research paper

haematologica 2002; 87:292-298
http://www.haematologica.ws/2002_03/292.htm

Predicting factors for admission to an intensive care unit and clinical outcome in pediatric patients receiving hematopoietic stem cell transplantation

MIGUEL ANGEL DIAZ,* MARTA G.VICENT,* MARTA PRUDENCIO,* FRANCISCO RODRIGUEZ,* CATALINA MARIN,° ANA SERRANO,° JULIAN SEVILLA,* JUAN CASADO,° LUIS MADERO*

*Department of Pediatrics, Division of Pediatric Hematology/Oncology, "Niño Jesus" Children's Hospital, Madrid; °Department of Pediatrics, Pediatric Intensive Care Unit, "Niño Jesus" Children's Hospital, Madrid, Spain

Correspondence: Miguel Angel Diaz MD, Department of Pediatrics, Division of Pediatric Hematology-Oncology, BMT Unit, "Niño Jesus" Children's Hospital, Menendez Pelayo 65, 28009 Madrid, Spain.
Phone: international +34.9.15035938.
Fax: international +34.9.15035902. E-mail: mtcanto@jazzfree.com

Background and Objectives. In children, hematopoietic stem cell transplantation (HSCT) implies life-threatening complications and some patients need admission to a pediatric intensive care unit (PICU). Few studies have been reported analyzing this issue in a pediatric population and most focused on risk factors predicting survival following PICU admission.

Design and Methods. We examined data of 240 pediatric patients who received HSCT (100 allogeneic and 140 autologous) in order to ascertain the incidence of life-threatening complications requiring PICU admission, the contributing risk factors and the patients' long-term survival.

Results. Forty-two (17.5%) (25 males and 17 females) of the transplanted children were admitted to the PICU. Twenty-nine of them (69%) had received an allogeneic transplant and thirteen (31%) an autologous transplant. Their median age was 7 years (range; 1-18). The most frequent reason for admission was respiratory failure (37 cases, 88%). The overall probability of developing complications requiring PICU admission was 21.2% (33.5% for allogeneic transplantation and 10.1% for patients receiving autologous grafts, p=0.0002). On univariate analysis, only the type of transplantation was significantly associated with PICU admission (allogeneic vs autologous RR 1.92, 95% CI: 1.46-2.53)(p = 0.0001). In allogeneic transplants, only the underlying disease (non-malignant) and the status of disease at transplantation within malignant diseases (advanced phase) were pre-transplant variables associated with PICU admission. Post-transplantation risk factors were presence of graft-versus-host disease (GvHD) (p = 0.046) and its grade (II-IV) (p = 0.002), as well as the presence of multiorgan dysfunction during the early post-infusion phase especially when the lung was the first failing organ (p = 0.0001). However, on multivariate analysis, only severe GvHD was statistically significant. In the autologous transplantation group, the underlying disease (solid tumor, p = 0.07) and status at transplantation (advanced phase, p = 0.0029) were the only risk factors. In the post-transplant phase, patients who develop multiorgan dysfunction during the neutropenic period and those with engraftment syndrome had an increased risk of requiring critical care. The overall event-free survival (EFS) at 3 years was 15.3%, (18.4% for autologous transplant recipients and 13.7% for those receiving an allogeneic graft, p = 0.4). Using a Cox regression model, multiorgan failure (MOF) present at admission was the only variable that had a negative impact on EFS (4.28% vs 35.71% for patients with no MOF, p = 0.016).

Interpretation and Conclusions. Despite high mortality, intensive care support can be beneficial for pediatric patients with life-threatening complications following HSCT. However, for patients with multiorgan failure involving the lungs, admission to the PICU should be avoided.

Key words: PICU admission, HSCT, GvHD, engraftment syndrome, mechanical ventilation, interstitial pneumonia, diffuse alveolar hemorrhage, children

Hematopoietic stem cell transplantation (HSCT) from bone marrow, peripheral blood or cord blood is the only curative treatment for some pediatric patients with malignant and non-malignant conditions. However, this procedure may cause life-threatening complications especially in the early post-transplant phase. Therefore, some patients need admission to a spe-

cialized pediatric intensive care unit (PICU). To date few studies have been reported analyzing this issue in a pediatric population and they have mainly focused on risk factors predicting survival following PICU admission. To the best of our knowledge, there are only two reported studies analyzing associations between pre-transplant and post-transplant factors with PICU admission and factors predicting long-term survival.[1,2] We examined our experience on pediatric patients who received HSCT in order to ascertain the incidence of life-threatening complications requiring admission to a PICU, the contributing risk factors and the patients' long-term survival.

