THE EFFECT OF EMOTIONAL QUALITY MANAGEMENT ON CORTISOL, TNF- r, AND IL-2 IN WOMEN WITH BREAST CANCER

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ABSTRAK

Wanita yang didiagnosis kanker payudara sering mengalami gangguan emosi dan psikososial. Distres ini dapat mempengaruhi sistem imun, kemungkinan penurunan kemampuan individu yang terkena kanker payudara untuk melawan penyakit dan penyebaran metastase. Emotional Quality Management (EQM) merupakan strategi yang memfokuskan peningkatan kematangan emosi. Kematangan emosi akan mengarahkan persepsi yang positif pada pasien dengan kanker payudara. Tujuan penelitian ini adalah untuk menjelaskan pengaruh pelatihan emotional quality management terhadap respons imunitas yang diukur melalui kortisol, TNF-r, dan IL-2 pada pasien kanker payudara. Dua puluh delapan wanita dengan kanker payudara yang menjalani kemoterapi di unit rawat jalan rumah sakit Soetomo yang terseleksi dibagi menjadi dua kelompok. Kelompok pertama diberikan pelatihan EQM selama 4 kali dan kelompok kedua sebagai control. Sampel darah perifes diambil untuk mengukur respons ketahanan tubuh: kortisol, TNF-r, dan IL-2. Hasil yang diperoleh setiap kelompok dianalisis dengan Uji T. Hasil penelitian ini membuktikan bahwa pelatihan EQM pada pasien kanker payudara secara signifikan menurunkan kortisol. Tidak ada perbedaan kadar TNF-r, IL-2 pada kelompok Control maupun kelompok Treatment. Sebagai kesimpulan, Emotional Quality Management memperbaiki respons ketahanan tubuh dengan menurunkan kadar kortisol, yang diikuti dengan kecenderungan peningkatan kadar TNF-r, IL-2. Kedua sitokin ini merupakan indikator perbaikan imunitas seluler yang sangat diperlukan bagi ketahanan tubuh pasien terhadap sel kanker payudara.(FMI 2013;49:1-7)

Kata Kunci: EQM, Respons Imun

ABSTRACT

Women with breast cancer are often diagnosed of having emotional and psychosocial problems. This distress can influence immune system, and may be decreasing individual's ability to fight the disease and metastasis. Emotional Quality Management (EQM) model is strategy with a focus to increase emotional maturity. Emotional maturity will lead to positive perception of women with breast cancer. The objective of this study was to find the effect of EQM training on immunity responses that were measured with cortisol, tumor necrosing factor alpha (TNF-r), interleukin-2 (IL-2) and interferon gamma in women with breast cancers. Twenty-eight women with breast cancer undergoing chemotherapy in Dr Soetomo hospital outpatient clinic were selected and divided into two groups. First group was given with EQM training four times and the second group served as control. Peripheral blood sample was used to measure immune responses: cortisol, TNF-r and IL-2. Results obtained from each group were analyzed using analysis of variance with T test. This study demonstrated that EQM training for women with breast cancer had significantly lowered cortisol level. No differences between the groups were seen for TNF-r and IL-2 levels. In conclusion, Emotional Quality Management improved perception of stress modulate the activity of the HPA axis, resulting in decreased cortisol levels, followed by a trend of increased TNF-r, and IL-2. These cytokines are indicators of improved cellular immunity that is necessary for the patient's body resistance against breast cancer cells. (FMI 2013;49:1-7)

Keywords: Emotional Quality Management, cortisol, TNF-r, IL-2.

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INTRODUCTION

Women who are diagnosed with breast cancer often experience emotional disturbances, especially of fear and loss of hope cured resulting in death (Luecken & Compas 2002). Emotional distress in cancer patients also have a devastating effect on the adjustment of children and families (Watson et al 2006), a higher probability of death over a period of 15 months, the lack of NK cell function (Levy et al 1990), the activity of NK cells is lower, decreased NK cell response against recombinant IFN-γ, and decreased lymphoproliferative response to mitogen (Andersen et al 1998). Previous research suggests that psychosocial interventions improve survival (Eysenck & Grossarth-Maticek 1991), a decrease in plasma cortisol and an increase in

circulating lymphocytes (Schedlowski et al 1994). Emotion management programs improve relations professionals and personnel (Bar-On 2006), higher job performance (Fariselli et al 2008), has a positive effect on quality of life and well-being in patients with type 2 diabetes (Yalcinet al 2008), and improve the quality of life of cancer patients (Coleet al2007). Emotional Quality Management (EQM) is a way to manage the emotions that attention to quality improvement stages of emotion that effectively lowers job stress of nurses (Tannar 2006). So far EQM has never been used and have not been able to explain the immunity improvement of breast cancer patients. This study wants to prove the effect of training on the quality management of emotional responses endurance represented by the levels of cortisol, TNF-α, IL-2 in breast cancer patients at the Oncology Outpatient Installation One-Stop Poly (POSA) Hospital Dr. Soetomo.

