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Hematopoietic Stem Cell Transplantation in Children with Leukemia: A Single Institution Experience with Respect to Donors

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Aim of this study was to compare the outcomes of transplantation by donor source and to help select the best alternative donor in children with leukemia. Donor sources included matched related donor (MRD, n = 35), allele-matched unrelated donor (M-UD, n = 10) or -mismatched (MM)-UD (n = 13) or unrelated umbilical cord blood (UCB, n = 11). UCB group had a significantly higher incidence of grade II-IV acute graft versus host disease (MRD, 11.8%; M-UD, 30.0%; MM-UD, 15.4%, UCB, 54.4%, $P = 0.004$) but there was no difference in incidence of chronic graft versus host disease between 4 groups. The 5-yr leukemia-free survival (LFS) was 76.7%, 60.0%, 69.2%, and 45.5%, respectively ($P = 0.128$). MRD group showed higher LFS rate than UCB group ($P = 0.022$). However, LFS of M-UD and MM-UD together (65.2%) was not different from that of MRD group (76.7%, $P = 0.325$), or from that of UCB (45.5%, $P = 0.190$). The relapse incidence at 5 yr was 17.1%, 20.0%, 15.4%, and 0%, respectively ($P = 0.460$). The 100-day treatment-related mortality was 2.9%, 20.0%, 7.7%, and 36.4%, respectively ($P = 0.011$). Despite the limitations of small number of patients, unrelated donor transplants including even allele-mismatched ones, seem to be as effective in children with leukemia lacking suitable relative donors. Also, UCB transplant may serve as another possible option in urgent transplants.

Key Words: Allogeneic Hematopoietic Stem Cell Transplantation; Leukemia; Unrelated Donor; Umbilical Cord Blood

INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (HSCT) is a potentially curative therapeutic modality for malignant hematologic disorders. The ideal donor for allogeneic HSCT is a human leukocyte antigen (HLA)-identical sibling. However, only 30% of all patients who need transplantation have a suitable sibling donor (1). For transplant candidates lacking an HLA-identical relative, the choice of the best donor is important but often difficult for pediatric patients.

Alternative donors as a candidate for stem cell sources are volunteer unrelated donors (UDs), unrelated umbilical cord blood (UCB), and haplotype-mismatched family members (1, 2).

To maximize posttransplant survival in unrelated transplant settings, high-resolution matching for HLA is recommended in recent studies (3-5). The most important HLA loci influencing post-transplant outcome are known to be HLA-A, -B, -C (class I loci) and -DRB1 (class II locus) (3, 4). However, the role of other class II loci (namely DQB1 and DP1 loci) remains controversial (4, 6). Recently, the National Marrow Donor Program (7) released the updated guidelines for the selection of an unrelated HSCT donor: Whenever possible, donors who are high-resolution matched at these 4 HLA loci should be sought, and if a mismatch is unavoidable, a single mismatched (MM)-donor (-A, -B, -C, or -DRB1) should be sought.

UCB has been widely used recently in unrelated transplant settings because of ready availability, less probability of viral contamination and lack of risk to a donor (8). Moreover, UCB is known to be associated with less graft versus host disease (GvHD) due to naive nature of the lymphocytes displaying a lower alloreactive potential than bone marrow (BM) or peripheral blood lymphocytes. Thus, less restriction in HLA matching (4-6/6 HLA) is required for transplantation (8). However, the most important factor influencing the patient outcome in UCB transplantation is infused cell dose, as a unit of cord blood has limited cell numbers. The cell dose per Kg of recipient body weight, expressed either as total nucleated cells or number of CD34+ cells, has a significant correlation with engraftment, adverse transplant-related events and survival (9-11).

The selection of unrelated UCB units has been based on the number of cells cryopreserved in the unit and HLA data, usually typed for HLA-A and -B by serology or low-resolution meth-

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od, and DRB1 by allele typing (12). Selection of cord blood units with no more than two HLA disparities and with cell numbers more than 3×10^7/kg before thawing and 2×10^7/kg after thawing is recommended (11, 13). Recently, double UCB transplantations or expanded UCB have been explored to overcome the cell dose limitation (14).

