VOLUME-7, ISSUE-1, JANUARY-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Oncology

CHEMOTHERAPY INDUCED EARLY TRANSIENT FEBRILE NEUTROPENIA DESPITE THE USE OF PEGYLATED GRANULOCYTE COLONY STIMULATING FACTOR

Dr. Vinayak V Maka* Department of Medical oncology M S Ramaiah Medical College MSRIT post, Bangalore, India, 560054 *Corresponding Author

Dr. Nalini Kilara Department of Medical oncology M S Ramaiah Medical College MSRIT post, Bangalore, India, 560054

ABSTRACT

Background: PEGylated Granulocyte – Colony stimulating factor(G-CSF) prophylaxis is given to prevent chemotherapy induced Febrile neutropenia and its complications.

Methods: Clinical study included 8 patients aged 30 to 59 years with varied hematologic & solid malignancies on combination chemotherapy. Blood counts are monitored for seven days in patients developing fever after receiving subcutaneous PEGylated G-CSF 6 micrograms.

Results: Six patients developed early febrile transient neutropenia after 1st cycle chemotherapy, one after 2nd cycle and one after 4th cycle. Six patients developed febrile neutropenia (early & transient) on day 7 post chemotherapy, two on Day 2. Profound neutropenia was found in 7 of the 8 patients. The mean time to recovery was 2.7days [2 to 5 days].

Conclusion: Despite PEGylated G-CSF support, patients can develop early, transient, uncomplicated, reversible febrile neutropenia which tends to recover within mean duration of 2.7days.

KEYWORDS : Peglated GSF, Febrile Neutropenia,

Introduction:

PEGylated G-CSF is given with the objective of preventing neutropenia and its complications. Transient febrile neutropenia is not reported to occur while administrating pegylated G-CSF subcutaneously. However, we are reporting eight patients in whom we have documented febrile neutropenia (early & transient) despite the use of PEGylated G-CSF to prevent neutropenia post chemotherapy.

Methods & materials:

Current study is observational prospective study of patients developing febrile neutropenia after receiving PEGylated G-CSF where Blood counts are monitored for seven days after administration of combination chemotherapy in various hematological and solid cancers. Patients sample is derived from medical oncology department for duration of six months who have given informed consent to be part of this study.

Results:

Table :1 baseline characteristics of patients in study

Age/ Sex	Diagnosis	Treatment	Chemotherapy cycle after which Early neutropenia developed	Post chemotherapy day on which early transient neutropenia developed	White cell count /Absolute neutrophil count at presentation of the early transient neutropenia (Nadir)	Time to Recovery from the early transient neutropenia
40/M	Non-Hodgkin's Lymphoma Stage III	E-CHOP	1st Cycle	Day 7	727 / 14	Day 12
37/F	Carcinoma Right Breast	Adjuvant TA	1st Cycle	Day 7	510 / 61	Day 9
40/F	Carcinoma left breast T2 N2	Adjuvant FEC	1st Cycle	Day 7	330 / 16	Day 10
47/F	Carcinoma left breast TX N2	Adjuvant FEC	2nd Cycle	Day 7	440 / 70	Day 11
56/F	Carcinoma left breast T2N2	Adjuvant FEC	1st Cycle	Day 7	640 / 32	Day 11
59	Metastatic Gastric carcinoma	Palliative DCF	1st Cycle	Day 2	800 / 160	Day 4
30/F	Locally Advanced Carcinoma right breast	Adjuvant TA	4th Cycle	Day 2	630/138	Day 4
51/F	Carcinoma left breast T3N1	Adjuvant FEC	1st Cycle	Day 7	330/66	Day 10

Our study had eight patients aged between 30 and 59 years of age with seven female and one male. These patients had varying diagnosis including hematologic & solid cancers as described in table. [Refer table 1]. All the patients received combination chemotherapy and the various chemotherapy regimens have been outlined in table 1. There were five patients with the diagnosis of Carcinoma breast, one with Non-Hodgkin's lymphoma & one with metastatic gastric carcinoma. Six patients developed early transient neutropenia after 1st cycle chemotherapy, one after 2nd cycle and one after 4th cycle. Six patients developed febrile neutropenia (early& transient) on day 7 post chemotherapy, two on Day 2. Profound neutropenia was found in 7 of the 8 patients. The mean time to recovery was 2.7days [range 2 to 5 days].

