Relation Between Hematological Recovery and Number of Transplanted Mononuclear Cells in Patients after High Dose Chemotherapy with Peripheral Blood Stem Cell Rescue

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ABSTRACT: The aim of the study is to investigate the relation between the hematological recovery in patients after high dose chemotherapy and peripheral blood stem cell (PBSC) rescue and the number of reinfused previously collected stem cells assessed by the number of mononuclear cells (MNCs), CFU-GMs and CD34(+) cells in the harvest. Forty nine patients mobilized with different techniques were transplanted. Our data indicate that the number of reinfused MNCs and CFU-GMS has a statistical significant relationship with the duration of leukopenia and thrombocytopenia following high dose chemotherapy and PBSC rescue in patients with various malignancies.

Keywords: peripheral stem cells, transplantation, hematological recovery

INTRODUCTION

Peripheral blood stem cell (PBSC) transplantation is a viable alternative to autologous bone marrow transplantation (ABMT) and has been successfully used in patients with malignant diseases (1,2) after high dose chemotherapy.

Despite the promising results of PBSC transplants, considerable uncertainty has remained about the timing of harvest and the number of cells and phereses required for an adequate collection. Various numbers of mononuclear cells (MNCs), CFU-GMs and CD34(+) cells have been proposed (3-6), but there is not a universally accepted best way for the qualitative assessment of the harvest.

We investigated the relation between the hematological recovery in patients after high dose chemotherapy and PBSC rescue with the number of reinfused previously collected stem cells assessed by the number of MNCs, CFU-GMs and CD34(+) cells in the harvest.

MATERIALS AND METHODS

In 49 patients at our department who received PBSC (with post transplant growth factor support) after high dose chemotherapy, PBSC were mobilized by 1) rHu-GCSF or rHu- GM-CSF 10 µg/kg/day subcutaneously, 2) high dose cyclophosphamide 6g/m^2 and rHu-GCSF 10 µg/day/subcutaneously, or 3) conventional chemotherapy and rHu-GCSF 10 µg/kg/day subcutaneously. PBSC were collected on a Cobe

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Spectra cell separator during one to five leukaphereses and cryopreserved by controlled freezing. All patients had received prior chemotherapy and part of them radiation too.

Our goal was MNC collection of $2x10^8$/kg and CD34(+) 2 $x10^6$/kg while extra harvested PBSC were stored ready for infusion if engraftment was delayed as evidenced by a neutrophil count less than $0.1x10^9$/L on day 11.

RESULTS

One to five phereses were necessary to obtain the planned number of PBSC based on circulating WBC number and time of recovery after chemotherapy and growth factor administration.

The collected reinfused cells at one to five aphereses and the hematological recovery following PBSC rescue are shown in table 1. Two of 49 patients died of infection prior to engraftment.

Statistical analysis with multiple linear regression of our results (figures 1, 2, 3) indicates that there is a statistically significant relation ($p<.05$) 1) between the reinfused MNCs and the days of leukopenia and thrombocytopenia; 2) between the reinfused CFU-GMs and the days of thrombocytopenia for transplanted patients after high dose chemotherapy.

An increase of reinfused MNCs by $1x10^8$/kg results in a decrease of the duration of leukopenia by 0.5 days and of thrombocytopenia duration by 1.7 days. Additionally, any increase of reinfused CFU-GMs by $1x10^4$/kg results in a decrease of the duration of thrombocytopenia by 0.3 days. The number of CD34(+) cells infused did not correlate with the duration of leukopenia or thrombocytopenia after high dose chemotherapy and PBSC rescue although it was always observed a significant increase of them on the day of leukapheresis.

