Neutropenia and First Cycle of Chemoradiotherapy: A Retrospective Analysis of 100 Cancer Patients

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Abstract

Introduction: Chemoradiotherapy-induced neutropenia can occur after the first cycle of treatment. It becomes a major dose-limiting factor and affects the further management of the patient.

Material and Medthod: A retrospective analysis of 100 patients who received chemoradiotherapy was done to know about percentage of reduction of low absolute neutrophilic counts after first cycle of treatment and their relation with absolute neutrophilic values before the treatment started.

Results: Post chemoradiotherapy reduction in absolute neutrophilic counts was seen in 25% and neutropenia in 4% of the cases irrespective of pre-treatment values. Majority of the neutropenic cases were of carcinoma breast.

Conclusion: It was observed that 4% of the total cases had neutropenia irrespective of pre-treatment absolute neutrophilic ounts.

Keywords: Chemotherapy, Carcinoma, Neutropenia, Absolute neutrophilic count, Blood Parameter.

Introduction

Chemotherapy unavoidably suppresses the hematopoietic system hence impairing host defence mechanisms. Neutropenia is the generally serious hematologic toxicity of chemotherapy.[1,2] Febrile neutropenia is a significant subject with a negative impact on quality of life, causing increased morbidity and mortality rates, and elevating treatment costs[3,4] Neutrophils are the first line of defence against infection as the first cellular component of the inflammatory response and a key component of innate immunity. In future, chemotherapy-induced neutropenia will become an even greater issue as elderly population increased in developed countries, leading to a higher prevalence of cancers and an increase in the age-related risk of chemotherapy-induced neutropenia.[5] The reported incidence and prevalence of neutropenia vary widely. The literature suggests an incidence of neutropenia in 7.83 cases per 1000 cancer patients.[6] In the current study retrospective analysis of absolute neutrophilic value was done before and after first cycle of chemoradiotherapy to assess the percentage and level of neutropenia.

Materials and Method

This study was a retrospective measure of the haematological toxicity risk in patients with solid tumours during their first chemotherapy cycle. Total of 100 patients with male and female ratio of 1:1.8 were taken into consideration with age range of 6-86 (55.1±15.1) years. Majority of the patients were females with predominant group of carcinoma breast (Table 1).

The pretreatment as well as post first cycle of chemoradiotherapy reports of all the blood samples collected in EDTA vacutainers and processed with automated hematology analyzer were re-collected. The pretreatment values of cases with reduction in ANC after first cycle of chemotherapy were categorised (Table 2) into neutrophilia, normal range and neutropenia.[7] Hematopoietic growth factors were given to neutropenic cases. Post treatment data obtained was analysed and discussed in detail.

Results

Pretreatment values of ANCs were compared with post treatment values after first cycle of treatment. Total mean value of ANC in pretreatment patients was 5.3±1.1× 10^9/L (mean±standard deviation) with post treatment value of 5.3±3.6× 10^9/L (Table 3). Total of 25 out of 100 cases (25 %) showed reduction in ANC after first cycle of chemoradiotherapy. When observed in total cases neutropenic patients were 1% only. Total out of 25% affected cases, 12% cases were having neutrophilia and 4% cases had pre-treatment neutropenia. Rest of the 87.6% cases had absolute counts within normal range. After further analysis, neutropenia was detected in 16% of the affected cases. But overall post treatment neutropenic cases were 4% including 3% patients of carcinoma breast.

Table 1: Distribution of various carcinomas

Organ affected	Type of carcinoma	Percentage (%)
Breast	Infiltrating ductal cell carcinoma	25%
Oral cavity	Squamous cell carcinoma	09%
Uterus	Adenocarcinoma endometriun	02%
Ovary	Cystadenocarcinoma	02%
Oesophagus	Squamous cell carcinoma	02%
Skin	Squamous cell carcinoma	02%
Axilla	Mucinous carcinoma skin	01%
Rectum	Adenocarcinoma	02%
Liver	Hepatocellular carcinoma	02%
Thyroid	Papillary carcinoma thyroid	02%
Lung	Squamous cell carcinoma	01%
Total		100%

Table 2: Showing distribution of absolute neutrophil count (ANC) in 25% cases of reduced post treatment values

ANC× 10^9/L	No of cases (Pre-treatment)	No of cases (Post treatment)
< 2	1	4
2-7	21	21
>7	3	Nil

