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Autologus Stem Cell Transplantation for Cancers: India: 2017

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Abstract

India is a well-known destination for health tourism including hematopoietic stem cell transplantation for various cancers like multiple myeloma, Hodgkin and non-hodgkin lymphoma. Hematopoietic stem cell transplant is cheaper in India as compared to developed countries and there is a huge cost difference. Here, the numbers of stem cell transplant centres and transplant activity are increasing. In this paper, we summarise present status of autologus stem cell transplant for various cancers in India including the basics of autologus stem cell transplant procedure and reported statistics. This will add to scarcely reported literature in this topic as well as encourage the Indian stem cell transplant activity.

Keywords: Metabolism; Graft venous host; Immunodeficiency; Stem cell transplantation

Introduction

Preclinical studies in animals showed that stem cell transplantation (SCT) can restore blood production. This created a new highway of curative therapy in many malignant and nonmalignant diseases (errors of inborn metabolism, congenital immunodeficiency and hemoglobinopathies). High dose chemotherapy (HDCT) and radiotherapy (RT) shows the steep dose response curves. This dose exceeds the normal tolerance of bone marrow. The fatal bone marrow aplasia (BMA) secondary to HDCT, if restored through autologous stem cells, it is called as autologous stem cell transplantation (ASCT). Hence the principle of ASCT is "more the better". ASCT depends on HDCT for eradication of malignancy as compared to allogenic transplant (allo SCT) which has additional graft versus host effect (GVHE) to counteract the malignancy. ASCT is also free of significant long term immunosuppression and delayed immune reconstitution. The chemotherapy and radiation therapy are regimen specific to particular diseases [1-8].

What are stem cells?

Hematopoietic stem cells (HPSC) identified by flow - cytometry detectable expression of CD34. CD34 + cells present in small quantities in bone marrow (0.5-1%) and in tiny quantities (0.05-0.1%) in circulating blood. Hematopoietic stem cells (HSC) also express human leukocyte antigen (HLA) antigens, but do not carry ABO blood group antigens. These pluripotent stem cells replenish themselves as well as differentiate in to multipotent progenitor cells and finally irreversibly form specific lineage-restricted cells. Age is a limitation factor to allogenic SCT, cut off being 55 years. This led to the development of the concept of ASCT. Phases of ASCT include Collection, Cryopreservation, HDCT, Thawing, Infusion of stem cells and Supportive care.

Pretransplant evaluation

Evaluation of disease status, Complete blood counts, Biochemistry, HIV, Hepatitis B and C, Pulmonary function test, 2 D Echo.

Indications

Indications according to worldwide reporting with descending order are multiple myeloma (50-55%), non-Hodgkin lymphoma (20-25%), Hodgkin lymphoma (8-9%), light chain amyloidosis (0.5%), and acute myeloid leukemia (0.5%). Especially acute promyelocytic leukemia, acute lymphoblastic leukemia (0.1%), chronic lymphoblastic leukemia(0.1%), germ cell tumour (1%). Unsuitable patients for ASCT are those with Karnofsky score<70, LVEF<40%, Compromised FEV1, DLCO<40% of predicted normal, Creatinine>3 mg/dl, heavily pretreated patients, and Chemorefractory patients.

Collection

Hematopoietic progenitor stem cells (HPC) for ASCT have 2 sources, bone marrow (BM) and peripheral blood (PBSC). After collection the stem cells are can be preserved at 2 to 4°C for use within 7 days or it can be suspended in a balanced salt solution with cryoprotectant (e.g. DMSO, dimethyl sulfoxide) in liquid nitrogen. For bone marrow (BM) collection usually the volume is 10 to 15 ml/kg patient weight (1000 ml approx). Minimum dose of stem cells should be 2 million CD 34 + cells/kg recipient body weight (>4 to 6 million cells/kg being the optimal). Mobilization of HPC is done either by cytokine only strategy (G-CSF) or with chemo-mobilization (low dose cyclophosphamide). Plerixafor is also used that works through disrupting the bonding of chemoreceptor type 4 and stromal derived factor to the marrow stromal cells and HPC. Mobilization is 4 fold increase of circulating progenitors. This term was used first in 1977 in experimental administration of endotoxin in healthy subjects. Growth factors alone or that after chemotherapy is used for collecting stem cells. According to CIBMTR reports, now virtually all ASCT are performed with mobilized hematopoietic stem cells. Mobilization with chemotherapy achieves antitumour activity as well.