Several clinical studies, both in adults and children, have demonstrated comparable outcomes in respect to engraftment, GvHD, and survival between UD bone marrow transplantation (BMT) and UCB transplants despite higher HLA disparity in the latter group (15-22). The excessive mortality from delayed engraftment and graft failure in UCB transplants might be balanced by lower mortality from other causes, including GvHD (23). To date, however, there have been no prospective studies that compare unrelated BMT with UCB transplants.

The aim of this retrospective study was to compare the clinical outcomes of allele-matched (M)-unrelated donor (UD) or -mismatched (MM)-UD transplantation and those of unrelated UCB and to help select the best alternative donor in children with leukemia. A comparison with matched related donor (MRD) transplantation was also made.

MATERIALS AND METHODS

Patients

A total of 83 children with leukemia less than 18 years of age underwent allogeneic HSCT at the Chonnam National University Hospital and Chonnam National University Hwasun Hospital between January 1996 and July 2009. The patients' medical records were retrospectively reviewed and analyzed as of June 2011. Patients were excluded if they were recipients of double UCB transplants (n = 4), UD grafts without HLA typing at allele-levels who were transplanted prior to June 2004 (n = 8), or haploidentical-related HSCT (n = 1). An extremely rare case of leukemia, CD52+ prolymphocytic leukemia was also excluded. For patients who underwent 2 allogeneic HSCTs, data of initial transplant were included (n = 5). Also, patients who received an initial autologous transplant followed by an allogeneic HSCT, only the data of allogeneic HSCT was analyzed (n = 2). For transplant candidates lacking an HLA-identical relative, M-UDs were searched. If not available, either MM-UD or UCB was chosen based on clinical urgency, cell dose of cord blood unit and HLA disparity.

Sixty-nine pediatric patients were the subjects for the analyses. Among them, 35 patients received HSCT from MRDs, 23 patients from UDs, and 11 from unrelated UCB (Table 1).

Patients were not considered to be evaluable for chronic GvHD if they died before 100-day posttransplant. Disease status was assessed immediately prior to transplantation, and at Day+28 and 3 months posttransplant. Patients were subsequently evaluated at least every 3 months in the first year, every 6 months in the second year, and yearly thereafter.

Donors and HLA-typing

The patients were divided into 4 groups according to the donor type: MRD, M-UD, MM-UD and UCB group. HLA typing was done by the best available methods at the time of transplantation. Patients who received an HSCT prior to September 2002 were typed for HLA-A, and -B by serologic techniques (24) and for -DRB1 by intermediate-resolution molecular techniques (25). Thereafter, high-resolution DNA typing was used for HLA-A, -B, -DRB1 at allele levels. Since June 2004, HLA-C matching has been included. All MM-UDs were accepted for transplantation only when they were 6/6 matched at antigen levels (HLA-A, -B, and DRB1) by serology, but incompatible at allele levels. All cord-blood units were HLA-typed at antigen levels for HLA-A and -B, and DRB1 at respective cord blood bank.

Conditioning

As the conditioning for transplant, total body irradiation (TBI)-based regimens were used in 37 patients, non-TBI regimens in 28, and reduced intensity conditioning (RIC) in 4. There was no significant difference in conditioning regimen among 4 groups.

A preparative regimen consisting TBI plus cyclophosphamide (CY) with or without cytarabine was used in the majority (80.6%) of patients with acute lymphoblastic leukemia (ALL, n = 36). The non-TBI regimen of busulfan (BU)/CY was used in 16 patients (72.7%) with acute myeloid leukemia (AML, n = 22). The RIC consisting of fludarabine/BU/antithymocyte globulin was given to each one patient from each group, respectively (Fanconi anemia with AML, secondary AML, relapsed ALL from lymphoblastic lymphoma, and AML in second remission after previous autologous peripheral blood stem cell transplantation, respectively).

Supportive care

The patients were kept in laminar airflow rooms. To prevent infections, all patients received prophylactic acyclovir, and itraconazole or fluconazole. All patients received granulocyte-colony stimulating factor (G-CSF) support from day 0. Transfusion support was provided with irradiated blood products. Stem cells were infused through a central venous catheter on day 0.

Definition of terminology

Disease status at transplantation was divided as standard and high risk groups: Standard risk: AML in first complete remission (CR), ALL in first or second CR and chronic leukemia in first chronic phase; High risk: more advanced status than standard risk leukemia or second stem cell transplantation (26, 27).

