

第 51 回日本輸血学会総会アジア輸血医学シンポジウムの報告 (その 2)

Cord Blood Transplantation and Cord Blood Banking in Korea

Hyun Ok Kim, M.D

Department of Laboratory Medicine, Yonsei University College of Medicine, Seoul, Korea

Introduction

The first cord blood transplantation (CBT) was performed in a patient with severe aplastic anemia using sibling cord blood in July 1996, and three cases of unrelated CBTs were reported in the same year in Korea. The cord blood bank was started at 1996 by the Bioventure Company for autologous cord blood bank and opened almost every year until the year 2001. Now there are thirteen cord blood banks in Korea, which were mainly operated by commercial companies for private banking. From the view point of cord blood banking, I reviewed the storage status of cord blood units in banking and the outcome of cord blood transplantation performed through the nationwide.

1. Cord blood banking

Between 1997 and February 2003, 14,208 cord blood units had been cryopreserved at three big commercial CBBs for mainly private and 3 non-profit medical CBB for public (Fig. 1). As shown in Figure 2, the average number of total nucleated cells (TNC) was $7.9 \times 3.6 \times 10^8$ in 14,208 cord blood units stored in six surveyed CBBs. The average number of CD34+ cell count is $2.0 \pm 1.9 \times 10^6$ in 3,183 unit (22.4% of total cryopreserved units) (Fig. 3). Most of the cord blood units contained $1 \sim 4 \times 10^6$ CD34+ stem cells. Figure 4

showed the data into actual number of TNCs per body weight for the proportion of available CB units for transplantation. When we use the cell dose thresholds for reliable neutrophil recovery above 2.5×10^7 /kg, which was recommended at the 3rd international Indiana Conference for CBS and progenitor cell transplantation 2001, about fifty percent of stored cord blood only could be available for transplantation below the body weight 30kg patients. The figure 5

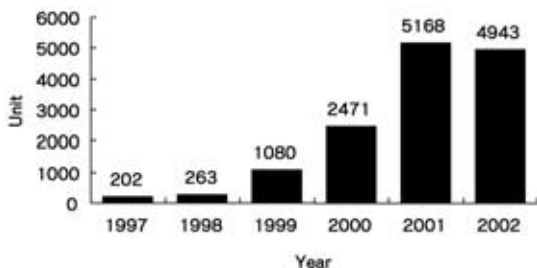


Fig. 1 Cord blood banking units in Korea. The number of cumulative cord blood was 14,208.

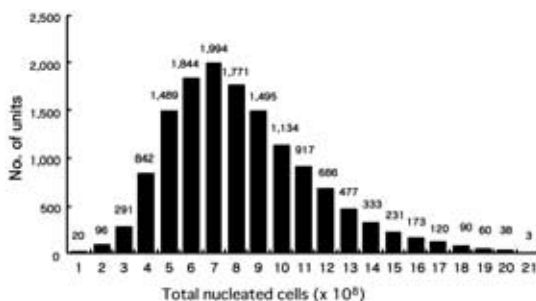


Fig. 2 The distribution of cord blood units according to the total nucleated cell counts in cord blood units. The number of TNC in average was $7.9 \pm 3.6 \times 10^8$.

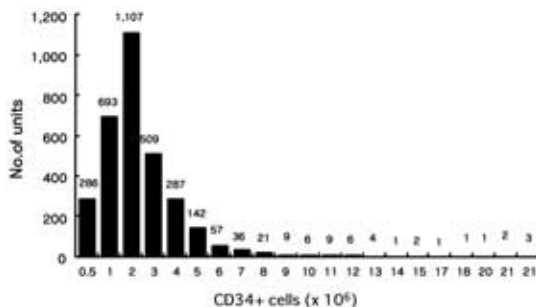


Fig. 3 The distribution of cord blood units according to the CD34+ cell counts in cord blood units. The number of CD34+ cells in average was $2.0 \pm 1.9 \times 10^6$.

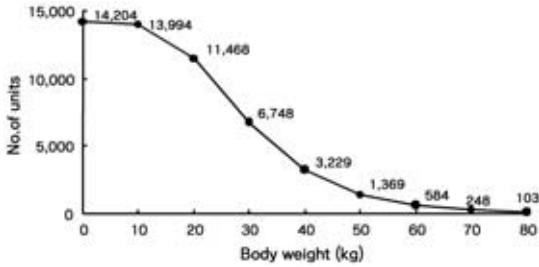


Fig. 4 The proportions of available cord blood units for transplantation using cord blood units with the cell count above 2.5×10^7 /kg, which was a recommended guideline for engraftment successfully within 1 month.

