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Brief Communication

Assessment of Granulocyte-Colony Stimulating Factors Use at a community-based teaching hospital and compliance with National Comprehensive Cancer Network guidelines

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Abstract

Objectives: Approximately 60,000 patients are hospitalised annually due to chemotherapy-induced febrile neutropenia (FN) in the United States alone. Febrile neutropenia is primarily managed by antibiotics and granulocyte-colony-stimulating factors (G-CSFs). However, there are inconsistent recommendations regarding dose, frequency, and duration for G-CSF therapy. We conducted this study to assess the use of G-CSFs in a community-based teaching hospital in compliance with the National Comprehensive Cancer Network (NCCN) guidelines.

Methods: We retrospectively reviewed medical records of adult patients diagnosed with non-myeloid malignancies who received filgrastim in a community-based teaching hospital from November 2014 to April 2015.

Results: Of 90 patients, 77% received filgrastim for FN treatment, 19% for primary prophylaxis, and 4% for secondary prophylaxis. The dose of filgrastim was appropriate in 93% of patients, while 7% received a sub-optimal dose without the worsening of their clinical outcomes. We could not assess the duration of therapy for 38 patients who either died or were discharged before achieving the desired absolute neutrophil count (ANC). Of the 69 patients treated for FN, only 33% received filgrastim until they achieved the ANC goal (1,500 −8,000/μL), while 36% continued to receive filgrastim treatment beyond the desired ANC goal.

Conclusion: In our study, filgrastim was correctly prescribed; however, the ANC goal was not achieved in 47% of the patients. If the recommended ANC range had been targeted, a minimum of 28 doses could have been potentially avoided. This approach would have saved approximately $56,000. Therefore, future protocols should focus on pharmacist-led interventions to optimise G-CSF usage.

Keywords: Chemotherapy-induced febrile neutropenia; Colony-stimulating factors; Filgrastim; Leukocyte count; Neutrophils

Introduction

According to the World Health Organization, cancer is considered one of the leading causes of death worldwide.[1] In 2016, an estimated 1,685,000 new cases of cancer were diagnosed in the United States, with 595,690 people dying from the disease.[1,2] Treatment with chemotherapy frequently leads to neutropenia, which affects more than one in three

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patients undergoing chemotherapy. Febrile neutropenia (FN) remains one of the most common adverse effects associated with chemotherapy, with approximately 60,000 patients being hospitalised annually for FN.[2]

Patients who develop chemotherapy-induced FN are at high risk of developing potentially life-threatening infections that often require hospitalisation, which costs approximately $16,000 per admission.[1] FN can also delay subsequent chemotherapy treatment regimens.[1,2] Hence, prompt prevention and management of febrile neutropenia are necessary. Prevention and management include identifying candidates for primary and secondary prophylaxis of FN. This is in addition to supportive management with antibiotics and granulocyte colony-stimulating factors (G-CSFs), which have been shown to reduce the duration and severity of neutropenia and the risk of FN development.[2]

According to the National Comprehensive Cancer Network (NCCN) Guidelines® for Myeloid Growth Factors, in cases of FN, G-CSFs are considered adjuncts to antibiotics. This is for patients at high risk for infection-associated complications or for those who have prognostic factors that are predictive of a poor clinical outcome, regardless of whether they have received G-CSFs prophylactically.[3] However, guidelines from the American Society of Clinical Oncology® (ASCO), the Infectious Diseases Society of America® (IDSA), and the European Society for Medical Oncology (ESMO) recommend against their routine use.[4,5]

Filgrastim is a G-CSF that has been shown to reduce the duration and severity of neutropenia and the risk of FN.[2] The indications for the use of filgrastim are similar to those for other G-CSF agents. Moreover, the NCCN guidelines for the use of myeloid growth factors address the use of available G-CSF products similarly.[3] However, there are inconsistent recommendations regarding dosing, frequency, and duration for G-CSFs. Hence, we aimed to assess the use of G-CSFs at a community-based teaching hospital and its compliance with the NCCN guidelines.