Mobilizing agents

These agents are used to mobilize stem cells from bone marrow to peripheral blood for ease of collection. The doses are as follows- Filgrastim is 10 mcg/kg/day SC at least 4 days prior to collection. Lenograstim is glycosylated form of GCSF yet to be standardized in practice. Sargramostim (GM CSF) is rarely used now. Cyclophosphamide 1-5 gm/m^2. It is more used as a part of conditioning regimen rather than mobilization purpose. Plerixafor is a CXCR4 antagonist reducing the binding and chemotaxis of HSC to BM stroma. After 4 days of filgrastim and 11 hours prior to apheresis -0.24 mg/kg SC qDay (max 40 mg per day) for up to 4 consecutive days.

Ancestim (recombinant human stem cell factor)

It is a soluble surface molecule on bone marrow stromal cells. It is used in conjunction with filgrastim -20 mcg/kg/day SC.

Insertion of catheter

A double lumen catheter is inserted in juglar or sublclavian vein, which serves both for collection of stem cells and intravenous access for transplantation. Table 1 Shows most commonly used conditioning regimens for various diseases. E.g. for multiple myeloma it is single agent melphalan, for lymphoma it is BEAM (BCNU, etoposide, Ara C, Melphalan), for AML it is BuCy(Busulphan, Cyclophosphamide). **Isolation**: The patient is nursed in an isolated environment till the newly infused normal marrow cells engraft and start functioning. This takes 3-4 weeks. Table 2 Shows various precautions for a hematopoietic stem cell marrow transplant unit. Isolation and asepsis are crucial in the process [9].

MM	Melphalan
lymphoma	BEAM, CBV
AML	BU, CY
Neuroblastoma	Busulfan + melphalan
Wilm tumour	no standard
Ewing sarcoma	no standard
Germ cell tumour	TICE

Table 1: Most Common Conditioning Regimens for Different Diseases

No sick visitors
Hand washing
Mask (optional)
Gowns(optional)
Gloves (optional)
Shoe coverings(optional)
HEPA filter and laminar flow are level 3 recommendations.

Table 2: Safety Precautions For Both Staff And Visitors [9]

Day of transplant
Fever
Chills
Hypotension
Chest tightness
Cough
During engraftment (weeks 1 to 4)
Infections: bacterial, viral, fungal
Nausea and vomiting
Fluid and electrolyte disturbance
Mucositis
Malnutrition
Bleeding and bruising
Need of blood components
Diffuse alveolar hemorrhage
Hepatic venoocclusive disease
Post-transplant (months to years)
Relapse of disease
Leukemia
Myelodisplastic syndrome
Interstitial pneumonitis
Hemorrhagic cystitis
Toxicity of the procedure and supportive care

Table 3: Complications of Autologus transplantation Day of Transplant

Table 3 Enumerates the toxicity of HSCT which induced by cytopenia and organ damage through HDCT. Oral mucositis, Diarrhoea, pain, infections, nausea, vomiting, alopecia, Anorexia, rash are usual. Cytopenias recover within 3 weeks. Further growth factor support (G CSF) enhances recovery by 4 days. Packed red cells (PRBC) and platelet transfusion (SDP preferably) are required to counteract the cytopenias. Transfusion associated graft versus host disease (GVHD) is prevented by irradiating all the blood products before transfusion. Stem cells are not to be irradiated. Major infections are gram negative bacteria, gram positive bacteria, clostridia, herpes and fungi in descending order. Prophylactic antibiotics, antivirals, antifungals, growth factors are recommended.

