FILGRASTIM DOSE HAS AN IMPACT ON INFECTIOUS COMPLICATIONS IN PATIENTS WITH LYMPHOMA FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANTATION

Peric Z[1], Kalac M[1], Jurenec S[1], Kovacevic V[2], Tambic-Andrasevic A[2], Bukovski-Simonoski S[2], Minigo H[1], Jaksic B[1], Vrhovac R[1]

[1]University Hospital "Merkur", [2]University Hospital for infectious diseases "Dr Fran Mihaljevic", Zagreb, Croatia

correspondence to: rvrhovac@mef.hr

BACKGROUND AND OBJECTIVES

Infections represent the leading cause of morbidity and mortality in patients with lymphoma treated with autologous stem cell transplantation.[1] Duration and depth of neutropenia following transplantation correlates with incidence and severity of infections in the post-transplant period.[2] Filgrastim shortens the duration of neutropenia[3,4] but its impact on the course and outcome of infections[5] as well as the preferred dose remain somewhat controversial.[6] The objective of this study was to evaluate infectious complications in patients with lymphoma treated with autologous peripheral blood stem cell transplantation (PBSCT) and investigate possible influence of different filgrastim doses on incidence, severity and outcome of these infections.

PATIENTS AND METHODS

120 consecutive patients (median age 42, range 19–71 yrs, 63M/57F) with relapsed or refractory Non-Hodgkin's Lymphoma (NHL, n=92) and Hodgkin's Disease (HD, n=28) treated with PBSCT in a single center have been evaluated for infectious complications following stem cell transplantation (Table 1). In the post-transplant period, all patients received filgrastim sc., starting from the day of WBC<1x10^6/L until the second consecutive day of WBC>1x10^6/L. Two different dose levels of filgrastim were used, "Low": 300 mcg/day, administered in 58 patients; and "Standard": median dose 600 mcg (SD 94, average 628 mcg), administered in 62 patients.

Table 1.
Patients' characteristics

		LOW DOSE FILGRASTIM	STANDARD DOSE FILGRASTIM	
TOTAL NUMBER		58	62	
GENDER				p=0.05
Male		36	28	
Female		22	34	
DIAGNOSIS				p=NS
Hodgkin's Disease		16	12	
Non-Hodgkin's Lymphoma		42	49	
AGE				p=NS
	Median	41	43	
	Range	22-63	19-71	
PREVIOUS THERAPY				p=NS
Lines of chemotherapy	Median	2	3	
	Range	2-5	1-7	
Cycles of chemotherapy	Median	8	8	
	Range	6-16	2-18	

Fig. 1.
Febrile neutropenia (FN) in lymphoma patients following PBSCT

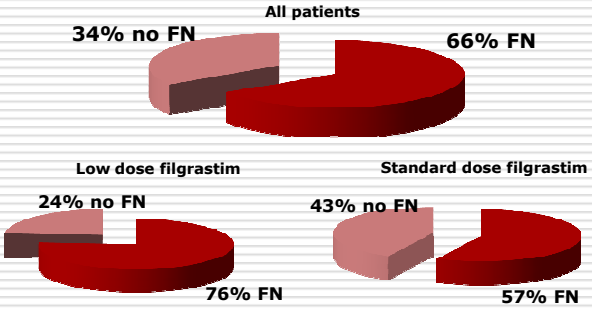


Fig. 2.
Causes of febrile neutropenia

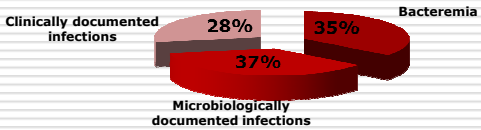


Fig. 3.
Bacteremias according to causative organism

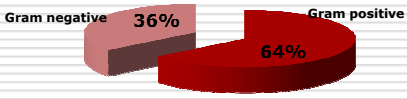
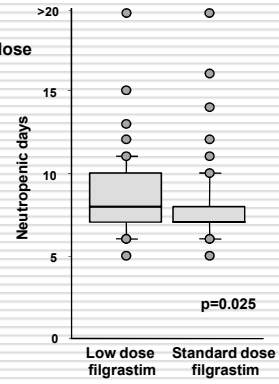


Fig. 4.
No. of neutropenic days according to filgrastim dose



RESULTS

Febrile neutropenia occurred in 79 (65.8%) patients (Fig. 1) at a mean of 6 days after transplantation (range 1–9, SD 1.65), more often in patients with longer duration of neutropenia post transplant (p=0.0003). In these patients, microbiological work-up was done and empirical antibiotic therapy was initiated; piperacillin-tazobactam was administered to all patients not having a history of penicillin allergy. Empirical therapy was modified according to recommended guidelines in 19 (24.1%) patients: vancomycin was added in 32 patients (40.5%), a systemic antifungal in 10 (12.7%) and both in 6 (7.6%) patients. Twenty-eight patients (35.4%) had proven bacteremias while 29 (36.7%) had other microbiologically documented infections (MDIs) (Fig 2.). Gram+ microorganisms were responsible for the majority (64.3%) of all bacteremias (Fig 3.). Patients receiving standard doses of filgrastim had significantly shorter duration of neutropenia (average of 9.06 vs. 9.82 days, p=0.02, Fig 4.) and developed febrile neutropenia less often than the group receiving lower doses of filgrastim (57.4% vs. 75.9%, p=0.03, Fig 1.). They also responded better to empirical therapy – addition of vancomycin was not needed as often as in the group receiving lower filgrastim doses (28.6% vs. 50%, p=0.05) and had shorter duration of antimicrobial treatment (average of 9.71 vs. 10.9 days, p=0.11).

CONCLUSIONS

Infections are serious but manageable complications of PBSCT. Gram-positive microorganisms remain the major cause of documented infections. In our patients treated with two dose levels of filgrastim, standard filgrastim doses were more efficacious in both shortening the duration of neutropenia and reducing the incidence of fever during neutropenia. Also, compared to the lower filgrastim doses, patients receiving standard filgrastim doses needed shorter antimicrobial treatment and fewer modifications of empirical antimicrobial regimen.

REFERENCES

1. Kirk JL Jr et al. Analysis of early infectious complications after autologous bone marrow transplantation. Cancer 1988; 62: 2445-2450.
2. Offidani M et al. Infectious complications after autologous peripheral blood progenitor cell transplantation followed by G-CSF. Bone Marrow Transplant 1999; 24:1079-1087.
3. Schmitz N et al. Results of a randomized, controlled, multicentre study of recombinant human granulocyte colony-stimulatimg factor (filgrastim) in patients with Hodgkin's disease and non-Hodgkin's lymphoma undergoing autologous bone marrow transplantation. Bone Marrow Transplant 1995; 15:261-266.
4. Linch DC et al. G-CSF after peripheral blood stem cell transplantation in lymphoma patients significantly accelerated neutrophil recovery and shortened time in hospital: results of a randomised BNLI trial. Br J Haematol 1997; 99:933-938.
5. Ojeda E et al. A prospective randomised trial of granulocyte colony-stimulating factor therapy after autologous blood stem cell transplantation in adults. Bone Marrow Transplant 1999;24:601-607.
6. Bolwell B et al. G-CSF post autologous progenitor cell transplantation: a randomized study of 5, 10, and 16 mcg/kg/day. Bone Marrow Transplant 1997; 19:215-219.