

Neutropenia onset, Severity and their Association with Solid Cancer Diseases

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Abstract

Background: Neutropenia is a decreased in the absolute neutrophil count lower than the normal that is < 1500 cell/ μ l. It has a detrimental effect on cancer patients' quality of life, also possibly resulting in a reduction in the chemotherapy dose which could lead to an increment in the size of a cancer. There are so many causative factors for neutropenia like hematological disorders, autoimmune diseases and infection, drugs reactions and chemotherapy or radiotherapy. So the main aim of this study is to find the association between solid cancer diseases with onset and severity of neutropenia.

Methods: This an observational retrospective study conducted on 117 solid cancer patients who received chemotherapy as a treatment and as a result of that they suffer from neutropenia, this study retrospectively cover the period between 1 January 2003 and 31 December 2006. Statistical analysis methods used were Chi-square test, Fisher's Exact test. The level of significance was set at $P < 0.05$.

Results: The total number of the patients involve was 117 neutropenic patients they suffer from 19th different solid cancer diseases. Breast cancer was the predominant once it was found (75, 64.1%) followed by nasopharyngeal cancer 9 (7.7%), rectal cancer 9 (7.7%) and many others. The main finding of this study was insignificant association between solid cancer diseases with both onset and severity of neutropenia since the P values for both tests > 0.05 .

Conclusion: Solid tumor is not considered as a risk factor for neither onset nor severity of neutropenia not like the hematological cancer diseases which play a risk role in these cases. Then the main risk factor for neutropenia within solid cancer patients is the chemotherapy intensity they receive for as a treatment.

Keywords: Neutropenia; Solid cancer; Association

Introduction

Neutropenia has been shown to be associated with solid tumor especially breast and lung cancers whereby about 25% of them developed neutropenia. This will happened as a results of bone metastases, because when cancer cell metastases to bone marrow this will cause bone marrow suppression which will leads to incidence of anemia, neutropenia and thrombocytopenia [1,2]. Neutropenia has a detrimental effect on cancer patients i.e., both solid and hematological patients which caused a decreases in their chemotherapeutics drug doses and delay in their schedule. So this gives a great chance for cancer disease to grown up more and its dangerous will increases. So the discovering of the main risk factor for neutropenia in case of solid cancer patients whether the solid cancer it self which play a major role within neutropenia onset or severity. This will help the physician in this field since there is a very few if not available of any studies which work on discovering whether solid cancer diseases are consider as a risk factor for neutropenia, since neutropenia consider as a major problem [1,2].

Neutrophil cells produce from stem cell of the bone marrow and represented about 60% - 70% of the total WBC in the blood their production need for about 10-14 days they have very short life about 6-10 hours in blood [1,2]. Neutropenia is a condition occurred when there is an actual decrease in the number of neutrophils cells in the whole blood. Therefore the body will lose its main defense mechanism and it will become under serious risk of bacterial or fungal infection [3,4]. Neutropenia is highly caused by antineoplastic drugs and regimens in case of solid cancer patients while neutropenia causes within patients with hematological malignant diseases different. These chemotherapeutics drugs or regimens will cause bone marrow

suppression lead to decreases in neutrophil cell production resulted in neutropenia, just like in breast cancer disease 78% of the patient their neutropenia is because of the uses of CMF (cyclophosphamide, methotrexate and 5-fluorouracil) [1-8]. But in many times these chemotherapeutics will not cause neutropenia this is because of their intensive effect is not high enough to cause bone marrow suppression also because of the interval period between one cycle and other in long enough so neutropenia will overcome and no increases in its severity beside the uses of G-CSF will also help in reducing the time for neutrophil cell production and reducing or preventing neutropenia onset and severity [9].

Materials and Methods

Data source

Ethical approval letter for conducting this study was obtained and granted from the clinical research center (CRC) of the hospital which identical and follow to the declaration of Helsinki guidelines in 1964. This is an observational retrospective study was conducted

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on solid cancer patients treated in this hospital. This study covered retrospectively the period between 1 January 2003 and 31 December 2006. A total number of 117 patients fulfilling the inclusion criteria were selected from the total number of 4503 solid cancer patients. All of 117 patients suffered from neutropenia after chemotherapy treatment. All of them were fulfilled to the inclusion criteria of the study.

Inclusion and exclusion criteria of the study

The inclusion criteria for this study were the patient must suffer from solid cancer, male or female adult ≥ 18 years old, treated with chemotherapy, their files must be found in the oncology clinic and record office of the hospital and must be admitted to ward C19. While the exclusion criteria were all the pediatric patients will excluded, all the patients who suffer from neutropenia as a result from hematological diseases not caused by chemotherapy, all the patients who treated with radiotherapy and a result of that they suffer from neutropenia and all the patients who did not admitted to ward C19.

Data collection

All the data collected were retrospectively from the patients files which were found in the oncology clinic and the record office of the hospital. These data were collected by the uses of a special data form sheet which was already design for this study. So all the patients who admitted to the hospital between 1 January 2003 and 31 December 2006 files were retrospectively reviewed. After that all the clinical information obtained were keyed into SPSS[®] software program, which by it all the statistical analysis to find if there is an association between neutropenia onset and severity on one side and with types of solid cancer diseases diagnosed on the other side.

