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RESEARCH ARTICLE

Efficacy of Filgrastim in Managing Chemotherapy-Induced Febrile Neutropenia in Iraqi Patients with Non-Small Cell Lung Cancer

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ABSTRACT

Filgrastim, a recombinant human granulocyte colony-stimulating factor, has been intensively researched as a systemic treatment for neutropenia, notably in cancer patients receiving myelosuppressive chemotherapy. The use of filgrastim has demonstrated considerable benefits in reducing the frequency and duration of febrile neutropenia, as well as in supporting the maintenance of chemothera-py dose intensity. The research findings that multiple doses regime of filgrastim has significant benefits observed in reducing the incidence and duration of fe-brile neutropenia, as well as in supporting the maintenance of chemotherapy dose intensity, highlight its valuable role in improving the quality of life and treatment outcomes for patients undergoing myelosuppressive chemotherapy. In conclusion, the research on multiple doses regime of filgrastim provides solid evidence for its usefulness in controlling neutropenia-related problems in cancer patients.

INTRODUCTION

Adjuvant chemotherapy for advance-stage lung cancer can result in neutropenia, leading to febrile neutropenia (FN), hospitalizations, decreased quality of life, and potential delays or changes in chemotherapy (1). FN and subsequent infections are the primary factors contributing to illness and death in many chemotherapy patients, despite conventional interventions such as hospitalization and antibiotics (2). Neutropenia is a prominent dose-limiting hazard and life-threatening complication of myelosuppressive chemotherapeutic agents. In times when neutropenic patients develop infections (3), generally expressed as FN, it can lead to hospitalizations that necessitate the need for administration of intravenous antibiotics as well as increased morbidity and mortality in as many as 10% of patients (4). Non-Small Cell Lung Cancer (NSCLC) is a term used to designate a group of lung cancers, including adenocarcinoma, squamous cell carcinoma, and large-cell carcinoma (5). Adenocarcinoma is associated with half of all NSCLC cases, making it the most common variety (6). Previously, squamous cell carcinoma was the most frequently diagnosed form of carcinoma, often originating in the tracheobronchial tree, but is now more commonly found in the outer parts of the lung (7).

Granulocyte colony stimulating factor (G-CSF) is the major cytokine for the control of neutrophil production that is clinically employed for the treatment of congenital and acquired neutropenia (8). Cytokine increases the number of circulating neutrophils in vitro and improves their

performance. More than 90% of patients respond to G-CSF by an increase of more than 1×10^9/L in ANC (Absolute Neutrophil Count) (9).

Most patients should take some kind of GCSF after chemotherapy as a single dose treatment or multiple type for at least six days. Therefore, the objective of this study is to compare the effectiveness between two protocols.

1. MATERIALS AND METHOD

1.1. Method

We collected data from multiple hospitals in the central and southern regions of Iraq between January 11, 2023, and February 1, 2024. A retrospective study was conducted 225 patients to evaluate the effect of Filgrastim on reduce chemotherapy induce FN in Iraqi patients with NSCLC. Patients in the single dose group received a single 300 mcg subcutaneous injection of filgrastim on the second day of each treatment cycle. In the multiple doses group, 300 micrograms of Filgrastim were given subcutaneously once day for six consecutive days in each chemotherapy cycle. Each week, patients received clinical evaluations, the blood-related parameters (White Blood Cell (WBC) count, hemoglobin (Hgb) level, platelet count, neutrophil count, lymphocyte count, and absolute neutrophil count).

Included criteria The patient must be at least 18 years old and have an absolute neutrophil count of 1.5×10^9 /l or higher, as well as a platelet count of 100×10^9 /l or higher. The serum creatinine level should be less than 1.5 times the upper limit of normal. Additionally, there should be evidence that the patient has received GCSF. The exclusion criteria: Elevated bilirubin, aspartate transaminase, or alanine transaminase levels, combined with elevated alkaline phosphatase levels, Radiation therapy within 4 weeks of study enrolment, Previous bone marrow or stem cell transplant, ejection fraction <40%, and liver cirrhosis.

1.2. Statistical analysis

For this study, all analyses were performed using Statistical Package for the Social Sciences version 26.0 (SPSS Inc.; Chicago, IL, USA). To compare differences between the patients that receive single dose and those that receive multiple doses of Filgrastim, a one-way ANOVA test for dependent samples with correction for multiple testing was conducted. Pairwise comparisons between groups were calculated using the Wilcoxon pairwise test corrected for multiple testing.