MATERIALS AND METHODS

This research is a quasi experimental design with a non-randomized pre-test-post-test control group. Subjects were 28 patients with breast cancer who are undergoing chemotherapy at the One-Stop Poly Oncology (POSA) General Hospital Dr. Soetomo. The subjects chosen convenience sampling, the inclusion criteria stage II-III, has never been operating, no wound infections and has not been getting EQM. Before conducting the study, researchers conducted: 1) a preliminary study to get an idea of the condition of the subjects in the population and ask the patient 's willingness to engage in research to fill out and sign a consent form. Initial data collection is done one week before the patients received chemotherapy, and the second data collection carried out two weeks after the patients undergoing chemotherapy. Giving EQM held twice before chemotherapy and twice after chemotherapy.

Cortisol measurement using FPIA (Fluorescence Polarization Immunoassay) using reagents Abbott AxSYM instrument. Morning cortisol standard range is 5-25 mg/dl and measurement of IL-2, and TNF-α ELISA method with immunofluorescence method. In the examination of the principle of cytokines, antigen antibody obtained by attaching a solid object, added material to be examined antigen and enzyme-labeled antibody (conjugate). The final step is adding a chromogenic substrate that causes discoloration due to reacting with the enzyme. The color changes according to the amount of enzyme attached and is also in line with the antigen levels checked. For examination of TNF-α, Reagent kits used for checking HS Human TNF Alpha is a product R & D Systems, Minneopolis, USA, Cat HSTAOOD, Lot : 272 881. Standard range is 0.5-32 pg/mL and a detection limit 0.106 pg/mL. For examination of IL-2, reagent kits used for checking HS Human IL-2 is the product Bender MedSystems, Vienna, Austria Cat BMS221HS, Lot : 53,944,010. Standard range is 0.94-60.00 pg/mL, the limit of detection 0:40 pg/mL. Data changes in immunologic response (cortisol, TNF-α, IL-2) is described by the mean and standard deviation for normally distributed and the data were analyzed with T test at 95% confidence level.

RESULTS

Based on the characteristics of the data showed that the proportion of education, cancer stage, and the source of financing the treatment of patients with breast cancer between the control group and the treatment group was relatively similar, ie have a low level of education (elementary/junior) (60%), aged 35-56 years, and experienced stage IIIb breast cancer (64%) (Table 1). In terms of understanding the emotions, on average they only know that emotion as temperamental or emotional disposition.

Table 1. Description of education, cancer stage and treatment of the source of financing of breast cancer patients.

Education	Control Group		Treatment Group	
	n	%	n	%
SD	6	42.9%	6	42.9%
SLTP	2	14.3%	4	28.6%
SLTA	4	28.6%	3	21.4%
Sarjana	2	14.3%	1	7.1 %
Jumlah	14	100%	14	100%
Stages	Control Group		Treatment Group	
	n	%	n	%
IIa	2	14.3%	1	7.1 %
IIb	1	7.1 %	2	14.3%
IIIa	2	14.3%	2	14.3%
IIIb	9	64.3%	9	64.3%
Total	14	100%	14	100%

Table 2. Means and standard deviations of variables changes in levels of cortisol, TNF-α, IL-2 before and after administration of EQM

Variables	KLP	N	Before EQM		After EQM	
			Mean	SD	Mean	SD
Cortisol	Control	14	11.879	5.8746	14.4500	5.69706
	Treatment	14	15.257	7.2416	12.9357	3.85120
TNF	Control	14	2.52429	0.682767	2.50307	0.793681
	Treatment	14	3.47086	1.315753	3.90093	4.000623
IL2	Control	14	1.47857	2.368355	1.26929	2.414764
	Treatment	14	0.69643	0.441651	0.61857	0.540582

The condition shows the average change in cortisol increased 2.5714 ± 4.48217 in the control group and the mean stress decreases -2.3214 ± 6.98572 in the treatment group. This showed increased stress responses in the control group and decreased in patients receiving EQM. The mean TNF-α -0.0212 ± 1.04397 decreased in the control group and increased by 0.4301 ± 4.28501 in the treatment group. Average IL-2 decreased -0.2093 ± 0.58609 in the control group and dropped -0.0779 ± 0.71783 in the treatment group (Table 2).Independent Samples Test results of the analysis of the variables change cortisol levels showed no difference (p = 0.036) were evident among patients who receive training EQM with controls. This means that training EQM lower cortisol levels in patients with breast cancer. While the levels of TNF-α (p = 0705) and IL-2 (p = 0.600) showed no difference between the treatment and control groups (Table 8). This means EQM training in breast cancer patients did not increase the levels of TNF-α. IL-2.

