Bone marrow transplantation from haploidentical donors compared to patients receiving bone marrow transplantation from matched unrelated donors

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Abstract

Traditionally the treatment for hematologic malignancy, including adults (>18 years old) has been a bone marrow transplant using either a matched related donor, such as a sibling, or matched unrelated donor using HLA typing. Only 30% of patients have a family member eligible to donate their bone marrow with the remaining 70% of patients left to find an HLA match through the registry[1].Haploidentical bone marrow transplants would provide a treatment option for numerous patients that have children or parents eligible to donate their bone marrow.

Introduction

Due to the fact that HLA markers are inherited, it is more likely that a patient will find a match within their own ethnicity. According to the Be The Match Registry, African American or Black patients have a 23% likelihood of finding a matched adult donor, Asian or Pacific Islander patients have a 41% likelihood of finding a matched adult donor, Hispanic or Latino patients have a 46% likelihood of finding a matched adult donor, and White patients have a 77% likelihood of finding a matched adult donor[4]. This clearly demonstrates the great disparity in the likelihood of finding a life saving donor match for bone marrow transplantation. Haploidentical bone marrow transplants would provide a treatment option for numerous patients that have children or parents eligible to donate their bone marrow while simultaneously expanding the availability of donor matches on the registry itself. The primary concern with the use of haploidentical donor matches in bone marrow transplantation has been surrounding the incidence of acute graft versus host disease, incidence of chronic graft versus host disease, and overall survival.

Methods

A literature search was conducted through PubMed and EBSCO in November 2019. Seven articles were selected based on their relevance to the research topic, study design, measurements, and results.

- Inclusion criteria: allogeneic bone marrow transplant, adult, humans, haploidentical, published in last 6 years.
- Exclusion criteria: relapse after second transplant, meta-analysis, animal models, umbilical cord, sickle cell anemia

Results

Based on the literature review, there is hopeful evidence that bone marrow transplantation from haploidentical donors may have lower incidences of adverse outcomes such as acute GVHD and chronic GVHD, as demonstrated by 6 out of the 7 studies analyzed in this paper. Only one study analyzed out of the 7 studies found patients receiving bone marrow transplantation from haploidentical donors to have higher incidences of acute GVHD and chronic GVHD. The cumulative incidence of grade II-IV acute GVHD was 49% in the haploidentical donor transplantation group and 24% in the identical sibling donor transplantation group. The cumulative incidence of grades III-IV was 15% in the haploidentical donor transplantation group and 4% in the identical sibling donor transplantation group. (Wang et al, 2011). In all of the other 6 studies, both acute GVHD and chronic GVHD incidences were found to be equal or lower when haploidentical donor matches were used for treatment.

Table 1. Comparison of Results

Study	aGVHD	cGVHD	OS
Sun Y et al. (2016)	S	NS	S
Piemontese S et al. (2015)	S	S	S
Raiola AM et al. (2014)	S	S	S
Wang Y et al. (2011)	NS	NS	S
Lorentino F et al. (2018)	S	S	S
Piemontese S et al. (2017)	S	S	S
Basquiera et al. (2019)	S	S	S

Key: aGVHD= acute graft versus host disease, cGVHD= chronic graft versus host disease, OS= overall survival, S= Significant, NS= Not Significant

Discussion

As seen in Table 1, 6 out of 7 of the studies found statistically significant differences between incidences of cGVHD, aGVHD, and OS with overall lower incidences in patients that received transplantation from haploidentical donors. One study by Wang Y et al. found aGVHD and cGVHD to be slightly higher in patients receiving transplantation from haploidentical donors. This was the only study with this finding, all other studies found overall lower incidences of aGVHD and cGVHD. In terms of validity, as seen in Appendix B, all studies did not demonstrate any bias and followed standardized criteria for the definition of aGVHD, cGVHD, and OS. The statistical power of all studies was deemed adequate except for the study by Sun Y et al. which had the lowest sample size at only 87. External validity was also unclear because bone marrow transplantation itself is a complex procedure where pre-existing health status and comorbidities can greatly impact the success of the transplant itself. These studies were unable to control for all of the variables that may exist in the patients themselves prior to transplantation such as presence or absence of hypertension, hyperlipidemia, diabetes, etc. Additionally, limitations across all studies include variation in preconditioning used prior to transplantation of donor stem cell and GVHD regimen following transplantation. These must be controlled for and then compared against one another to ensure that it is the difference in donor and not any difference in preconditioning regimen or post transplant GVHD prophylaxis that is causing the change in aGVHD, cGVHD, or overall survival.

Conclusion

If further research does continue to demonstrate that haploidentical bone marrow transplantation is at least comparable if not even better than matched donor transplantation, the implications would extend as far as decreasing racial difference in transplantation among ethnic minorities. Overall, while there certainly is hope for the future of bone marrow transplantation, further research must be conducted prior to making large changes in protocol.