SHORT COMMUNICATION

Hematopoietic Stem Cell Transplantation in India-2017 Annual Update

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Abstract There has been a steady rise in number of transplant centers in India over last few years. This year many papers related to bone marrow transplants were presented in annual conference of Indian society of Hematology and Transfusion Medicine. All oral and poster presentations which were published were reviewed. There were many publications on autologous transplant, allogeneic transplant and lab aspects of transplant. Centers shared their data on autologous transplants in newly set-up units with resource constraints with good outcomes. Encouraging data from across India is likely to boost more centers to set up transplant centers.

Keywords Bone marrow transplant · India · Recent developments

Introduction

Hematopoietic stem cell transplantation (HSCT) is curative therapy in benign and malignant diseases [1]. Adequate transplant facilities are still lacking in large part of India [2]. Indian stem cell transplant registry (ISCTR) Nov 2017 data suggests that we have a significant increase in the total number of HSCT centers reporting from 52 to 65 and total number of HSCTs also continue to increase by around 10% per year with 2016 seeing 1878 transplants reported to ISCTR (personal communication). It was heartening to see progress made as presented during annual conference of

Indian Society of Hematology and Transfusion Medicine (ISHTM) in 2017 in Guwahati, India.

Methodology

All oral and poster presentations which were published were reviewed. Six abstracts were rejected-two due to duplication and four to failure to mention author names and affiliations. Key findings are being highlighted.

Allogeneic Bone Marrow Transplants

Refractory acute myeloid leukemia (AML) is a difficult clinical challenge with dismal outcomes. European Society of Blood and Marrow Transplantation reported 25% leukemia free survival in this population after matched sibling donor (MSD) or matched unrelated donor (MUD) transplants [3]. One center presented data on 17 allogeneic HSCT in refractory acute myeloid leukemia with active disease at the time of transplant [4]. Median age of study cohort was 25 years. Nine patients underwent MSD, 3 MUD and 5 underwent haploidentical HSCT. Four patients received reduced intensity conditioning (RIC) and rest all received variable myeloablative conditioning regimes. Four patients died before engraftment. Day 30, day 100 and day 180 mortality was 41%, 59% and 76% respectively. Four patients were alive at median follow-up of 843 days which is similar to international data even though numbers were small.

Sharma et al. [5] reported outcomes of 32 allogeneic HSCT in primary immunodeficiency disorders over last 20 years. Wiskott Aldrich syndrome (n = 8) and severe combined immunodeficiency (n = 7) were the commonest

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immune deficiencies. There were 10 MSD, 5 MUD, 5 matched family donors and 12 haploidentical transplants. Six children succumbed to infectious complications before day 30. Severe acute GVHD occurred in 8 children. Bacterial, viral and fungal infections were noted in 22 (68%), 19 (59%) and 11 (34%) patients respectively in peritransplant period. Six children died due to GVHD and 8 due to infections.

The 2-year OS and EFS for the entire cohort was 51.3 and 48.7% respectively. At 2 years the OS in MSD, MUD/MFD and haploidentical transplants was 88.9, 33.3 and 40.0% respectively ($p = 0.033$). Outcomes of haploidentical HSCT in present series are inferior to international data with infections being major cause of mortality.

A 7-year male with transfusion dependent anemia secondary to pyruvate kinase deficiency was reported cured after myeloblastic conditioning and a MSD transplant [6].

Autologous Bone Marrow Transplants

More and more new centers are now reporting their transplant outcomes even though smaller numbers. A new center from Eastern India reported their data on 42 patients over 4.5 years [7]. There were 8 lymphomas, 1 acute promyelocytic leukemia and rest were plasma cell dyscrasias. All lymphoma patients received BEAM while APL patient received busulfan cyclophosphamide conditioning while myeloma patients received high dose melphalan. Median stem cell dose was $5.3 \times 10^6/\text{kg}$ with median neutrophil engraftment on day + 11 (day + 9 to day + 15). Day 30 mortality was nil.

