Yan-Wisnu-Prajoko-ARTIKEL6

by Yan Wisnu Prajoko

Submission date: 29-Jan-2024 08:46AM (UTC+0700)
Submission ID: 2280605318
File name: eifera_Extract_on_CPK_and_Quality_of_Life_-_farah_febriyanti.pdf (365.71K)
Word count: 2972
Character count: 16643

Journal of Medicinal and Chemical Sciences 6 (2023) 2750-2755

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Original Article

The Effect of Moringa Oleifera Extract on CPK and Quality of Life of Breast Cancer Hpatinnts Reseiving Aromatase Inhibitor Therapy

Yan Wisnu Prajoko[1]*, Sugeng Pramono[2], Agung Hartanto[2], Mada Aji Prakoso[2]

[1]*Staff of the Sub Division of Surgical Oncology at Universitas Diponegoro, Semarang, Indonesia*
[2]*General Surgery Resident at Universitas Diponegoro, Semarang, Indonesia*

ARTICLE INFO

Article history

Receive: 2023-04-31
Received in revised: 2023-06-23
Accepted: 2023-07-02
Manuscript ID: JMCS-2305-2087
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Fatima Ramezani
Editor who approved publication:
Dr. Ali Delpisheh

DOI:10.26655/JMCHEMSCI.2023.11.19

KEYWORDS

Breast cancer
Aromatase inhibitor
AIMSS
CPK
FACT-B

ABSTRACT

Aromatase inhibitors (AI) are commonly used adjuvant therapy drugs for women with hormone receptor-positive postmenopausal breast cancer. Frequently AI associated side effects include severe joint and muscle pain. Aromatase Inhibitor - Associated Musculoskeletal Syndrome (AIMSS) is a condition that primarily affects the hands, wrists, and knees. This study aimed to determine the efficacy of Moringa oleifera extract as an adjuvant when taken with AI to postmenopausal breast cancer patients with ER (+), PR (+), and observed the CPK levels as inflammation indicators. The Functional Assessment of Cancer Therapy-Breast (FACT-B) can assess subjects' emotional, physical, functional well-being, social, and also the breast cancer subscale. The research sample consisted of 40 postmenopausal cancer patients with ER (+) and PR (+) immunohistochemistry and as outpatients at the Kasuari facility, Dr. Kariadi Semarang, who experienced pain due to the administration of aromatase inhibitors. The results of the changes in CPK and FACT-B scores in the group that received additional therapy with Moringa oleifera extract were obtained in this study. The treatment group showed CPK level of post-test lower than pre-test (105.30 ± 50.19 vs. 88.10 ± 48.24, p <0,001). In addition, treatment group showed lower FACT-B score than control group (83.45 ± 5.11 vs. 75.25 ± 4.05, p<0,001). Moringa oleifera extract has a strong anti-inflammatory effect especially for patient with post-menopause breast cancer who received ER (+), PR (+), and aromatase inhibitor treatment. Its anti-inflammatory properties will upgrade breast cancer patient's quality of life, treatment adherence, long period of breast cancer therapy and outcomes.

GRAPHICAL ABSTRACT

* Corresponding author: Yan Wisnu Prajoko
✉ E-mail: yanprajoko7519@gmail.com

Introduction

Cancer is an uncontrolled cell proliferation that can penetrate and spread throughout the human body [1].

The prevalence and number of fatalities from cancer are rising quickly worldwide. There is a 3.1% increase in the incidence of breast cancer every year. Around 2 million new cases of breast cancer were identified in 2018, with 600,000 dying from the disease globally. Breast cancer death accounts for 6.6% of all cancer-related fatalities globally. It becomes major cause of mortality case in female [2].

Breast cancer accounted for 58,256 instances, or 16.7% of all cancer cases reported in Indonesia in 2018, according to World Health Organization (WHO) data [3].

