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Body Weight and Hematological Parameter Change in Advanced Breast Cancer Following Adjuvant Chemotherapy

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Abstract

Background: Body weight change commonly occurs in breast cancer patients who receive adjuvant chemotherapy. However, there was lack of information associated with weight loss and hematological parameter change. The purpose of this study was to evaluate the body weight and hematological parameter change following adjuvant chemotherapy in advanced breast cancer.

Methods: This prospective observational study included 50 advanced breast cancer (Stage IIIB and stage IV) subject who were receiving adjuvant chemotherapy with Doxorubicin and Cyclophosphamide regiment. Body weight, Body Mass Index (BMI), Body Surface Area (BSA) and hematological parameter were measured before the onset of chemotherapy, then after first and second cycles of chemotherapy.

Results: Based on the study results, the subject body weight was decrease after first and second cycles chemotherapy from 60.06 ± 11.16 kg to 61.33 ± 16.61 and 58.69 ± 10.41 kg ($p<0.05$), respectively. The BMI was also decrease from 25.66 ± 4.10 kg/m^2 to 25.33 ± 4.12 and 25.05 ± 4.12 kg/m^2 ($p<0.05$), respectively. Body surface area also decrease from 1.58 ± 0.16 m^2 to 1.58 ± 0.16 and 1.57 ± 0.15 m^2 ($p<0.05$), respectively.

Hemoglobin and Total Lymphocyte Count (TLC) level significantly decrease after first and second cycles of chemotherapy. Hemoglobin level decrease from 12.04 ± 1.35 g/dL to 11.29 ± 1.32 and 10.97 ± 1.47 g/dL ($p<0.05$), and TLC decrease from 2235.61 ± 701.02/mm^3 to 1916.42 ± 670.77 and 1894.82 ± 712.13/mm^3 ($p<0.05$), respectively.

There was no significant decrease in leukocyte and Absolute Neutrophil Count (ANC) level after first and second cycles of chemotherapy ($p=0.06$ and $p=0.56$).

Conclusion: Body weight, BMI and BSA significantly decrease after first and second cycles of chemotherapy. Hemoglobin and TLC level also significantly decrease but there is no significant decrease in leukocyte and ANC level. Appropriate nutritional management interventions with follow-up programs are needed.

Keywords: Breast cancer; Adjuvant chemotherapy; Body weight; Hematological parameter changes

Introduction

The majority of breast cancer patients are treated with adjuvant chemotherapy often in combination with other systemic treatment [1,2]. Weight gain commonly occurs in western breast cancer patients who receive adjuvant chemotherapy [3-6]. Weight gain is also associated with cancer recurrence and poor prognosis [7-10].

Several studies have demonstrated that the majority of breast cancer survivors exhibited a mean body weight gain of 1-6 kg following chemotherapy and identified adjuvant chemotherapy as an independent prognostic factor for weight gain, with a potential long-term effect [11,12]. However, other studies did not report a significant difference in weight gain between breast cancer patients receiving adjuvant chemotherapy and healthy controls [3,13,14].

The causes of weight gain may include reduced physical activity and menopause prior to diagnosis. However, the exact mechanisms have not been fully elucidated. In addition, the previous observations were focused on patients from the USA and also patients from Western Europe [3].

There is lack of information associated with body weight decrease in advanced breast cancer patients following adjuvant chemotherapy in Indonesian population. Information about hematological parameter change in advanced breast cancer patients following adjuvant chemotherapy is also very limited.

Therefore, we conducted an observational analytical study among women treated with adjuvant chemotherapy for advanced breast cancer. The purpose of this study was to evaluate the body weight and hematological parameter change following adjuvant chemotherapy in advanced breast cancer.

Methods

Data collection

This study was conducted in the period of September 2016 to March 2017 in 50 patients who newly diagnosed with breast cancer and will get chemotherapy at the Hospital in Cirebon, West Java, Indonesia.

Diagnosis of breast cancer based on pathological anatomy result from patient undergoing mastectomy or biopsy. Breast cancer stage is determined based on the results of physical examination, anatomical pathology result and imaging.