Diagnosis and clinical grading of acute and chronic GvHD were made according to the established criteria (28). Treatment-related mortality (TRM) was defined as death during a continu-

Table 1. Patients' clinical and transplantation characteristics

Parameters	MRD (n = 35) (%)	M-UD (n = 10) (%)	MM-UD (n = 13) (%)	UCB (n = 11) (%)	*P* value
Age, median					
Recipient (yr)	10.5 (1.1-18.6)	9.1 (0.7-16.6)	8.7 (1.3-14.2)	6.3 (0.6-15.0)	0.307
Disease, No. (%)					0.686
ALL	14 (40.0)	6 (60.0)	8 (61.5)	8 (72.7)	
AML	14 (40.0)	1 (10.0)	4 (30.8)	3 (27.3)	
Mixed phenotype leukemia	2 (7.6)	2 (20.0)	0	0	
Chronic leukemia	5 (14.3)	1 (10.0)	1 (7.7)	0	
Median follow-up months after transplant (range)	67.0 (1.0-179.0)	36.0 (0.7-83.0)	43.0 (1.7-83.0)	9.0 (0.3-106.0)	0.002
Disease status at transplantation*					0.547
Standard risk	33 (94.3)	9 (90.0)	13 (100.0)	8 (72.7)	
High risk	2 (5.7)	1 (10.0)	0	3 (27.3)	
Conditioning					0.548
TBI regimen	17 (48.6)	4 (40.0)	8 (61.5)	8 (72.7)	
Non-TBI regimen	17 (48.6)	5 (50.0)	4 (30.8)	2 (18.2)	
RIC	1 (2.9)	1 (10.0)	1 (7.7)	1 (9.1)	
GvHD prophylaxis					0.000
CsA/MTX	28 (80.0)	2 (20.0)	1 (7.6)	0	
Tacrolimus/MTX	0	8 (80.0)	12 (92.3)	0	
CsA only	2 (5.7)	0	0	9 (81.8)	
Tacrolimus/MMF	0	0	0	2 (18.2)	
MTX only	4 (11.4)	0	0	0	
No	1	0	0	0	
HLA disparity, No. (%)					
Serological match	35 (100.0)	10 (100.0)	6 (46.2)	1 (9.1)	
1 antigen mismatch	0	0	7 (53.8)	9 (81.8)	
2 antigen mismatch	0	0	0	1 (9.1)	
8/8 allele match	35	10 (100.0)	0	ND	
1 allele mismatch	0	0	7 (53.8)	ND	
2 alleles mismatch	0	0	5 (38.5)	ND	
3 alleles mismach	0	0	1 (7.7)	ND	
Stem cell source and numbers, median (range)					
BM/PBSC/CB	33/2/0	6/4/0	8/5/0	0/0/11	0.634
TCC (× 10^8/kg)	5.8 (1.4-115.0)	6.2 (1.6-12.2)	4.1 (1.8-14.8)	0.50 (0.15-1.20)	0.968†
MNC (× 10^8/kg)	5.6 (1.5-81.0)	4.6 (0.9-11.6)	3.0 (1.7-14.3)	-	0.863†
CD34+ (× 10^6/kg)	6.0 (0.6-89.0)	7.1 (0.6-14.3)	5.5 (2.8-11.0)	0.19 (0.07-0.73)	0.451†

*Standard risk is AML in 1st complete remission (CR), ALL in 1st or 2nd CR and chronic leukemia in 1st chronic phase. High risk is more advanced status than standard risk leukemia or 2nd stem cell transplantation; BM, bone marrow; PBSC, peripheral blood stem cell; CB, cord blood; TCC, total nucleated cell; MNC, mononuclear cell; Chronic leukemia including chronic myeloid leukemia (n = 6) and chronic eosinophilic leukemia (n = 1); †M-URD vs MM-URD vs MRD. MRD, matched related donor; M-UD, matched unrelated donor; MM-UD, mismatched unrelated donor; UCB, umbilical cord blood; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; TBI, total body irradiation; RIC, reduced intensity conditioning; CsA, cyclosporine; MTX, methotrexate; MMF, mycophenolate mofetil; ND, not done.

ous remission from any cause other than relapse. Leukemic-free survival (LFS) was defined as survival without relapse or death by any cause.

