

Chemotherapy in Different Cancers; an Observational Study Highlighting the Association of Febrile Neutropenia with Various Hematological Parameters

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Abstract

Objective: This study was aimed to evaluate of febrile neutropenia in patients receiving chemotherapy and find out its association with haematological parameters.

Methodology: This was an observational study conducted in the Oncology Department of Jinnah Postgraduate Medical Centre, Karachi. The study was done for duration of 6 months from November 2017 till April 2018. Data was collected using non-probability convenient sampling technique after taking informed consent from 318 patients diagnosed as having cancer on histopathology, undergoing treatment with chemotherapeutic agent and having neutropenia along with fever as a single oral temperature of >38.3 °C. Patients who had comorbid conditions such as diabetes, heart disease, or psychiatric illness were excluded from this study. The variables recorded were age, gender, chemotherapy protocol, number of days of chemotherapy, haemoglobin, total leukocyte count, neutrophils, monocytes, platelets and creatinine. Patients were divided into 2 groups based on presence and absence of febrile neutropenia receiving the chemotherapeutic regimen, Group 1 consisted of those patients that have developed febrile neutropenia and Group 2 consisted of those patients that have not developed febrile neutropenia. SPSS version 20.0 was used for data analysis. T-test was used to assess the association. P-value of < 0.05 was taken as significant

Results: The mean age of Group 1 patients was 39.88 ± 15.2 years while that of group 2 was 44.84 ± 12.2 years. In our study significant difference exists in some of the hematological parameters. In our study, group 1 had total leukocyte count of 1411.0180 ± 641.48 cells/cmm, neutrophil count of 17.64 ± 14.01/mm³ and group 2 had total leukocyte count 3597.41 ± 1673.90 cells/cmm, neutrophil count 52.20±12.08/mm³ which is significantly different among two groups (p-value < 0.05).

Conclusion: Our study showed that significant difference exists in some of the hematological parameters including hemoglobin levels, platelet count, total leukocyte count, neutrophil count, monocyte count and absolute neutrophil count in patient treat with different chemotherapeutic drugs suffering from febrile neutropenia.

Keywords: Febrile Neutropenia; hematological association;

Introduction

Cancer chemotherapy causes a lot of complications among them one is febrile neutropenia which leads to decrease in efficiency of treatment due to reduction in dosage of chemotherapy. Higher mortality rate has been demonstrated due to febrile neutropenia [1]

Febrile neutropenia in patients having hematological malignancies is apparently about ≥ 80% while in patients having solid tumor, the incidence ranges from 10%-50% [2]. Aggressive antimicrobial treatment and hospitalization is required in febrile neutropenia associated with high mortality [3]. Mortality rate of about 18% and 5% have been documented in patients having gram negative and gram positive bacteraemia respectively [4].

Febrile Neutropenia according to the European Society for Medical Oncology (ESMO) defined as 'An oral temperature of > 38.5°C or two consecutive readings of > 38.0°C for 2 h and an absolute neutrophil count (ANC) of < $0.5 \times 10^9/l$, or expected to fall < $0.5 \times 10^9/l$ ' [5]. Neutrophils are basically the first line defence against infection and are the most numerous circulating wbc's [6]. Neutropenia causes several symptoms. As the patient is already immune compromised because of chemotherapy and are more prone to progress to infection [7]. Chemotherapy affects the bone marrow and suppresses the cell lineage majorly affecting neutrophils [8]. With the increase of severity and duration of neutropenia there is the increase risk of infection and mortality along with the persistence of fever wherein the duration of neutropenia is typically 7–10 days, with variations depending upon the type and strength of the chemotherapeutic regimen [9]. Heterogeneous grouping exists among febrile neutropenia patients, so development of infection and outcome is related to individual patient factors such as: age, stage and tumor type, severe comorbidity or hospital admission previously [10,11].

Moreover, febrile neutropenia commonly compromises the chemotherapeutic treatment being administered by necessitating a reduction in dose and/or interruption of treatment cycles, thereby directly affecting treatment efficacy, patient survival and quality of life [12]. As during initial cycles of chemotherapy it is common to develop febrile neutropenia, US and European guidelines recommend the use of stimulating growth factors in patients having > 20% risk of developing febrile neutropenia [13,14]. Elder are more prone to have metastatic disease and have more comorbidity than younger patients who usually present with less severe disease so elder show poor performance status [15,16].