Design and Methods

Study design and patients' characteristics

All patients who underwent a first allogeneic or autologous hematopoietic transplantation at the Niño Jesus Children Hospital between November 1993 and January 2001 (n=240) were included in our study. As of June 2001, the minimal follow-up period from time of transplant was 6 months. All data were retrieved from clinical information collected prospectively during the transplantation procedures. Patients' characteristics, including demographic data, underlying diseases, their status at transplant, source of hematopoietic stem cells and HSCT-related parameters are shown in Table 1. Conditioning regimens varied according to underlying disease and type of transplantation. In general, patients over 5 years old with acute lymphoblastic leukemia (ALL) were conditioned with total body irradiation (TBI)(12 Gy fractionated in 6 sessions) plus cyclophosphamide (120 mg/kg total dose in 2 days). ALL patients under five years old and acute myelogenous leukemia patients were conditioned with busulphan (BU)(16 mg/kg total dose in 4 days) and cyclophosphamide (120 mg/kg total dose in 2 days). Most patients with solid tumors received busulphan-containing regimens.[3] In the autologous setting, mobilized peripheral blood progenitor cells were used as the sole source of stem cells. Details of the mobilization protocols and collection procedures used have been previously reported elsewhere.[4]

Graft-versus-host disease (GvHD) prophylaxis

For patients receiving allogeneic transplants, different GvHD prophylaxis regimens were used according to institutional protocols or co-operative trials. GvHD was diagnosed and graded according to standard criteria.[5]

Table 1. Characteristics of 240 hematopoietic stem cell recipients.

	Autologous transplant recipients, n=140 (%)	*Allogeneic transplant recipients, n=100 (%)*
Age years		
median (range)	8 (1-18)	7 (1-18)
Gender		
Male	89 (63)	58 (58)
Female	51 (37)	42 (42)
Diagnosis		
ALL	17 (12)	51(51)
AML	18 (13)	9 (9)
CML		15 (15)
HD	5 (3.5)	1 (1)
NHL	12 (9)	1 (1)
Solid tumors	88 (63)	
Immunodeficiency		5 (5)
Osteopetrosis		5 (5)
Severe aplastic anemia		5 (5)
Adrenoleukodystrophy		6 (6)
Thalassemia		1 (1)
Histiocytosis		1 (1)
Disease status at transplantation		
Early	66 (47)	29 (39)
Intermediate	30 (21)	21 (28)
Advanced	44 (32)	25 (33)
Source of stem cells		
Bone marrow		40 (40)
Peripheral blood	140 (100)	44 (44)
Cord blood		16 (16)
Type of allogeneic transplantation		
Related identical HLA		54 (54)
Related non-identical HLA		12 (12)
Unrelated identical HLA		19 (19)
Unrelated non-identical HLA		15 (15)
Conditioning		
Cy-TBI	11 (8)	34(34)
BuCy	30 (21)	42 (42)
BuMel	48 (34)	1 (1)
BuTh	16 (11)	
Other	35 (25)	23 (23)
GvHD prophylaxis		
Csa+MTX		58 (58)
Csa+ PRD		16 (16)
Csa		26 (26)
Cytokines post-infusion		
Yes	104 (74)	56 (56)
No	36 (26)	44 (44)

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CML, chronic myeloid leukemia, HD, Hodgkin's disease; NHL, non-Hodgkin's lymphoma; Cy, cyclophosphamide; TBI, total body irradiation; Bu, busulphan; Mel, melphalan; Th, thiotepa; Csa, cyclosporin A; MTX, methotrexate; PRD, prednisone.