Hepatic veno-occlusiove disease (hepatomegaly, jaundice, fluid retention) and idiopathic pneumonia syndrome, acute respiratory distress can also occur. Transplant related mortality (TRM) is usually <3%, ideally it should be 0%. Relapses are more common in ASCT than allo SCT. Causes of death are primary disease (65-69%), infections (6-8%), organ failure (3-4%), secondary malignancies (1-2%) and other (16-18%)

Infection prophylaxis

It takes one to 2 years for immunological recovery after HSCT. Usually neutrophil engraftment takes within 3 weeks in ASCT. Isolation is done till day + 30 post transplant. Oral cavity, skin and perianal hygiene is to be maintained.

Bacterial prophylaxis

It includes Ciprofloxacin 500 -750 PO BID or alternatively ceftriaxone 2gm IV. Other newer fluoroquinolones are not active against polyoma virus.

Fungal prophylaxis

It usually includes Fluconazole or Posaconazole or Voriconazole. Fluconazole decreases candida infection but not Aspergillosis. Posaconazole may be preferred in allo SCT where the risk of fungal infection is more.

Viral prophylaxis

It includes Acyclovir for HSV Prophylactic Ganciclovir for CMV is controversial in ASCT. In allo SCT, post-transplant if CMV PCR is positive one can start treatment with Ganciclovir before clinical manifestations.

Parasite and *Pneumocystis jirovaci* prophylaxis

We use oral Albendazole 400 mg single dose on day 9 and oral Cotrimoxazol DS alternate day from day -14 to day -2 and then from engraftment till 6 months or till GVHD resolves whichever is later.

Transfusion strategy

SDP transfusion if Platelet count is <20,000/c.mm and Packed red cells if Hemoglobin is <8.0 gm is to be supported. All the blood products should be irradiated to prevent graft versus host disease.

Stem cell transplantation

Actual process of autologous stem cell infusion is same as blood transfusion. Hence the precautions are same as that of regular blood transfusion. Mannitol and diuretics are used when hemolysis is suspected after stem cell transfusion (suspected with reddish urine or decreased urine output).

Recovery (supportive care)

Peritransplantation: Indications for various blood products are as follows: RBC, platelet, and plasma indications for transfusion do not differ significantly from non-HSPC patients. RBC "threshold" hemoglobin 7 or 8 g/dL (higher in cardiac patients). Platelet threshold commonly 10,000/μL for prophylactic transfusion, 50,000 for bleeding patients. FFP indications are not well-established (as is true elsewhere); FFP is not widely used in HPC transplants.

Post-transplant

Irradiated products are used (probably forever) and Leukocyte-reduced products used for HLA immunization prevention.

Engraftment

The date of neutrophil recovery is scored as the first of 3 consecutive days with ANC 0.5 × 109/L or greater and unsupported platelet count ≥ 20 × 109/L on 3 consecutive days.

Multiple myeloma

Multiple myeloma (MM) is incurable. ASCT has proved to prolong both event free survival (EFS) and overall survival (OS). There are 3 transplant strategies in MM for ASCT, upfront ASCT, delayed ASCT and ASCT on relapse. The Intergroup Francophone myeloma (IFM) and Medical Research Council trials showed significant increased OS, EFS and complete remission (CR) rates with ASCT than conventional dose chemotherapy (CDCT). For a young patient (<65 years) Melphalan 200 mg/m^2 is the standard conditioning regimen for MM. Elderly patients usually receive 100-140 mg/m^2 Melphalan (preferably 140 mg/m^2). As the stem cells can be stored at 2 to 4°C for up to 5 days, ASCT in MM may be done without use of DMSO. Also during thawing, residual DMSO can cause histamine release syndrome, hypotension, abdominal pain and renal failure. Some patients who are not in very good partial response (VGPR) at the time of first ASCT can be offered tandem ASCT (second ASCT within 6 months), with prior storage of adequate stem cells using DMSO. This approach was proved to increase OS and EFS at 7 years in IFM94 trial. Delaying ASCT at the time of relapse is not as effective as the upfront consolidation ASCT protocol. High risk biology e.g. t (4:14), del (17p) or high β2 microglobin predict poor prognosis even with ASCT. When patient is not in VGPR at the time of stem cell collection, it is practice to use intermediate dose cyclophosphamide or plerixafor based mobilization. Melphalan, overuse of Lenalidomide and RT are to be avoided if ASCT is in consideration. The optimum dose of CD 34 cells in collection should be 6 to 10 million.Post transplantation maintenance of thalidomide, lenalidomide and bortezomib have demonstrated superior progression free survivals (PFS), but the risks of secondary malignancies should be explained. Second transplants are beneficial to patients who have PFS >36 months after first ASCT. Third ASCT are usually not beneficial [10-15].

