' incubation in 5% CO<sub>2</sub> and 100% humidity at 37°C, the number of CFU-GM with >40 cell per colony was scored.

### Catheter-related complications

Catheter-related complications were classified as follows:

- Infection: skin erythema, purulent drainage, and pain at the site of catheter insertion were considered signs of local infection. Systemic infection was defined as fever and bacteriemia.
- Catheter malfunction: inadequate blood flow for the procedure or failure of blood withdrawal.
- Catheter obstruction: persistence of catheter malfunction after appropriate manoeuvres.
- Vascular thrombosis: clinical and/or ultrasound evidence of catheter-associated thrombosis.
- Bleeding: insertion-related haemorrhage or haematoma. Haematomata were classified as grade I (< 2 cm diameter), grade II (2–5 cm diameter), and grade III (> 5 cm diameter). Echographic control was undertaken in grade III cases.

### Results

Over the period of study, 108 femoral venous catheters were placed in 95 patients (49 male, 46 female) for collecting PBSC. The average age of patients was 46.5 years (range 12–69). In all, 13 patients had two catheters because they required two different collections at different times to achieve the target count of CD34+. No patient required more than one catheter for the same collection. The longest duration a catheter was left *in situ* was 5 days, with an average duration of 3.6 days (range 1–5), making a total of 286 catheter days.

A total of 232 sessions were performed, with a median of 2.4 (range 1–4) apheresis sessions for collection. More than 60% of patients required only one or two sessions, and only

**Table 2** PBSC collections

Sessions per collection	No patients (%) <sup>a</sup>	Total no. of sessions	CD34+ × 10 <sup>6</sup> /ml initial	Patients blood volume processed	CD34+ × 10 <sup>6</sup> /kg collected
1	24 (22,2)	232	60 (1–618)	10.2 (3–23)	6.09 (0.6–33.3)
2	49 (45,4)				
3	30 (27,8)				
4	5 (4,6)				

<sup>a</sup>In all, 13 patients had two different collections.

five patients required more than three sessions to reach the target number of CD34+ cells (Table 2). The median inlet flow rate for all procedures was 80 ml/min (range 54–108). Nine patients needed reduction of the flow rate to less than 65 ml/min due to symptoms of hypocalcaemia in spite of IV calcium administration. On the day of the first leukapheresis, blood leucocyte count ranged from 6.7 to 63.9 × 10<sup>9</sup>/l, and the median CD34+ counts was 60 × 10<sup>6</sup>/ml (range 1–618).

The mean TBV (patient blood volume) processed per collection and per session was 10.2 and 4.5, respectively. The mean number of CD34+ cells collected was 6.09 × 10<sup>6</sup>/kg of BW (range 0.6–33.32).

Almost all patients tolerated the procedures well. The most frequent side effect was paraesthesia, reversible dizziness, and hypotension, which were interpreted as adverse reactions due to citrate-related hypocalcaemia. This was managed with calcium supplements and/or slower flow rates. Three patients required anticoagulation with heparin due to severe citrate intolerance, seven patients needed i.v. calcium administration, and the blood flow had to be reduced in nine patients.

No local or systemic infection was diagnosed. No symptomatic venous thrombosis was recorded. Catheter malfunction was evident in 29/232 apheresis sessions. It was resolved by reversing the catheter bloodlines in 20, and partially removing the catheter in eight. Only one catheter (<1%) had to be removed due to obstruction when starting the third session, but by then the target count had been achieved.

There were no important complications related to insertion. Haematoma occurred at the site of catheter placement in 15 patients: only two were grade III, but ultrasound examination ruled out an arteriovenous fistula, and they resolved without complications. There were two minor bleeds at the site of insertion (one patient was receiving anticoagulant therapy). No other complications relating to the insertion or maintenance of the femoral catheter were recorded.

Catheter removals were simple and safe, with no acute or delayed bleeding.