Discussion:

Pegfilgrastim, a pegylated formulation of G-CSF, has a prolonged half-life, permitting the administration of a single dose rather than daily administration. The recommended dose (6 mg in adults; 100 microgram/kg [maximum 6 mg] in children is given 24 hours after chemotherapy, with at least 14 days elapsing until the next planned chemotherapy dose. It is used to decrease the incidence of infection, by stimulation of granulocyte production, in patients with non-myeloid malignancies receiving myelosuppressive therapy associated with a significant risk of febrile neutropenia. It stimulates the production, maturation, and activation of neutrophils. Pegylated G-CSF activates neutrophils to increase both their migration and cytotoxicity. Pegfilgrastim has a prolonged duration of effect relative to filgastrim and a reduced renal clearance. Multiple randomized trials have shown that Pegfilgrastim is as effective as and more convenient to administer than G-CSF for primary prophylaxis in patients requiring CSF treatment during myelosuppressive chemotherapy. (1-4) The reported significant adverse reactions are: Peripheral edema (12%), Headache (16%) Vomiting (13%) Bone pain (31% to 57%), myalgia (21%), arthralgia (16%), weakness (13%)

Fever in a neutropenic patient is usually defined as a single oral temperature >38.3ºC (101ºF), or a sustained temperature >38ºC (100.4ºF) for more than one hour [1]. However, on occasion a neutropenic patient may not present with fever despite the presence of infection. This may occur more commonly in elderly patients or those receiving glucocorticoids. It is defined as an absolute neutrophil count (ANC) <500 cells/microL [1], or <1000 cells/microL with a predicted nadir of <500 cells/microL. Profound neutropenia is defined as an ANC ≤100 cells/microL.

Factors that are used to categorize patients as high-risk or low-risk for severe infection include presenting signs and symptoms, the underlying cancer, the type of therapy for the underlying cancer, and medical co morbidities [1]. Important factors include age more than 65 years, poor performance status concurrent chemotherapy & radiation therapy, prior episodes of neutropenic fever, extensive prior therapy, extensive bone marrow involvement by tumor as well as other comorbidities [1]. Contributory factors to the pathogenesis of febrile neutropenia include the direct effects of chemotherapy on mucosal barriers and immune deficits related to the underlying malignancy [1]. An infectious source is identified in approximately 30 percent of febrile neutropenic episodes [2]. Despite PEGylated G-CSF patients can develop early transient neutropenia and fever, Neutropenia tends to be early and transient and recovers with a mean of 2.7days. Patients are usually stable despite profound neutropenia without any organ dysfunction and uncomplicated recovery

Conclusion:

PEGylated G-CSF- can be associated with neutropenic fever (early & transient) before causing a rise in the ANC, which requires further study.

Reference

1. Green, M. D., Koelbl, H., Baselga, J., Galid, A., Guillem, V., Gascon, P., ... & Zani, V. (2003). A randomized double-blind multicenter phase III study of fixed-dose single-administration Pegfilgrastim versus daily filgastrim in patients receiving myelosuppressive chemotherapy. Annals of Oncology, 14(1), 29-35.
2. Holmes, F. A., O'shaughnessy, J. A., Vukelja, S., Jones, S. E., Shogan, J., Savin, M., ... & Neumann, T. A. (2002). Blinded, randomized, multicenter study to evaluate single administration Pegfilgrastim once per cycle versus daily filgastrim as an adjunct to chemotherapy in patients with high-risk stage II or stage III/IV breast cancer. Journal of Clinical Oncology, 20(3), 727-731.
3. Vose, J. M., Crump, M., Lazarus, H., Emmanouilides, C., Schenkein, D., Moore, J., ... & Liang, B. C. (2003). Randomized, multicenter, open-label study of Pegfilgrastim compared with daily filgastrim after chemotherapy for lymphoma. Journal of Clinical Oncology, 21(3), 514-519.
4. Fox, E., Widemann, B. C., Hawkins, D. S., Jayaprakash, N., Dagher, R., Aikin, A. A., ... & Steinberg, S. M. (2009). Randomized trial and pharmacokinetic study of Pegfilgrastim versus filgastrim after dose-intensive chemotherapy in young adults and children with sarcomas. Clinical Cancer Research, 15(23), 7361-7367.