Future directions in myeloma ASCT

Novel conditioning regimens, Pet CT scan and minimal residual disease (MRD) are being increasingly incorporated to enhance the ASCT outcomes of MM.

Landmark trials in myeloma ASCT

Child et al. [10] reported CR rate of 44% with Melphalan 200 mg/m2 as compared to 8% with chemotherapy on population less than 65 years of age with MM. Both OS and EFS were superior for ASCT than chemotherapy.

Lymphoid malignancies

Relapsed Hodgkin and relapsed, aggressive non Hodgkin lymphoma demonstrate 45% cure rate with ASCT. In heavily pretreated patients cytokine only based mobilization may be inadequate and chemotherapy or plerixafor based mobilizations are preferred. CBV and BEAM are standard conditioning regimens for ASCT in lymphoma. Radioimmunotherapy based conditioning regimens are not favoured in various studies [16-23].

Follicular lymphoma, first remission

The routine use of upfront ASCT consolidation in follicular lymphoma is not recommended in the rituximab era because though ASCT may offer better event free of progression free survival, it does not associated with better overall survival rather it is associated with increased TRM and greater percentage of secondary malignancies [16].

Follicular lymphoma (FL), relapsed

ASCT is reserved for chemotherapy sensitive, relapsed FL in patients who are not candidates for allogenic transplantation. CIBMTR-2004 retrospective data shows better overall and event free survival with purged ASCT (62% *vs.* 55%).

Transformed FL

ASCT is indicated for transformed FL with nonbulky and chemosensitive disease.

Mantle cell lymphoma (MCL)

ASCT is recommended for chemosensitive, relapsed MCL patients, who are candidates for allogenic HSCT. Hermine et al. [19] demonstrated near doubled EFS (84 months *vs.* 49 months) with marked OS advantage with R-DHAP induction ASCT. Rituximab and addition of Cytarabine in induction improved the OS [20].

Waldenstrom macroglobulinemia(WM)

ASCT is indicated in relapsed chemosensitive WM patients who have received 2 or 3 different therapies.

Marginal zone lymphoma (MZL)

In relapsed, chemosensitive MZL, ASCT is recommended.

Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)

ASCT is not beneficial in CLL/SLL.

Diffuse large B cell lymphoma (DLBCL), first remission

Upfront ASCT is not indicated in DLBCL.

DLBCL, relapsed disease

ASCT is standard treatment for relapsed, chemosensitive DLBCL. CORAL study (2010) established the role of ASCT (EFS 53%) for relapsed DLBCL after RICE and RDHAP based salvage [23].

Burkitt lymphoma (BL)

ASCT is not required in BL in first CR, but in relapsed chemosensitive BL gives 3 year PFS of 30%.

Hodgkin lymphoma (HL), relapsed or primary refractory

ASCT is curative and standard procedure in relapsed chemosensitive HL as well as primary refractory cases. CIBMTR (2001, 1999) data shows that patients in second CR have better outcomes and upto 40% of primary refractory patients can be salvaged by ASCT [22].

T cell lymphoma (TCL)

ASCT can be considered for relapsed, chemosensitive TCL patients who are not candidates for allo SCT. Tumour cell contamination in Autograft: *In vivo* (rituximab based) or *ex vivo* (by monoclonal antibodies, CD34+ selection) purging have not been successful till date to increase the survival by decreasing the tumour cell contamination in autograft.

