Published in final edited form as:

Support Care Cancer. 2018 June ; 26(6): 1927–1931. doi:10.1007/s00520-017-4023-y.

Transfusion Practices at End of Life for Hematopoietic Stem Cell Transplant Patients

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Abstract

Purpose—Limited data exist regarding transfusion practices at end of life (EOL) for hematopoietic stem cell transplant (HSCT) patients. The purpose of this study was to examine RBC and platelet transfusion practices in HSCT patients who enrolled or did not enroll in hospice.

Methods—This was a single-center, retrospective chart review in deceased HSCT patients. The primary objective was to determine the mean difference between the last transfusion and death in HSCT patients (n=116) who enrolled or did not enroll in hospice.

Results—Sixteen (14%) and 100 (86%) patients were enrolled in hospice and not enrolled in hospice, respectively. Hospice patients observed a larger mean difference between death and last transfusion (45.9 ± 66.7 vs. 14.6 ± 48.1 days, $p < 0.0001$). A higher amount of platelet, but not RBC, transfusions occurred in patients not enrolled in hospice ($p = 0.04$). The last transfusion that occurred more than 96 hours before death was observed in 12 (75%) and 22 (22%) in hospice and non-hospice patients, respectively. For HSCT patients not enrolled in hospice, 17 patients received a transfusion on the same day of death and 31 patients received the last transfusion 24 hours before death.

Conclusions—Blood transfusion practices differed in HSCT patients enrolled and not enrolled in hospice. For most patients not enrolled in hospice, the last transfusion occurred 24 hours before death. Future efforts should explore if limited access to blood products is a barrier to hospice enrollment for HSCT patients.

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Presented in part at the 2016 ASCO Palliative and Supportive Care in Oncology Symposium, San Francisco, CA, 2016.

CONFLICT OF INTEREST The Authors declare no conflict of interest related to this article.

Keywords

hematologic malignancies; stem cell transplantation; blood transfusion; hospice; end of life

Introduction

Hematopoietic stem cell transplant (HSCT) is a high-risk procedure with treatment goals focusing on a potential cure even in advanced or high-risk disease. Red blood cell (RBC) and/or platelet transfusions are a resource in the HSCT population for symptom management. Although patients feel better with less fatigue, weakness, bleeding, and dyspnea [1–4], there is a lack of conclusive evidence that such treatments provide a benefit based on objective measures in patients at or near end of life (EOL). A recent, retrospective study evaluated RBC transfusions in 31 palliative care unit patients [5]. Clinician and patient-reported subjective benefit was high (>80%), but incremental changes in Likert scale-based measures of symptoms (i.e., Symptom Assessment Score) or physical function (i.e., Australia-modified Karnofsky Performance Status) were observed. Based on the same scale-based measures of symptoms or physical function, deterioration after transfusion was prevalent [5].

Existing evidence also shows a quality gap in EOL care in HSCT patients. Fewer HSCT patients receive palliative or hospice care compared to solid tumor patients [6, 7]. A reluctance to discontinue transfusions at the EOL by patients and/or their clinicians may be a major barrier to hospice enrollment and quality EOL care in HSCT patients [2, 3, 8]. Furthermore, although transfusions are not explicitly excluded from the Medicare hospice benefit, most hospices are unable to provide transfusions due to cost, resource availability, and staff. Although pricing will vary based on region, the mean cost for one unit of RBCs to hospitals is approximately \$211-\$344 [9]. Hospices that are able to maintain a higher daily census are better suited to negotiate prices and absorb cost, but most hospices are not large enough to provide these treatments [10]. In 2008-2009, 40% of 591 U.S. hospices surveyed refused to provide transfusions [11]. A recent review on transfusion practices in the palliative care setting suggested a need for additional clinical, ethical, and infrastructure guidance of such practices given the fixed financial and human resources that are available [12]. The authors also cited an absolute lack of randomized controlled trials or clinical guidelines [12]. This is problematic in that transfusion practices are not standardized and are based from empiric evidence.

In the inpatient palliative care setting, Chang and colleagues demonstrated that almost half of hematological malignancy patients received a RBC and platelet transfusion within the last week of life at their institution [13]. Another study in 73 advanced cancer patients reported a mean number of days between the last transfusion and death was 47 ± 57.1 days, with 14% (n=10) of patients dying within seven days of the last transfusion [14]. We were interested in evaluating such measures in HSCT patients by utilizing a subset of data from a larger retrospective study that examined advanced care planning and palliative care integration in over 600 HSCT patients at our institution [15]. In the aforementioned study, initial and final code status documentation in the outpatient setting was low (3-24%). Allogeneic transplant

and age were significantly associated with greater rates of advance directive and/or Physician Orders for Life-Sustaining Treatment (POLST) completion [15]. In contrast to the current study, the primary purpose was to examine RBC and platelet transfusion practices in deceased HSCT patients who enrolled or did not enroll in hospice. We hypothesized that HSCT patients enrolled in hospice would have lower use of blood transfusions compared to non-hospice patients at or near EOL.

