

THE AMOUNT OF LYMPHOCYTES BEFORE AND AFTER CEMOTHERAPY IN BREAST CANCER AT ULIN GENERAL HOSPITAL BANJARMASIN

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Abstract: *Breast cancer is the most common malignancies among woman in Indonesian. One of breast cancer treatment is chemotherapy which resist cancer's cells to grow. But chemotherapy also cause DNA damage that interfere lymphocyte proliferation. Depletion on lymphocyte counts will increased patient's susceptibility to opportunistic infection. The aim of this research was to knowing the difference of lymphocyte counts because of chemotherapy on breast cancer patients in general hospital Ulin Banjarmasin. This research was an observational analytic with cross sectional approach. The sampling technique was non-probability sampling followed by consecutive sampling. Total samples were 61 patients that match with inclusion criteria. Paired T-test was used to analyze the hypothesis with the result of pvalue=0.000 ($p < 0.05$), that means there's a significant decrease in the number of lymphocyte counts after receiving chemotherapy in general hospital Ulin Banjarmasin, January 2014 to December 2015 period.*

Keywords: *chemotherapy, lymphocyte, breast cancer*

INTRODUCTION

Global statistical data show that breast cancer is the second most common cancer in the world after lung cancer. So far, breast cancer most often affects women with an estimated 1.67 million new cases diagnosed in 2012. In addition to the large number of cases, an estimated 522,000 people die with a case fatality rate (CFR) of 31.7%.¹ Incidence breast cancer sufferers in Indonesia is quite high. According Basic National Research (Riskesdas) 2013, it reached 100 per 100,000 women and made breast cancer as the top case in women in Indonesia.²

Cancer treatment may include surgery, radiotherapy and systemic treatment such as chemotherapy. Chemotherapy can be given as induction therapy, primary, adjuvant, as well as neoadjuvant therapy. Giving chemotherapy is based on the degree of ferocity and type of cancer.³

Chemotherapy works by inhibiting growth and killing cancer cells. But in the other hand, chemotherapy drugs affect the physiological system and cells that function physiologically such as the immune system mediated by lymphocytes. Lymphocytes play a role in the prevention of infection and eradication of the causes of chronic infections such as the process of elimination of cancer cells. Lymphocytes will attack foreign cells, make antibodies and maintain immunity. The decline in the number of post-chemotherapy lymphocytes has been widely studied and it is said that some chemotherapy agents result in DNA damage that causes a large effect on lymphocyte proliferation. Decrease of the number of lymphocytes indirectly will cause patients who get chemotherapy more susceptible to infection.⁴ Case data of post-chemotherapy infections remain unknown, especially in Indonesia. However, several incidences of infection such as fungal infections, viral infections and bacterial infections have been reported.

Ulin Hospital Banjarmasin is an A type hospital and top referral hospital in South Kalimantan. Patients with malignancy will generally be referred to Ulin Hospital to obtain appropriate management, including chemotherapy. In 2014 and 2015 respectively recorded there were about 167 and 204 new patients with breast cancer who came to treatment at Ulin Hospital.⁵ Until now not many studies that reveal the linkage of lymphocytes to chemotherapy. Therefore, it is necessary to investigate the number of lymphocyte patients of breast cancer before and after chemotherapy at Ulin Hospital Banjarmasin.

RESEARCH METHODS

This research was an observational analytic with cross sectional study design. This approach was intended to see the effect of independent variables on the dependent variable at the same time. The independent variable is the administration of chemotherapy and the dependent variable is the number of lymphocytes before and after receiving chemotherapy in breast cancer patients at Ulin Hospital Banjarmasin.

The population of this study were all breast cancer patients undergoing chemotherapy at Ulin Hospital Banjarmasin which recorded in medical record from January 2014 until December 2015. The sampling technique using non-probability sampling method followed by consecutive sampling method. Inclusion criteria were IIB and IV breast cancer patients who underwent chemotherapy at Ulin Hospital Banjarmasin, obediently undergoing chemotherapy at least 3 cycles, received the same combination chemotherapy, data identity and complete recorded laboratory results in medical record status.

Instrument used in this research is secondary data in the form of medical record data and result of complete blood laboratory examination before and after

administration of chemotherapy in breast cancer patient at RSUD Ulin Banjarmasin.