Post-transplant maintenance therapies for lymphoma

Post-transplant rituximab maintenance has shown to increase the PFS in FL but not in DLBCL.

PET scan in ASCT

Pet negative state before or after ASCT is predictive of improved ASCT outcomes.

Rarer plasma cell dyscrasias

High dose therapy with melphalan has been effective in Light chain amylodosis, light chain deposition disease, and POEMS syndrome but randomized clinical trials are yet awaited.

Acute myeloid leukemia (AML)

Patients of AML with favourable or intermediate risk cytogenics can be considered for ASCT after induction therapy when suitable donor is not available.

Acute lymphoid leukemia (ALL)

Routine ASCT in ALL in first line as consolidation or maintenance or in relapsed patients is not recommended in current scenario. Some older studies have demonstrated similar EFS with ASCT as compared to allo SCT in selected patients. However, Philadelphia chromosome positive patients receiving tyrosine kinase inhibitors with chemotherapy can be considered for ASCT when suitable donors are not available.

Germ cell tumour (GCT)

ASCT is recommended in high risk GCT who are relapsed after or refractory to first line chemotherapy.

Late complications of ASCT

ASCT decreases the life expectancy and have increased risk for opportunistic infections, iron overload, endocrine disturbances, osteoporosis and second malignancies.

Preventive maintenance after transplant

It is also recommended to follow healthy practices i.e. not using tobacco and alcohol, having healthy foods, exercise and regular sunscreen use.

Blood tests: Annual complete blood count (CBC), blood glucose level, serum lipid levels, liver function tests, renal function tests, thyroid hormone levels.

Dental: To maintain good oral health and having routine dental examinations after transplant. One can resume routine dental

cleanings and treatments after 6 months of ASCT. One should avoid routine dental treatment if he had an ASCT less than 6 months before. This precaution does not prevent you from receiving dental treatment that is necessary. If dental treatment is medically necessary, it is important to take antibiotics before the treatment for preventing infections. Dentist should know that patient has had a transplant. The risk for osteonecrosis persists for many years, even after treatment with the bisphosphonate drug has been stopped. Children who had a transplant before the age of 10 should have a Panoramic dental x-ray taken approximately every year to assess tooth development and eruption.

Eyes: Evaluation is done for cataract annually.

Lungs: Pulmonary function tests one year and five years after transplant, or annually if respiratory symptoms.

Bones: Bone density test / DEXA scan at one year post-transplant, to be repeated annually if the initial test shows decreased density. Patients taking prednisone should do a DEXA scan annually.

Colon: Test for blood in the stool every year and a colonoscopy at age 50 years.

Females: Annual Pap smear, breast examination and mammogram (after age 45).

Patients with CML: BCR/ABL test annually.

Children: Every 6 months height should be measured. Growth hormone levels should be tested every year until age of 16 years. Pulmonary function tests should be done annually after age 6. The transplant related treatments with chemo-radiation increase the risk of second cancers e.g. skin cancer, head and neck cancer, breast cancer, thyroid cancer (papillary thyroid carcinoma), and brain cancers (astrocytomas). The risk of hepatocellular carcinoma is increased in patients with hepatitis C infection. We recommend that all patients should follow a healthy lifestyle. Exercise, walking and weight-bearing for 20-60 minutes every day for stamina and to prevent bone loss; a healthy, balanced diet with five daily servings of fruits and vegetables; vitamin and mineral supplements of calcium and vitamin D, to prevent bone loss when the diet doesn't contain recommended 1500 mg of calcium and 800 i.u. of vitamin D per day; avoiding exposure to direct sunlight by using a hat, long-sleeves and sunscreen; regular hand-wash.

