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Cardiotoxicity Proceeding Stem Cell Transplantation

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Introduction

HSCT is a process in which there is intravenous infusion of progenitor cells and hematopoietic stem cells to revive normal hematopoiesis. When stem cells are taken from patient's own body, this is called autologous HSCT. When stem cells are taken from identical twin of the patient, this is called syngeneic HSCT. When stem cells are taken from body other than patient (siblings), this is called allogeneic HSCT [1].

During the procedure, autologous or allogeneic stem cells are infused into veins in order to restore normal hematopoietic function.

- Evaluation of health status: It involves following steps (complete history and physical exam, Evaluation of your psychological and emotional strengths, HLA tissue typing, Blood tests, such as a complete blood count, blood chemistries, and screening for viruses like hepatitis B, CMV, and HIV, CT (computed tomography) scan or MRI (magnetic resonance imaging), ECG or echocardiogram, chest x-ray and PFTs (pulmonary function tests).

- Conditioning treatment: It is also known as bone marrow preparation, is treatment with high-dose chemo and/or radiation therapy. It's the first step in the transplant process and usually it takes a couple of weeks.

- Infusion of stem cells: Infusion of cells is done through central venous catheter, much like a blood transfusion. If frozen stem cells are taken, patient might get some drugs before the stem cells are given. These drugs are used to prevent the reaction to the preservatives that are used when freezing the cells.

Stem cell transplantation is curative in a number of otherwise fatal hematological diseases.

In an autologous transplant, stem cells are collected from the patient themselves, harvested, frozen and stored, then given back to the patient after intensive therapy. An autologous stem cell transplant is different from an allogeneic stem cell transplant, which uses stem cells from a matching donor.

One of the most potential life threatening late effects of stem cell transplant is cardiovascular disease. In some of the previous reports, a range of Stem cell transplant related cardiotoxicity have been revealed which includes, pericardial effusion, hypertension, valvular diseases, congestive heart failure, arrhythmias and pericarditis [2-6]. Some of the studies which were done earlier states that incidence of arrythmias taken place during autologous or allogeneic Stem cell transplant is 9-27% [7-12]. Those transplant recipients with increasing age experience more pre-stem cell transplant comorbidities, like arrhythmias [13-15]. With the help of clinical cardiac evaluation in pre-stem cell transplant patients, major cardiotoxic events including cardiac tamponade and heart failure have been reported to be uncommon (<1% of patients) but incidence of supraventricular arrhythmias is high and is complicating the clinical course of such patients [16]. Arrhythmias, especially supraventricular arrhythmias, however more commonly complicate the clinical course of these patients [17-20]. This fact become more clear by a report by Olivieri et al in 1998, which reported 5 complicated cases of atrial fibrillation in recipients of stem cell transplant who were on high dose Melphalan [21]. Some more studies suggested the incidence of supraventricular arrhythmias is 4-10% in bone marrow transplant recipients [17-20]. Cyclophosphamide-induced cardiomyopathy or hemorrhagic pericarditis, thiopental-related acute myocarditis and brady-arrythmias during the infusion of progenitor cells cryopreserved with dimethylsulfoxide (DMSO) are some of the acute cardiac toxicities occurring during conditioning and immediate post-transplant period [23,24]. These cardiac complications can occur acutely (within 100 days) or as a chronic complication. Some studies revealed that most common arrhythmias includes, atrial fibrillation, atrial flutter and supraventricular tachycardia [25]. Older age, baseline renal dysfunction, prior anthracycline use, history of prior arrhythmias, a lower ejection fraction at baseline and presence of premature supraventricular complexes on baseline screening electrocardiogram are some of the risk factors for development of arrhythmias [26]. According to a study, post-transplant arrhythmias are associated with greater risk for death within a year of transplant, these results were confirmed by another study which proved 40% risk of mortality in patients who developed arrhythmias during first 100 days of transplant [27,28]. Most preoperative regimen for allogeneic stem cell transplant use Cyclophosphamide and its high dose can induce myocardial necrosis which manifest as tachycardia, decreased QRS voltage, hypertension and dyspnea within 10 days of drug administration. Histology samples taken from these patients showed unique pattern of fibrin micro-thrombus in capillaries, fibrin strands

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in interstitium and fibrin strands in myocytes [29].

Methodology

This cross-sectional study was conducted from January 2014 - December 2017 in South-East Asia. Patients above 20 years of age were recruited in this study. Sample size was 786. A history and examination form designed from an application "Forms", particularly for the study. For data analysis SPSS 16.0 software was used. Seven eighty six patients undergoing allogeneic (n=550) or autologous (n=236) BMT were evaluated by physical examination, history, rest and exercise ECG, chest x-ray, two-dimensional echocardiography, and radionuclide ventriculography (RNV) before BMT, and monitored for 5 months thereafter.

Results

Following stem cell transplantation, cardiac toxicity occurred in two hundred and eighty eight patients (36.64%). One forty three patients (18.2%) developed life-threatening toxicity (pericardial effusion and left ventricular failure, n=72; sudden cardiac arrest, n=71). Thirty-eight patients (4.83%) had pathologic findings before transplantation. In 62 patients, left ventricular ejection fraction (EF) determined by RNV was reduced to less than 55%. This was the only abnormality in 71 patients and was generally mild, with a lowest EF of 42%. 184 had no cardiac events after stem cell transplantation. Cardiotoxic events occurred more frequently in patients with a reduced EF (P<.05). Life-threatening cardiac toxicity was not significantly increased in patients with pathologic results before transplant. Moreover, none of the patients with an EF less than 50% developed cardiac toxicity.

Discussion

Stem cell transplantation is well and truly underway in South East Asia. High-dose chemoradiotherapy is the major cause of organ toxicity. Cardiac complications have been described in HSCT with the majority of reported cardiac complications during HSCT attributed to the use of high-dose cyclophosphamide [30].

We observed that acute, major cardiotoxic events attributable to stem cell transplant are uncommon, occurring with a frequency of <5%. These data suggest that with appropriate pre-transplant clinical evaluation, high-dose cyclophosphamide and irradiation in the BMT preparative phase does not result in frequent, clinically relevant short-term cardiac toxicity [31].

Patients who undergo bone marrow transplantation are generally immunosuppressed with a dose of cyclophosphamide which is usually calculated based on the patient's weight. At these high doses, serious cardiotoxicity may occur [32].

Although the occurrence of cardiac toxicity is correlated with a reduction of EF before BMT, life-threatening cardiac toxicity cannot be predicted in individual patients [33].

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