Statistical analysis

Overall survival (OS) and LFS were calculated using the Kaplan-Meier method. The log-rank test was used for group comparisons. Data for patients alive and in continuous remission were censored at the time of last follow-up. LFS was calculated from the beginning of transplant until relapse or death. The cumulative incidences of relapse, TRM and GvHD were estimated by treating deaths as competing risk. Gray's method was used for group comparison of cumulative incidence (29).

Patient and transplant characteristics were compared across donor type subgroups. Statistical comparison of continuous variables was performed by the Kruskal-Wallis test or ANOVA. Differences in categorical factors were tested across subgroups by the use of the chi-square test or Fisher's exact test. *P* values < 0.05 were considered as statistically significant. Analyses were performed using the SPSS software (Statistical Package for the Social Science, version 18.0, SPSS Inc, Chicago, IL, USA) and R soft ware (version 2.13.0).

Ethics statement

The present study was approved by the Institutional Review Board of the Chonnam National University Hwasun Hospital (IRB No. 2011-35). A written informed consent was obtained from each patient's guardian.

RESULTS

Patient characteristics

Patients' clinical characteristics and transplant details across the 4 donor groups are shown in Table 1. The numbers of trans-

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plants by each donor type were as follows: MRD, 35; M-UD, 10; MM-UD, 13; and UCB, 11. All the MM-UD patients were matched at 6/6 antigens (HLA-A, -B, and -DRB1) by serology, but 7 had mismatches in HLA-C. By allele typing of 8 antigens, one locus was mismatched in 7 patients, two loci in 5, and three loci in 1. In UCB group, only one patient was full matched, and the remaining 10 patients were antigen-mismatched (1 antigen MM in 9; 2 antigen MM in 1).

There were no significant differences in age at transplantation, disease type, disease status at transplantation and conditioning regimen between the 4 groups. The proportion of high risk patients was higher in UCB group (27.3%) than other groups, but it was not significant. The median follow-up duration after transplant was longer in MRD group (67.0 months) than in other groups (P = 0.002), as unrelated transplants were more commonly applied recently. Also, median follow-up duration after transplant was the shortest (9 months) in UCB group as six patients died prior to 9 months after transplant but the median follow-up was 90.0 (75.0-106.0) months in the remaining UCB patients.

GvHD prophylactic regimens were quite different across the 4 donor groups. Cyclosporine (CyA) plus short-course methotrexate (MTX) were used in the majority of MRD group (80.0%), while tacrolimus was substituted for CyA in M-UD (80.0%) and MM-UD groups (92.3%). CyA alone was used in most of UCB group (81.8%).

Stem cell properties and engraftment kinetics

The BM was the most frequent source of stem cells (n = 47, 68.1%). The proportion was especially higher in MRD grafts (97.3%) than that in M-UD (60.0%) or MM-UD (61.5%) transplants (Table 1).

There were no significant differences in infused total nucleated cells (TNC), mononuclear cells and CD34 cell counts among the 3 groups except for UCB group, which contained one-log smaller amount of TNCs. However, only 3 patients were infused less than TNC 3 × 10^7/kg of recipient body weight. CD34+ cell numbers in UCB group were even lower than 1/10 of other groups.

Engraftment failure was not observed. The speed of neutrophil and platelet recovery was different according to the donor type. The median day to absolute neutrophil counts ≥ 500/μL was 15 in MRD, 16 in M-UD, 18 in MM-UD, and 21 in UCB, respectively (P = 0.01). The median day to platelets ≥ 20,000/μL without transfusion for 7 consecutive days was 19 in MRD, 23 in M-UD, 30 in MM-UD, and 45 in UCB, respectively (P < 0.01). Among alternative donor groups, UCB group showed slower recovery of both neutrophils and platelets than M-UD group (P = 0.008, P = 0.001, respectively), or MM-UD group (P = 0.051, P = 0.01, respectively).

The engraftment speed between M- or MM-UD group and MRD group, or between M- and MM-UD groups was not different.

Acute and chronic GvHD

The cumulative incidence of grade II-IV acute GvHD was significantly higher in UCB group: 11.8% (n = 4) for MRD, 30.0% (n = 3) for M-UD, 15.4% (n = 2) for MM-UD, and 54.4% (n = 6) for UCB (P = 0.004).