Statistical analysis

The power of this study according to its sample size was more than 87.5% i.e., since the power of the study > 80 then the results of this study can be dependable for future studies. The type of the data collected were a categorical data which included the information of 19th of different solid cancer diseases diagnosed all those suffer from

Cancer Disease	Number of Patients	Percentage
1 Breast cancer	75	64.1
2 Nasopharyngeal cancer	9	7.7
3 Rectal cancer	9	7.7
4 Brain cancer	4	3.4
5 Bone metastasis cancer	3	2.6
6 Lung cancer	3	2.6
7 Kidney cancer	2	1.7
8 Astrocytoma cancer	1	0.9
9 Stomach cancer	1	0.9
10 Ileo-caecal cancer	1	0.9
11 Pancreatic cancer	1	0.9
12 Liver cancer	1	0.9
13 Adinocarcinoma cancer	1	0.9
14 Left tonsil cancer	1	0.9
15 Colon cancer	1	0.9
16 Osteosarcoma cancer	1	0.9
17 Left maxillary carcinoma	1	0.9
18 Squamous cell carcinoma	1	0.9
19 Bladder cancer	1	0.9
Total	117	100

Table 1: Types of solid cancer diagnosed among neutropenic patients studied (n=117).

Characteristic	Test	Neutropenia	P value
Cancer Diagnosis (n=117)	Chi-square test	Onset	0.218
	Fisher's Exact test		0.158
	Chi-square test	Severity	0.379
	Fisher's Exact test		0.378

Table 2: Association of cancer types diagnosed with neutropenia.

neutropenia beside of their cancer diseases. While on the other side it include neutropenia onset depend on the time when its start after chemotherapy administration and its classified as the following within the first week after receiving chemotherapy ≤ 7 days, within two weeks after chemotherapy administration 8-13 days and more than or after two weeks ≥ 14 days and neutropenia severity which classified according to absolute neutrophil count (ANC) which include (Mild when ANC < 1500 cell/ μL and > 1000 cell/ μL , Moderate when ANC < 1000 cell/ μL and > 500 cell/ μL , Severe when ANC ≤ 500 cell/ μL). These data are not normally distributed this has been confirm after the uses of the SPSS[®] program since the ($P= 0.003$, Kolmogorov-Smirnov test). Since this study is observational designs then its main objective is the looking for association of neutropenia with types of solid cancers diagnosed i.e., risk factors and since the data was categorical then the main statistical test which is suitable is Chi-square test and Fisher's Exact test significance was set at P value < 0.05 . The confidence interval for this test is 95%. These data were analyzed by using SPSS[®] version 15 program to see the association between these solid cancer diseases diagnosed with neutropenia onset and severity.

Results

The main results that show the types of solid cancers diseases that with them neutropenia was taken place cleared in Table 1. Breast cancer disease is the predominance type of solid cancer with it neutropenia occur or take place ($n= 75$; 64.1%) while the other types of cancer diseases show different values and levels. Nasopharyngeal cancer was in the second rank ($n= 9$; 7.7%), rectal cancer was in the third rank ($n= 9$; 7.7%) and so one. Statistical results show that insignificant association between solid cancer diseases with both neutropenia onset (i.e., early and late onset) and severity (i.e., all levels of severity mild, moderate and severe) since P values for Chi-square test = 0.218 and Fisher's Exact test= 0.158 with the onset. While with severity the Chi-square test = 0.379 and Fisher's Exact test = 0.378. These statistical results all consider insignificant since P values for all of them were > 0.05 , all these tests are shown in Table 2.

Discussion

The reason for breast cancer patients were the highest group in this study is most probably because breast cancer is the most common solid cancer among Malaysian women. It represents 30.4% of occurrence among all the others cancer diseases as reported by the [10,11]. Also it has been mentioned by Penang Cancer Registry (2003) and Kaur et al. [13] that the breast cancer is the highest cancer type that occur or take place in Island of Penang [12].

The explanation for insignificant association is that patient with solid cancer is different from those with hematological malignancy. That solid cancer patient usually have normal neutrophil cell function unlike that in case of hematological malignant patient his neutrophil cell function is completely abnormal and suffers from neutropenia. Also for solid cancer patients their neutropenia usually started after chemotherapy and severe neutropenia may last for 7-10 days. For this reason solid tumor patients who developed neutropenia are consider as low risk patients since neutropenia depend on chemotherapy

intensity not the cancer it self [14]. Just like in case of breast cancer is the highly solid cancer associated with neutropenia about 78% but when specific intensive chemotherapy regimen used which is the CMF (cyclophosphamide, methotrexate and 5-fluorouracil). So by changing the protocol as in this study since CEF (cyclophosphamide, epirubicin, 5-fluorouracil) is the highly used and it is less intensive than CMF for this reason neutropenia not highly associated with solid tumor [9].

Also one of the main important factors that play a role in this insignificant association is the uses of (G-CSF, filgrastim) that will reduce the occurrence of neutropenia and increases the rate for the neutrophil cell production and decreases the period and severity of neutropenia [8]. Rahman et al. [15] and Rolston (2001) mentioned that the patients with solid tumors were not immunocompromised (i.e., not significantly immunosuppressive as those with hematological malignancies).

Now many centers consider solid tumor patients as having low risk towards neutropenia. Thus this will also explain the insignificant association between the solid cancer and neutropenia as seen in this presented study.

Conclusion

The main limitation of this present study that it is a retrospective study but as it is clear from its results, solid tumor is not a risk factor for onset and severity of neutropenia not like the hematological cancer diseases.

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