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THE ROLE OF POST GRANULOCYTE COLONY-STIMULATING FACTOR WHITE BLOOD CELL COUNTS IN PREDICTING THE MOBILIZATION ADVERSE EVENTS AND YIELDS

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Background: To evaluate the incidences of adverse events of granulocyte colony-stimulating factor (G-CSF) and the impacts of post G-CSF white blood cell (WBC) counts on adverse events and mobilization yields in healthy peripheral blood stem cell donors.

Materials and Methods: Four hundred seventy-six healthy donors were given G-CSF of 10μg/kg/day for 5-6 consecutive days. The WBC counts were determinated at baseline, after third dose (before the forth dose on Day4) and after fifth dose (before leukapheresis on Day5) of G-CSF administration. Performance status and symptoms were recorded everyday before G-CSF injection. The incidences of adverse events and mobilization yields were compared between different donor characteristic groups. Multivariate analysis was used to analyze the correlations between the adverse events and donor factors.

Results: Bone pain (64.9%), myalgia/arthralgia (58.2%), fatigue (44.1%) and headache (33.0%) were the most common side effects. The third day and fifth day median WBC counts were 35,050/μL and 45,905/μL. Donors with WBC ≥ $50x10^3$/μL after 3 doses of G-CSF experienced more fatigue, myalgia/arthralgia and chills (p = 0.0314, 0.0066 and 0.0121) but post G-CSF $CD34^+$ cells were similar (72.6/μL *vs* 68.7/μL, p = 0.5916). Although the $CD34^+$ cells were higher in donors with WBC ≥ $50x10^3$/μL after 5 doses of G-CSF (89.3/μL *vs* 59.1/μL, $p < 0.0001$), the incidences of side effects were similar. Female donors more frequently had headache, nausea/anorexia, vomiting, fever (p = 0.003, < 0.0001, 0.0016 and 0.0392) and lower post G-CSF $CD34^+$ cell count than male donors did (78.0/μL *vs* 59.0/μL, $p < 0.0001$). Donors with body mass index ≥ 25 had higher incidences of sweat and insomnia (p = 0.0211 and 0.0318) and also higher $CD34^+$ cell count (79.9/μL *vs* 64.9/μL, $p < 0.0001$). Donor receiving G-CSF ≥ 10μg/kg tended to have bone pain, headache and chills (p = 0.0085, 0.0270 and 0.0085). The side effects and $CD34^+$ cells were not different between young and old donors.

In multivariate analysis, female donor experienced more fatigue, nausea, vomiting, bone pain, myalgia/arthragia, headache, fever and insomnia. Higher BMI donor had more fatigue, myalgia/arthragia and sweats. G-CSF dose was associated with bone pain and the WBC count post the third G-CSF was associated with fatigue only.

Conclusion: Female and high BMI donors are associated with higher risk of side effects of PBSC mobilization by G-CSF. Routine monitor of the post G-CSF WBC count provide minimal benefit in predicting side effects. Reducing dose or discontinuation of G-CSF should mainly base on the clinical severity of adverse events.

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AFFECT OF CARDIAC COMPLICATIONS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FROM VARIOUS STEM CELL SOURCES

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Background: Cardiac complications after Allogenic Hematopoietic Stem Cell Transplantation (allo-SCT) have varied among studies. Furthermore, various stem cell sources have increasingly been used as a therapeutic option, it remains unknown the affect of cardiac complications after allo-SCT from various stem cell sources.

Patients and Methods: We retrospectively reviewed 172 patients underwent allo-SCT at Okayama University Hospital between May 2004 and October 2010, for whom electrocardiography (ECG) and ultrasound cardiography (UCG) within 3 months before transplantation. The median age at allo-SCT was 50 years (range: 16-74). Donor sources were related peripheral blood in 41, related bone marrow in 13 and unrelated bone marrow in 66, and umbilical cord blood in 52 cases, respectively. 80 (46.5%) patients had high risk disease at the time of transplantation.

Results: We identified 31 patients (18%) with grade 2-4 cardiac complications within 28 days after allo-SCT according to the Common Terminology Criteria for Adverse Events v3.0 (CTCAE). 4 patients (0.02%) developed grade 3-4 cardiac complications. The median time of onset after allo-SCT was 9 days (range: -7-23 days). Manifestation of cardiac complications was mainly pulmonary congestion in 19, while hypertension in 5, arrhythmia in 3, pericardial effusion in 2, cardiac ischemia in 1 and hypotension in 1 case, respectively. 2 patients died of cardiac causes after the onset of severe cardiac complications. The cumulative 1-year overall survival in patients with or without cardiac complication was 46.8% and 57.2%, respectively (p = 0.29). There was no difference in the ECG/UCG findings, the cumulative dose of anthracyclines and between patients with and without cardiac complications. Furthermore, no difference in rate of cardiac complications was observed in among stem cell sources.

Conclusion: Although from a retrospective study, these results suggest that cardiac complications were associated with relatively poor survival but not with stem cell sources although this finding must be considered with caution due to the small sample size.

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LINEAGE-SPECIFIC CHIMERISM ANALYSIS IS A SENSITIVE PREDICTOR OF OUTCOME AFTER ALLOGENEIC MYELOABLATIVE AND NONMYELOABLATIVE STEM CELL TRANSPLANTATION

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Monitoring chimerism in allogeneic hematopoietic stem cell transplant (HSCT) recipients is of great clinical significance after different conditioning regimens. Analysis of lineage-specific leukocytes provides useful information in predicting the clinical outcome and plays a critical role in the management of HSCT patient. We have analyzed donor-type chimerism in CD3+ T cells, CD19+ B cells, CD15 + myeloid cells and CD34+ progenitor cells in patients who had undergone myeloablative and nonmyeloablative HSCT for acute myeloid leukemia (AML) and non-AML. The engraftment analysis was performed by PCR-based detection of donor- and recipient-specific short tandem repeats (STR) using enriched T cells, myeloid cells, B cells and progenitor cells from peripheral blood and bone marrow samples prior to isolation of DNA. Chimerism analysis performed on CD34+ progenitor cells was most useful in early detection of relapse in AML patients than unfractionated whole blood analysis due the increased sensitivity in the enriched cell subpopulations. Monitoring of leukemia- and lymphoma-affected cell lineage predicted relapse. Determination of the level of donor T cells appears to be critical for successful engraftment and predict graft versus host disease in transplant patients who underwent nonmyeloablative HSCT. Donor-type chimerism in lineage-specific cell population appears to impact outcome and allows early intervention.

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SAFETY OF LIPOSOMAL AMPHOTERICIN B IN ALLOGENIC HEMATOPOIETIC TRANSPLANTATION (HSCT) RECIPIENTS

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In the patients performed HSCT, liposomal amphotericin B (L-AMB) is one of useful antifungal agents because of its broad-spectrum. However, little was known about the safety of L-AMB in allogenic HSCT setting. There were 90 patients administrated L-AMB around allogenic HSCT in our institute from December 2007 to November 2009 consecutively. Thirty-two of those 90 patients were administrated L-AMB at least for 1 week during in day -30 to 120 after HSCT. We analyzed those 32 patients, included 23 males and 9 females, retrospectively. Median age was 58 (29-68) yrs. Stem cell sources of HSCT were 22 CB, 7 unrelated BM and 3 sibling-PB respectively. Two patients used L-AMB as prevention to invasive fungal infections (IFIs) and 30 treatment. Thirty-one patients received other prior anti-fungal therapies. Median follow up period from the day starting L-AMB was 71.5 (7-466) days. Median