Chronic GvHD developed in 14 of 61 evaluable patients (22.9 %). Six patients had extensive diseases. The cumulative incidence of chronic GvHD was not significantly different between the groups (P = 0.523); 18.3% (No./evaluable patients, 5/34) for MRD, 27.1% (3/8) for M-UD, 33.3% (4/12) for MM-UD, and 28.6% (2/7) for UCB.

The incidence of extensive type chronic GvHD was higher in MM-UD group than MRD group (P = 0.029). In UCB group, all 2 patients with chronic GvHD had extensive diseases. Each one

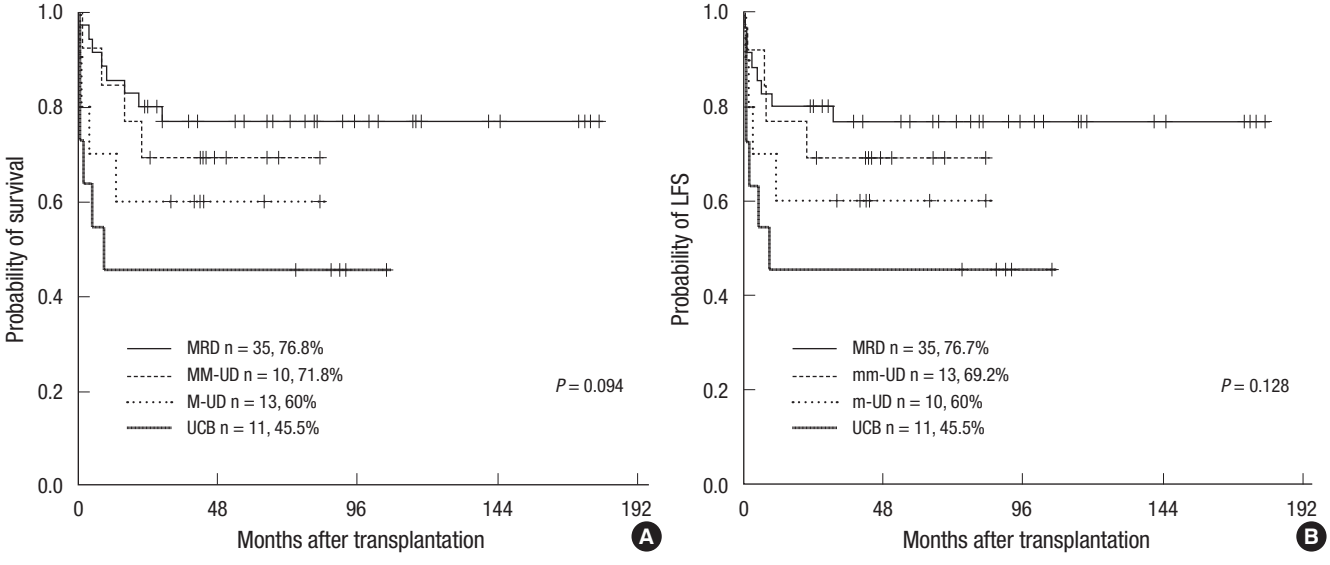

Fig. 1. Probability of Kaplan-Meier 5-yr overall survival (**A**) and leukemic-free survival (**B**) by different donor groups.

from MM-UD and UCB group died of chronic GvHD.

Overall survival and leukemia-free survival

The Kaplan-Meier 5-yr OS by donor group was the best in MRD group (76.8%), followed by MM-UD (69.2%), M-UD (60.0%) and UCB (45.5%) group (P = 0.094) (Fig. 1A). The Kaplan-Meier 5-yr LFS showed the same tendency: MRD (76.7%) MM-UD (69.2%), M-UD (60.0%), and UCB (45.5%), respectively (P = 0.128) (Fig. 1B). MRD group showed higher OS and LFS rate than UCB group (P = 0.015, P = 0.022. respectively). However, Kaplan-Meier survival rates (OS, 65.2%; LFS, 65.2%) of all UD groups together (M- and MM-) were not different from those of MRD group (OS, 76.8%, P = 0.288; LFS, 76.7%, P = 0.325), and also from those of UCB group (OS, 45.5%, P = 0.179; LFS, 45.5%, P = 0.190), respectively.

Relapse

Eleven patients relapsed at the median of 6.0 (2.0-31.0) months post-transplantation. All the patients who relapsed died of progressive disease. Most relapses occurred within the first year posttransplant with only one patient relapsing after one year and none after 3 yr.