Definitions

Only patients needing critical care such as mechanical ventilation for respiratory failure or acute neurologic events or multiorgan failure or hemodynamic support with inotropic drugs other than dopamine and dobutamine or dialysis for oliguric renal failure were admitted to a PICU. Organ dysfunction and failure were defined according to criteria previously reported by other authors.[6,7] Engraftment syndrome was defined as the presence of fever, rash, and evidence of respiratory dysfunction during the peri-engraftment period in the autologous setting.[8]

Statistical analysis

The patients' demographic data, disease and HSCT-related variables were analyzed for association with PICU admission by univariate and multivariate analysis using a logistic regression model. The probabilities of PICU admission and event-free survival (EFS) after this were estimated by the Kaplan-Meier method.[9] Time was censored at relapse or death or last follow-up if none of the previous events ocurred. The log-rank test was used to compare survival curves. Statistical analyses were carried out for the whole group and separately for autologous and allogeneic transplant recipients. Results are presented as relative risk (RR) and 95% confidence intervals (CI). For multivariate analysis, parameters with a probability higher than 0.1 were excluded from the regression analysis.

Results

Patients and reasons for PICU admission

Forty-two (17.5%) of a total of 240 transplanted patients were admitted to a PICU. Twenty-nine of them (69%) had undergone allogeneic transplantation and thirteen (31%) autologous transplantation. The clinical characteristics of these patients are outlined in Table 2. Their median age was 7 years (range; 1-18). The main reason for admission was respiratory failure (37 cases, 88%). Thirteen of them (35%) had interstitial pneumonia (CMV was isolated by bronchoalveolar lavage (BAL) in 6 cases, HHV 6 in two, *Pneumocystis carinii* in one; four cases had idiopathic disease). A diagnosis of diffuse alveolar hemorrhage (DAH) was made in ten cases (27%). In five cases (13.5%) a fungal infection was documented by BAL (three *Aspergillus fumigatus* and two *Candida albicans*). *Mycobacterium tuberculosis* was isolated in one case. In eight (22%) an etiologic diagnosis could not be established.

Table 2. Characteristics of 42 patients admitted to the PICU after HSCT.

	Autologous transplant recipients, n=13 (%)	*Allogeneic transplant recipients, n=29 (%)*
Age years		
median (range)	9 (1-17)	5 (1-18)
Gender		
male	8 (61.5)	17 (59)
female	5 (38.5)	12 (41)
Diagnosis		
Acute lymphoblastic leukemia	3 (23)	12 (41)
Acute myeloblastic leukemia		3 (10)
Chronic myelogenous leukemia		1 (3)
Hodgkin's disease		1 (3)
Severe combined immunodeficiency		4 (14)
Osteopetrosis		2 (6)
Severe aplastic anemia		3 (10)
Adrenoleukodystrophy		2 (6)
Histiocytosis		1 (3)
Central nervous system tumors	4 (31)	
Ewing's sarcoma	2 (15)	
Wilms' tumor	1 (8)	
Rhabdomyosarcoma	2 (15)	
Neuroblastoma	1 (8)	
Type of allogeneic transplantion		
Related identical HLA		12 (41)
Related non-identical HLA		6 (21)
Unrelated identical HLA		7 (24)
Unrelated non-identical HLA		4 (14)
GvHD		20 (69)
Reasons for admission		
Respiratory failure/MV	13 (100)	24 (83)
Refractory shock		2 (7)
Renal failure/dialysis		2 (7)
Coma		1 (3)
Days to admission		
median (range)	14 (2-45)	20 (6-600)

Factors predicting PICU admission

The overall probability of developing complications requiring PICU support was 21.2±3.7%. This probability was 33.5±5.4% for patients who had undergone allogeneic transplantation and 10.1±2.5% for patients in the autologous setting ($p = 0.0002$) (Figure 1). On univariate analysis only type of transplantation was significantly associated with PICU admission; patients receiving allogeneic transplants had a RR of 1.92 (95% CI: 1.46-2.53) ($p = 0.0001$). Among this group of patients, underlying disease (non-malignant), and status of disease at transplantation within malignant diseases (advanced phase) were pretransplant variables associated with PICU admission (Table 3).