We performed body weight and height assessment as well as complete laboratory examination including hematology parameter before chemotherapy. Data on body weight and hematological parameters are followed up during patients undergoing first and second cycle of chemotherapy.

We collected pathological anatomic diagnosis, age, body weight, body height and hematological parameter including hemoglobin, leucocyte, differential count and thrombocyte on adult patient newly diagnosed with advanced breast cancer (stage IIIB and IV) and undergoing chemotherapy with doxorubicin and cyclophosphamide regimen.

Data analysis

Data processing using the program *SPSS version 21.0 for windows*. Categorical data is presented with the number/frequency and percentage whereas the numerical data is presented with the mean, median, standard deviation and range.

Numerical data were analyzed using Kolmogorov Smirnov test to determine the data distribution the data were analyzed by using the Repeated Anova test if the data were normally distributed and Friedman's test if the data were not normally distributed.

Body mass index, hemoglobin and TLC data are normally distributed so that the Repeated Anova test is performed while body weight, BSA, platelets, leukocytes and ANC data are not normally distributed. So, Friedman test is performed. The significance criterion is determining using p value. The p value is statistically significant if $p \leq 0.05$ and not statistically significant if $p>0.05$.

Results

A number of 50 patients with advanced breast cancer (stage IIIB and IV) were treated with doxorubicin and cyclophosphamide adjuvant chemotherapy in the participating hospitals. The mean age of the study subjects was 46.44 ± 9.68 years, whereas the mean body weight and BMI of the subjects before the illness were 60.98 ± 13.10 kg and 26.05 ± 4.65, respectively (Table 1).

Variable	N=50
Age	
Mean ± Std	46.44 ± 9.68
Median	44.5
Range	28.00-70.00
Height (cm)	
Mean ± Std	152.80 ± 5.32
Median	153
Range	144.00-170.00
Body weight before illness (kg)	
Mean ± Std	60.98 ± 13.10
Median	60
Range	43.00-113.00
BMI before illness	
Mean ± Std	26.05 ± 4.65
Median	25.53
Range	18.73-39.10

Table 1: Baseline characteristics. Categorical data presented in number/frequency or percentage while numerical data presented in mean, median, standard deviation and range.

Based on the study results, the subject body weight was decrease after first and second cycles chemotherapy from 60.06 ± 11.16 kg to 61.33 ± 16.61 and 58.69 ± 10.41 kg ($p<0.05$), respectively. The BMI was also decrease from 25.66 ± 4.10 kg/m^2 to 25.33 ± 4.12 and 25.05 ± 4.12 kg/m2 ($p<0.05$), respectively. Body surface area also decrease from 1.58 ± 0.16 m2 to 1.58 ± 0.16 and 1.57 ± 0.15 m2 ($p<0.05$), respectively (Table 2).

Variable	Group Before Chemotherapy Cycle			p
	I	II	III	
	N=50	N=50	N=50	
Body weight				**0.000****
Mean ± Std	60.06 ± 11.16	61.33 ± 16.61	58.69 ± 10.41	
Median	60	59	58	
Range	41.00-104.00	40.00-148.00	40.00-95.00	
BMI				**0.000****
Mean ± Std	25.66 ± 4.10	25.33 ± 4.12	25.05 ± 4.12	
Median	25.47	25.43	25.2	
Range	17.04-35.98	16.64-35.64	16.64-35.88	
BSA				**0.001****
Mean ± Std	1.58 ± 0.16	1.58 ± 0.16	1.57 ± 0.15	
Median	1.58	1.57	1.56	
Range	1.32-2.21	1.31-2.21	1.31-2.11	

Table 2: Comparison of body weight, BMI, and BSA in chemotherapy group before cycle I, II and III. For numerical data p value is tested by

Repeated Anova test if normal distributed data and Friedman alternative test if the data is not normally distributed. The significance value is based on the p value <0.05. The * mark shows the value of p<0.05 means statistically significant.

