Serum Interleukin-17 level in Breast Cancer

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Original article

Serum interleukin-17 (IL-17) level in breast carcinoma before and after chemotherapy☆

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ABSTRACT

Objectives: Breast cancer is a cellular disease which occurs from breast tissue with manifestation that failing to control the cellular proliferation and mutation. The purpose of this study is to identify the IL-17 level in breast carcinoma before and after chemotherapy.
Methods: This research was a cross-sectional study with comparative analysis. Sampling was conducted using accidental sampling method. Interleukin-17 was analyzed using the Elisa method. Data were analyzed using paired *T*-test with an error tolerance of 0.05.
Results: The results showed significant differences before and after chemotherapy in breast cancer, with an increase in IL-17 levels of 46.36 pg/mL. Nonetheless, all the characteristics of good age, stage of cancer, and menopausal status, all experienced an increase in IL-17 levels after chemotherapy Patients with stage 2 cancer stages had the highest increase in IL-17 levels compared to the others, which was 62.09 pg/mL.
Conclusion: IL-17 is a potential predictive biomarker for breast cancer therapy.

Introduction

Breast carcinoma is cancer in women with the highest frequency in the world and one of the main cause of death in a developed country. Breast cancer is the second most prevalent cancer after lungs cancer.[1,2] Cancer patients should increase their antibody since some of the lymphocyte cells will secrete cytokine, such as interleukin.[3] Interleukin (IL)-17 is a cytokine which acts as an effective mediator in delaying the expression by increasing the chemokines production in several tissues. The previous study found that IL-17 has an essential function in pushing mediation of the proinflammatory response in which to regulating immune in cancer patients.[4]

Evidence shows that IL-17 is related with the tumour growth and angiogenesis, IL-17 expression in some tumour patients, such as cervical cancer, hepatocellular carcinoma, ovarium cancer, trachea, breast colon cancer, and CRC, was increasing. IL-17 is directing a significant effect on tumour initiation and development through an antitumor immune response. It means that the IL-7 activates Src/PI3K/Akt/nuclear factor κ B (NF κ B), MAPK, STAT3, and COX-2 ways. This line plays essential roles in tumorigenesis, angiogenesis, and metastatic.[5]

IL-17 roles in cancer start with the early step of tumorigenesis as the early tumour development with the increase of micro tumour.[6] There is strong evidence of the roles of IL-17 in the increase of tumour severity.[7] This is caused by the accumulation of IL-17 that secrete Foxp3+ in micro tumour deficiency with double proinflammation function and local cell-T regulation function.[8] Despite the evidence on the roles of IL-17 in cancer, there is a contraindication showing that IL-17, especially when added through immunization could increase anti-tumour response and causing the decrease in tumour size.[4]

Based on this evidence, it is important to understand about the interleukin-17 process. Moreover, due to the high prevalence of breast carcinoma cases, it is necessary to determine the roles of interleukin-17 to find the right intervention in early step as the prevention of breast carcinoma among women. This study will determine the interleukin-17 level of breast carcinoma before and after therapy.

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Method

This study was a cross-sectional study conducted in Ibnu Sina Hospital on 6 February to 23 March 2018. The population were all patients diagnosed with breast cancer during this study; the total sample was 20 women. The sample was selected using accidental sampling.

Interleukin-17 serum level was analyzed using ELISA method while the breast carcinoma status was determined using medical diagnosis and hepatology results and patients medical records. Wilcoxon test was applied to determine the difference of interleukin-17 serum before and after chemotherapy with the cutoff for significance was 0.05.

Results

Most of the respondents were aged ≥ 45 years old (13 women, 65%), the average age of respondents was 46.4 years old. A total of 13 women (65.0%) was menopause, and 7 of women was not menopause. Most of the respondents were high school graduate (17 women, 85%), and the rest of them were diploma and undergraduate. Most of the respondents were in stage two of cancer (11 women, 55%), and the rest of them were in stage three. Average respondent's height was 153.4 cm with an average weight of 40.5 kg before chemotherapy and 39.7 kg after chemotherapy. Highest chemotherapy frequency was < 3 times (Table 1).

The characteristics that showed significant differences before and after chemotherapy, with an increase in IL-17 levels of 46.36 pg/mL. Nonetheless, all the characteristics of good age, stage of cancer, and menopausal status, all experienced an increase in IL-17 levels after chemotherapy Patients with stage 2 cancer stages had the highest increase in IL-17 levels compared to the others, which was 62.09 pg/mL (Table 2).

Table 1
Characteristics of respondents ($n = 20$).