The procedure in this research was: preparing the preliminary study permission at Ulin Banjarmasin. Then conduct a preliminary study by accessing data on patient register book in Edelweiss Room or PDE (electronic data search) Ulin Hospital. Therefore, data submitted to the Medical Record Division to obtain each patient's medical record status. Each medical record status was identified to conform to the inclusion criteria and exclusion criteria in the study. After the patient is declared in accordance with the criteria of research, then the recording of data is done.

The data analysis was preceded by the normality test using the Kolmogorov-

Smirnov test. If the obtained data is normally distributed, then it can be continued data analysis using paired T test with result p value <0.05 to declare if there is significant difference.

RESULTS AND DISCUSSION

This study was conducted to determine differences in the number of lymphocytes before and after receiving chemotherapy in breast cancer patients in RSUD Ulin Banjarmasin. The study obtained 61 samples that meet the inclusion criteria. Of the 61 study samples, the characteristics of the study sample according to age, type of staging and drug regimen used.

Table 1. Characteristics of Breast Cancer Patients at Ulin Hospital Banjarmasin 2014-2015

| Characteristic | Total | % |
|----------------|-------------|-----|
| 1. Age | | |
| 21-30 year | 1 patient | 2% |
| 31-40 year | 11 patients | 18% |
| 41-50 year | 31 patients | 51% |
| 51-60 year | 18 patients | 29% |
| 2. Stadium | | |
| IIIB | 56 patients | 92% |
| IIIC | 1 patient | 2% |
| IV | 4 patients | 6% |
| 3. Regimen | | |
| TAC | 42 patients | 69% |
| TEC | 19 patients | 31% |

Based on table 1, it can be seen from 61 research samples that most breast cancer patients are in range around 41-50 years which is counted 31 people (51%) and only 1 person (2%) at 20-30 years. According to the type of stadium suffered,

most is stage IIIB with the number 56 people (92%). According to the chemotherapy regimen used, the most is TAC that is 42 people (69%). The number of lymphocytes before and after the third cycle of chemotherapy is presented in Figure 1.

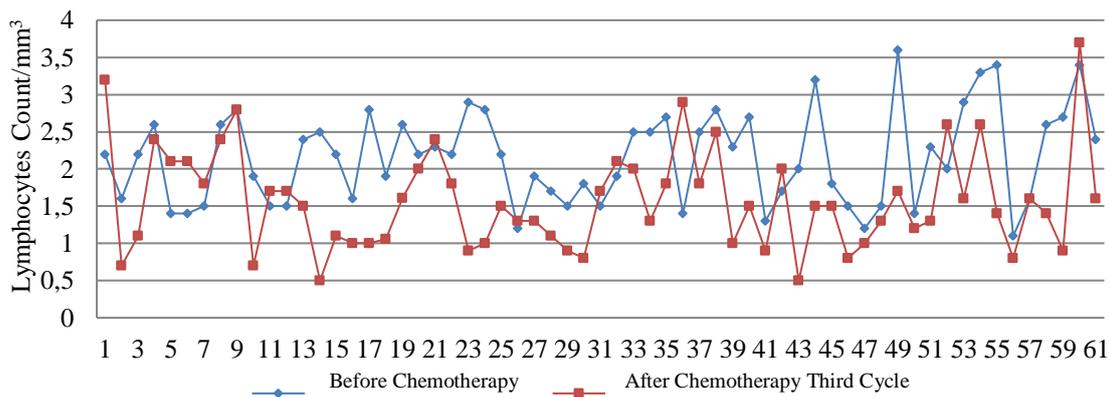


Figure 1. The amount of lymphocyte before and after 3rd chemotherapy cycle.