It is observed that there are variations of haematological parameters in patients receiving chemotherapy on febrile neutropenia basis. Therefore, this study was aimed to focus on frequency of patients receiving chemotherapy and having febrile neutropenia, so that the appropriate chemotherapeutic plan can be devised to manage the patients accordingly. This may help decrease mortality and morbidity in future.

Materials and Methods

This was an observational study conducted in the Oncology Department of Jinnah Postgraduate Medical Centre, Karachi Pakistan. The study was done for duration of 6 months from November 2017 till April 2018 by utilizing non-probability convenient sampling technique. The study comprised of a total of 316 patients after receiving informed consent. The Ethical approval was taken from Ethical Review Board of Jinnah Postgraduate Medical Centre.

Patients diagnosed as having cancer on histopathology, undergoing treatment with chemotherapeutic agent were included in this study. The different chemotherapeutic agents used were antibiotics like bleomycin, doxorubicin, and alkylating agents like cyclophosphamide, dacarbazine, and microtubular inhibitors like docetaxel, paclitaxel, vincristine, vinorelbine, and steroids like prednisone and other agents like cisplatin, asparaginase and etoposide. Patients who had comorbid conditions such as diabetes, ischemic heart disease, or psychiatric illness and incomplete data were excluded from this study. The patients were divided into 2 groups based on presence and absence of febrile neutropenia receiving the chemotherapeutic regimen, Group 1 consisted of Group 1 (n=167) consisted of those patients that have developed febrile neutropenia and Group 2 (n=151) consisted of those patients that haven't developed febrile neutropenia. The variables including age, weight, height, gender and body surface area, type of cancer, chemotherapy protocol, and number of days of chemotherapy, haemoglobin, total leukocyte count, neutrophils, monocytes, platelets, and creatinine were recorded.

Data was analysed using SPSS version 20. Demographic and haematological variables were presented as mean, standard deviation. Qualitative data was expressed as frequency and percentages. T-test was applied to find significant difference between quantitative variables. Chi-square test was applied to find significant difference in febrile neutropenia between genders. P-value < 0.05 was considered to be significant.

Results

Our study comprised of 318 patients in total, out of which Group 1 had 167 patients and Group 2 had 151 patients. The mean age of Group 1 patients was 39.88 ± 15.29 years while that of group 2 was 44.84 ± 12.20 years. Group 1 had mean weight of 55.99 ± 12.71 kg, mean height of 158.50 ± 11.06 cm, Haemoglobin level of 9.08 ± 1.82 gm/dl, platelet count of 131724.55 ± 108855.91 cells/cumm, total leukocyte count of 1411.01 ± 641.48 cells/cumm, neutrophil count of $17.64 \pm 14.01/mm^3$, monocytes of $7.05 \pm 9.88/mm^3$, absolute neutrophil count of $241.35 \pm 167.87/mm^3$ and duration of chemotherapy was 10.62 ± 3.49 days. Group 2 had mean weight of 58.56 ± 11.06 kg, height of 158.84 ± 9.33 cm, Haemoglobin level 10.39 ± 1.51 gm/dl, platelet count $203359.5232 \pm 109505.7270$ cells/cumm, total leukocyte count 3597.41 ± 1673.9 cells/mm³, neutrophil count $52.2 \pm 12.08/mm^3$, monocytes $9.07 \pm 6.69/mm^3$, absolute neutrophil count $2012.21 \pm 1406.0/mm^3$ and duration of chemotherapy 10.86 ± 2.92 days.

There was a significant difference (p-value < 0.05) in age, hemoglobin, neutrophils, platelet count monocyte count, total leukocyte count and absolute neutrophil count between the two groups table 1.