2. RESULTS

2.1. Patient demographics and clinical characteristics

In this study, the demographic and clinical characteristics of people who were treated with either a single dosage or many doses were investigated. As compared to the multiple dose group, the single dosage group had an average age of 57.8 ± 4.04, whereas the multiple dose group had an average age of 53.7 ± 5.23. In terms of age, body mass index (BMI), LN that was excised, LN that was involved, Ki-67 index, education level, marital status, and employment status, there were no significant differences between the two groups.

2.2. CHANGES IN BLOOD PARAMETERS BETWEEN GROUP

The study analysis found that there were no significant alterations in hematologic values such as hemoglobin (Hgb) and lymphocyte count during the first two sessions of chemotherapy. However, during the third session of chemotherapy, there were no significant variations in Hgb values solely. When comparing white blood cell (WBC), platelet, neutrophil, and absolute neutrophil count (ANC) counts, statistically significant differences ($p<0.05$) were identified between the two study groups as showed in Table 1 as well as figure 1 and 2. This shows that indicated multiple doses of drug have influence of chemotherapy on these hematologic parameters may vary during the course of treatment.

Table 1: The changes in hematologic variables during the three courses of chemotherapy in the two groups

The changes in hematologic variables during the three courses of chemotherapy in the two groups				
Time	**Variable**	**Single** **Mean ± SD**	**Multiple** **Mean ± SD**	**P value**
1st course (day 7)	WBC	3223.08 ± 292	5937 ± 404	< 0.001
	Hgb	11.26 ± 0.91	11.2 ± 1.01	
	Platelet*10^5	1.4 ± 0.07	2.3 ± 0.03	< 0.001
	Neutrophil	46.5 ± 5.19	67.6 ± 4.3	< 0.001
	Lymphocyte	52.97 ± 6.57	51.3 ± 6.6	
	ANC	1662 ± 137	3896 ± 162	< 0.001
1st course (day 15)	WBC	2918.42 ± 121.6	5827 ± 127	< 0.001
	Hgb	11.52 ± .95	11.76 ± 1.107	
	Platelet*10^5	1.2 ± 0.07	2.9 ± 0.09	< 0.001
	Neutrophil	85.18 ± 5.4	84.66 ± 5.54	
	Lymphocyte	45 ± 4.75	55 ± 5.57	
	ANC	1255 ± 292	4089.1 ± 154	< 0.001
2nd course (day 7)	WBC	2686.84 ± 250	5953.16 ± 202	< 0.001
	Hgb	10.36 ± 1.03	12.44 ± 1.06	
	Platelet*10^5	1.3 ± 0.006	2.9 ± 0.07	< 0.001
	Neutrophil	47.71 ± 6.21	85.52 ± 8.98	< 0.001
	Lymphocyte	51.23 ± 6.09	68.21 ± 10.82	
	ANC	1324 ± 476	3819 ± 1891	< 0.001
2nd course (day 15)	WBC	2405.52 ± 803	5693.42 ± 831	< 0.001
	Hgb	10.25 ± .96	12.4 ± 1.18	
	Platelet*10^5	1.2 ± 12,622	2.8 ± 0.02	< 0.001
	Neutrophil	56.73 ± 5.75	86.34 ± 4.39	< 0.001
	Lymphocyte	14.02 ± 8.14	82.89 ± 3.67	< 0.001
	ANC	1250 ± 4351	4009 ± 808	< 0.001
3rd course (day 7)	WBC	2610.52 ± 1345.1	6660.52 ± 277.09	< 0.001
	Hgb	9.14 ± .93	12.23 ± 17.99	
	Platelet*10^5	1.7 ± 0.14	3.0 ± 0.13	< 0.001
	Neutrophil	47.4 ± 6.9	81.18 ± 4.57	< 0.001
	Lymphocyte	41.97 ± 6.52	87.55 ± 5.25	< 0.001
	ANC	1215 ± 582	4359 ± 636	< 0.001
3rd course (day 15)	WBC	3961.31 ± 668.86	6993.68 ± 717.65	< 0.001
	Hgb	10.06 ± .92	12.14 ± 17.99	
	Platelet*10^5	1.0 ± 0.14	3.45 ± 0.24	< 0.001

	Neutrophil	37.1 ± 5.05	87.87 ± 4.47	< 0.001
	Lymphocyte	12.81 ± 5.11	82 ± 4.6	< 0.001
	ANC	1064 ± 431	4010 ± 450	< 0.001