Materials and Methods

A retrospective chart review was conducted, which included adult patients diagnosed with non-myeloid malignancies between 1 November 2014 and 30 April 2015, and who received filgrastim during admission. Patients who received other G-CSFs were excluded. Data collected for every patient included the following: dates of hospital admission and discharge, age, gender, weight, oncology-related diagnosis, daily absolute neutrophil count (ANC), daily temperature, indication for G-CSF therapy, G-CSF dose, duration of G-CSF therapy, number of doses of G-CSF, patient's current chemotherapy regimen, and patient's risk factors. Our primary objective was to evaluate the percentage of patients who received G-CSF for the proper indications, while the secondary objectives were to assess the percentage of patients who received an accurate dose of G-CSF and whether they achieved the ANC goal. To these ends, we used descriptive statistics.

Results

We reviewed 135 patient charts, out of which 45 were excluded. Of these patients, 56% were male, with a mean age of 62.7 ± 13.5 years. Most patients (68%) had carcinoma, 19% had lymphoma, and 6% and 4% had myeloma and sarcoma, respectively (Table 1).

Table 1: Patient characteristics.

Characteristics	Descriptive Statistics
	N = 90
Age: mean in years (range)	63.8 (18–83)
Gender: male (%)	51 (56)
Cancer type (%)	
Carcinoma	58 (68)
Lymphoma	21 (19)
Myeloma	7 (6)
Sarcoma	4 (4)

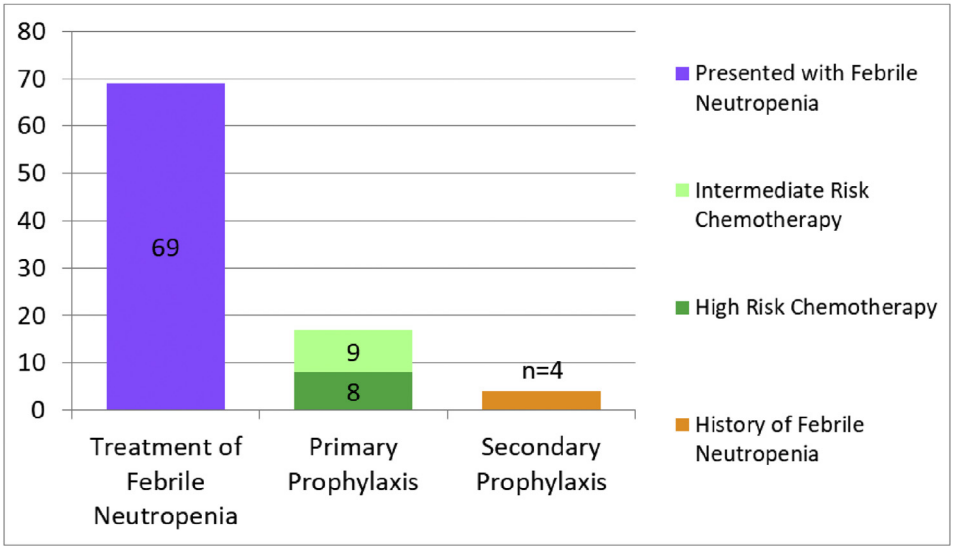

Figure 1: Filgrastim indications

For the primary objective, all patients received G-CSFs for appropriate indications as recommended in the NCCN guidelines. A total of 69 patients (77%) received G-CSFs for the treatment of febrile neutropenia, 17 patients (19%) for primary prophylaxis, and four patients (4%) for secondary prophylaxis (Figure 1).

For the secondary objective, 84 patients (93%) were dosed appropriately in accordance with the recommended dosing range of 5–10 μg/kg, while 7% of the patients received a suboptimal dose. Of the 69 patients treated for FN, 23 (33%) received treatment until the ANC goal was achieved, 13 (19%) were discharged on G-CSF before achieving the ANC goal, 25 (36%) received treatment beyond the ANC goal, four (6%) had their treatments discontinued before reaching the ANC goal, and four (6%) died before achieving the ANC goal.

