Changes in immunological recovery in patients who received post-transplant G-CSF or GM-CSF after autologous peripheral blood stem cell transplantation (PBSCT) 1


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Abstract—In this prospective study, the effects of granulocyte colony-stimulating factor (G-CSF) and granulocyte–macrophage colony-stimulating factor (GM-CSF) on immunological reconstitution after autologous peripheral blood stem cell transplantation (PBSCT) were investigated for 6 months. Thirty-five patients received G-CSF 5 μg/kg per day and 26 patients received GM-CSF SC 5 μg/kg per day from day 1 to leukocyte engraftment (>1000 per mm³). Peripheral blood samples were obtained on 14, 28, 100, and 180 days after transplantation for immunological evaluation. CD3+, CD4+, CD8+, CD19+, and CD56+ cells were analysed by flow cytometry. Immunoglobulin levels (IgG, IgA, and IgM) and complement levels (C3c and C4) were measured by nephelometry. Both G-CSF and GM-CSF groups were comparable with respect to age, sex, the period from diagnosis to transplantation, total nucleated cells infused, the number of CD34+ cells, conditioning regimens (TBI and non-TBI), and post-transplant infection. CD3+ and CD8+ cells on day 14 following autologous PBSCT + G-CSF were significantly higher than following autologous PBSCT + GM-CSF (p = 0.008 and p = 0.021, respectively). The number of CD4 cells and the CD4/CD8 ratio were not different at several time points between the two groups. CD19+, CD56+ cells and immunoglobulin levels showed a faster recovery pattern in the autologous PBSCT + G-CSF group. The effect of G-CSF on immune reconstitution after autologous PBSCT is more prominent than that of GM-CSF. The possible role of haematopoietic growth factor on immune recovery and its clinical importance should be investigated in further studies.

Key words: Autologous PBSCT; G-CSF; GM-CSF; immune recovery.

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INTRODUCTION

The success of post-transplant immune recovery depends on the haematopoietic reconstitution and the interactions of various haematopoietic cytokines and growth factors. Nowadays, different haematopoietic progenitor cell transplantation models are being used as graft sources (bone marrow, mobilized peripheral blood, cord blood) and graft origins (allogeneic, autologous). It has been shown that haematopoietic growth factors such as G-CSF or GM-CSF accelerate myeloid recovery in the course of haematopoietic progenitor cell transplantation by reducing both the infectious complications and the need for post-transplant supportive treatment [1].

Studies of the effects of GM-CSF and G-CSF have concentrated basically on the acceleration of the myeloid series improvement provided by these factors [2–4]. Limited information is available on the effect of haematopoietic growth factors on the immunological reconstitution after autologous BMT. The information available is generally related to major T, B, and NK cell populations [5–7] and there are very few data on other lymphoid cell subsets that may play a key role in the immune system.

There are no GM-CSF and G-CSF receptors in normal lymphocytes [8]. However, these haematopoietic growth factors may influence the immune response by exhibiting their effects on accessory cells [8, 9]. It is suggested that GM-CSF increases IL-2 mediated T-cell proliferation [10] and the activation of NK cell function together with a possible decrease in leukaemic relapse [11]. G-CSF can also restore IL-2 production in the blood of HIV-infected patients [12]. TNF-α and IFN-γ release from lipopolysaccharide-stimulated blood is suppressed by G-CSF in the blood of healthy volunteers [13]. There is only one randomized study comparing the effects of G-CSF or GM-CSF, used in the post-transplant period, on lymphoid reconstitution [14]. B-cell reconstitution is not affected by the use of different haematopoietic growth factors [15]. It has also been reported that NK cell activity is not affected by the use of different growth factors [15].

In this large, prospective trial, the kinetics of immunological reconstitution of T and B lymphocytes and NK cells; the immunoglobulin and complement levels; and the effects of G-CSF and GM-CSF on immunological recovery in autologous PBSCT in the early post-transplant period (0–180 days) were investigated in patients who underwent autologous PBSCT.

MATERIALS AND METHODS

Patients

Between January 1997 and February 1999, 61 patients who underwent autologous PBSCT in the GATA BMT center were studied prospectively regarding immunological reconstitution in the early post-transplant period (0–180 days). Of the 61