Hemoglobin levels in the group before chemotherapy, after first and second cycle of chemotherapy had an average of 12.04 ± 1350, 11.29 ± 1.32, and 10.97 ± 1.47, respectively. Platelet levels in the group before chemotherapy, after first and second cycle of chemotherapy had an average of 363380.00 ± 108989.24, 404788.00 ± 127744.36, and 381276.00 ± 122192.573, respectively. Total lymphocyte count in the group before chemotherapy, after first and second cycle of chemotherapy had an average of 2235.61 ± 701.02, 1916.42 ± 670.776 and 1894.82 ± 712.13, respectively. Hemoglobin level decrease from 12.04 ± 1.35 g/dL to 11.29 ± 1.32 and 10.97 ± 1.47 g/dL (p<0,05), and TLC decrease from 2235.61 ± 701.02/mm^3 to 1916.42 ± 670.77 and 1894.82 ± 712.13/mm^3 (p<0,05), respectively. Base on study result, Hemoglobin, thrombocyte and TLC level significantly decrease before and after chemotherapy. (Table 3).

Variable	Group Before Chemotherapy Cycle			p
	I	II	III	
	N=50	N=50	N=50	
Hemoglobin level				**0.000****
Mean ± Std	12.04 ± 1.35	11.2 9 ± 1.32	10.97 ± 1.47	
Median	12.05	11.5	11.15	
Range	8.00-14.40	7.50-14.20	8.00-14.70	
Thrombocyte level				**0.030****
Mean ± Std	363380.00 ± 108989.24	404788.00 ± 127744.36	381276.00 ± 122192.57	
Median	335500	387700	364500	
Range	214000.00-704000.00	164000.00-675000.00	114000.00-646000.00	
TLC				**0.003****
Mean ± Std	2235.61 ± 701.02	1916.42 ± 670.77	1894.82 ± 712.13	
Median	2299.2	1937.5	1814.5	
Range	950.00-3680.00	540.00-4048.00	540.00-3640.00	

Table 3: Comparison in Hemoglobin level, Thrombocyte level and TLC in chemotherapy group before cycle I, II and III. For numerical data p value is tested by Repeated Anova test if normal distributed data and Friedman alternative test if the data is not normally distributed. The significance value is based on the p value<0.05. The * mark shows the value of p<0.05 means statistically significant

Leukocyte levels in the group before chemotherapy, after first and second cycle of chemotherapy had an average of 9129.40 ± 3081.53, 8252.60 ± 3167.50, and 7713.60 ± 2815.23, respectively. The ANC in the group before chemotherapy, after first and second cycle of chemotherapy had an average of 6817.82 ± 4824.36, 5756.96 ± 3023.06, 5262.68 ± 2439.06, respectively. Leukocyte level decrease from 9129.40 ± 3081.538, 8252.60 ± 3167.507, and 7713.60 ± 2815.230/mm^3 (p=0.062), respectively, while the ANC level also decrease from 6817.82 ± 4824.366, 5756.96 ± 3023.061 and 5262.68 ± 2439.062/mm^3 (p=0.568), respectively. Base on study result, there is no significant decrease in leukocyte and ANC level after first and second cycles of chemotherapy (Table 4).

Variable	Group Before Chemotherapy Cycle			p
	I	II	III	
	N=50	N=50	N=50	
Leucocyte level				**0.062**
Mean ± Std	9129.40 ± 3081.53	8252.60 ± 3167.50	7713.60 ± 2815.23	
Median	8590	7550	7150	
Range (min-max)	4300.00-20760.00	3200.00-15900.00	3800.00-15740.00	
ANC				**0.568**
Mean ± Std	6817.82 ± 4824.36	5756.96 ± 3023.06	5262.68 ± 2439.06	
Median	5365	4693	4810.5	
Range (min-max)	2450.00-33245.00	1664.00-13578.00	1638.00-12277.00	

Table 4: Comparison in Leucocyte level and ANC in chemotherapy group before cycle I, II and III. For numerical data p value is tested by Repeated ANOVA test if normal distributed data and Friedman alternative test if the data is not normally distributed. The significance

value is based on the p value<0.05. The * mark shows the value of p<0.05 means statistically significant.