Breast cancer treatment modalities include surgery, radiation therapy, cytotoxic drugs, immunotherapy, and hormone therapy [3, 4]. Aromatase inhibitor is used in hormone treatment for postmenopausal women who tested positive for hormone receptors. Significant joint and muscular problems are frequently linked to the side effects of AI, affecting the hands, wrists, and knees, also called Aromatase Inhibitor-Associated Musculoskeletal Syndrome (AIMSS). Stopping AI medication would lead to the cessation of these symptoms, but as soon as it is started again, these symptoms will reappear. AIMSS negatively impacts the life quality of many patients in terms of health, impairs adherence to AI breast cancer treatment, increases blood inflammation, and raises creatine phosphokinase levels (CPK). This study focuses on developing novel chemicals derived from medicinal plants that act as analgesics and anti-inflammatory agents. In most cases, the use of medicinal plants is based solely on tradition, without sufficient scientific evidence. Moreover, derived medicinal plants are known to treat joint pain effectively. One is Moringa oleifera, a tropical plant widely used in traditional medicine, including anti-inflammatory drugs for treating pain [5, 6]. Multiple researches for Moringa oleifera gave information that 100 grams of Moringa oleifera contains twelve times the vitamin C in oranges, ten times the vitamin A in carrots, nine times the protein in yogurt, fifteen times the potassium in bananas, seventeen times the milk, ten times the calcium, and twenty-five times the iron of 100 grams of beef and spinach. In both human and animal metabolic processes, this nutritional content is crucial. Monosaccharide-containing, rhamnose-containing, glucosinolate, and isothiocyanate chemicals are abundant in the Moringa oleifera plant. Cyclooxygenase 2 (COX2) produces isothiocyanate, which reduces inflammation brought on by nitric oxide synthase (i-NOS).

This study aimed to investigate the impact of Moringa oleifera extract as a supplementary treatment alongside aromatase inhibitors on postmenopausal breast cancer patients with ER (+) and PR (+), specifically focusing on the variations in CPK levels, an indicator of inflammation.

Furthermore, the study measured the subjects' well-being using the FACT-B scale, which assessed their physical, social, emotional, functional, and breast cancer subscale well-being. The research findings are expected to promote the use of Moringa oleifera as a beneficial addition to aromatase inhibitor therapy for ER (+) and PR (+) postmenopausal breast cancer patients.

Materials and Methods

This study is experimental research with two groups' parallel pre-test and a post-test control group design. Breast cancer patients who met the research criteria and received treatment at RSUP Dr. Kariadi Semarang during the study period made up the research sample.

As soon as the Institutional review board permission is given, research and data collection will begin until the minimum number of samples is reached. The Biochemistry Laboratory of the Sido Muncul Ungaran factory produced the Moringa oleifera extract. Patients with breast cancer were treated at Dr. Kariadi's Kasuari Installation. The Clinical Pathology Laboratory, headed by Dr. Kariadi, conducts the laboratory examination process.

Breast cancer patients who had undergone menopause, tested positive for ER and PR

immunohistochemistry, had undergone aromatase inhibitor therapy (Anastrozole, 1 mg) and had consented to participate in the study met the inclusion criteria while emergency cases needing surgery and unwillingness to participate in the study were exclusion factors in this study. Dropout criteria in this study were being unable to follow up for 30 days after the study began and obtaining therapy in addition to the research method.

These calculations show that 44 research subjects are required since each group requires 22 postmenopausal breast cancer patients with ER (+) and PR (+). The stages in this research are patients with inclusion and exclusion criteria and already gave permission to join as research subjects. These subjects were randomized and divided into 2 groups. 1 group for intervention and the other for control group. The therapy was given according to the research group for 30 days.

A 10 ml venous blood sample was taken from each patient after 12-14 h fasting at the baseline and at the end of the study. Serum was separated by centrifugation at 3000 rpm and frozen at -80º C until the end of the study. Serum levels of Creatine phosphokinase (CPK was accomplished by the ELISA method at baseline and after 30 days of treatment. Subjects were also assessed using the FACT-B to measure emotional, physical, social, functional well-being, and also the breast cancer subscale.

After data collection, data cleaning, coding, and also tabulation is carried out. The data analysis is done through descriptive analysis and hypothesis testing. CPK levels and FACT-B scores are presented as the mean and +/- SD if the data is normally distributed, or the minimum, the median, and the maximum ranges if the data distribution is abnormal are presented by descriptive analysis.

In this research, there were more than 50 samples, the Kolmogorov-Smirnov test was done for determining whether the data were normal. If the research data were normally distributed, the paired t-test was employed to test this hypothesis, or else Wilcoxon test was used for non-normally distributed data.