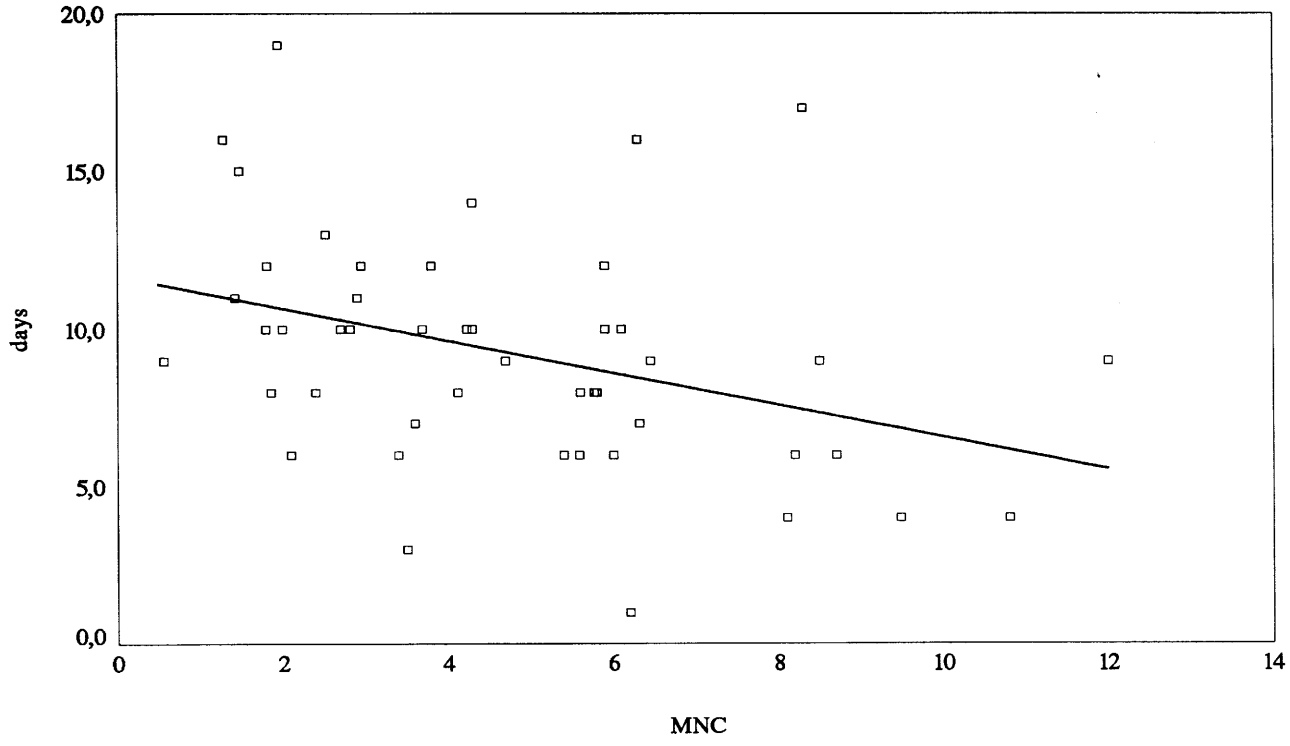

Figure 1. Effect of MNCs on WBC<1000 days

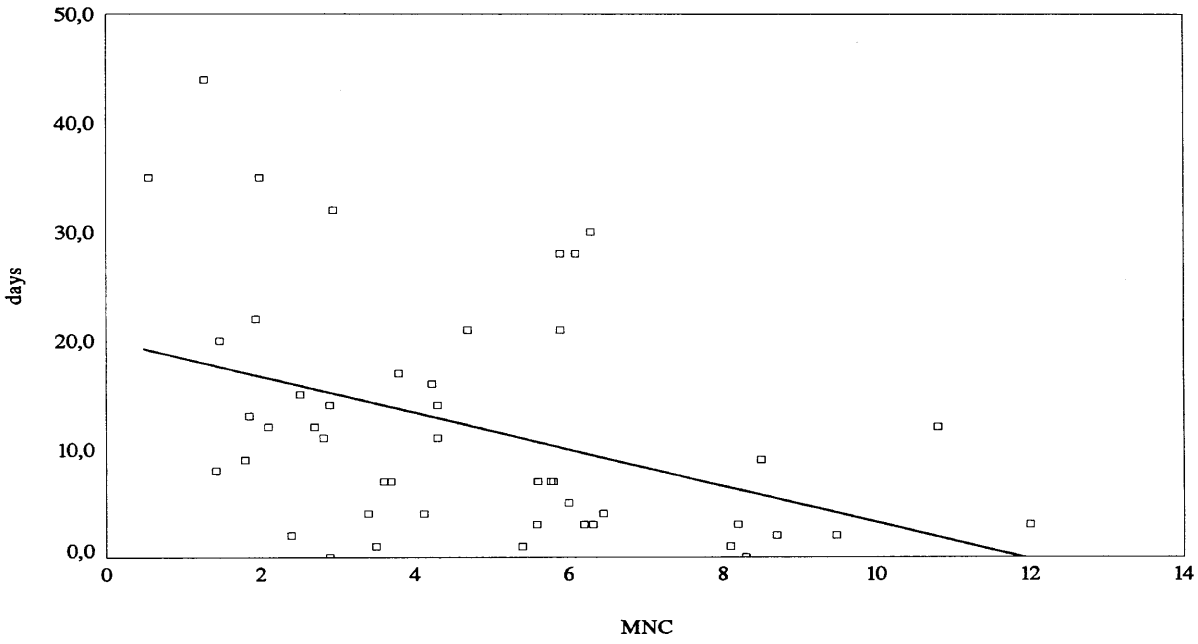

Figure 2. Effect of <MNCs on PLT<20000 days

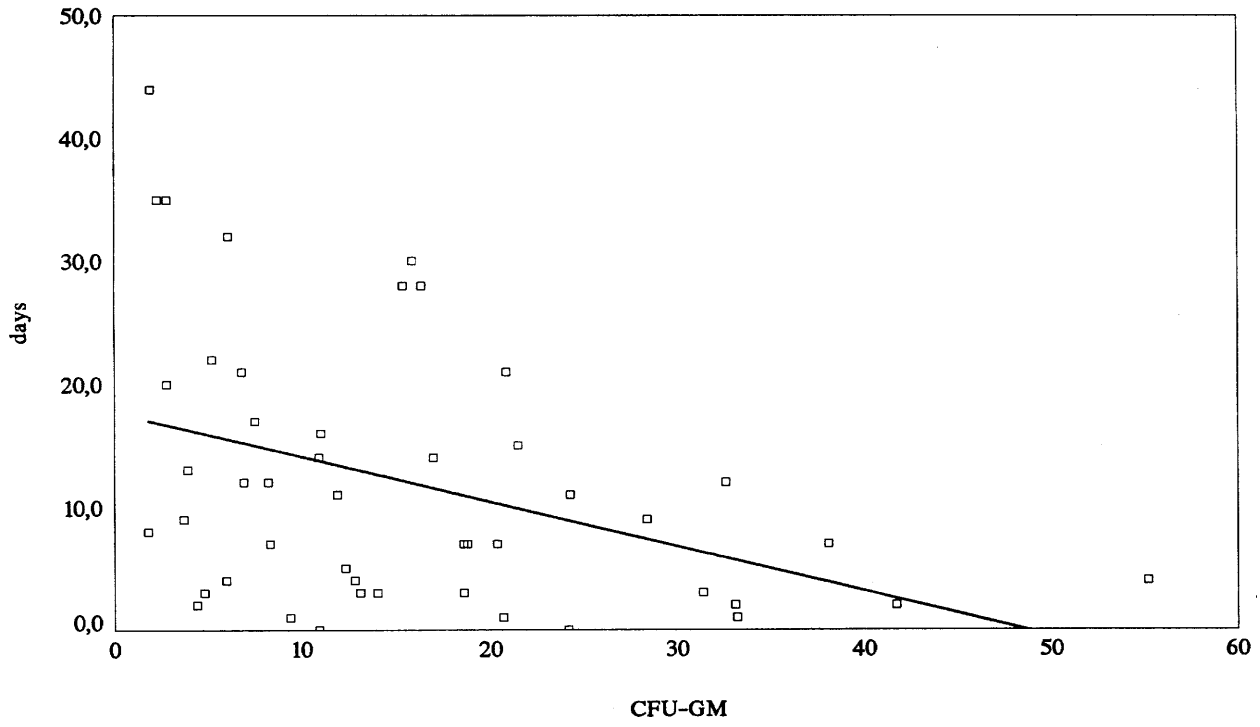

Figure 3. Effect of CFU-GMs on PLT<20000 days

Table 1. Reinfused cells and hematological recovery following PBSC (in 47 patients)

	Total MNC ($x10^8$/kg)	CFU-GM ($x10^4$/kg)	CD34(+) ($x10^6$/kg)	Days to ANC $0.5x10^9$/L	Days to WBC $1.0x10^9$/L	Days to Plt $20x10^9$/L
Median	4.3	12.8	3.38	9	9	11
Range	(0.56-12.0)	(1.8-55.2)	(0-11.8)	(2-19)	(1-19)	(1-135)

DISCUSSION

Our observations are in contrast with similar studies of Siena et al (7) in which the duration of grade IV neutropenia correlated inversely with the number of autografted CD34(+) cells and agree with the findings of Elias et al (8) who was not able to show any correlation of the number of colonies or percent CD34(+) with subsequent reconstitution. The time of collection did not affect recovery times, and it appears that one apheresis with high circulating WBCs is equivalent to multiple aphereses performed at lower WBC number of $<5x10^9$/L.

In conclusion our data indicate that the number of reinfused MNCs and CFU-GMs has statistical significant relation with the duration of leukopenia and thrombocytopenia following high dose chemotherapy and PBSC rescue in patients with various malignancies. The role of the number of CD34(+) cells remains to be elucidated in relation to the above parameters of recovery in patients undergoing high dose chemotherapy and PBSC rescue.

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