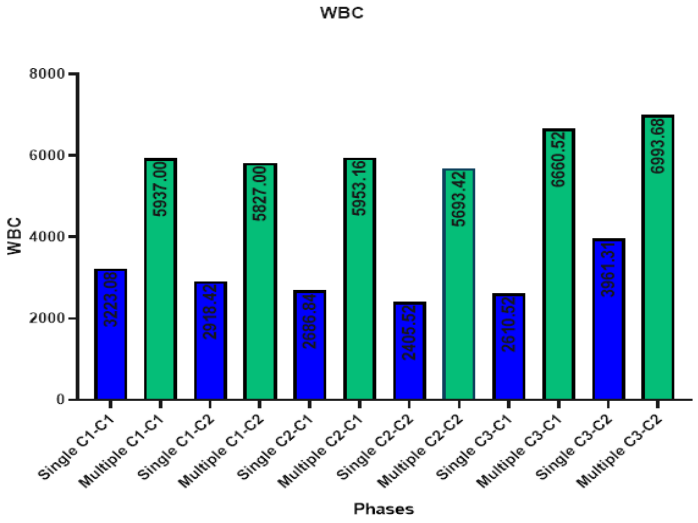

Figure 1: effect of single vs multiple dose on elevation of WBCS among cycles

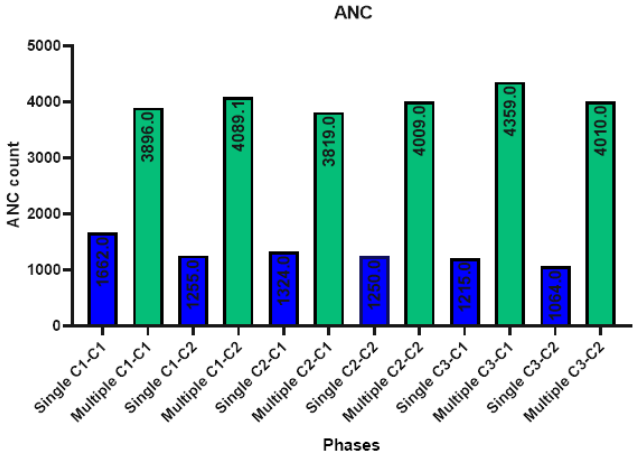

Figure 2: effect of single vs multiple dose on elevation of ANC among cycles

3. DISCUSSION

This study used chemotherapy drugs that caused more than 10% neutropenia without GCF in all chemotherapy regimens used. WBC, platelets, neutrophils, and ANC levels differed significantly between the two treatment protocols. Both study groups did not show statistically significant differences in Hgb and lymphocyte hematologic parameters during chemotherapy.

The chemotherapy regimens as shown in other studies, medications comprised known to cause more than 10% neutropenia without G-CSF (10-12). The results demonstrated substantial variations in WBC, platelet, neutrophil, and ANC alterations between the two treatment regimes. However, there were no statistically significant variations in the changes of Hgb and lymphocyte hematologic parameters between the two study groups during the sessions of chemotherapy. After conventional chemotherapy regimens, the drop in leukocytes and platelets in the peripheral circulation happened more faster, but with G-CSF, this pace was slowed, potentially reducing harmful side effects (13, 14). In one study enrolling the patients who received Filgrastim were compared on the second to seventh day of the cycle were compared with control. The results were

showed that the WBC and ANC values were significantly different between the two groups, and neutropenia with fever was less common in the patients who took Filgrastim in multiple doses.

Another trial that randomized patients with breast cancer to receive multiple doses of filgrastim versus a single dose found that the multiple doses had a positive side effect profile and good effectiveness, with febrile neutropenia being less common among those who received the single dosage (13% vs. 20%) (15, 16).

4. CONCLUSION

Multiple administrations of filgrastim have higher efficacy and also less hazardous than single dosage. Its prescription as a medication that effective treatment for chemotherapy-induced neutropenia.

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Conflicts of Interest:

The authors declare no conflicts of interest.