Differences in CPK levels and FACT-B assessment between the treatment and control groups will be tested using an unpaired t-test for normal data distribution and the Mann-Whitney test for abnormal data distribution.

The difference is considered significant for $p<0.05$ with 95% confidence interval, and then data analysis was performed with SPSS software Ver. 26.0 for Windows.

Results and Discussion

Aromatase inhibitors (AI) are frequently used as adjuvant therapy for postmenopausal breast cancer patients with positive hormone receptor malignancy. The numbers of aromatase inhibitor side effects include arthralgia, fractures, and a reduction in bone mineral density (BMD). Postmenopausal onset and natural aging may contribute to joint issues. Twenty to seventy percent of postmenopausal women who use an aromatase inhibitor will experience joint pain [7-9].

Our study used experimental methodologies and a parallel pre- and post-test control group design with two groups. Forty postmenopausal cancer patients with ER (+) and PR (+) immunohistochemistry treated as outpatients at the Kasuari facility by Dr. Kariadi Semarang and with discomfort complaints after receiving aromatase inhibitors made up the research sample.

Before conducting the study, the sample complied with the inclusion and exclusion criteria and provided written consent. The mean age of all subjects is 54.88 ± 9.23 y.o and senior high school (32.5%) is the most populated education (Table 1).

Both groups showed no significant difference on mean age and education ($p>0.005$, Table 2).

The management of AI-induced arthralgia puts a greater emphasis on counselling and education. Therapy using this regimen is administered for 5 years. Since arthralgia side effects can start to manifest as early as 2 months after therapy and last as long as 6 months after that, patients are advised to undergo follow-up every 2 or 6 months.

Table 1: Characteristics of subject

Variable	F	%	Mean ± SD	Median (min-max)
Group				
Treatment(P1)	20	50.0		
Control (K)	20	50.0		
Age			54.88 ± 9.23	53.5 (38 – 18)
Education				
No school	1	2.5		
Primary school	10	25.0		
Junior high school	6	15.0		
Senior high school	13	32.5		
Graduate	10	25.0		

Table 2: Characteristics of data by treatment group and placebo

Variable	Group		P-value
	Control (20)	Treatment (20)	
Age	53.85 ± 9.60	55.90 ± 8.97	0.490§
Education			
No school	0 (0%)	1 (100%)	0.300‡
Primary school	3 (30%)	7 (70%)	
Junior high school	4 (66.7%)	2 (33.3%)	
Senior high school	8 (61.5%)	5 (38.5%)	
Graduate	5 (50%)	5 (50%)	

Table 3: Statistic Test of CPK levels

CPK	Group		P-value
	Treatment (20)	Control (20)	
Pretest	105.30 ± 50.19	100.10 ± 38.67	0.808‡
Post-test	88.10 ± 48.24	102.60 ± 39.40	0.091‡
P	<0.001†*	0.015†*	
Δ	-17.20 ± 16.60	2.50 ± 24.19	<0.001‡*

**Description*: *Significant (p < 0.05); ‡ Mann Whitney; and † Wilcoxon

Table 4: Statistic test of FACT-B

FACT-B	Group		P-value
	Treatment (20)	Control (20)	
Pretest	69.85 ± 3.27	73.90 ± 4.68	0.012‡*
Post-test	83.45 ± 5.11	75.25 ± 4.05	<0.001§*
p	<0.001†*	0.009¶*	
Δ	13.60 ± 4.48	1.35 ± 2.06	<0.001‡*

**Description: *Significant (p < 0.05); § Independent t; ‡ Mann Whitney; ¶ Paired t; and † Wilcoxon*

In addition, patients can strengthen their muscles by adopting healthy lifestyle changes, including decreasing weight and engaging in regular exercise. To relieve pain, acetaminophen/ibuprofen or other NSAIDs may be used. Opioids or tricyclic antidepressants may assist people with higher VAS scales to feel less pain [10].

The pain manifestation is one of the adverse effects frequently reported for using aromatase inhibitor medication (AIA-Aromatase Inhibitor-associated Arthralgia). Aromatase inhibitors are believed to reduce estrogen production, and this drop in estrogen will result in lower pain thresholds. As a result, during regular activities, the pain sensation may happen independently [11].

Due to the adverse effects of AI medication, Moringa oleifera extract with sodium diclofenac can reduce inflammation and subsequently pro-inflammatory cytokines. Serum CPK levels can be used to measure decreased pro-inflammatory cytokine levels [12].