Table 1: Association of demographic and hematological parameters in different groups

Variable	Group 1 (n=167)	Group 2 (n=151)	P-Value
	Mean ± SD	Mean ± SD	
Age (years)	39.88 ± 15.29	44.84 ± 12.20	0.002
Weight (kg)	55.99 ± 12.71	58.56 ± 11.06	0.057
Height (cm)	158.50 ± 11.06	158.84 ± 9.33	0.77
Body Surface Area (m ²)	1.55 ± 0.199	1.58 ± 0.178	0.121
Hemoglobin (mg/dl)	9.08 ± 1.82	10.39 ± 1.51	<0.001
Platelets (cells/mm ³)	131724.55 ± 108855.91	203359.52 ± 109505.72	<0.001
Total Leucocyte Count (cells/mm ³)	1411.01 ± 641.48	3597.41 ± 1673.90	<0.001
Neutrophils (%)	17.64 ± 14.01	52.2 ± 12.08	<0.001
Monocytes (%)	7.05 ± 9.88	9.07 ± 6.69	0.029
Absolute Neutrophil Count /(mm ³)	241.35 ± 167.87	2012.21 ± 1406.0	<0.001
Creatinine (mg/dl)	0.79 ± 0.44	0.73 ± 0.28	0.132
Chemotherapy (days)	10.62 ± 3.49	10.86 ± 2.92	0.501

Discussion

In our study total 318 cancer patients receiving chemotherapeutic agents, were divided into 2 groups depending on the presence and absence of febrile neutropenia. Chemotherapy causes hematological and also non-hematological unfavorable medication responses. The most serious toxicity in hematological parameters that get disturb is neutropenia, which can cause deadly septicaemia by smothering the generation of neutrophils and by cytotoxic effects on the cells that line the gastrointestinal tract permitting bacterial increase and invasion [17]. Neutropenia with fever (Febrile Neutropenia [FN]) is a serious consequence of myelosuppressive chemotherapy that results in hospitalization and the requirement for intravenous anti-biotics agents. FN may result in delays, reduction or even discontinuation of chemotherapy, which thus, may compromise patient's outcome. It is important to recognize which patients are at high risk for developing FN with the goal that patients can get optimal chemotherapy while their risk for FN is appropriately managed. Older age, poor execution status, certain comorbidities, low baseline blood cell counts, low body surface area, treatment with myelosuppressive chemotherapies, and particular hereditary polymorphisms connected with the risk of developing FN [18].

Severe complications are related to febrile neutropenia caused by chemotherapy that includes changes in hematological parameters, pneumonia, sepsis and others. In one of the study 78 patients out of 81 got febrile neutropenia. In about 25 (30.8%) episodes of serious complications were identified, that include latency of the first dose of antibiotics, pneumonia and platelet counts ≤ 50,000/mm³ were identified as independent factors associated with serious complications [19]. In our study platelets count (mm³) noted in group 1 was 131724.55 ± 108855.91 and group 2 was 203359.52 ± 109505.72 (p= < 0.001)

In one of the study to determine febrile neutropenia, among

the 215 patients who participated in that study, the mean age was documented to be 51.53 years [20]. In another study the mean age of febrile neutropenia patients was 61.5 years that was carried out by [21] Patients aged 65 years or above after 1 cycle of chemotherapy were associated with greater (66%) chances of having febrile neutropenia

[22] In an Indian study the mean age of patients that developed febrile neutropenia during chemotherapy treatment was reported to be 54 years [23]. On the contrary in our study, the mean age of febrile neutropenia patients was reported to be 39.88 ± 15.29 years in Group 1 patients and 44.84 ± 12.20 years in Group 2, which is younger age than in the studies mentioned above.

The quantitative approach of this study has approved that we have sampled the extensive range of patients with cancer chemotherapy. However the study might not be immune from observer and selection bias. Considering the views of the above studies and to what extend the association of febrile neutropenia with hematological parameters will be consistent with different chemotherapeutic drugs would be revealing to discover more facts about febrile neutropenia.

Conclusion

Our study showed that significant difference exists in some of the hematological parameters including hemoglobin levels, platelet count, total leukocyte count, neutrophil count, monocyte count and absolute neutrophil count in patient treat with different chemotherapeutic drugs suffering from febrile neutropenia.

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