CORRESPONDENCE

Hematopoietic Stem Cell Transplant in Elderly Patients: Experience from a Tertiary Care Centre in Northern India

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Dear Editor,

One-fifth of the world's population resides in India. The burden of hematological diseases both malignant and non-malignant is huge in the country. According to the registry data the total number of leukemia and lymphoma patients living in India in 2010 was about 100,000 [1]. The estimated size of the elderly population in India is expected to rise from 77 million in 2001 to 140 million by 2021. With the increasing awareness about hematological diseases and the rising economy, many patients are opting for hematopoietic stem cell transplant (HSCT) as a definite treatment for many hematological diseases. The role of HSCT for various hematological diseases in young patients is well established. Older patients have traditionally been considered ineligible for stem cell transplantation and data of HSCT in elderly is scarce, particularly from developing countries. Here we report our experience with stem cell transplantation in the elderly population in India.

We reviewed the transplant database at Bone Marrow Transplant (BMT) centre, BLK Superspeciality Hospital, New Delhi. The conditioning regimen for allogeneic HSCT was reduced intensity conditioning (with fludarabine 30 mg/m² for 5 days and melphalan 140 mg/m² for 1 day). For autologous HSCT for multiple myeloma and lymphoma, melphalan 200 mg/m² and BEAM regimens (BCNU 300 mg/m², etoposide 200 mg/m², cytarabine 200 mg/m² and melphalan 200 mg/m²) respectively were used as conditioning regimens. The transplants were

performed in High Efficiency Particulate Air (HEPA) filtered rooms. Peripheral blood stem cell harvest was done after granulocyte-colony stimulating factor (G-CSF) mobilization. Graft versus host disease (GVHD) prophylaxis for allogeneic HSCT included cyclosporine and methotrexate. Patients received standard anti-viral prophylaxis with acyclovir and *Pneumocystis jirovecii* prophylaxis with trimethoprim-sulfamethoxazole. Patients were treated with broad spectrum antibiotics at the time of their first neutropenic fever, and with antifungal agents as per institutional policy. The study was approved by the Institutional Review Board.

Out of 440 patients who underwent HSCT at BLK Superspeciality hospital from February 2010 to August 2015, 19 (4.32 %) were ≥60 years of age. Median age was 63 years (range 60–73 years). There were 14 males and 5 females. Seven patients underwent allogeneic HSCT and 12 patients underwent autologous HSCT. All patients had normal liver and kidney functions and normal left ventricular ejection functions prior to HSCT. Six patients had diabetes well controlled with oral hypoglycemic agents. All allogeneic HSCTs were sibling matched peripheral blood stem cell transplantations. The most common indications for allogeneic and autologous HSCT were acute myeloid leukemia (AML) and multiple myeloma (MM) respectively (Table 1). The donors for allogeneic HSCT were females in five cases and males in two cases with a median age of 56 years (range 51–62 years). The median CD34+ stem cell dose was 3.7 × 10⁶/kg recipient body weight (range 1.88–8.77 × 10⁶/kg). Neutrophil engraftment occurred at a median of 11 days (range 9–13 days) and platelet engraftment at 15 days (range 11–26 days). None of the patients had cytomegalovirus (CMV) reactivation. One patient developed grade 2 acute gut GVHD and three patients had limited chronic skin GVHD. Twelve patients

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Table 1 Characteristics of elderly patients who underwent HSCT

Total patients	19
Males	14
Females	5
HSCT	
Allogenic	7
Autologous	12
Indications	
Multiple myeloma	11 (5 in CR, 4 in VGPR, 2 in PR)
Acute myeloid leukemia	6 (3 in 1st CR, 3 in 2nd CR)
Non Hodgkin lymphoma	1 (in 2nd CR)
Acute lymphoblastic leukemia	1 (in 2nd CR)
Co-morbidities	
Diabetes mellitus	6
Hypertension	4
Coronary artery disease	1
Conditioning regimens	
Flu/Mel	7
Melphalan	11
BEAM	1
Median CD 34+ stem cell count (range) $\times 10^6/\text{kg}$	3.7 (1.88–8.77)
Median neutrophil engraftment, days (range)	11 (9–13)
Graft versus host disease	
Acute	1
Chronic	3
Infections	
Bacterial	3
CMV reactivation	0

HSCT hematopoietic stem cell transplant, *CR* complete remission, *PR* partial response, *VGPR* very good partial response, *CMV* cytomegalovirus)

developed grade II–IV oral mucositis. Median follow-up was 14 months (range 7–44 months). One patient with relapsed AML in second complete remission died on day +10 post allogeneic transplantation due to gram negative sepsis. During follow-up two patients with multiple myeloma post autologous stem cell transplant relapsed, one of whom expired because of progressive disease.