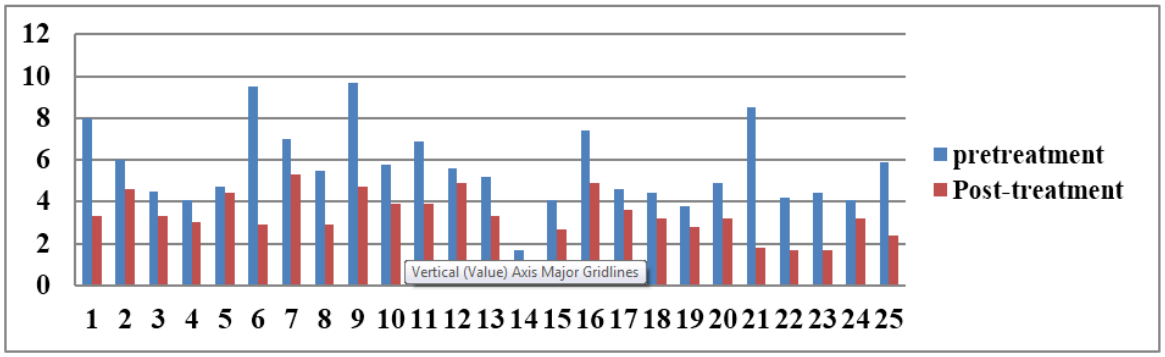

Fig. 1: Showing pre-treatment and post-treatment values of ANC

Discussion

Neutropenia or febrile neutropenia is one of the major haematological complications of chemotherapy. In the current study, post chemotherapy neutropenia was detected in 4% after first cycle of treatment. Incidence and prevelance of neutropenia varies widely. However depending on the cancer type, disease staging, patient functional status and chemotherapy regimen, neutropenia has been observed in 6–50% of patients.[8] It is amongst dose-limiting toxicities seen in clinical oncology practice. Neutropenia is clinically significant

As pre-treatment neutropenia was detected in 1% cases, only these patients were identified as at risk and hematopoietic growth factors were given. The work conducted by Chang has manifested marked benefits in patients, if they were identified as high risk patients prior to chemotherapy. In time use of growth factors can avoid the occurrence of delay in therapy as well as dose reduction.[11] Although with the use of hematopoietic growth factors incidence, severity and duration of neutropenia can be reduced. But these agents are negatively associated with bone pain, fever. And also not all chemotherapy regimens bear the same risk of neutropenia. So these factors are not recommended for use in all the patients. On the other hand total of 4% cases including previous 1% cases of low ANC, showed neutropenia after treatment. So patient's selection should be improved for the use of these types of factors.[12,13]

In our study it was found that 75% neutropenic cases were of carcinoma breast only. This may be correlated with the higher number of cases of carcinoma breast (25%) who were planned for chemotherapy. However many authors have also mentioned the need for a tool to identify high-risk patients among that undergoing adjuvant chemotherapy as it causes increased morbidity and mortality rates and possibly compromised treatment outcomes, and excess healthcare costs. A study done by Shirdel EA and associates predicted the significant fall in neutrophilic counts in patients receiving chemotherapy treatment.[9] In the review of literature it was found that research in quantitative analysis of neutropenic complications and their risk, may help in the near future to target patients at greater risk. So that appropriate preventive measures can be taken up to maximizing the benefits and minimizing the costs of chemotherapy.[10] for early-stage breast cancer.[12,13,14] Several studies had been done to know the correlations between risk groups and blood count data in various malignancies for any particular regimens. But none of them have produced any predictor that can suggest tumour type or treatment regimen to make a distinction between high risk patients from low risk patients especially in carcinoma breast.[15-21] A study done on 35 patients also have shown significant fall in ANC in cases where pre-treatment ANC counts were low.[21]

Conclusion

Neutropenia is the commonest adverse effect amongst all post chemotherapy complications. In our observation it was 4% of the total cases and can occur in any case irrespective of prechemotherapy ANC counts. ANC values of post first cycle chemotherapy treatment can play important role in the further plan of treatment in cancer patients.

References

1. Bodey GP, Buckley M, Sathe YS, Freireich EJ. Quantitative relationships between circulating leukocytes and infection in patients with acute leukemia. Ann Intern Med. 1966;64:328–40.