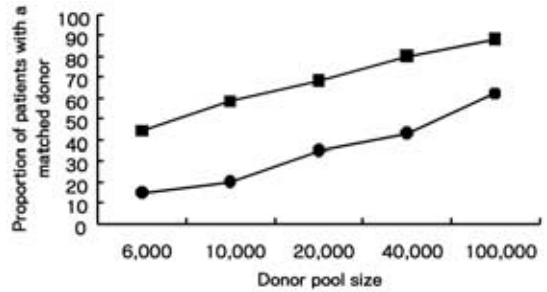


Fig. 5 Relation between normal bone marrow donor pool size and probability of finding a matched donor in Korea
 — : a full matched, — : a one antigen mismatched

shows the probability of finding a matched donor in the donor pool in Korea. It is rather hard to find a matched donor when the donor pool is below 10,000 but when we find the HLA one antigen mismatched donor in these pool, the probability increase up to the 60% in the same donor pool size. Because of available of HLA three mismatched cord blood for transplantation, the pool size of cord blood units is enough of smaller size compared to the normal bone marrow donor pool.

2 . Methods of isolation and cryopreservation of mononuclear cells from cord blood

There is no national standard for CB collection, processing and storage in Korea. Every cord blood bank has an institutional SOP for not only reducing storage space but also reducing the volume of DMSO. Informed consent was obtained according to institutional guidelines. Cord blood units were collected at the end of term deliveries. CB was collected by gravity into sterile CB collection bag (Green Cross, Seoul, Korea) containing anticoagulant CPDA-1. The cord blood was usually processed up to 24 h later after collection in the bank and tested for screening of infectious marker as anti-HCV, anti-HIV, HBs antigen, and syphilis test. All cord blood samples were typed for HLA class I and class II antigens by DNA genotyping for public cord blood banking, but HLA typing is not tested for autologous cord blood We usually use a technique, New York Blood Center developed, for red cell depletion and mononuclear cell concentration us-

ing 6%hydroxyethyl starch in a ratio of 1 volume HES to 5 volumes blood. A final concentration of 10% DMSO with at least 20%autologous plasma for cryopreservation techniques and a controlled rate freezer is used before transfer into liquid nitrogen at - 180 or lower. The cord blood reference samples are kept for further study. We seal the attached tube from the bag and keep three reference samples We keep two vials of plasma or serum, two vials of intact mononuclear cells that contains 1 to 2×10^6 cells per vial and two vials of purified DNA or frozen cells, which could be used for the purification of genomic DNA later.

3 . Outcomes of cord blood transplantation in Korea

There are 39 patients who received cord blood transplantation from 1997 to February 2002 at five cord blood transplantation centers in Korea. These patients had either no suitable bone marrow donor or urgent medical indications for transplantation. Fourteen patients had acute myelogenous leukemia, six with ALL, four with CML one with MDS, five with SAA, and two with genetic disease. In HLA-A, B and DR types, 4, 8, 15, and 5 cases were full-matched, one-, two-, and three-locus mismatched transplantation, respectively. Table 1 shows the characteristics of the recipients and outcome of CB transplantation at two different active cord blood transplantation centers. The overall survival rate was 60% and 70.6%, and event free survival rate was 53.3% and 58.2%, respectively.

Table 1 Clinical Data of Cord Blood Transplantation in Korea (Jul. 1997 Feb. 2002)

| | Group 1 (n=15) | Group 2 (n=17) |
|-----------------------------|---------------------|---------------------|
| Age (month) | 84 | 20 |
| Body weight (kg) | 21 | 18 |
| Infused cell | | |
| TNC ($\times 10^7$ /kg) | 3.7 | 3.8 |
| CD34+ ($\times 10^6$ /kg) | 1.9 | 2.8 |
| Engraftment | | |
| Neutrophil | D37 | D18 |
| Platelet | D78 | D54 |
| Survival (%) | | |
| Overall survival rate | 60 | 70.6 |
| Event free survival | 53.3 | 58.2 |

Discussions

Many data provide the good results that cord blood

transplants are regularly engrafted, with a relatively low rate of GVHD, and produce survival rates similar to those with transplantation of bone marrow from unrelated donors. In Korea cord blood transplantation were financially covered by the National health insurance since January 2003. Now, we are looking forward to set up the information network that can be shared nation wide. Now, we are preparing to make a national guideline for cord blood banking and transplantation, which will contain cord blood collection, cord blood processing, cord blood transport and data collection for clinical outcome. The " Cord Blood Research Committee " was organized in the Korean Society of Hematopoietic Stem Cell Transplantation this year (2003) and we are expecting some enthusiastic exchange of research results and information inside the country and abroad.