Indian data

Most common indication for ASCT in India is MM which comprises half population of ASCT cases, lymphoma being the next common. There are 52 HSCT centres in india. Though the population of India is several times more than USA, the HSCT activity in india is 10 times less than USA. This is the failure to deliver standard of care curative treatment strategies in cancer. But the graphical representation of estimated HSCT activity in Figure 1 and Figure 2 shows that the HSCT activity in India in exponentially increasing and hopefully soon the unmet need will be covered. In total 52 centers across all over India overall 10381 stem cell transplantations were reported since 1983 to 2015. Out of these 6240 were allo SCT whereas 4141 were ASCT. The graph shows gradual but persistent increase in the SCT activity. In initial decade the numbers counted less than 10 per year but presently it has reached more than a thousand per year. Sixty percent of this counts allogenic and 40% is autologous SCT activity.

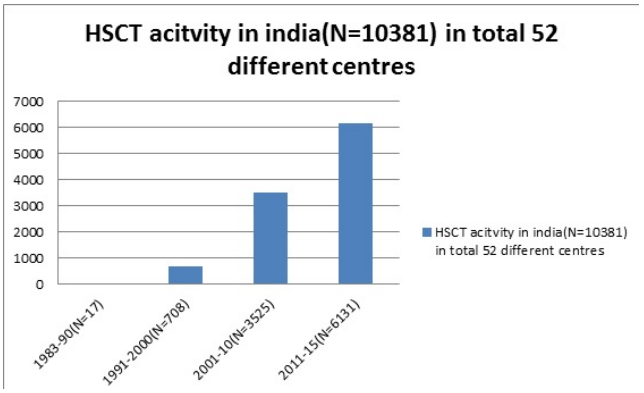

Figure 1: Yearwise growth of overall hematopoetic stem cell transplant activity in India

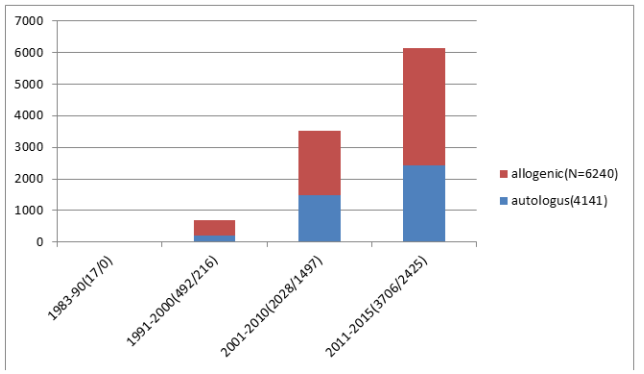

Figure 2: Yearwise growth in autologus and allogenic stem cell transplant activity in India.

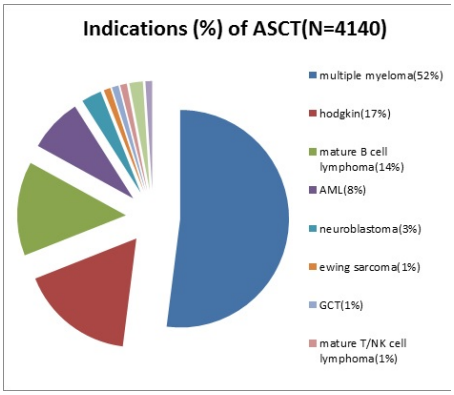

Figure 3: Percentage representation of various diseases undergoing autologous hematopoetic stem cell transplant in India.

Out of 4140 autologus transplants, 52% were multiple myeloma, 14% were mature B cell lymphoma, 17% were Hodgkin lymphoma.

Cost of ASCT in India

ASCT is not an expensive mode of therapy in developing countries as compared to west but it is still unaffordable to most of Indian patients. It costs 5 to 10 lakh. This cost is 20 times more in developed countries. Therefore india has a good scope and potential for medical tourism in HSCT. Majority of the bacterial infections documented from western world has dominance of gram positive organisms but in India, gram negative organisms dominate the culture reports. Also, there are a few reports from India showing good outcome of HSCT even in compromised infrastructure e.g. without HEPA filters. The trend of "ASCT with bone marrow proper" collection has been shifted to "peripheral blood stem cell based ASCT" without compromising efficacy. Still the major hurdle seems to be financial problems and lack of awareness about HSCT leading to less referral for HSCT in Indian medical practice. Provided the curative potential of HSCT even in relapsed/ refractory cases the serious efforts and awareness should be increased along with the formal training of the procedure (Figure 3).

