Abstract
Background: Primary immunodeficiency disorders (PIDs) are an important but under-diagnosed cause of childhood morbidity and mortality. HSCT is the curative treatment for PIDs. Finding a matched donor is a stumbling block. Moreover, presence of severe infections at the time of transplants increases the transplant-related mortality (TRM. Poor infrastructure in developing world adds to the Gordian knot. So, RIC HSCT has been reported as a safer modality.
Objectives: To describe the feasibility and outcome of RIC HSCT for PIDs.
Methods: Twelve children with various PIDs, from August 2013 to August 2016 who underwent HSCT under our care were included. Clinical records were analyzed retrospectively.
Results: Twelve children (SCID-2, DOCK-8 deficiency-1, Chediak-Higashi Syndrome-1, WAS-3, HLH-2, GATA2 mutation-1 and CVID-1, HO-1 deficiency-1) with mean age 5.72 year underwent HSCT. Male: Female ratio was 11:1. Mean follow-up 419 days (9 to 1209 days). Eight underwent haploidentical HSCT three had matched sibling donor (MSD) HSCT, and one had MUD HSCT. In seven T-cell replete haploidentical and one MUD HSCT the conditioning was with serotherapy (Alemtuzumab-4 or Rabbit Anti-Thymoglobulin-4) along with Fludarabine, Cyclophosphamide, Thiotepa and TBI in 5, Fludarabine and Treosulfan in 2 and Fludarabine and Busulfan in 1. All received post transplant cyclophosphamide 50 mg/kg on day 3 and 4 for GVHD prophylaxis along with tacrolimus and MMF. In one, TCR alpha-beta/CD19 depleted haploidentical HSCT the conditioning was Alemtuzumab, Fludarabine, Treosulfan and Thiotepa with no GVHD prophylaxis. Two MSD were conditioned with Anti-Thymoglobulin, Fludarabine and Cyclophosphamide and GVHD prophylaxis was cyclosporine and methotrexate and one MSD was given Alemtuzumaab, Fludarabine, Cyclophosphamide and TBI with Tacrolimus and MMF for GVHD prophylaxis. Mean $CD34^+$ cell dose was 14.24×10^6/kg for 8 patients with PBSC graft and 32.1×10^6/kg for 4 patients who got bone marrow. Ten patients engrafted and two died prior to engraftment with bacterial sepsis on day +8 and day+14 respectively. Mean neutrophil engraftment was on 16.8 day. One patient died with thrombotic microangiopathy on day+28. Eight survivors are fully donor (>95%) and one had mixed chimerism (85%). Acute GVHD grade I-II developed in 4 children. Chronic GVHD of skin developed in two. CMV reactivation was seen in two and BCG reactivation in two. Overall survival 75% and TRM 25%.
Conclusion: RIC HSCT constitutes a feasible option for PIDs in developing world and gives a ray of hope for these patients.

SCT-1_V1.2
HAPLOIDENTICAL STEM CELL TRANSPLANTS WITH POST TRANSPLANTATION CYCLOPHOSPHAMIDE FOR HEMATOLOGICAL MALIGNANCIES IN CHILDREN

