Utilisation of Therapeutic Plasma Exchange in Treating Transplant-Associated Thrombotic Microangiopathy: A Single Centre Retrospective Cross-Sectional Cohort Study

Wong YS[1], Sharifah Shahnaz SAK[1], Ho KW[1], Ong TC[1], Tan SM[1]
[1]Department of Haematology, Ampang Hospital, Selangor, Malaysia.

Introduction

Transplant-associated thrombotic microangiopathy (TA-TMA) is an established complication of allogeneic haematopoietic stem cell transplantation (HSCT) that results in significant morbidity and mortality. Despite it being a recognised post-transplant sequelae, there are no well defined treatment algorithms to guide the management of this condition. The objectives of this study are to identify the clinical outcomes of allogeneic HSCT patients who have undergone therapeutic plasma exchange (TPE) for the treatment of TA-TMA, and to determine certain therapy related factors such as the median duration of treatment with TPE.

Methodology

The electronic medical records of all allogeneic haematopoietic stem cell transplantation patients with TA-TMA in Ampang Hospital diagnosed over a 5 year period (January 2017 to December 2021) who were treated with therapeutic plasma exchange were reviewed. Collected data consisted of patients' demographics, clinical characteristics, therapeutic interventions and clinical outcomes. TA-TMA was diagnosed according to the criteria proposed by the International Working Group of the European Group for Blood and Bone Marrow Transplantation (IWG-TMA, 2007), with the notable exception of serum haptoglobin concentration due to the lack of availability of this investigation in our institution. The diagnostic criteria we employed included: (1) increased percentage (>4%) of schistocytes in peripheral blood; (2) de novo, prolonged or progressive thrombocytopenia (platelet count less than $50x10^9$/L or a 50% or greater decrease from previous counts); (3) sudden and persistent increase in LDH; (4) decrease in hemoglobin concentration or increased red blood cell transfusion requirement. The date of TA-TMA diagnosis was recorded when all the above criteria were met.

Results

Table 1: Patient and Transplant Related Characteristics

Characteristic	Total subjects (n=25)
Age at transplant, years	34.8
Gender, n (%)	
Male	14 (56%)
Female	11 (44%)
Underlying haematological diagnosis, n (%)	
Acute myeloid leukaemia	14 (56%)
Acute lymphoblastic leukaemia	8 (32%)
Hodgkin and Non-Hodgkin lymphoma	3 (12%)
Intensity of conditioning used, n (%)	
Myeloablative	23 (92%)
Reduced intensity	2 (8%)
Type of conditioning used, n (%)	
Bu/Cy	9 (36%)
Flu/Bu	4 (16%)
Flu/Cy	1 (4%)
Flu/Mel	2 (8%)
TBI/Flu	2 (8%)
TBI/Bu	4 (16%)
TBF	3 (12%)
GVHD prophylaxis used, n (%)	
CSA/MMF	15 (60%)
CSA/MTX	10 (40%)

Table 2: TA-TMA and TPE Related Characteristics

Characteristic	Total subjects (n=25)
TA-TMA occurrence, n (%)	
Early TA-TMA (within 100 days post-HSCT)	20 (80%)
Late TA-TMA (after 100 days post-HSCT)	5 (20%)
Concomitant transplant related morbidity, n (% of total cases)	
VOD/SOD	1 (4%)
Graft versus host disease	14 (56%)
CMV reactivation	19 (76%)
Bacterial infection	8 (32%)
Fungal infection	3 (12%)
Organ involvement, n (% of total cases)	
Renal	18 (72%)
Central nervous system	8 (32%)
Pulmonary	7 (28%)
Gastrointestinal	8 (32%)
Time to TPE from TA-TMA diagnosis, n (%)	
Less than 72 hours	25 (100%)
More than 72 hours	0 (0%)
Median number of TPE cycles	6 (range, 1 to 56)
Other treatment uses, n (% of total cases)	
Rituximab	1 (4%)
Narsoplimab (as part of a clinical trial)	1 (4%)

Table 3: Outcomes of TPE Treatment

Response	Responded to TPE		Did not respond to TPE	
	8 (32%)		17 (68%)	
Survival beyond 100 days post commencement of TPE	Yes	No	Yes	No
	6 (24%)	2 (8%)	0 (0%)	17 (68%)
Cause of death	-	Patient 1: Sepsis Patient 2: GVHD	-	13 (52%) patients: TA-TMA 4 (16%) patients: Sepsis

Discussion

Despite the increasing frequency of allogeneic haematopoietic stem cell transplants globally, TA-TMA remains a poorly researched and understood transplant related complication. To date, the optimal approach to the treatment of TA-TMA is not known. Pharmacological agents such as rituximab, eculizumab and defibrotide have shown promise as potential therapeutic options.[1-3] Encouragingly, a recent real world cohort study investigating the use of TPE in TA-TMA patients has provided some optimism that TPE offers significant clinical utility in selected patients.[4]

Conclusion

There is a paucity of data regarding the use of TPE in the treatment of patients with TA-TMA, particularly amongst adult patients. This study sheds some light on the utility and value of TPE in this population of patients, and provides optimism that TPE represents a viable and useful treatment option in resource-limited settings with restricted access to novel therapeutic agents.

References

1. Au WY, Ma ES, Lee TL, Ha SY, Fung AT, Lie AKW, et al. Successful treatment of thrombotic microangiopathy after haematopoietic stem cell transplantation with rituximab. Br J Haematol. 2007;137:475–8.
2. Jodele S, Dandoy CE, Lane A, Laskin BL, Teusink-Cross A, Myers KC, et al. Complement blockade for TA-TMA: lessons learned from large pediatric cohort treated with eculizumab. Blood. (2020)
3. Corti P, Uderzo C, Tagliabue A, Della Volpe A, Annaloro C, Tagliaferri E, et al. . Defibrotide as a Promising Treatment for Thrombotic Thrombocytopenic Purpura in Patients Undergoing Bone Marrow Transplantation. Bone Marrow Transplant (2002)
4. Yang LP, Zhao P, Wu YJ, Fu HX, He Y, Mo XD, Lv M, Wang FR, Yan CH, Chen YH, Chang YJ, Xu LP, Liu KY, Huang XJ, Zhang XH. Treatment outcome and efficacy of therapeutic plasma exchange for transplant-associated thrombotic microangiopathy in a large real-world cohort study. Bone Marrow Transplant. 2022