Pediatric Hematology Abstract Categories

Stem Cell Transplantation
OP 24

BUSULFAN-CYCLOPHOSPHAMIDE OR TREOSULFAN-FLUDARABINE-THIOTEPA-BASED MYELOABLATIVE CONDITIONING FOR CHILDREN WITH THALASSEMIA MAJOR, SINGLE CENTRE EXPERIENCE

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Objective: Hemoglobinopaties are the most common genetic disorder worldwide. Patients with transfusion-dependent thalassemia major (TDT) are deficient in β-globulin chain production, resulting in ineffective erytropoiesis and hemolysis. Consequently, patients with TDT suffer from primary and secondary iron overload, leading to severe organ dysfunction. In despite of significant improvements in supportive care, especially monitoring and treatment of iron overload and its complications, organ dysfunction progresses in adulthood, resulting in significant morbidity and mortality. Allogeneic haematopoietic stem cell transplantation (HSCT) is the current standart of care for patients with thalassemia major, except clinical trials on gene therapy and gene editing as alternative curative options. Despite improvements in supportive care, blood transfusions and organ damage from iron overload situation before HSCT, predict worse outcome. Recent studies have reported a rate of graft rejection of 8 to 12 % in pediatric patients with TDT undergoing HSCT. Furthermore, the role of conditioning regimen in the outcome has been extensively investigated. Busulfan, treosulfan, fludarabine, thiotepa, cyclophosphamide are common agents of the conditioning regimen for HSCT. Busulfan is an alkylating agent that is mainly eliminated through the liver. Busulfan is associated with sinusoidal obstruction syndrome, pulmonary toxicty, seizures, chronic gonadal dysfunction, and late mortality. Treosulfan is the prodrug of L-epoxybutane, a water-soluble, bifunctional alkylating agent. Treosulfan-containing regimens achieve a high rate of stable donor engraftment, reduced transplant-related mortality and low rate of GVHD. Therefore, treosulfan has been considered to replace busulfan in conditioning regimens in patients with TDT. Experience with treosulfan-based conditioning in pediatric patients is more limited than studies in adult series. However, the data has promising results. Thus, here were reported a retrospective study of patients with TDT undergoing HSCT, in which we compared those with busulfan and those with treosulfan in their conditioning regimen. **Methodology:** We retrospectively evaluated all the consecutive cases of pediatric patients underwent allogenic HSCT and busulfan-based or treosulfan-based conditioning regimens between 2015 and 2021 at Istanbul Medipol University Pediatric Bone Marrow Transplantation Unit. 47 patients were included to the study. Patients between 0 and 18 years of age that unerwent allogenic HSCT for TDT with a treosulfan or busulfan base conditioning regimen during the period of the study were included. In our center, Busulfan-Cyclophosphamide was the conditioning regimen between 2015-2017. Busulfan dose was adjusted according to patient's weight (3-15 kg: 5,11mg/kg/d; 15-25 kg: 4,9mg/kg/d; 25-50 kg: 4,1mg/kg/d; 50-75 kg: 3,3mg/kg/d; 75-100 kg: 2,7mg/kg/dd), and then recalibrated according to AUC. Cyclophosphamide dose was 50mg/kg/d, 4 days. We started using treosulfan-based conditioning in patients with any risk factor for busulfan toxicity in 2018. Conditioning regimen is; treosulfan 10-12-14 g/m^2/d (based on age) 3 days, fludarabine 40 mg/m^2/d 4 days, thiotepa 10mg/kg/d 1 day. GVHD prophylaxis was administered as ATG, methotrexate and cyclosporine. Prophylaxis of venoocclusive disease (VOD) with defibrotide was administered whether the patient had a risk factor or not. **Results:** A total of 47 patients undergoing 49 allogenic HSCT were included: 32 HSCT (65%) with busulfan and 17 (35%) with treosulfan based conditionings. Median age was 7,16 years (2,15-15,9), with no significant difference between the busulfan and treosulfan cohorts (7,9; 7,15). There were 22 (47%) girls and 25 (53%) boys. In the total study population, an HSCT was received from a matched sibling donor (MSD) by 31 patients (65%) and from a 10/10 matched unrelated donor (MUD) by 14 patients (29%). One patient had an 6/6 matched mother and one patient had a 6/6 matched father. There was a significant difference between busulfan and treosulfan cohorts: An HSCT was performed with a MSD by 26 patients (86%) in the BU-Cy group versus 5 (33%) in the TREO-FLU group. The stem cell source was bone marrow (BM) for 75% (n=37) of transplantations and peripheral blood stem cells (PBSC) for 22% (n=11). In one transplantation, both BM and PBSC were used. There was a significant difference between the groups: BM in 87% of transplantations for BU-Cy group; and 47% of transplantations in TREO-FLU group. Thirteen patients experienced acute graft versus host disease (GVHD): 8 patient with skin GVHD (17%: 5 in BU-Cy group, 15%; 3 in TREO-FLU group, 15%), 3 patients with gastrointestinal (GIS) GVDH (6%: 1 in BU-Cy group, 3%; 2 in TREO-FLU group, 11%), 2 patienst with both skin and GIS GVHD (4%, both of two were in the BU-Cy group). However, there were significant differences in donor types and stem cell sources between two groups. There are 3 patients following-up with chronic GVHD: 2 with bronchiolitis obliterans (1 in BU-Cy group and 1 in TREO-FLU group) and 1 patient with ocular GVHD (in BU-Cy group) Ten patients had VOD and all of them were in BU-Cy group (21% of whole population, 30% of BU-Cy group) .Four of 10 patients were followed-up in intensive care unit, and 3 of them had seizures therewithal. We did not have mortality due to VOD. In the total study population, primer engraftment failure number was 3 (6%: all in BU-Cy). We performed second HSCT in 2 of 3, and 1 of 3 died. Number of secondary graft rejection was 2 (4%: 1 in BU-Cy, 1 inTREO-FLU). Their bone marrow turned into TDT with normal series of granulocytes and platelets and parents did not prefer the second transplantation. Number of prolonged isolated thrombocytopenia was 2 (4%: both in BU-Cy): One had platelet recovery with eltrombopag treatment and the other died due to severe GIS GVHD. The median follow-up of all patients was 6 years (2-7 years). OS was 93,75% in the BU-Cy group and 100% in the TREO-FLU group. We had 2 transplant-related mortality: One patient was 15-year-old boy, underwent BU-Cy based allogenic HSCT