Malhotra et al. [8] have published a larger series of 94 patients with myeloma who were conditioned with high dose melphalan. The mean time to neutrophil and platelet engraftment was 11 and 12 days respectively. Thirteen percent patients succumbed to their illness of which 3 patients died within 30 days of transplant. Median OS was 76.7% at 6.5 years. Autologous HSCT for multiple myeloma is very much feasible in India and the results are comparable to international data.

Lab Aspects of Bone Marrow Transplants

There has been significant development in laboratory aspects of HSCT in India. In one presentation, short tandem repeat (STR) analysis was compared with variable number of tandem repeats (VNTR) in 15 patients for chimerism analysis [9]. Both revealed comparable qualitative results in the majority of cases. The incidence of mixed chimerism by STR analysis was 13% compared to 0% in cases evaluated by VNTR analysis. Authors concluded that

STR analysis is more sensitive, can be done with lesser DNA and is more rapid and accurate quantitative assessment of post-transplant chimerism. Another group compared therapeutic tacrolimus levels post BMT by chemiluminescent microparticle enzyme immunoassay versus immunoassay technique. They studied 83 samples and discovered that results by both assays were similar with regression value of $R = 0.911$ [10].

Two patients with haploidentical HSCT were reported wherein after engraftment there was graft loss and auto recovery of patient cells without disease relapse [11]. In both cases there was KIR activating receptor match and stronger iKIR mismatch in graft versus host (GvH) direction. This resulted in removal of leukemic cells, since there was no inhibition of NK cell activity. Moreover, in the host versus graft (HvG) direction, the stronger aKIR match led to graft rejection. These cases highlight the importance of knowing KIR mismatches in GvH and HvG directions before selecting a donor for haploidentical HSCT.

Supportive Care

Stem cell apheresis in smaller children can be difficult. Vascular access, extracorporeal circuit volume, blood flow rates are the main limiting factors for PBSC collection in small children. These require central vascular access for apheresis which may require either general anesthesia or conscious sedation [12]. Donors are generally hospitalized in ward for these procedures. Interestingly, a retrospective analysis of 164 PBSC harvests under anesthesia in day care setting in children with a median age of 5 years (1–12 years) was presented. In 50% of the cases, induction of anaesthesia was by sevoflurane followed by total intravenous anaesthesia while in 32% it was sevoflurane induction followed by sedation. Propofol was the most commonly used maintenance agent (67%). One child developed acute pulmonary edema secondary to infusion of blood products requiring a short stay in ICU for one donor. Authors concluded that Pediatric PBSC harvest can be safely done under anesthesia with due precautions in the day care setting [13].

Infections especially early bacterial infections are major threat to success of any transplant program. Sixty-five HSCT centers from 25 countries in Europe, Australia, and Asia reported data on 655 GNR episodes and 704 pathogens in 591 patients. Unfortunately, half of gram negative bacteria were fluoroquinolone and noncarbapenem resistant; 18.5% carbapenem resistant; 35.2% multidrug resistant [14]. Interestingly, total resistance rates were similar in community-acquired infections. Gram negative sepsis has been major cause of mortality and morbidity in India. Kamble et al. [15] reported data on 516 blood culture

samples received from 74 patients from different sites. Sixty-three cultures were positive in 21 patients (12%). These included *Pseudomonas aeruginosa* (2), Coagulase negative *Staphylococci* (11), *Klebsiella pneumoniae* (5), *E. coli* (2), and others (6). Unfortunately, all 5 *Klebsiella pneumoniae* and both *pseudomonas aeruginosa* isolates were resistant to carbapenems and one isolate was resistant to colistin too. This is worrisome trend. We need to see data from other centers to understand our situation and make India specific guidelines.

Conclusions

There have been sufficient developments in field of HSCT in India. Newer centers developing transplant capabilities in Eastern India with limited resources was encouraging. At least there were no short-term mortalities which are important morale booster for new centers and it also encourages other centers to proceed with establishment of BMT facilities.

Compliance with Ethical Standards

Conflict of interest The author declares that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants performed by any of the authors.

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