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Abstract
Background/Objectives: Donor availability remains one of the major challenges for performing hematopoetic stem cell transplantation (HSCT) in the treatment of hematologic malignancies. Matched sibling or unrelated donor cannot be identified or mobilized in time for many patients. HLA-haploidentical donor transplantation (HIDT) using T cell replete grafts and post-transplantation cyclophosphamide (PTCY) for control of alloreactivity has emerged as an important option for patients who lack a donor. Post-transplant cyclophosphamide (PTCY) is not toxic to hematopoietic stem cells because of high expression of enzyme aldehyde dehydrogenase but it induces selective allodepletion by killing host and donor T cells proliferating in response to donor and host cells, respectively. Thus, PTCY decreases GvHD but doesnot effect GvL. We report here the feasibility and outcome of HIDT in a developing world setting.
Designs/Methods: Six children with hematological malignancies and no available matched donor underwent HIDT from Dec2013 to Sept2016. The clinical records and investigation sheets were analyzed retrospectively. Patient's follow-up ranged from Day+10 to Day+732 (Mean Day+278)
Results: Mean age was 4.88 year (1.6-9 years). M:F = 3:3. All had hematological malignancies (High risk Acute myeloid leukemia-2, Relapsed acute lymphoblastic leukemia-4) and all were in complete remission (CR) at the time of transplant. Conditioning was Fludarabine ($40mg/m^2$/day) from Day-8 to day-5, Cyclophosphamide (14.5mg/kg/day) on Day-4 and Day-3, Thiotepa (8mg/kg/day) on Day-2 and TBI (2Gy) on Day-1. All patients received haploidentical peripheral blood stem cells. Mean $CD34^+$ cell dose was 12.7×10^6/kg/recipient weight. PTCY (50 mg/kg/day) was given on Day+3 and Day+4. Tacrolimus and MMF were started from Day+5 for Graft-Vs-Host disease (GvHD) prophylaxis. Supportive care along with Voriconazole and Valacyclovir for antifungal and antiviral prophylaxis was given. Five patients engrafted while one awaits engraftment (short follow-up). Mean neutrophil engraftment was on 18.6 day. Immediate post-transplant period was uneventful. Only one patient had viral reactivation, who had Adenovirus induced hemorrhagic cystitis on Day+44 which was successfully treated with Cidofovir. Chimerism studies showed fully donor in all patients who were post Day+100. One patient of Pre-B ALL relapsed on Day+406 of HIDT. This patient was very difficult to bring in remission even before the transplant and is now being taken up for the next transplant. Acute GVHD was not seen in any patient. Chronic GVHD of skin was seen in two patients which was conservatively managed. All six patients are alive.
Conclusion: In hematological malignancies patients who have no matched donor available, HIDT with PTCY constitutes a feasible and effective option.

SCT-1_V1.3
HALF MATCHED BUT TWICE AS GOOD – HAPLOIDENTICAL STEM CELL TRANSPLANTATION FOR BENIGN DISORDERS IN CHILDREN – CHALLENGES AND OUTCOME FROM A TERTIARY CARE CENTRE IN INDIA

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Background: Haploidentical stem cell transplantation in children with benign haematological disorders offers a unique opportunity to cure a child who has no matched family donor. However, the associated challenges are different to conventional allograft making the options suboptimal so far. Recent advances have made this procedure feasible in very young children and we describe our experience in the use of this technique.
Patients and methods: The study was conducted at the blood and marrow transplantation unit at Apollo Hospital, Chennai. Children aged up to 18 years who underwent haploidentical transplantation from 2002 to 2016 were included in the study.
Results: A total of 23 paediatric haploidentical stem cell transplantations have been performed at our centre so far. Of these 16/23 (69.5%) have been for benign disorders including Fanconi anaemia in 3, Haemophagocytic LymphoHistiocytosis in 2, 1 with severe aplastic anaemia and 10 with primary immunedeficiency disorders namely, severe combined immunedeficiency in 6, 1 each with Wiskott Aldrich syndrome, Hyper IgM syndrome, MSMD and Adrenoleukodystrophy. The sources of stem cells were from sibling and parent and bone marrow and peripheral blood in equal numbers. Techniques of T depletion used were CD 34 selection in 1, Campath in the bag in 1, TCR alpha/beta depletion 2, CD3/19 depletion in 1 and post transplant cyclophosphamide (PTCy) in 11 children.
In transplants where PTCy was used, conditioning included Fludarabine/ Treosulphan in primary immunedeficiency, Fludarabine/ Treosulphan/ single dose TBI 200cGy in HLH, Fludarabine/ Cyclophosphamide/ single dose TBI 200cGy in Fanconi anaemia and severe aplastic anaemia. In the child with ZAP70 mutation where TCR alpha/beta depletion was used, conditioning regimen included Fludarabine/ Treosulphan/ Thiotepa/ ATG. 12/16 (75%) transplants resulted in engraftment by Day 16-21 post HSCT with sustained complete chimerism. Hyper IgM syndrome and MSMD were 2 conditions where primary rejection resulted in autologous reconstitution. Acute skin and gut GVHD of grade 2-3 was noted in 5/16 (31%) which was responsive to steroids. Chronic skin and mouth GVHD has been noted in 1 child. CMV reactivation was noted in 5/16 (31%) children wherein 4 children achieved negative CMV copies on treatment with Valganciclovir.
Mortality among this group of patients was found to be 6/16 (37.5%). In the PTCy group, 3 children died of aspergillosis, severe ARDS and ruptured peliosis hepatis respectively. Campath use resulted in refractory CMV