## Discussion

The collection of PBSCs requires venous access that ensures withdrawal and reinfusion of blood at high flow rates, and allows repeated leukaphereses. The majority of candidates for PBSC transplantation do not have adequate peripheral veins for collection due to repeated cannulation and

chemotherapy. A CVC is therefore required. Standard catheters are generally not adequate for apheresis procedures due to problems of pressure and difficulty in keeping the inlet flow constant. Different types of catheters have been used for PBSC, but those specifically designed for haemodialysis seem to work better; their large lumen and thicker wall provide high flow rates without collapse of the catheter, reducing the number of leukapheresis sessions.<sup>2–6</sup>

Long-term tunnelled dialysis CVCs have been used for stem-cell harvesting and high-dose chemotherapy, with the intention of reducing the number of peripheral venous cannulae or CVCs inserted in patients requiring PBSC transplantation. However, a high complication rate has been reported with this kind of CVC, most of them being removed before the start of high-dose treatment.<sup>3</sup>

Non tunnelled CVCs have been found to be an excellent cost-effective alternative to tunnelled CVCs. The most common location of apheresis catheters is the superior vena cava, entered through the subclavian or internal jugular vein, although tip occlusions, catheter obstruction, and infection are common problems experienced with their use.<sup>4–6</sup> Other complications are those related to insertion such as pneumothorax, haemothorax or nerve lesions.<sup>7</sup>

Femoral vein catheterization is an alternative: it is feasible in the vast majority of patients, and is associated with a low complication rate during insertion. This approach is commonly used by nephrologists in patients with acute renal failure, or patients with temporary loss of permanent access.<sup>8</sup> Studies of CVC placement have documented the use of femoral access and the low incidence of associated complications.<sup>9–11</sup> The femoral site has several anatomic advantages over the subclavian or jugular approach that reduces the insertion-related complications: the anatomy is easily learned, the arterial pulse provides a reliable landmark for insertion, and haemostasis can be achieved by direct compression. The use of the femoral vein avoids pneumothorax, thrombosis, brachial plexus injury, and positional problems that often complicate subclavian or jugular catheterization. Moreover, radiographic confirmation of location or ultrasound guidance for placement are not necessary. However, the use of femoral venous access has traditionally been discouraged due to the high incidence of infection or thromboembolic complications,<sup>2,12–13</sup> and patient discomfort. Some authors have used short-term dialysis catheters for PBSC collection, but experience using the femoral vein is limited.<sup>15,16</sup>

We have shown that the use of femoral dialysis catheters in the setting of PBSC collection is safe and effective. In spite of the traditionally higher risk of infection or thrombosis using this location, our results are superior to

those seen with subclavian or jugular catheters. It is known that the risk of catheter-related infection increases over time,<sup>14</sup> and the absence of infection in our series may be explained by the short-term use of the catheters (less than the 7–10 days recommended for the femoral vein CVC). Also, the low rate of thrombosis and malfunction in our series is noteworthy although no prophylactic antithrombotic therapy was used. This low incidence contrasts with the higher incidence using other kinds of CVCs.

With respect to the patient comfort, the need for hospitalization is balanced by the simplicity and efficacy of the apheresis, which allows rapid harvesting with a reduced number of sessions. We preferred to keep the patients hospitalized, although they were allowed to stroll, while the catheter was in place. However, no problems were recorded when patients were discharged home with the catheter *in situ*.<sup>15</sup> The short time the catheters were *in situ* does not affect patient comfort to the extent that would be the case with simultaneous use of different peripheral veins and/or another kind of CVC with a higher complication rate.

Our experience also demonstrates the efficacy of this location for PBSC collection: the mean values of apheresis variables are similar to those series using subclavian or jugular venous access.

In conclusion, the short-term use of femoral dialysis catheters in the setting of large volume leukapheresis for PBPC collection is associated with minimal complications. The high flow rates achieved permit reduction of the number of apheresis sessions, simplifying PBSC collection, improving patient comfort, and reducing cost.

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