Discussion

Studies have demonstrated that adjuvant chemotherapy correlates with weight gain in Western breast cancer patients following adjuvant chemotherapy [15,16]. In our study, patients with advanced stage breast cancer exhibited significant decrease in body weight (60.06 ± 11.16 to 58.69 ± 10.4, p<0.05), BSA (1.58 ± 0.16 to 1.57 ± 0.15, p<0.05), and BMI (25.66 ± 4.10 to 25.05 ± 4.12, p<0.05) following two cycles of adjuvant chemotherapy with doxorubicin and cyclophosphamide regimen. Thus, unlike the dominant weight gain observed in Western populations, patients in our study have a significant decrease in body weight, BSA and BMI.

There are several factors contributing to weight change following adjuvant chemotherapy, such as age and weight at diagnosis, menopausal status, chemotherapeutic regimen, receptor status, clinical stage and number of chemotherapy cycles. Other factors, such as lifestyle, educational level and economic status were also shown to affect weight gain [17]. We observed that patients age over 40 years were more likely to decrease in body weight compared to those aged less than 40 years. This study also shown that patient's body weight over 60 kg before chemotherapy may be associated with the greatest weight loss than patient's age less than 60 kg (Data not shown).

The menopausal status was previously reported to be a positive predictor for weight gain in women receiving adjuvant chemotherapy [18-20]. Although it was also reported that menopausal status did not affect body weight [21]. Our study does not analyse the correlation of menopausal status and hormonal receptor status to body weight. However, all subjects in this did not receive hormonal therapy because they newly planned to get chemotherapy first and also did not have ovarian ablation. Our study did not analyse correlation between different chemotherapy regimen and body weight change because all subject have the same chemotherapy regimen (doxorubixin and cyclophosphamide).

Previous studies in animal have demonstrated that doxorubicin correlates with neutropenia and thrombocytopenia [22,23]. Meta-analysis study also shown that doxorubicin and cyclophosphamide causing neutropenia and thrombocytopenia [24]. Our study found that there is influence of chemotherapy on hematological parameters. Hemoglobin, platelet and TLC levels decreased significantly after chemotherapy but no significant decrease in leukocyte and ANC counts.

Our study had several limitations, due to it's from a single centre and the relatively small sample size and we involve analyses only of two cycle of chemotherapy with doxorubicin and cyclophosphamide regimen. We did not assess additional factors which would potentially affect weight change, including energy intake, exercise, education and psychological status. Further multicentre, long-term and random case-control studies are required to further address these issues. However, this study was the first to report that adjuvant chemotherapy in advanced breast cancer may be associated with weight change in Indonesian breast cancer patients. The differences between Asian and Western populations may be attributed to racial genetic differences, a subject that requires further investigation.

Conclusion

Body weight, body mass index and body surface area is significantly decreased during chemotherapy in advanced breast cancer patients even when given dietary recommendations. Hemoglobin and including TLC level also decrease during chemotherapy. There is no significant decrease in leukocyte and ANC level after first and second cycles of chemotherapy. Appropriate weight management interventions with nutritional follow-up and physical activity programs are needed.