HSCT is considered as a high risk procedure with a higher morbidity and mortality in older patients and many institutions avoid transplanting patients above 60 years. We analyzed our transplant data and found only one transplant related mortality among the elderly patients who underwent HSCT conducted at the BMT centre. Among the seven allogeneic HSCT recipients only three developed limited chronic GVHD and none had extensive chronic GVHD. After a median follow-up of 14 months two patients with multiple myeloma had relapsed with an overall survival of 89.5 %.

In myelodysplastic syndrome (MDS) and AML, various studies have shown that age alone has no significant

adverse effect on overall survival in patients undergoing reduced intensity conditioning allogeneic HSCT, and older age should not make an otherwise eligible patient ineligible [2, 3]. Moreover, AML, MDS, lymphoma and multiple myeloma are most common in people aged over 65 years who could be denied the deserved curative treatment based on age alone. These patients now comprise 25–30 % of all HSCT recipients, according to the National Marrow Donor Program (NMDP) and the Center for International Blood & Marrow Transplant Research (CIBMTR) [3]. In NMDP and CIBMTR data there was no difference in rates of non-relapse mortality, grade 2–4 GVHD, chronic GVHD, or relapse in patient less than or more than 60 years [3]. Similarly, age at transplantation has no prognostic significance on outcome in autologous HSCT [4]. Our results also showed that age alone has no impact on outcome in elderly patients undergoing stem cell transplantation.

Older age is associated with co-morbidities which could preclude stem cell transplantation, but in otherwise fit elderly patients, HSCT can be safely performed. The

percentage of elderly patients who underwent HSCT at our center was only 4.3 % compared to 16–24 % in USA and Australia [3, 5]. Based on our experience, we conclude that stem cell transplant is feasible in the elderly population in developing countries, with good outcomes and should be considered in eligible patients. As the population ages worldwide including in developing countries more people will be in need of HSCT in future. Age alone should not be a cause of denial of a potentially lifesaving treatment. The relatively low cost associated with the transplant in the developing world [6] makes it an attractive and definite treatment option for hematological disorders whose benefit should be extended to all well selected patients irrespective of age.

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Compliance with ethical standards

Conflict of interest None.

References

1. Takiar R, Nadayil D, Nandakumar A (2010) Projections of Number of Cancer Cases in India (2010–2020) by Cancer Groups. *Asian Pac J Cancer Prev* 11:1045–1049
2. Koreth J, Aldridge J, Kim HT, Alvea EP, Cutler C, Armand P, Ritz J et al (2010) Reduced intensity conditioning hematopoietic stem cell transplantation in patients over 60 years: hematologic malignancy outcomes are not impaired in advanced age. *Biol Blood Marrow Transplant* 16:792–800
3. Majhail NS, Tao L, Bredeson C, Davies S, Dehn J, Gaiewski JL, Hahn T et al (2013) Prevalence of hematopoietic cell transplant survivors in the United States. *Biol Blood Marrow Transplant* 19:1498–1501
4. Merz M, Neben K, Raab MS, Sauer S, Egerer G, Hundemer M, Hose D et al (2014) Autologous stem cell transplantation for elderly patients with newly diagnosed multiple myeloma in the era of novel agents. *Ann Oncol* 25:189–195
5. Nivison-Smith I, Bradstock KF, Dodds JA, Hawkins PA, Ma DD, Moore JJ et al (2007) Hematopoietic stem cell transplantation in Australia and New Zealand, 1992–2004. *Biol Blood Marrow Transplant* 13:905–912
6. Sharma SK, Choudhary D, Gupta N, Dhamija M, Khandelwal V, Kharya G et al (2014) Cost of hematopoietic stem cell transplantation in India. *Mediterr J Hematol Infect Dis* 6(1):e2014046