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Unrelated donor umbilical cord blood transplantation versus unrelated donor bone marrow transplantation in adult and pediatric patients: A meta-analysis

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ABSTRACT

The effect of unrelated donor bone marrow transplantation (UBMT) and unrelated donor cord blood transplantation (UCBT) on the outcome of patients with hematological diseases remains controversial. We conducted a meta-analysis using data from controlled clinical trials comparing UCBT to UBMT in patients undergoing hematopoietic stem cell transplantation. Pooled comparisons of studies of UCBT and UBMT in children found that the incidence of chronic graft-versus-host disease (GVHD) was lower with UCBT (relative risk [RR] = 0.41; 95% confidence interval [CI] (0.25, 0.68)), and the incidence of grades II–IV aGVHD was also significantly different (RR = 0.69; 95% CI (0.55, 0.86)). The incidence of relapse was also lower with UCBT (RR = 0.72; 95% CI (0.59, 0.87)). There was no difference in OS in children when studies were pooled (Hazard ratio [HR] = 1.25; 95% CI (0.87, 1.78)). For adults, OS (HR = 1.26; 95% CI (1.13, 1.40)) was statistically different. Thus, UCBT led to inferior outcomes than UBMT in adults.

1. Introduction

Allogeneic hematopoietic stem cell transplantation (HSCT) is a treatment largely employed for a number of hereditary and/or hematological disorders, both malignant and non-malignant. For the first 20 years (namely between 1968 and 1988), bone marrow (BM) was the only source of hematopoietic stem cells (HSC) [1,2]. However, BMT is limited by HLA-matching requirements, high risk of graft-versus-host disease (GVHD), opportunistic infection, and donor availability. Since the first successful allogeneic cord blood transplant (CBT) performed in 1988 to treat a child with Fanconi anemia [2], cord blood (CB) has been increasingly used as an alternative stem cell source to BM or peripheral blood stem cells to treat hematologic disorders primarily in children, but its use in adults is increasing.

A number of controlled clinical trials (CCTs) [3–12] have been conducted to evaluate the benefit of CBT for hematologic disorders compared with BMT, but whether the real influence of unrelated donor CBT on outcome of recipients is still controversial and not fully established. A prospective randomised clinical trial is the accepted standard to compare different treatments such as different graft types for unrelated donor transplantation. To randomize patients in a study comparing unrelated CBT and BMT, each patient would need an unrelated CB and BM donor available at the point of randomization. However, conducting such a study has not been possible to date. The main purpose of this analysis was to critically assess the safety and efficacy of unrelated CBT compared with BMT from unrelated donors.

2. Methods

To aid in making treatment decisions for patients needing allogeneic HSCT, we systematically reviewed all data on comparative studies of UCBT versus UBMT in which survival was the key outcome measure. To obtain reliable evidence on the relative effect of UCBT versus UBMT in the primary treatment of adults and children with malignant and non-malignant disorders, results from independent and comparable studies were integrated to increase statistical power. The primary outcome of interest for our analysis was survival; secondary outcomes studied included engraftment, GVHD, transplantation-related mortality (TRM), and relapse.

3. Search strategy

Following established guidelines, relevant studies were identified through a computerized literature search of the MEDLINE, EMBASE, the Cochrane controlled trials register, the Cochrane Library, and the Science Citation Index databases. The search terms used were “cord blood,” “bone marrow,” and the alternate search terms “transplant,” “transplantation,” and “transplants.” We included all journal articles and limited the search terms to the title. Full text papers were obtained to extract the data for this analysis.

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References of retrieved articles were also checked for any relevant trials. Studies published by June 2009 were eligible.

4. Selection criteria

All comparative studies of UCBT versus UBMT were selected. Only studies published as an abstract or journal article were eligible for this analysis. Data for TRM, GVHD, and overall survival had to be available. Each study was critically appraised for validity based on consistency, accuracy, and balance between treatment groups. Data were independently abstracted by two reviewers and consensus was reached on any disagreement. Study authors were contacted if important data were not available in the published study. Studies without comparable data between the two comparative groups were excluded. Studies with <20 patients per arm and T-cell-depleted UBMT were excluded.