The cumulative incidence of relapse at 5 yr was not different by donor groups: 17.1% for MRD; 20% for M-UD; 15.4% for MM-UD; and 0% for UCB (P = 0.460). Of note is that there was no relapse case in UCB group. Although none of 7 patients who had grade III-IV acute GvHD relapsed, acute GvHD was not associated with decreased relapse rate (8.3% vs 20.3%, P = 0.391). Also, chronic GvHD was not associated with decreased relapse rate (8.3% vs 21.6%, P = 0.252).

Treatment-related mortality and cause of death

Eleven patients died of treatment-related causes. All the cases of early deaths before 100 days (n = 8) were TRM: GvHD, 1; veno-occlusive disease, 2; interstitial pneumonia, 3; infection, 1; and massive hemorrhage, 1. The cumulative incidence of 100-day TRM was higher in UCB group than in other groups: 2.9% for MRD; 20.0% for M-UD; 7.7% for MM-UD; and 36.4% for UCB group (P = 0.001). There was no TRM after post-transplant 100 days in other groups except UCB group. The 5-yr cumulative TRM rate showed a significant pattern with the highest in UCB (54.4%; P = 0.001). In UCB group, causes of TRM were as follows: GvHD, 2; veno-occlusive disease, 1: interstitial pneumonitis, 2; and infection, 1. Fourteen patients died after 100 days posttransplant. Leukemia relapse (n = 11, 78.6%) was the leading cause of late death, followed by GvHD (n = 2) and infection (n = 1).

DISCUSSION

The HSCT has been the primary treatment modality and the curative option for certain childhood leukemia, such as high risk ALL, most of AML, and relapsed leukemia (26, 27). MRD transplantation is usually preferred, with the LFS rate being 32%-65% in high-risk childhood ALL and 60%-70% in childhood AML (26, 27). Alternative donors for patients without an HLA-identical relative are UD, unrelated UCB and haploidentical family donors (1, 2). Each alternative donor has advantages and limitations, which should be considered in choosing the best possible donor.

Recently, a meta-analysis of pooled data on comparative studies of UCBT and UBMT was published which comprised all patients requiring HSCTs (17). There was no difference in 2-yr OS between UCBT and 6/6 antigen matched UBMT in children. On behalf of the Center of the International Bone Marrow Registry (CIBMTR) and the New York Cord Blood Program, Eapen et al. (18) reported comparative results on more restricted population of acute leukemia less than 16 yr. Outcomes of 503 children transplanted with UCB were compared with 8/8 allele-M BMT (n = 116) and 1 or 2 allele-MM BMT (n = 166). Of UCBTs, 35 were matched at the HLA-A, -B (antigen level) and -DRB1 (allele level) and 201 mismatched at one locus and 267 mismatched at two loci. The 5-yr probabilities of LFS for 1-antigen MM UCB with a cell dose greater than 3×10^7 nucleated cells/kg (45%) and 1-antigen MM UCB with low cell dose (36%), and 2-MM UCB (33%) were similar to M-UD (38%). Smith et al. (30) reported transplantation outcome of children with ALL in CR2 by the type of available donors. The LFS at 5 yr was lower in recipients of MM-UD grafts, but was comparable in all other groups (MSD, 41%; M-UD, 57%; MM-UD, 19%; UCB, 43%, respectively P = 0.05). In a recent Korean report on 56 children with acute leukemia the LFS was 57.1% in UCB transplants, which was comparable to 63.2% in UD BMT (19).

In the present study, the Kaplan-Meier 5-yr LFS by donor group was the best in MRD group (76.7%), followed by MM-UD (69.2%), M-UD (60.0%) and UCB (45.5%) group (P = 0.128). Although UCB showed the lowest survival rate, it was not statistically different from that of M- or MM-UD. Moreover, 5-yr LFS rate of UCB group in our study (45.5%) was not inferior to the survival rate of other reports: 45% from 1-antigen MM UCB with high cell dose, or 33% from 2-antigen MM UCB from CIBMTR and New York Cord Blood Program (18); 43% from University of Minnesota (16); 31% 2-yr LFS from Eurocord (15); or 57.1% from Korean study (19).

As reported in other studies (15-19), the engraftment was slower in UCB group than UD groups in this study. However, graft failure was not observed despite three patients received TNCs less than 3×10^7/kg of recipient body weight.