Methods

A retrospective data analysis was conducted in deceased HSCT patients at a single, academic, comprehensive cancer center. Institutional Review Board approval was granted from the Human Research Protections Program at the University of California, San Diego. Data were extracted from a single electronic medical record and included patients who underwent HSCT at UC San Diego from January 2011 to December 2015. These patients included in this analysis were a subset from a larger dataset of 602 HSCT patients whereby advance care planning and palliative care integration was evaluated [15]. From the previous study [15], 118 HSCT patients died during the evaluated study period and were thus utilized for analysis. Inclusion criteria were patients $\geq$ 18 years of age who underwent a HSCT and who died within the data collection period (January 2011 to December 2015).

HSCT data were differentiated between patients who were enrolled in hospice and not enrolled in hospice. Baseline demographics such as age at transplant, sex, type of HSCT, and hematologic malignancy type were collected. Allogeneic HSCTs included match related donor, match unrelated donor, mismatched, cord blood, and haploidentical. Transfusion data were collected from a single electronic medical record and included the date of the last transfusion, transfusion type, and the number of units of RBC and/or platelets administered for each documented transfusion. For each patient who died in hospice, a telephone encounter was conducted to confirm no transfusion(s) were provided to the patient while enrolled in hospice.

To evaluate possible patient demographic differences regarding age, sex, and transplant type between hospice and non-hospice patients, a Wilcoxon-Mann-Whitney test and Fisher's exact test were used, as appropriate. For any statistically significant demographic differences, simple logistic regression or Spearman correlation versus the dependent (outcome) variables were performed. The dependent (outcome) variables were the mean difference between death and last transfusion, mean number of RBC transfusions, and mean number of platelet transfusions. These were further analyzed by the Wilcoxon-Mann-Whitney test between hospice and non-hospice patients. A p-value $\leq$ 0.05 was considered statistically significant. Data were collected on an MS Excel™ spreadsheet and analyzes performed with SAS version 9.3 (SAS Institute, Cary, NC).

Results

Six-hundred and thirty-three HSCTs were performed. As of January 2016, 118 HSCT patients died. One patient was excluded as the patient had no documented transfusion(s) in the electronic medical record and another patient was excluded since his/her last transfusion

was prior to 2011. The final sample size was 116 HSCT patients. One-hundred patients and 16 patients were enrolled versus not enrolled in hospice, respectively. Patient demographics are summarized in Table 1. Age and transplant type were significant between hospice and non-hospice patients ($p < 0.05$, Table 1). Age and transplant type were not statistically significant predictors of RBC and platelet transfusions. There was no association between age ($r = -0.02$; $p = 0.78$), as well as transplant type ($r = -0.16$; $p = 0.08$), versus the ranked difference between death and the last transfusion.

The difference between death and the last transfusion was 45.9 ± 66.5 (mean $\pm$ SD) and 14.6 ± 48.1 days between hospice and non-hospice patients. A larger mean difference was observed in hospice versus non-hospice patients ($p < 0.001$, Table 2). There was no difference between HSCT patients enrolled in hospice versus not enrolled in hospice regarding mean number of RBC transfusions ($p = 0.6$). In contrast, a significantly higher mean number of platelet transfusions in patients not enrolled in hospice was observed ($p < 0.05$, Table 2).

Table 3 summarizes the last transfusion relative to death for HSCT patients. For HSCT patients enrolled in hospice ($n = 16$), the last transfusion that occurred more than 96 hours before death was observed in 12 (75%) patients. For HSCT patients not enrolled in hospice ($n = 100$), the most frequent time point of the last transfusion was at 24 hours before death ($n = 31$, Table 3). Moreover, 17 (17%) of HSCT patients not enrolled in hospice received a last transfusion on the same day of death (Table 3).

Discussion

The primary purpose of this study was to examine RBC and platelet transfusion practices at EOL in HSCT patients who enrolled or did not enroll in hospice. The reported mean RBC and platelets transfused in HSCT patients (Table 2) is consistent with a previous study of patients admitted to an inpatient palliative care setting whereby the majority of patients received 2 units of blood (range: 1-6) [16]. The mean difference between death and the last transfusion was 45.9 ± 66.5 days for HSCT patients enrolled in hospice. This result parallels a previous study in 73 advanced cancer patients in the inpatient palliative care setting that reported a mean difference of 47 ± 57.1 days [14]. Upon evaluation in non-hospice patients, the difference between death and the last transfusion was shorter (14.6 ± 48.1 days) and significantly less compared to hospice patients ($p < 0.0001$, Table 2). To the best of our knowledge, this is a novel finding. Additional prospective studies with a robust sample size are needed to confirm findings as well as examine the impact of quality of life measures on the evaluated outcome variables in this study.

