

Safe and sufficient dose of total body irradiation for unrelated donor transplants in aplastic anemia.

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Hematopoietic stem cell transplantation from unrelated donor is often attempted for patients with acquired severe aplastic anemia. Overall survival of unrelated donor transplant for aplastic anemia is lower than that of sibling donor transplant because of higher rate of transplant related mortality (TRM) and graft failure, which are deeply influenced by the intensity of pretransplant conditioning. We conducted a prospective study to determine the sufficient and safe dose of total body irradiation (TBI) as a pretransplant conditioning which was combined with the fixed dose of cyclophosphamide 120 mg/kg in unrelated donor transplantation setting for adult aplastic anemia. The starting dose was 1,200 cGy and the dose was to be escalated or de-escalated by 200 cGy according to toxicity and graft failure. Twenty eight patients were enrolled, all of whom were heavily transfused and poorly responded to immunosuppressive therapy. The numbers of the patients who received 1200, 1000 and 800 cGy of TBI were 5, 9 and 14, respectively. Corresponding probabilities of overall survival at 3 years were 40.0, 44.4 and 92.9 %, respectively. Three of five patients (60%) who received 1200 cGy of TBI and five of nine (55.6%) patients who received 1000 cGy of TBI died of transplant related complications. Only one of the patients whose TBI dose was 800cGy died of posttransplant thrombotic microangiopathy. The causes of death of the patients who received 1000 cGy or more of TBI were infection(4/8), chronic GVHD(3/8) and graft rejection(1/8). According to univariate Cox proportional-hazards regression analysis, the prognostic factors for overall survival were the TBI dose (P=0.01), the transfusion amount before transplants (P=0.02), the level of resolution of HLA typing (P=0.04) and the presence of chronic GVHD (P=0.03). We concluded that 800cGy of TBI combined with 120 mg/kg of cyclophosphamide was safe and sufficient for pretransplant conditioning for acquired aplastic anemia in unrelated donor stem cell transplantation setting.

Pro475Ser polymorphism of ADAMTS13 gene is associated with decreased ADAMTS-13 activity

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Background : The proline to serine polymorphism in codon 475 (C1423T) of the ADAMTS-13 gene was found to impair ADAMTS-13 activity in vitro study, but it remains to be clarified whether heterozygote individuals with this mutation show the reduced activity or not. We investigated the frequency of the C1423T polymorphism and its effect on the plasma ADAMTS-13 activity in Korean healthy individuals. **Methods :** The study population was enrolled from January 2004 to February 2004 from patients who visited Bundang CHA Hospital's health promotion center(n=250). The genotype was determined by polymerase chain reaction, digestion with RsaI and separation on a 2% agarose gel. The activity of plasma ADAMTS-13 was detected by fluorescence resonance energy transfer assay. **Results :** The allele and heterozygote frequency of C1423T polymorphism were 4% and 8% respectively. The median (range) activity of CT type was 78 (55-95)%, which was significantly lower than that of CC type, 85 (72-127)% (p=0.014). **Conclusion :** C1423T mutation of ADAMTS-13 gene contributes to decreased ADAMTS-13 activity in heterozygote individuals.