Some UCB studies reported that more than 2-antigen MM increased acute GvHD compared with full matching (13) but HLA matching did not impact chronic GvHD (18). Another study (17) reported that the incidence of chronic GvHD was lower with

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UCBT (relative risk [RR] = 0.26; $P = 0.16$), but the incidence of grade III-IV acute GvHD did not differ (RR = 1.46; $P = 0.55$). Our results show that the incidence of grade II-IV acute GvHD was significantly higher in UCB group (54.4%) than other groups ($P = 0.004$). The incidence in our study was higher than that from the Eurocord (35.8%) (13). The discrepancy might be HLA-DRB1 mismatch at allele level because allele level data was not available in our study. Also, the use of CsA alone as GvHD prophylaxis in most of UCB group (81.8%) might be associated with higher incidence of acute GvHD in our study. But, chronic GvHD did not significantly differ in the 4 groups, although the incidence was the lowest in MRD group.

Eapen et al. (18) reported the higher TRM rates in 1- and 2-antigen MM-UCB was counterbalanced by the lower relapse rates. Thus, LFS was not statistically different from 1 or 2 antigen MM CBT compared with M-UD BMT. Our 5-yr non-relapse mortality rate (54.4%; $P = 0.001$) and the 100-day TRM rate (36.4%; $P = 0.001$) was highest in UCB group, which was consistent with other reports (15-19). Most relapses occurred within the first year posttransplant. The relapse rates were similar among M-UD and MM-UD and MRD groups ($P = 0.53$). Although no relapse occurred in the UCB group, the true relapse rate should be analyzed in large series of patients. As previous reports, even if our UCB group showed the lowest survival rate, it was not statistically different from that of other groups.

In UD transplants, the level of HLA mismatching has an impact on the development of GvHD and survival (4-6). On behalf of the CIBMTR, Lee et al. (4) suggested that single mismatches at HLA-B or HLA-C appear to be better tolerated than mismatches at HLA-A or HLA-DRB1. Mismatching at HLA-DQ and HLA-DP did not influence the outcome in large series of UD BMT (3, 5). Thus, it is usually recommended that high-resolution 4 loci of HLA-A, -B, -C, and -DRB1 be typed for the selection of UD for transplant (3-5). In our study, all the MM-UD patients were matched at 6/6 antigens (HLA-A, -B, and -DRB1) by serology, but 7 had mismatches in HLA-C at antigen levels. By allele typing, 1 locus mismatching was found in 7 patients and 2 more loci were mismatched in 6. However, OS rate, relapse rate and TRM rate were not significantly different between M-UD and MM-UD groups in this small series of patients.

The authors have summarized the transplant results at a single center comparing transplant outcomes by different stem cell donor sources for children with leukemia. The 5-yr Kaplan-Meier OS was not different between the 4 groups, although MRD group showed the best, while UCB group being the worst ($P = 0.013$). However, among the alternative groups other than MRD group, the OS rate of UD group, either M- or MM-, was not different from that of UCB group ($P = 0.153$). Although no relapse was found in UCB group, the benefit was offset by the high TRM early posttransplant. However, the 5-yr LFS in our UCB group (45.5%) was not inferior to that from other reports.

In conclusion, despite the limitations of small number of patients from a single institution, our results suggest that UD transplants, even allele-MM, are effective treatment modality in children with leukemia lacking suitable relative donor. Also, UCB transplant may also serve as another possible option in urgent transplants. These results may justify the simultaneous search of unrelated BM donors and unrelated UCB units when a child with acute leukemia is in need of an alternative transplant.

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AUTHOR SUMMARY

Hematopoietic Stem Cell Transplantation in Children with Leukemia: A Single Institution Experience with Respect to Donors

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We compared the outcomes of transplantation according to the donor source for children with leukemia. The matched related donor (MRD) group showed higher overall survival and leukemia-free survival (LFS) rate than the umblical cord blood (UCB) group. However, the LFS of allele-matched (M)-unrelated donor (UD) or -mismatched (MM)-UD groups together was not different from that of MRD group, or from that of UCB. Moreover, 5-yr LFS rate of the UCB group was consistent with the findings of other reports. UD transplants including even allele- MM ones, seem to be as effective in children with leukemia lacking suitable relative donors. Also, UCB transplant may serve as another possible option in urgent transplants.