2. Blackwell S, Crawford J. Filgrastim (r-metHuG-CSF) in the chemotherapy setting. In: Morstyn G, Dexter TM, Foote M, editors. Filgrastim (r-metHuG-CSF) in clinical practice. New York: Marcel Dekker, 1994:103–106.
3. Talcott JA, Siegel RD, Finberg R, Goldman L. Risk assessment in cancer patients with fever and neutropenia: a prospective, two-center validation of a prediction rule. Journal of Clinical Oncology. 1992;10: 316–22.
4. Hughes WT, Armstrong D, Bodey GP, Bow EJ, Brown AE, Calandra T et al. 2002 guidelines for the use of antimicrobial agents in neutropenic patients with cancer. Clinical Infectious Diseases. 2002;34:730–51.
5. Lyman GH, Kuderer N, Agboola O, Balducci L. Evidence-based use of colony-stimulating factors in elderly cancer patients. Cancer Control. 2003;10:487–99.
6. Caggiano V, Weiss RV, Rickert TS, Linde-Zwirble WT. Incidence, cost, and mortality of neutropenia hospitalization associated with chemotherapy. Cancer. 2005;103:1916-24.
7. Lewis S. (2006) Reference ranges and normal values. In: Dacie and Lewis Practical Hematology, 10th edn. (eds SM Lewis, BJ Bain & I Bates) Churchill Livingstone, Philadelphia, pp. 11–24.
8. Smith TJ, Khatcheressian J, Lyman GH, Ozer H, Armitage JO, Balducci L et al. 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. Journal of Clinical Oncology. 2006;24:3187–205.
9. Crawford J, Dale DC, Lyman GH. Chemotherapy-induced neutropenia: risks, consequences, and new directions for its management. Cancer. 2004;100:228–37.
10. Schimpff SC, Gaya H, Klastersky J, Tattersall MH, Zinner SH. Three antibiotic regimens in the treatment of infec-tion in febrile granulocytopenic patients with cancer. The EORTC international antimicrobial therapy project group.Journal of Infectious Diseases. 1978;137:14–29.
11. Chang J. "Chemotherapy dose reduction and delay in clinical practice, evaluating the risk to patient outcome in adjuvant chemotherapy for breast cancer." European Journal of Cancer. 2000;36(1):S11–S4.
12. Lyman GH, Kuderer N, Greene J, Balducci L. "The economics of febrile neutropenia: implications for the use of 8 Advances in Bioinformatics golony-stimulating factors," European Journal of Cancer. 1998;34:(12):1857–64..
13. Silber JH, Fridman M, DiPaola RS, Erder MH, Pauly MV, Fox KR."First-cyclebloodcountsandsubsequent neutropenia, dose reduction, or delay in early-stage breast cancertherapy." Journal of Clinical Oncology. 1998;16(7):2392–400.
14. Uyl-de Groot CA, Vellenga E, Rutten FFH. "An economic Model to assess the savings from a clinical application of haematopoietic growth factors," European Journal of Cancer. 1996;32(1):57–62.
15. Jenkins P, Freeman S. "Pretreatment haematological laboratory values predict for excessive myelosuppression in patients receiving adjuvant FEC chemotherapy for breast cancer," Annals of Oncology. 2009; 20(1):34–40.
16. Dranitsaris G, Rayson D, Vincent M, Chang J, Gelmon K, Sandor D et al. "Identifying patients at high risk for neutropenic complications during chemotherapy for metastatic breast cancer with doxorubicin or pegylated liposomal doxorubicin: the development of a prediction model," American Journal of Clinical Oncology. 2008; 31(4):369–74.
17. Rivera E, Haim Erder M, Fridman M, Frye D, Hortobagyi GN, "First-cycle absolute neutrophil count can be used to improve chemotherapy-dose delivery and reduce the risk of febrile neutropenia in patients receiving adjuvant therapy: a validation study." Breast Cancer Research. 2003;5(5):R114–R20.
18. Matsubara J, Ono M, Negishi A, Ueno H, Okusaka T, Furuse Jn et al. "Identification of a predictive biomarker for hematologic toxicities of gemcitabine."Journal of Clinical Oncology. 2009;27(13):2261–8.
19. Uys A, Rapoport BL, Fickl H, Meyer PWA, Anderson R. "Prediction of outcome in cancer patients with febrile neutropenia: comparison of the multinational association of supportive care in cancer risk-index score with procalcitonin, C-reactive protein, serum amyloid A, and interleukins-1β, -6, -8 and -10." European Journal of Cancer Care. 2007;16(6):475–83.
20. Moreau M, Klastersky J, Schwarzbold A, Muanza F, Georgala A, Aoun M et al. "A general chemotherapy myelotoxicity scoretopredictfebrileneutropenia in hematological malignancies." Annals of Oncology. 2009; 20(3):513-9.
21. Rolston KVI."Prediction of neutropenia," International Journal of Antimicrobial Agents.2000;16(2):113–5.