Future

Current national capacity is suboptimal to meet the needs for India's population (with an estimated incidence of 1,000,000 new cancer patients/year). Existing centers need to focus on the development of regimen/ strategies tailored to our needs. For instance, cancers like MM are diagnosed very early in our population. They are in the most productive phase of their lives and are fit to tolerate dose intensive therapy. Hence they should be subject to strategies that lead to a curative outcome. HSCT is the only curative mode of treatment for several cancers. Gene therapy is yet to standardize its application with HSCT.

Medical Tourism in India

By 2020 India is projected to a growth about 8 billion dollars in medical tourism. India is preferred medical hub by UK and USA due to low cost of treatment while Bangladesh and Afghanistan patients prefer Indian healthcare due to poor infrastructure in respective countries and close proximity to India. Russia and Middle East country patients contribute in next rank. Major destinations in India include Chennai, Kolkata, Mumbai, Hyderabad, and Delhi-NCR. Indian healthcare is advancing to international qualities and patients all over the world face lesser language barrier day by day. There are approximately 25 JCI accredited hospitals in India. Visa on arrival scheme allows foreign patients to stay about a month which decreases the difficulty of foreign patients taking treatment in India. Some hospitals also have hired the facility of language translators to facilitate foreign patients.

Advantages
No need to identify donor if peripheral blood is uninvolved by tumour at the time of collection
No immunosuppression, less risk of infections
No GVHD
Dose intensive therapy can be used for older patients(usually up to age 70)
Low early treatment related mortality (2%-5%)
Disadvantages
Not feasible if peripheral blood stem cells/ marrow involved
Possible marrow injury leading to late myelodysplasia (either from prior chemotherapy or transplant regimen)
No graft versus tumour effect
Not all patients can be mobilized to give adequate cell doses for reconstitution.

Table 4: Advantages And Disadvantages Of Autologous Stem Cell Transplantation (ASCT)

Year and author	Analysis	Institution	Contribution
2017, prinja et al. [23]	cost effectiveness of ASCT	PGI Chandigarh	Cost effectiveness of ASCT improved with early detection and initiation of treatment.
2016, Raut et al. [24]	ASCT in HD	GCRI Ahmedabad	DFS 65% and OS 70%
2016, Kumar et al. [24]	ASCT for myeloma: long term results	AIIMS new Delhi	CR following ASCT associated with good long term outcome. PFS:32 months, OS: 85.5 months
2015, Raut et al. [25]	safety of Eltrombopag in post HSCT thrombocytopenia	GCRI Ahmedabad	25–50 mg OD Eltrombopag for post-HSCT thrombocytopenia is well tolerated, appears efficacious and offers transfusion independence.
2015, Shah et al. [5]	data from western India	Apollo hospital, Gandhinagar	comparability with international standards

2014, Shah et al. [26]	ASCT in MM in Non university hospital of developing country	Apollo hospital, Gandhinagar	ASCT feasible in Non university hospital
2014, sharma et al. [3]	cost of HSCT in India	BLK superspeciality hospital New Delhi	ASCT cost12500 USD(10331-39367)
2014, Kumar [27]	CR after ASCT in MM	AIIMS New Delhi	those who receive one line of induction therapy before transplant have superior outcome,
2013, Kayal et al. [14]	ASCT using non cryopreserved peripheral blood stem cells	AIIMS New Delhi	Noncryopreserved PBSC is simple, effective and safe.
2012, Mukhopadhyay et al. [7]	Data from Eastern India	NCRI Kolkata	ASCT cost 3-4 lakhs
2010, Kumar et al. [18]	ASCT for HL and NHL	AIIMS New Delhi	pretransplant chemosensitive disease and CR after transplant had better survival

Table 5: Summarizing latest scientific reports with their inputs in ASCT activity in India

Compliance with Ethical Standards

We didnot violate any of the ethical concerns in this study.

Funding

This study was not funded.

Conflict of Interest

Author declared no conflicts of interest in any form. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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