Characteristics	Total (n)	Percentage (%)
Age		
<45 y.o	7	35.0
≥45 y.o	13	65.0
Latest education		
≤High school	17	85.0
>High school	3	15.0
Menopause status		
Postmenopause	13	65.0
Premenopause	7	35.0
Stages of cancer		
Stage II	11	55.0
Stage III	9	45.0
Height		
≤155 cm	16	80.0
>155 cm	4	20.0
Weight before chemotherapy		
<40 kg	10	50.0
≥40 kg	10	50.0
Weight after chemotherapy		
<40 kg	10	50.0
≥40 kg	10	50.0
History of chemotherapy		
<3 times	12	60.0
≥3 times	8	40.0

Discussion

Our finding shows significant differences before and after chemotherapy with an increase in IL-17 levels of 46.36 pg/mL. Nonetheless, all the characteristics of good age, stage of cancer, and menopausal status, all experienced an increase in IL-17 levels after chemotherapy. Patients with stage 2 cancer stages had the highest increase in IL-17 levels compared to the others, which was 62.09 pg/mL.

The increase in IL-17 level was linear with the severity of cancer. Based on the research, stage three of the carcinoma has a higher IL-17 level before chemotherapy and increase during the chemotherapy.[9]

According to the cancer duration characteristics, there was a significant association of IL-17 serum with breast carcinoma. Patients who were experiencing cancer will stimulate Th17 cell from T-cell in human, then modify β-cell (TGF-β) which increase with another cytokine (IL-21, IL-6, and IL-23) and induct the transcription factor (ROR-gamma) which directed to the development of T-cell to cells that produce IL-17 (17).[10] Therefore, the longer a person has cancer, the IL-17 level will also increase.

It is still unclear why IL-17 level increase after chemotherapy, this study found that IL-17 level increase along with the increase of cancer severity, including breast cancer. It might happen due to the roles of IL-17 in the pathogenesis of breast cancer. In this study, it was based on the assumption that IL-17 serum level increased along with the increase of cancer severity and the emergence of some additional complaints among breast cancer patients. Cancer is a condition in which the cells development is abnormal

Table 2
Relationship of Interleukin-17 (IL-17) with Characteristics of Respondents.

Characteristics	Interleukin 17				Mean difference	*p-Value*
	Pre		Post			
	n	Mean ± SD (pg/mL)	n	Mean ± SD (pg/mL)		
Age						
≤45 y.o	7	225.31 ± 44.89	7	255.93 ± 143.46	30.62	0.059
>45 y.o	13	179.82 ± 44.56	13	223.63 ± 64.49	43.81	0.063
Cancer duration						
≤1.5 years	5	194.96 ± 67.16	5	242.72 ± 163.9	47.76	0.525
>1.5 years	15	185.98 ± 44.3	15	232.34 ± 70.8	46.36	0.031
Stages of cancer						
Stage II	11	174.81 ± 50.05	11	236.90 ± 108.1	62.09	0.076
Stage III	9	204.62 ± 45.3	9	232.54 ± 87.3	27.92	0.357
Menopause status						
Menopause	13	173.37 ± 43.26	13	213.16 ± 49.4	39.79	0.316
Was not menopause	7	215.81 ± 50.4	7	275.37 ± 147.8	59.56	0.780

and uncontrollable. Killing and stopping cancer development could be done with chemotherapy. Chemotherapy might have several effects on the respondents, such as nausea, vomit, hair loss, and bone pain.

Women with breast carcinoma are experiencing significant failure in body immune; such as serum IL-17 concentration was significantly associated with IL-17 in cancer tissue. This cytokine level was higher among breast cancer patients who have been metastasized. IL-17 concentration in tissue was associated with tumour size. IL-17 level was increasing in the tumour size ≥ 50 mm.[11]

IL-17 could increase angiogenesis through upregulation of some growth factors, such as TGF-β, fibroblast growth factor β, hepatocyte growth factor, and endothelium vascular factor (VEGF), important for neovascularisation.[12] IL-17 could also increase the proinflammation factor such as anti-microbial peptide (AMPs), an angiogenic factor, and chemokines such as CCL20 which pulled both Th17 cell and dendritic cell (DCs). A study by Chung et al. shows that IL-7 indirectly increase the M2 macrophage differentiation through COX-2 line/PGE2 in the cancer cell so that IL-7 plays a role in regulating the micro tumour environment.[13]

Based on our study and other related concepts, we assumed that the increase of serum IL-7 on breast carcinoma is getting higher together with the increase of cancer cell growth. Our finding is linear with the working mechanism of serum IL-17, which is stimulating the cancer development by activating and inducting neovascularisation tumour and immunosuppression.

Conclusion

IL-17 is a potential predictive biomarker in breast cancer therapy.

Conflict of interest

The authors declare no conflict of interest.

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