Regarding the timing of last transfusion before death, 12 (75%) of HSCT patients enrolled in hospice received a last transfusion that occurred greater than 96 hours before death. In contrast, the most common time to receive a last transfusion for HSCT patients not enrolled in hospice was one day before death ($n = 31$, Table 3). Furthermore, 17 versus zero patients received a last transfusion on the same day of death in non-hospice versus hospice patients, respectively. Comparing these findings to other studies is challenging. Two previous studies reported a last transfusion received within 7 days of death of 14% and 33-48% of patients [13, 14]. However, no results were reported regarding the additional differentiation as

described in the current study regarding last transfusion on same day of death, 24 hours before death, and other defined time periods (Table 3).

This was a retrospective analysis with a small sample size of HSCT patients who were enrolled in hospice. We acknowledge the inherent limitations of a retrospective study design and small sample size adversely affecting statistical power. This study was conducted at a single academic medical center and may not reflect general practices at other institutions. In addition, this study was unable to determine transfusion clinical benefit as objective and subjective measures were not recorded.

Transfusion use may be a barrier to preventing HSCT patient access to hospice. The cause of the shorter time to last transfusion in non-hospice patients cannot be determined based on the study design. However, we speculate that HSCT patients may be more willing to enroll in hospice if transfusion requirements are low and/or palliative benefit from blood products is minimal. Active palliative transfusion requirements to prevent spontaneous bleeding or to target a symptom (e.g., dyspnea, chest pain) may prevent HSCT patients from enrolling in hospice. Alternatively, this may reflect that HSCT patients enrolled in hospice are more willing to forgo transfusions despite ongoing transfusion needs. Yet, as data in hematologic malignancy and HSCT EOL care continues to grow, we continue to recognize how unique hematologic malignancy patients are from those with solid tumors [17]. Not only do HSCT patients have unique treatments and related side effects, but they have different symptom clusters and thus different palliative and hospice needs. Perhaps the next step in bridging the gap between palliative and hospice care in HSCT patients is the expansion of the hospice benefit to permit blood transfusions necessary to palliative symptoms highly prevalent in HSCT patients. We aim to work collectively with other researchers in this area to explore the barriers to hospice enrollment for HSCT patients and ultimately advocate for policy change to promote the optimal care of these patients.

Acknowledgments

Dr. Roeland's research is supported by a UC San Diego Clinical Translational Research Institute KL2 Career Development Award (#KL2TR001444), and Cambia Health Foundation Sojourns Scholars Leadership Program

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Table 1

Patient characteristics of deceased HSCT patients (n=116).

Patient characteristics	Enrolled in hospice (n=16)	Not enrolled in hospice (n=100)	Total (n=116)	p-value ^a
Age (mean± SD, years)	60.9 ± 12.3	53.4 ± 13.2	54.4 ± 13.3	p<0.05
Sex				
Female	3	46	49	p=0.06
Male	13	54	67	
Transplant type				
Autologous	12	29	41	p<0.05
Allogeneic	4	71	75	
Hematologic malignancy type				
Acute myelogenous leukemia	1	26	27	
Non-Hodgkin's lymphoma	5	22	27	
Multiple myeloma	6	13	19	
Myelodysplastic syndrome	0	15	15	
Acute lymphocyte leukemia	1	11	12	
Hodgkin's lymphoma	1	5	6	
Aplastic anemia	0	3	3	
Chronic myelogenous leukemia	1	1	2	
Myelofibrosis	0	2	2	
Other	1	2	3	

^a p-value based on analyzes between hospice versus non-hospice patients

Table 2

Mean difference between death and last transfusion and mean number of red blood cells and platelets transfused in HSCT patients.

Variable	Enrolled in hospice n=16	Not enrolled in hospice n=100	p-value
Mean difference between death and last transfusion, (mean $\pm$ SD, days)	45.9 $\pm$ 66.5	14.6 $\pm$ 48.1	p<0.0001
Mean number of red blood cells transfused, (mean $\pm$ SD, units)	0.7 $\pm$ 0.8	0.7 $\pm$ 1	p=0.6
Mean number of platelets transfused, (mean $\pm$ SD, units)	0.8 $\pm$ 0.8	1.2 $\pm$ 1	p<0.05

Table 3

Last transfusion relative to death for HSCT patients enrolled (n=16) or not enrolled in hospice (n=100).

Timing of last transfusion before death	Enrolled in hospice (n, %)	Not enrolled in hospice (n, %)
Last transfusion occurred on same day of death	0	17 (17%)
Last transfusion occurred at 24 hours before death	1 (6%)	31 (31%)
Last transfusion occurred 25 to 48 hours before death	0	10 (10%)
Last transfusion occurred 49 to 72 hours before death	0	12 (12%)
Last transfusion occurred 73 to 96 hours before death	3 (19%)	8 (8%)
Last transfusion occurred > 96 hours before death	12 (75%)	22 (22%)