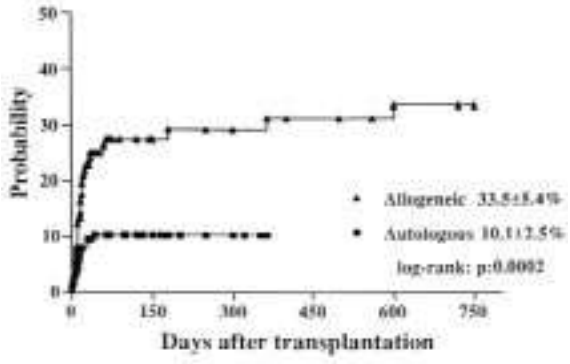

Figure 1. Probability of PICU admission according to type of transplantation.

Age, gender, conditioning, source of stem cell, type of donor, and GvHD prophylaxis used were not significantly associated with PICU support (data not shown). Post-infusion factors associated with a high risk of PICU admission were developing GvHD ($p = 0.046$) and its grade (III-IV) ($p = 0.002$) and the presence, during the early post-infusion phase, of multiorgan dysfunction syndrome especially when the lung was the first failing organ ($p = 0.0001$) (Table 3). On multivariate analysis only severe GvHD was statistically significant. Among patients undergoing autologous transplantation underlying disease (solid tumor, $p = 0.07$), and status at transplantation (advanced phase, $p = 0.0029$) were risk factors with statistical value.The preparative regimen used and a specific diagnosis within solid tumor patients did not increase the risk of needing PICU support. In the post-infusion phase, patients who developed multiorgan dysfunction during the neutropenic period and those with engraftment syndrome had an increased risk of requiring critical care (Table 3).

Clinical outcome and survival after PICU admission

A total of thirteen [9 (31%) out of the 29 patients in the allogeneic group and 4 (31%) out of the 13 patients in the autologous group] were discharged from the PICU. For 29 patients in the allogeneic group, need for mechanical ventilation had a negative impact on discharge from PICU. So, 5 (21%) out of 24 intubated patients were discharged compared to 4 out of 5 not receiving mechanical ventilation support ($p = 0.02$). The median number of days of mechanical ventilation was 13 (range 1-40). However, the need for mechanical ventilation (MV) did not influence long-term survival after PICU admission. The one year EFS was 20±17.8% for patients with no MV compared to 16.6±7.6% for patients on MV (p = NS). In addition three years later, 4 out of 5 patients discharged following extubation are alive and disease-free compared to none of four patients who did not need intubation. At the time of analysis 24 out of 29 (83%) allogeneic patients had died. The causes of death for these patients were as follows: GvHD 8 patients (33.3%), ADRS 8 patients (33.3%), refractory shock 3 patients (12.5%), multiorgan failure 2 patients (8%), leukemia relapse 2 patients (8%) and veno-oclusive disease of liver one patient (4%). All of the 13 patients admitted to the PICU in the autologous

Table 3. Factors predicting PICU admission.

	Univariate			*Multivariate*		
	RR	*95% CI*	*p*	*RR*	*95% CI*	*p*
Allogeneic transplant						
Underlying disease	2.36	1.33-4.19	0.0084			
Status at transplantation	9.66	1.35-69.14	0.0017			
GvHD (yes)	1.98	0.97-4.03	0.0460			
GvHD (III-IV)	8.50	1.23-58.39	0.0020	15.95	2.12-120.67	0.01
Multiorgan dysfunction syndrome	38.67	5.47-273.2	0.0001			
Lung as 1st organ failure	1.62	1.03 - 2.53	0.0043			
Autologous transplant						
Underlying disease	1.99	0.58-6.61	0.070			
Status at transplantation	3.06	1.06-8.86	0.0029	9.97	1.15-84.77	0.01
Engraftment syndrome	7.66	2.74-21.42	0.0002	14.92	3.53-63.11	0.0002
Multiorgan dysfunction syndrome during neutropenia period	17.07	6.61-44.04	0.0001			

group needed intubation and at the time of analysis 2 out of 4 patients discharged were alive and disease-free. Eleven patients (85%) had died. The causes of death for these patients were as follows: multiorgan failure 8 patients (73%), secondary graft failure 2 patients (18%) and ADRS one patient (9%). The probability of EFS at 3 years for the whole group was 15.38±5.7%, being 18.4±11.5% for autologous transplant recipients and 13.7±6.4% for allogeneic transplant recipients ($p = 0.4$). Using a Cox regression model, MOF present at admission was the only variable that had a negative impact on EFS (4.28±3.13% vs 35.71±12.8% for patients with no MOF (hazard ratio 0.42, 95% CI 0.20-0.85, $p = 0.016$).