Data from Table 3 showed paired difference test in the treatment and control groups is significant. In the unpaired difference test, the CPK pre and post-CPK were not significant, while the difference in CPK was significant. Creatine phosphokinase (CPK) is one of the enzymes that can catalyse the creatine and adenosine triphosphate (ATP) to become phosphocreatine and adenosie diphosphate (ADP). This enzyme can be found in muscle tissue. The study by Leverenz *et al.* found that the rheumatological cause of most cases of elevated CPK was idiopathic inflammatory myopathies (IIMS). IIMS is a group of diseases who manifested as abnormal inflammation in muscle tissue that constituted a large proportion of musculoskeletal problems. The additional Moringa oleifera extract has proven to reduce blood levels of CPK in patients using Aromatase Inhibitors.

Data form Table 4 is significant paired difference tests on Group Treatment and control. The FACT-B pre, FACT-B post, and FACT-B differences were significant in the unpaired difference test. Subjects were assessed with FACT-B for both before and after administration of Moringa oleifera extract. FACT-B will assess emotional, physical, functional well-being, social, and the breast cancer subscale. In the unpaired difference test, the FACT-B pre, FACT-B post, and FACT-B differences were significant, indicating an upgrade for subject's quality of life in the treatment group.

Moringa leaf extract shows a solid anti-inflammatory potential in patients with postmenopausal breast cancer receiving ER (+), PR (+), and aromatase inhibitor therapy. Its anti-inflammatory properties will enhance patients' quality of life, increase medication adherence, and, over time, significantly aid breast cancer treatments and outcomes. The author is aware that several gaps in this research should be filled for it to be finished. This study could be expanded to include more people and cancer patients where feasible.

Conclusion

It has been demonstrated that using Moringa oleifera extract as an additional therapy can lower serum CPK levels. By preventing prostaglandin synthesis, cyclooxygenase-2 (COX-2) activity, and the nuclear translocation of anti-inflammatory nuclear transcription factor (NF) factors, Moringa oleifera extract reduces inflammation. Pro-inflammatory cytokines, which prevent inflammation, are decreased by -B. It was discovered that an upgrade in subject's quality of life for Group Treatment in the FACT-B for both before and after administration of Moringa oleifera extract.

Acknowledgements

The authors would like to thank their institution, doctor, nurse, and staff who have taken care the subjects during treatment. Furthermore, they would like to thank their subjects who voluntary contributed to the study.

Disclosure Statement

No potential conflict of interest was reported by the authors.

Funding

This study was obtained an ethical approval from Institutional Review Board of RSUP Dr. Kariadi Semarang No. 1126/EC/KEPK-RSDK/2022.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Orcid

Yan Wisnu Prajoko
https://orcid.org/0000-0003-2659-9923

References

[1]. Lim W.F., Mohamad Yusof M.I., Teh L.K., Salleh M.Z., Significant decreased expressions of CaN, VEGF, SLC39A6 and SFRP1 in MDA-MB-231