from his MSD. He had primer engraftment failure with aplasic bone marrow. The other was 12-year-old boy, underwent BU-Cy based allogenic HSCT from his MSD. He had severe GIS GVHD and prolonged isolated thrombocytopenia. **Conclusion:** Despite busulfan based conditionings used to be more common approach in pediatric patients underwent allogenic HSCT for TDT, treosulfan-based conditioning is gaining acceptance. Our retrospective study confirms the efficiacy and safety of both agents. Treosulfan, fludarabine and thiotepa seem to be appropriate for minimizing the risk of complications, particularly for VOD.

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OP 25

EFFECT OF GRAFT VERSUS HOST DISEASE PROPHYLAXIS ON THE LEUKEMIA FREE SURVIVAL IN PEDIATRIC PATIENTS WHO HEMATOPOETIC STEM CELL TRANSPLANTED FOR LEUKEMIA

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Objective: Hematopoietic stem cell transplantation (HSCT) is an important treatment modality for leukemia, the most common childhood malignancy. Graft versus host disease, one of the most important complication of transplantation, is the most important cause of morbidity and mortality. In our study, we aimed to show the effect of methotrexate doses given in transplants due to leukemia, the development of acute or chronic GVHD, on leukemia-free survival. **Methodology:** Patients who underwent HSCT due to leukemia, between April 2010-October 2020 at a pediatric transplantation unit were included in the study. Methotrexate doses given to patients; were grouped as 10mg/m^2 on day 1,3,6; 10mg/m^2 on day 1,3, 5mg/m^2 on day 6; 10mg/m^2 on day 1, 3; 10mg/m^2 on day 1 and 5 mg/m^2 on day 3,6; 10 mg/m^2 on day 1 and also 5 mg/m^2 on day 1. The effects of these groups on event-free and overall survival were evaluated. **Results:** Recurrence was not observed in 72 of 93 patients evaluated in the ALL group (77.4%). The conditioning regimens were considered TBI-Busulfan-based regimens. No significant difference was observed in terms of LFS. The absence of aGVHD in the ALL patient group significantly prolongs LFS, when evaluated according to CR1-2-3 groups, CR2 significantly extended the LFS time. Effect of GVHD prophylaxis on LFS was evaluated no significant effect of methotrexate dose on LFS was observed. **Conclusion:** The most important factor affecting leukemia-free survival is the state of remission. The longest duration of LFS was detected in CR1. The effect of methotrexate dose as GVHD prophylaxis has not been determined. There was no consensus in the studies on methotrexate doses in the literature. It is necessary to study with a larger cohort.

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Pediatric Oncology Abstract Categories

Rare Tumours and Histiocytosis

OP 26

LANGERHANS CELL HISTIOCYTOSIS IN TURKISH CHILDREN; 30 YEARS OF EXPERIENCE FROM A SINGLE CENTER

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Objective: Langerhans-Cell Histiocytosis, the most common histiocytic disorder, is characterized by inflammatory lesions with infiltrating CD1a+/CD207+ pathologic dendritic cells. The extent of disease is highly variable, from single lesion disease to life-threatening disseminated multisystem disease. We aimed to determine the demographic characteristics and the clinical outcomes of children with LCH. **Methodology:** The files of 81 patients diagnosed with LCH in Ankara Oncology Hospital, Dışkapı Children's Hospital and Ankara City Hospital between 1993 and 2023 were retrospectively analyzed. Data collected from the files included characteristics, age, sex, symptoms, physical examination findings, site of involvement, laboratory findings at diagnosis, procedure applied, treatment type used, and outcome. **Results:** The median age was 5 (0.1-17) with a median follow-up of 3 years (0.1-14) (Table1). The most common complaint was a bone lesion-related symptom; swelling (31%), pain (19%). Surgery was the only treatment in 19, chemotherapy in 22, radiotherapy in 1, surgery + chemotherapy in 35 (43%). Vinblastine + prednisolone was most commonly (36%) used. A patient with BRAF600VE was treated with vemurafenib. Recurrence was detected in 13 (16%) patients. Three patients died (3.7%) with refractory disease. **Conclusion:** Bone and skin were the most frequently involved systems in our study. Prognostic factors affecting event-free survival (EFS) were multisystem disease (5-year EFS 62% versus 87%, p=0.01) and hematologic system involvement (5-year EFS 42% versus 82%, p=0.02). Consistent with the literature, our overall survival (OS) rate was found to be high (5-year OS 95%). Patients with single-system disease had excellent survival (100%).

	No (n=81)	%
Median age at diagnosis (range)	5 (0,1-17 years)	
Age distribution		
≤24 ay	22	27
>24 ay	59	73
Sex		
Male	55	68
Female	26	32
Staging		
Single-system disease	57	70
Multisystem disease	24	30
Sites of involvement		
Bone isolated	38	47