For the 23 patients who had received treatment until the ANC goal was achieved, the mean ± SD duration of treatment was 2.6 ± 2.3 days, while the mean ANC upon discontinuation was 4,300 ± 1,900/μL. For the 25 patients who continued their treatment beyond the ANC goal, the mean duration of therapy was 2.4 ± 0.6 days, while the mean ANC upon discontinuation was 15,100 ± 7,500/μL. Four patients had their treatment discontinued before the ANC goal; they had a mean treatment duration of one day, and the mean ANC upon discontinuation was 730 ± 410/μL.

Discussion

In this retrospective analysis, we found that 36% of patients continued to receive filgrastim treatment beyond the ANC goal, which led to a waste of 28 unnecessary doses with an approximate cost of ≈ $56,000. Nevertheless, we found that G-CSFs were prescribed exclusively for the indications recommended in the NCCN guidelines. All the patients had met the criteria recommended by the NCCN guidelines for receiving G-CSFs as prophylaxis or FN treatment.

The dosing recommendation for filgrastim is 5 μg/kg as a starting dose, whether it is indicated for FN treatment or as prophylaxis. This dose was increased up to 10 μg/kg if no response was noted in cases of FN treatment and was rounded to the nearest vial size.[6,7] Hence, 84 patients (93%) were found to be dosed appropriately between 5 and 10 μg/kg, while 7% of the patients received a sub-optimal dose. However, no worsening of clinical outcomes was noted in those patients.

The exact ANC goal was not defined in the NCCN guidelines, and ANC normalisation was considered to be per 'laboratory standards'.[3] However, the literature shows a consensus in defining the ANC range of 1,500 to 8,000/μL as being normal.[7] Hence, we identified the appropriate duration of treatment such as the use of G-CSFs until the goal ANC of 1,500 to 8,000/μL was achieved. A total of 21 patients in the prophylactic group were discharged, died, or discontinued treatment before achieving the ANC goal, while 23 patients in the treatment group continued treatment until the ANC goal was achieved. Further, 25 patients in the treatment group continued treatment beyond the ANC goal, at which point 28 doses could potentially have been avoided and resulted in cost avoidance of approximately $56,000 from a provider's perspective.

Literature has shown the benefits of pharmacist-managed therapeutic drug monitoring, especially for drugs with a narrow therapeutic index. These benefits include reductions in the length of hospital stay, adverse drug reactions, and cost of care, while still improving the quality of care.[8,9] Hence, we recommend conducting further studies to measure the impact of pharmacist-managed therapeutic drug monitoring for G-CSFs.

The study limitations include the following: small sample size; retrospective design; difficulty in assessing the appropriateness of therapy duration in 47% patients who were discharged, died, or discontinued treatment before achieving the ANC goal; and lack of a standard protocol for discontinuing G-CSFs based on ANC.

Conclusion

G-CSFs were appropriately prescribed based on the indications. However, 7% of the patients received sub-optimal dosing, 4% discontinued treatment before achieving the ANC goal, and 36% continued treatment beyond the ANC goal. If the recommended ANC range of 1,500 to 8,000/μL had been used, 28 doses could potentially have been avoided and resulted in cost avoidance of approximately $56,000 from a provider's perspective. Hence, opportunities for clinical pharmacists to optimise G-CSFs use and reduce unnecessary costs exist.

Recommendations

We recommend further research to assess the pharmacist-led therapeutic drug monitoring of G-CSFs and their impact on minimising waste and unnecessary cost.

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Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

Ethical approval was obtained from the Integrity board panel.

Authors contributions

Both authors (AAA and MWM) have contributed equally in conceiving and designing the study, conducting the research, providing the research materials, obtaining ethical approvals, collecting and analysing the data, interpreting results, writing and reviewing the manuscript, and approving the final draft for publication. All authors have critically

reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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