Discussion

Hematopoietic transplantation, especially in the allogeneic setting, continues to be associated with a high rate of clinical complications. Some of these complications need to be managed with critical care in a specialized ICU. Many reported studies in adults have shown a poor overall outcome for patients admitted to an ICU.[10-14] During the last decade very few studies have been conducted regarding risk factors for PICU admission and prognostic factors affecting survival following admission in pediatric patients undergoing HSCT.[1,2, 15-17] In fact, only two large series analyzing both subjects have been published.[1,2] This kind of study should help clinicians to make a decision on whether a patient should be admitted to PICU when a life-threatening complication is present or not. In this retrospective study, we present the clinical factors that predicted PICU admission and outcome in 240 pediatric patients who underwent HSCT at a single institution during the last seven years. Our results regarding the incidence of patients who required critical care are similar to those previously reported by others.[1,2,15-17] Analyzing pre-transplant variables for the whole transplanted group, we found that underlying disease had a significant influence on risk of needing PICU admission. Patients with immune deficiency, metabolic disorders and solid tumors had a higher rate of PICU admission and mechanical ventilation than patients with other malignant diseases. This finding concurs with those of the largest series reported.[1] Warwick *et al.*[1] found that a diagnosis of immune deficiency, metabolic disease or neuroblastoma was associated with an increased risk of requiring MV. As pointed out by them, pre-existing infectious conditions, aggressive chemotherapy received before transplantation and the need of intubation for upper airway control during conditioning in some metabolic disorders are reasons that might explain this association. However, Crawford *et al.*,[10] found an increased risk of requiring MV in patients with underlying malignancies, especially those with advanced disease at the time of transplantation. In our series, advanced phase at transplantation, both in the allogeneic and autologous settings, among patients with malignancies was also associated with an increased risk of admission for critical care. Moreover, in the autologous transplantation group, advanced disease was an independent risk factor for critical care support in the multivariate analysis. Other authors did not find any association between underlying disease and critical care requirements.[2] Regarding the type of transplantation, patients in the allogeneic transplant group had an almost 2-fold higher risk than patients in the autologous group. Among the allogeneic transplant group, the source of stem cells, CMV status, conditioning used, and HLA disparity were not associated with a significant risk of requiring PICU support. The presence of acute GvHD and its grade and developing multiorgan dysfunction syndrome, especially when the lung was the first failing organ, were post-transplant events with increased risk. However, severe acute GvHD was the only post-transplant event with an independent risk in the multivariate analysis. Other post-infusion events such as multiorgan dysfunction syndrome did not reach statistical significance in multivariate analysis, likely because patients with severe acute GvHD had a higher incidence of multiorgan dysfunction syndrome than patients with moderate or no GvHD. This finding is in keeping with those of other reported pediatric series.[1] An increase in pulmonary complications with higher grades of acute GvHD, especially viral pneumonitis and progressive airway obstruction, have been reported.[18,19]

Among patients receiving an autologous transplant, engraftment syndrome as a post-infusion event was correlated with higher risk of multiorgan dysfunction especially pulmonary complications and PICU admission for mechanical ventilation. Engraftment syndrome occurs as result of release of tumor necrosis factor and other cytokines during hematopoietic engraftment. This syndrome results clinically in hypoalbuminemia, weight gain, bilateral pulmonary infiltrates, hypoxia and non-infectious fever during the recovery phase of hematopoiesis.[8] Engraftment syndrome has been described as a cause of respiratory failure needing mechanical ventilation[8] and has been associated with breast cancer,[20] number of hematopoietic cells infused,[21,22]