References

1. Winkels RM, Beijer S, Lieshout RV, Barneveld DV, Holfstede J, et al. (2014) Changes in body weight during various types of chemotherapy in breast cancer patients. e-SPEN Journal 9: e39-e44.
2. Sukel MP, van de Poll-Franse LV, Nieuwenhuijzen GA, Vreugdenhil G, Herings RM, et al. (2008) Abstract. Eur J Cancer 44.
3. Wang JS, Cai H, Wang CY, Zhang J, Zhang MX. (2014) Body weight changes in breast cancer patients following adjuvant chemotherapy and contributing factors. Mol Clin Oncol 2: 105-110.
4. van den Berg MM, Winkels RM, de Kruif JT, Van Laarhoven HW, Visser M, et al. (2017) Weight change during chemotherapy in breast cancer patients: a meta-analysis. BMC Cancer 17: 259.
5. Heideman WH, Russell NS, Gundy C, Rookus MA, Voskuil DW (2009) The frequency, magnitude and timing of post diagnosis body weight gain in Dutch breast cancer survivors. Eur J Cancer 45: 119126.
6. Tredan O, Bajard A, Meunier A, Roux P, Fiorletta I, et al (2010) Body weight change in women receiving adjuvant chemotherapy for breast cancer: a French prospective study. Clin Nutr 29: 187-191.
7. LaubySecretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, et al. (2016) Body Fatness and Cancer--Viewpoint of the IARC Working Group. N Engl J Med 375: 794-798.
8. Yung RL, Ligibel JA (2016) Obesity and Breast Cancer: Risk, Outcomes, and Future Considerations. Clin Adv Hematol Oncol 14: 790-97.
9. Kroenke CH, Chen WY, Rosner B, Holmes MD (2005) Weight, weight gain, and survival after breast cancer diagnosis. J Clin Oncol 23: 1370-1378.
10. TrenthamDietz A, Newcomb PA, Nichols HB, Hampton JM (2007) Breast cancer risk factors and second primary malignancies among women with breast cancer. Breast Cancer Res Treat 105: 195-207.
11. Saquib N, Flatt SW, Natarajan L, Thomson CA, Bardwell WA, et al (2007) Weight gain and recovery of pre-cancer weight after breast cancer treatments: evidence from the women's healthy eating and living (WHEL) study. Breast Cancer Res Treat 105: 177-186.
12. Irwin ML, McTiernan A, Baumgartner RN, Baumgartner KB, Bernstein L, et al (2005) Changes in body fat and weight after a breast cancer diagnosis: influence of demographic, prognostic, and lifestyle factors. J Clin Oncol 23: 774-782.
13. Freedman RJ, Aziz N, Albanes D, Hartman T, Danforth D, et al (2004) Weight and body composition changes during and after adjuvant chemotherapy in women with breast cancer. J Clin Endocrinol Metab 89: 2248-2253.
14. Lorincz AM, Sukumar S (2006) Molecular links between obesity and breast cancer. Endocr Relat Cancer 13: 279-292.
15. Demark-Wahnefried W, Peterson BL, Winer EP, Marks L, Aziz N, et al (2001) Changes in weight, body composition, and factors influencing energy balance among premenopausal breast cancer patients receiving adjuvant chemotherapy. J Clin Oncol 19: 23812389.
16. Goodwin PJ, Ennis M, Pritchard KI, McCready D, Koo J, et al (1999) Adjuvant treatment and onset of menopause predict weight gain after breast cancer diagnosis. J Clin Oncol 17: 120129.
17. Villarini A, Pasanisi P, Raimondi M, Gargano G, Bruno E, et al (2012) Preventing weight gain during adjuvant chemotherapy for breast cancer: a dietary intervention study. Breast Cancer Res Treat 135: 581-589.

18. Rock CL, Flatt SW, Newman V, Caan BJ, Haan MN, et al (1999) Factors associated with weight gain in women after diagnosis of breast cancer. Women's Healthy Eating and Living Study Group. J Am Diet Assoc 99: 1212-1221.
19. Shapiro CL, Recht A (2001) Side effects of adjuvant treatment of breast cancer. N Engl J Med 344: 19972008.
20. Basaran G, Turhal NS, Cabuk D, Yurt N, Yurtseven G, et al. (2011) Weight gain after adjuvant chemotherapy in patients with early breast cancer in Istanbul Turkey. Med Oncol 28: 409-415.
21. Lankester KJ, Phillips JE, Lawton PA (2002) Weight gain during adjuvant and neoadjuvant chemotherapy for breast cancer: an audit of 100 women receiving FEC or CMF chemotherapy. Clin Oncol (R Coll Radiol) 14: 64-67.
22. Gatti DM, Weber SN, Goodwin NC, Lammert F, Churchill GA (2018) Genetic Background Influences Susceptibility to Chemotherapy-Induced Hematotoxicity. Pharmacogenomics J 18: 319-330.
23. Fayyaz TB, Memon Z, Baig MT, UL Ain AN (2017) Extract of Olive (Olea Europaea L.) cures hematologic toxicosis induced by Doxorubicin. Fuuast J Biol 7: 75-79.
24. Rafiyath SM, Rasul M, Lee B, Wei G, Lamba G, et al. (2012) Comparison of safety and toxicity of liposomal doxorubicin vs. conventional anthracyclines: a meta-analysis. Exp Hematol Oncol 1: 10.