Table 2. Pattern of Lymphocyte Amount Before and After 3rd Chemotherapy Cycle

| Lymphocyte Change | Amount | % |
|---|-------------|-----|
| Improved but still within normal range | 14 patients | 23% |
| Decreased but still within normal range | 28 patients | 46% |
| Lymphopenia | 19 patients | 31% |
| Lymphocytosis | 0 patient | 0% |

There are various patterns of changes in lymphocyte count before and after chemotherapy as shown in Figs. 1 and 2. Based on Table 2 it is concluded that the decline in the number of lymphocytes was 28 people (46%) although still within the normal range; lymphopenia was 19 people (31%); an increasing compared to before chemotherapy was 14 people (23%); and no lymphocytosis. Decreasing the number of low lymphocytes even below normal is associated with exposure to chemotherapy that occurs continuously without offset by self repair of blood progenitor cells in the body. In addition, 14 people had an

increase in the number of lymphocytes, although still within the normal range, were associated with uncontrollable confounding variables such as patients taking immunostimulant that were sold freely under chemotherapy period.

Normality test using Kolmogorov Smirnov test obtained that the data is normally distributed ($p > 0.05$). Then T-paired test results obtained significance value of 0.000 ($p < 0.05$), which means there is a significant difference between the number of lymphocytes before undergoing chemotherapy and after undergoing chemotherapy.

Table 3 Mean Lymphocyte Count Before and After Chemotherapy First, Second Cycle and Third

| | Mean Lymphocyte Count |
|----------------------------------|-----------------------|
| Before Chemotherapy | 2.159 |
| Before Chemotherapy first cycle | 1.629 |
| Before Chemotherapy second cycle | 1.614 |
| Before Chemotherapy third cycle | 1.586 |

Based on table 3, it can be seen that generally the number of lymphocytes is

decreased in each cycle of chemotherapy with the distance between cycles is 21 days. According to John Barret *et al* states

that spinal cord suppression from chemotherapy may occur soon or later. In immediate response of bone marrow, the effect on lymphocyte counts reaches the lowest value on day 8 to day 14. In bone marrow suppression that occurs later, a decrease in lymphocyte count may occur around the fourth week after chemotherapy. This is due to the lymphocytes as one part of the leukocytes, the type of blood cells which most significantly affected by cytostatic due to rapid proliferation of leukocyte precursors and short life span (6-12 hours).^{6,7}

This is in accordance with previous research by Denny IM *et al.*, Which states that there is a decrease in the number of leukocytes in patients who get TAC chemotherapy regimen in Ulin Hospital Banjarmasin.⁸

Chemotherapy agents also become one of the important factors in decreasing the number of lymphocytes in patients. When a single chemotherapy agent clearly has an effect on the number of lymphocytes and immunities, so does combination chemotherapy.

In this study we found a decrease in the number of lymphocytes due to chemotherapy in the combination of TAC and TEC, where this regimen contains docetaxel, anthracycline, and cyclophosphamide. This is in accordance with the research of Maria YH *et al* which states every type of chemotherapy drugs from any combination of TAC or TEC will have antitumor effects and are immunosuppressive. Docetaxel induces lymphopenia in all subset of lymphocytes especially T cells (CD4+ and CD8+), then anthracycline becomes an active agent in the process of destruction of cancer cells but also potentially large cytotoxic that will induce apoptosis of lymphocyte cells especially T lymphocytes. It is said cyclophosphamide may causes lymphopenia in prolonged use.^{9,10}

TAC regimens alone have much better efficacy when compared to combination chemotherapy regimens such

as FAC, AC and FEC. But in addition, the combination regimen of TAC and TEC have a hematologic toxicity effect, especially leukocytes that are much larger than other chemotherapy regimens.¹⁰

In addition, the decreasing number of lymphocytes in each of these cycles is related to the ability to repair DNA (DNA repair) from damaged progenitor cells affected by chemotherapy and bone marrow deposits keep decreasing with increasing levels of persistent chemotherapy exposure.¹¹ This cause the number of blood cells is in the lower limit even below normal and decreased the ability of the immune system to fight the opportunistic infection in the future.¹²

CONCLUSIONS

Based on the research, it can be concluded that the average number of lymphocyte of breast cancer patients before undergoing chemotherapy is 2.159 thousand/ mm³, whereas the mean number of lymphocyte of breast cancer patients after undergoing the third cycle chemotherapy is 1.586 thousand/ mm³. Therefore, it can be concluded that there is a decrease in the number of lymphocyte patients of breast cancer before and after receiving third cycle chemotherapy at Ulin Hospital Banjarmasin during the period of January 2014-December 2015.

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