mobilized peripheral blood as source of stem cells for autologous transplantation[21] and use of granulocyte colony-stimulating factor (G-CSF) after infusion to accelerate neutrophil recovery.[22] However, there are no reported studies evaluating predicting factors for engraftment syndrome in pediatric patients undergoing autologous transplantation. Our preliminary results show that a diagnosis of solid tumor, especially neuroblastoma and Ewing's sarcoma family tumors, and mobilization with high doses of G-CSF might be associated with an increased risk of engraftment syndrome (*data not shown*). Respiratory failure was the main cause of PICU admission and 37 (88%) patients admitted needed mechanical ventilation which represents a similar proportion to that in other pediatric series.[2] After PICU admission it is very important to identify patient characteristics that are predictive factors not only for successful extubation but also long-term survival. In fact, rates of successful extubation may be as high as 40-46%.[1] Our results regarding successful extubation are similar to other previously reported ones[1,2] but we were unable to find pre- or post-transplantation variables related to successful extubation. Warwick *et al.*[1] found that successful extubation was correlated with underlying disease and the presence of GvHD. Previous pediatric series[1,2] recorded a poor outcome among patients who needed MV compared to among those who did not. In fact, poor short- and long-term survival rates have been reported in children who needed intubation after bone marrow transplantation.[15,23] However, in this study, the need for mechanical ventilation did not influence long-term survival after PICU admission, probably because of the negative influence of other later events such as relapsing disease, secondary graft failure or chronic GvHD. In our series, long-term survival estimated from the time of PICU admission was not affected by duration of mechanical ventilation, successful extubation, type of transplant or the presence of GvHD. However, the presence of multiorgan failure including respiratory failure at time of admission resulted in a worse event-free survival. In fact, this survival rate (<5%) is near to the chance of success (1%) that some investigators have proposed as a quantitative approach to medical futility[24] and identifies a poor prognostic features among patients requiring mechanical ventilation following HSCT, as has been recently published by others.[25]

In conclusion, our data suggest that despite high mortality, intensive care support can be beneficial for pediatric patients with life-threatening complications following HSCT. This life-sustaining measure should be established as early as possible since some delay could be critical to the final outcome. However, for patients with multiorgan failure including respiratory failure the always hard decision of not admitting a patient to the PICU seems to be justified. This point should be explained to parents before starting hematopoietic transplantation.

Contributions and Acknowledgments

MAD and MGV were the main investigators, designed the study and wrote the paper. MP, FR, AS, CM and JS collected, analyzed and interpretated data and critically reviewed the literature along with main investigators. LM and JC critically revised the study and all authors approved the revised version.

Disclosures

Conflict of interest: none.

Redundant publications: no substantial overlapping with previous papers.

References

1. Warwick AB, Mertens AC, Shu XO, Ramsay NK, Neglia JP. Outcomes following mechanical ventilation in children undergoing bone marrow transplantation. Bone Marrow Transplant 1998; 22:787-94.
2. Díaz de Heredia C, Moreno A, Olive T, Iglesias J, Ortega JJ. Role of the intensive care unit in children undergoing bone marrow transplantation with life-threatening complications. Bone Marrow Transplant 1999; 24:163-8.
3. Díaz MA, G. Vicent MG, Madero L. High-dose busulfan/melphalan as conditioning for autologous PBPC transplantation in pediatric patients with solid tumors. Bone Marrow Transplant 1999; 24:1157-9.
4. Díaz MA, Villa M, Alegre A, Lamana ML, de la Vega A, Granda A, et al. Collection and transplantation of peripheral blood progenitor cells mobilized by G-CSF alone in children with malignancies. Br J Haematol 1996; 94:148-54.
5. Przepiorka D, Weisdorf D, Martin P, Klingemann HG, Beatty P, Hows J, et al. 1994 Consensus Conference on Acute GVHD Grading. Bone Marrow Transplant 1995; 15: 825-8.
6. Haire WD, Ruby EI, Stephens LC, Reed E, Tarantolo SR, Pavletic ZS, et al. A prospective randomized double-blind trial of antithrombin III concentrate in the treatment of multiple-organ dysfunction syndrome during hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 1998; 4:142-50.
7. Wilkinson JD, Pollack MM, Glass NL, Kanter RK, Katz RW, Steinhart CM. Mortality associated with multiple organ system failure and sepsis in paediatric intensive care unit. J Pediatr 1987; 111:324-8.
8. Lee CK, Gingrich RD, Hohl RJ, Ajram KA. Engraftment syndrome in autologous bone marrow and peripheral stem cell transplantation. Bone Marrow Transplant 1995; 16:175-82.
9. Kaplan EL, Meier P. Nonparametric estimation from in-