xenograft breast tumor mice treated with Moringa oleifera leaves and seed residue (MOLSr) extracts, *Nutrients*., 2020, **12**:2993 [Crossref], [Google Scholar], [Publisher]
[2]. Harbeck N., Penault-Llorca F., Cortes J., Gnant M., Houssami N., Poortmans P., Ruddy K., Tsang J., Cardoso F., *Breast Cancer Nat Rev Dis Primers.*, 2019, **5**:66 [Crossref], [Google Scholar], [Publisher]
[3]. International Agency for Research on Cancer WHO, 2018 [Publisher]
[4]. Mustafa Y.F., Chemotherapeutic applications of folate prodrugs: A review, *NeuroQuantology*., 2021, **19**:99 [Crossref], [Google Scholar], [Publisher]
[5]. Fakri Mustafa Y., Riyadh Khalil R., Tareq Mohammed E., Bashir M.K., Khudhayer Oglah M., Effects of structural manipulation on the bioactivity of some coumarin-based products, *Archives of Razi Institute*., 2021, **76**:1297 [Crossref], [Google Scholar], [Publisher]
[6]. Mohammed E.T., Khalil R.R., Mustafa Y.F., Phytochemical analysis and antimicrobial evaluation of quince seeds' extracts, *Journal of Medical and Chemical Sciences*., 2022, **5**:968 [Crossref], [Google Scholar], [Publisher]
[7]. Mustafa Y.F., Abdulaziz N.T., Hymecromone and its products as cytotoxic candidates for brain cancer: A brief review, *NeuroQuantology*., 2021, **19**:175 [Crossref], [Google Scholar], [Publisher]
[8]. Seagal Z.M., opographical and pathotopographical medical Atlas of the chest, abdomen, lumbar region, and retroperitoneal space, *John Wiley & Sons*., 2018 [Crossref], [Google Scholar], [Publisher]
[9]. Sharif S., Moran A., Huson S.M., Iddenden R., Shenton A., Howard E., Evans D.G.R., Women with neurofibromatosis 1 are at a moderately increased risk of developing breast cancer and should be considered for early screening, *Journal of medical genetics*., 2007, **44**:481 [Crossref], [Google Scholar], [Publisher]
[10]. King M.C., Marks J.H., Mandell J.B., Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2, *Science.*, 2003, **302**:643 [Crossref], [Google Scholar], [Publisher]
[11]. O'Sullivan C.C., Loprinzi C.L., Haddad T.C., Updates in the evaluation and management of breast cancer, *In Mayo Clinic Proceedings, Elsevier*., **93**:794, 2018 [Crossref], [Google Scholar], [Publisher]
[12]. Leverenz D., Zaha O., Crofford L.J., Chung C.P., Causes of creatine kinase levels greater than 1000 IU/L in patients referred to rheumatology, *Clinical rheumatology.*, 2016, **35**:1541 [Crossref], [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE
Yan Wisnu Prajoko*, Sugeng Pramono, Agung Hartanto, Mada Aji Prakoso.The Effect of Moringa Oleifera Extract on CPK and Quality of Life of Breast Cancer hpatinnts reseiving Aromatase Inhibitor Therapy. *J. Med. Chem. Sci.*, 2023, 6(11) 2750-2755.
DOI: https://doi.org/10.26655/JMCHEMSCI.2023.11.19
URL: https://www.jmchemsci.com/article_175379.html

Yan-Wisnu-Prajoko-ARTIKEL6

ORIGINALITY REPORT

8%	5%	5%	2%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Julia Hamer, Rachel McDonald, Liying Zhang, Sunil Verma et al. "Quality of life (QOL) and symptom burden (SB) in patients with breast cancer", Supportive Care in Cancer, 2016 Publication	1%
2	Mustafa Moaied Rabeaa, Muna Ismael Khalaf. "Modification and Characterization of Some New Levofloxacin Heterocyclic Derivatives as COX-2 Enzyme Inhibitors and Evaluate Their Efficacy Pharmacokinetics by Molecular Docking and the Swiss ADME Studies", Baghdad Science Journal, 2023 Publication	1%
3	dmsjournal.biomedcentral.com Internet Source	1%
4	Submitted to Universitas Indonesia Student Paper	1%
5	Fatemeh Pourteymour Fard Tabrizi, Mahdieh Abbasalizad Farhangi, Maryam Vaezi, Salar Hemmati. "The Effects of Thylakoid-Rich Spinach Extract Combined with the Calorie-	1%

	Restricted Diet on Cardiometabolic Risk Factors in Obese Women with Polycystic Ovary Syndrome: A Randomized Controlled Clinical Trial", Research Square, 2020 Publication	
6	theediblegardeninggal.com Internet Source	1 %
7	Madanikia, Sara Aileen, Amanda Bergner, Xiaobu Ye, and Jaishri O'Neill Blakeley. "Increased risk of breast cancer in women with NF1", American Journal of Medical Genetics Part A, 2012. Publication	<1 %
8	ijbs-udayana.org Internet Source	<1 %
9	ijessr.com Internet Source	<1 %
10	www.orthopaper.com Internet Source	<1 %
11	ejournal3.undip.ac.id Internet Source	<1 %
12	ejournal.almaata.ac.id Internet Source	<1 %
13	e-journal.unair.ac.id Internet Source	<1 %
	ojs.unpkediri.ac.id	

14	Internet Source	<1%
15	www.helsedirektoratet.no Internet Source	<1%

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	On		

Yan-Wisnu-Prajoko-ARTIKEL6

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6