6. REFERENCES

1. Serifoglu I, Sen N. Lung Cancer Emergencies. Airway diseases: Springer; 2023. p. 1-51.
2. Rapoport BL, Cooksley T, Johnson DB, Anderson R, Shannon VR. Treatment of infections in cancer patients: an update from the neutropenia, infection and myelosuppression study group of the Multinational Association for Supportive Care in Cancer (MASCC). Expert review of clinical pharmacology. 2021;14(3):295-313.
3. Kuderer NM, Desai A, Lustberg MB, Lyman GH. Mitigating acute chemotherapy-associated adverse events in patients with cancer. Nature Reviews Clinical Oncology. 2022;19(11):681-97.
4. Lyman GH, Kuderer NM, Aapro M. Improving outcomes of chemotherapy: established and novel options for myeloprotection in the COVID-19 era. Frontiers in Oncology. 2021;11:697908.
5. Lantuejoul S, Fernandez-Cuesta L, Damiola F, Girard N, McLeer A. New molecular classification of large cell neuroendocrine carcinoma and small cell lung carcinoma with potential therapeutic impacts. Translational Lung Cancer Research. 2020;9(5):2233.
6. Daly ME, Singh N, Ismaila N, Antonoff MB, Arenberg DA, Bradley J, et al. Management of stage III non–small-cell lung cancer: ASCO guideline. Journal of Clinical Oncology. 2022;40(12):1356-84.
7. Lazarus DR, Strange CD, Ahuja J, Shroff GS, Sabloff BS, de Groot PM, et al. Non-Small Cell Carcinoma. The Thorax: Medical, Radiological, and Pathological Assessment: Springer; 2023. p. 311-72.
8. Theyab A, Algahtani M, Alsharif KF, Hawsawi YM, Alghamdi A, Alghamdi A, Akinwale J. New insight into the mechanism of granulocyte colony-stimulating factor (G-CSF) that induces the mobilization of neutrophils. Hematology. 2021;26(1):628-36.
9. Suzuki K, Yamada M, Kurakake S, Okamura N, Yamaya K, Liu Q, et al. Circulating cytokines and hormones with immunosuppressive but neutrophil-priming potentials rise after endurance exercise in humans. European journal of applied physiology. 2000;81:281-7.
10. You Z, Zhang H, Huang Y, Zhao L, Tu H, Zhang Y, et al. Assessing the Optimal Regimen: A Systematic Review and Network Meta-Analysis of the Efficacy and Safety of Long-Acting Granulocyte Colony-Stimulating Factors in Patients with Breast Cancer. Cancers. 2023;15(14):3675.

11. Hobbs J, Lowe J, Ferdinand A, Shook A, Beck B, Blais D, et al. Efficacy of same-day versus next-day administration of pegfilgrastim for the prevention of chemotherapy-induced febrile neutropenia in breast cancer patients receiving dose-dense doxorubicin and cyclophosphamide: A retrospective multi-site analysis. Journal of Oncology Pharmacy Practice. 2023;29(8):1853-61.
12. Clemons M, Fergusson D, Joy AA, Thavorn K, Meza-Junco J, Hiller JP, et al. A multi-centre study comparing granulocyte-colony stimulating factors to antibiotics for primary prophylaxis of docetaxel-cyclophosphamide induced febrile neutropenia. The Breast. 2021;58:42-9.
13. Lazarus HM, Ragsdale CE, Gale RP, Lyman GH. Sargramostim (rhu GM-CSF) as cancer therapy (systematic review) and an immunomodulator. A drug before its time? Frontiers in immunology. 2021;12:706186.
14. Li N, Huang C, Zhang J, Zhang J, Huang J, Li S, et al. Chemotactic NO/H2S nanomotors realizing cardiac targeting of G-CSF against myocardial ischemia-reperfusion injury. ACS nano. 2023;17(13):12573-93.
15. Clemons M, Fergusson D, Simos D, Mates M, Robinson A, Califaretti N, et al. A multicentre, randomised trial comparing schedules of G-CSF (filgrastim) administration for primary prophylaxis of chemotherapy-induced febrile neutropenia in early stage breast cancer. Annals of Oncology. 2020;31(7):951-7.
16. Najafi S, Ansari M, Kaveh V, Haghighat S. Comparing the efficacy and side-effects of PDLASTA®(Pegfilgrastim) with PDGRASTIM®(Filgrastim) in breast cancer patients: a non-inferiority randomized clinical trial. BMC cancer. 2021;21:1-12.
17. Jam, F. A., Singh, S. K. G., Ng, B., & Aziz, N. (2018). The interactive effect of uncertainty avoidance cultural values and leadership styles on open service innovation: A look at malaysian healthcare sector. *International Journal of Business and Administrative Studies*, *4*(5), 208-223.
18. Kanval, N., Ihsan, H., Irum, S., & Ambreen, I. (2024). Human Capital Formation, Foreign Direct Investment Inflows, and Economic Growth: A Way Forward to Achieve Sustainable Development. *Journal of Management Practices, Humanities and Social Sciences*, *8*(3), 48-61.