complete observations. J Am Stat Assoc 1958; 53:457-81.
10. Crawford SW, Schwartz DA, Petersen FB, Clark JG. Mechanical ventilation after marrow transplantation. Risk factors and clinical outcome. Am Rev Respir Dis 1988; 137:682-7.
11. Crawford SW, Petersen FB. Long-term survival from respiratory failure after marrow transplantation for malignancy. Am Rev Respir Dis 1992; 145:510-4.
12. Paz HL, Crilley P, Weinar M, Brodsky I. Outcome of patients requiring medical ICU admission following bone marrow transplantation. Chest 1993; 104:527-31.
13. Faber-Langendoen K, Caplan AL, McGlave PB. Survival of adult bone marrow transplant patients receiving mechanical ventilation: a case for restricted use. Bone Marrow Transplant 1993; 12:501-7.
14. Torrecilla C, Cortes JL, Chamorro C, Rubio JJ, Galdos P, Dominguez de Villota E. Prognostic assessment of the acute complications of bone marrow transplantation requiring intensive therapy. Intensive Care Med 1988; 14:393-8.
15. Todd K, Wiley F, Landaw E, Gajewski J, Bellamy PE, Harrison RE, et al. Survival outcome among 54 intubated pediatric bone marrow transplant patients. Crit Care Med 1994; 22:171-6.
16. Hayes C, Lush RJ, Cornish JM, Foot AM, Henderson J, Jenkins I, et al. The outcome of children requiring admission to an intensive care unit following bone marrow transplantation. Br J Haematol 1998; 102:666-70.
17. Schneider DT, Lemburg P, Sprock I, Heying R, Gobel U, Nurnberger W. Introduction of the oncological pediatric risk of mortality score (O-PRIMS) for ICU support following stem cell transplantation in children. Bone Marrow Transplant 2000; 25:1079-86.
18. Krowka MJ, Rosenow EC 3rd, Hoagland HC. Pulmonary complications of bone marrow transplantation. Chest 1985; 87:237-46.
19. Sommer SE, Emanuel D, Groeger JS, Carlon GC. Successful management of CMV pneumonia in a mechanically ventilated patient. Chest 1991; 100:856-8.
20. Moreb JS, Kubilis PS, Mullins DL, Myers L, Youngblood M, Hutcheson C. Increased frequency of autoaggression syndrome associated with autologous stem cell transplantation in breast cancer patients. Bone Marrow Transplant 1997; 19:101-6.
21. Edenfield WJ, Moores LK, Goodwin G, Lee N. An engraftment syndrome in autologous stem cell transplantation related to mononuclear cell dose. Bone Marrow Transplant 2000; 25:405-9.
22. Ravoet C, Feremans W, Husson B, Majois F, Kentos A, Lambermont M, et al. Clinical evidence for an engraftment syndrome associated with early and steep neutrophil recovery after autologous blood stem cell transplantation. Bone Marrow Transplant 1996; 18:943-7.
23. Nichols DG, Walker LK, Wingard JR, Bender KS, Bezman M, Zahurak ML, et al. Predictors of acute respiratory failure after bone marrow transplantation in children. Crit Care Med 1994; 22:1485-91.
24. Schneiderman LJ, Jecker NS, Jonsen AR. Medical futility: its meaning and clinical implications. Ann Intern Med 1990; 112:949-54.
25. Bach PB, Schrag D, Nierman DM, Horak D, White P Jr, Young JW, et al. Identification of poor prognostic features among patients requiring mechanical ventilation after hematopoietic stem cell transplantation. Blood 2001; 98:3234-40.

Peer Review Outcomes

Manuscript processing

This manuscript was peer-reviewed by two external referees and by Prof. Franco Locatelli who acted as an Associate Editor. The final decision to accept this paper for publication was taken jointly by Prof. Locatelli and the Editors. Manuscript received October 8, 2001; accepted December 18, 2001.

What is already known on this topic

This study provides information on factors which predict admission into a pediatric intensive care unit of children given hematopoietic stem cells.

What this study adds

This paper can contribute to a better definition of the outcome of these patients, identifying children who despite an intensive approach have a negligible probability of survival.

Potential implications for clinical practice

Few studies focused on children have been published on this issue and this manuscript adds an useful piece of information.

Franco Locatelli, Associate Editor