5. Statistical analysis

To estimate the treatment effects, outcomes were calculated as either relative risks (RR) or hazard ratios (HR), with their respective 95% confidence intervals (CIs). HRs were the preferred form of data

Table 1
Study characteristics.

Study	Study population	Study arm	Number of patients	Median age (range, years)	HLA-matching
Rocha et al. [3]	Acute leukemia children	UCBT	99	6 (2.5–10)	8% 6/6 HLA-matched 43% 1 antigen-mismatched 41% 2 antigen-mismatched 8% >3 antigen-mismatched
		UBMT	262	8 (5–12)	80.5% 6/6 HLA-matched 17.6% 1 antigen-mismatched 0.4% 2 antigen-mismatched
Barker et al. [4]	Hematologic diseases children	UCBT	26	4.5 (0.2–17.9)	19% 6/6 HLA-matched 46% 1 antigen-mismatched 31% 2 antigen-mismatched 4% 3 antigen-mismatched
		UBMT	26	4.7 (0.6–17.7)	100% 6/6 HLA-matched
Dalle et al. [5]	Hematologic diseases children	UCBT	36	7.5 (0.1–19.5)	6% 6/6 HLA-matched 50% 1 antigen-mismatched 44% 2 antigen-mismatched
		UBMT	28	6.8 (0.4–1.2)	100% 6/6 HLA-matched
Jacobsohn et al. [6]	ALL children	UCBT	26	3.9 (0.3–11.9)	15.4% 6/6 HLA-matched 38.5% 1 antigen-mismatched 42.3% 2 antigen-mismatched 3.8% 3 antigen-mismatched
		UBMT	23	2.5 (0.3–15.4)	87% 6/6 HLA-matched 13% 1 antigen-mismatched
Laughlin et al. [7]	Hematologic diseases adults	UCBT	150	NR	0% 6/6 HLA-matched 23% 1 antigen-mismatched 77% 2 antigen-mismatched
		UBMT	367	NR	100% 6/6 HLA-matched
Rocha et al. [8]	Acute leukemia adults	UCBT	98	24.5 (15–55)	6% 6/6 HLA-matched 51% 1 antigen-mismatched 39% 2 antigen-mismatched 4% 3 antigen-mismatched
		UBMT	584	32 (15–59)	100% 6/6 HLA-matched
Takahashi et al. [9]	Hematological malignancy adults	UCBT	68	36 (16–53)	0% 6/6 HLA-matched 21% 1 antigen-mismatched 54% 2 antigen-mismatched 25% >3 antigen-mismatched
		UBMT	45	26 (16–50)	87% 6/6 HLA-matched 13% 1 antigen-mismatched
Barker et al. [10]	Hematological malignancy children	UCBT	60	8 (0.5–18)	17% 6/6 HLA-matched 35% 1 antigen-mismatched 48% 2 antigen-mismatched
		UBMT	52	8 (0.6–18)	58% 6/6 HLA-matched 38% 1 antigen-mismatched 4% 2 antigen-mismatched
Eapen et al. [11]	Acute leukemia children	UCBT	503	NR	7% 6/6 HLA-matched 40% 1 antigen-mismatched 53% 2 antigen-mismatched
		UBMT	282	NR	41% 6/6 HLA-matched 59% antigen-mismatched
Atsuta et al. [12]	AML adults	UCBT	173	38 (16–69)	7% 6/6 HLA-matched 20% 1 antigen-mismatched 73% 2 antigen-mismatched
		UBMT	311	38 (16–60)	100% 6/6 HLA-matched
Atsuta et al. [12]	ALL adults	UCBT	114	34 (16–58)	7% 6/6 HLA-matched 22% 1 antigen-mismatched 71% 2 antigen-mismatched
		UBMT	222	32 (16-59)	100% 6/6 HLA-matched