Table 3. Independent Sample Test Results of the analysis of the variable changes in levels of cortisol, TNF-α, and IL-2 between treatment groups

Variables	T value	Sig. (2-tailed)
Cortisol Change	2.206	0.036
TNF Change	-0.383	0.705
IL2 Change	-0.531	0.600

DISCUSSION

EQM and Cortisol

Emotional Quality Management training is a form of experiential learning that refers to the use of experience to help a person adjust to emotional problems, cope with changes in life, creating affective changes, is also spurring the growth and development of the personality (Johnson & Johnson 2000) and creating interactions that are therapeutic (Berry & Hynes 1994). At EQM training with the help of a facilitator, assisted breast cancer patients expressing feelings or emotions, recognize the emotions associated with either disease or other problems associated with the treatment of breast cancer. Patients are also encouraged to explore the feelings and the usual response they appear in the face of disease, validating emotions that arise, as well as the truth about the motives underlying thoughts, feelings or behaviors related illness. Patients were also asked to compare and contrast themselves against the usual response generated by mismatch repair -related emotions or behavior of breast cancer is less precise, with a variety of alternative approaches to the problem. Patients were asked to practice what has been given during the training so that at the end of the training EQM breast cancer patients are able to recognize and be aware of the emotions of self and others, able to motivate yourself and optimism, as well as able to establish interpersonal relationships with patients and or others.

Emotions affect the way responded to certain situations (Martin 2006, 2008). Emotions that accompany a diagnosis of breast cancer, among others, reject or shock, anger, stress and depression, guilt and fear, accept, adjustment, against and hope, fear of side effects, and withstand the test results. Emotions that accompany the treatment of breast cancer, among others, fear of recurrence, freshly wounded, fear of pain and fear of death (Stephan 2009), puts the woman on the emotional distress that can affect the psychology and behavior and immune function (Luecken & Compas 2002).

If the individual is not able to manage and control their emotions well, then the individual can respond in a negative situation that will cause stress. Acceptance of emotions, after controlling emotional distress has lowered the predicted mortality (Weihs et al 2008). It is also in accordance with the recognition of the subjects during the study that said that before and during cancer,

patients often experience negative emotions and can not manage that stress and increased illness complaints.

Individuals who are able to manage and control emotions may well respond positively to situations that do not cause stress. Conversely, a low emotional expression or suppression of high emotion with greater breast cancer progression and survival were low (Ader, 2007). It is also in accordance with the recognition of the subjects during the study. They say to get to know the patient's emotions and managing emotions are better able to understand themselves as well as the symptoms of the disease, better able to understand and interact with others, have learned not to get angry and offended by other people, so as to reduce the stress of illness.

EQM training in breast cancer patients shown to lower cortisol levels p = 0.036 (α< 0.05) (Table 2). Training EQM increase positive perceptions of breast cancer as an input, either visual, auditory and somatosensory in the limbic system that is forwarded to the lateral amygdala via through sensory association cortex, forwarded to the central of the amygdala (CEA), then headed to the Lateral Bed Nucleus of the striae terminalis (BNST) which is the primary effector structure of emotional response. Of BNST, forwarded to paraventricular nucleus (PVN), which further inhibits pituitary-adrenal cortex axis so that cortisol levels decreased, on the contrary, the input stress causes breast cancer cortex adrenal axis activation. Some evidence suggests that dysregulation of the HPA axis is accompanied by disease progression of metastatic breast cancer in women (Maier & Watkins 1998). Cortisol is a key hormone produced in response to physical and psychological stressors in humans. Cortisol is commonly known as a stress hormone involved in the response due to anxiety and stress (Sephton et al 2000). The tendency of a decrease in cortisol levels that are in line with the reduction in stress scores in breast cancer patients show an effect in reducing the EQM training stress followed by decreased levels of cortisol.

In healthy individuals, cortisol levels are usually higher before waking and decreased during the day, but nearly 70% of patients with breast cancer showed a flattened profile circardian, consistently at a high level or irregular fluctuations. Although the cause of circadian dysregulation in cancer can not be determined, cortisol dysregulation associated with physical stress and psychological stress of cancer. Psychological distress accompanying cortisol irregularities in a number of cancer patients. Cortisol can accelerate tumor growth through immunosuppressive action or effect of metabolic processes (Lointier et al 1992). Changes in cortisol rhythm also showed impaired circulation patterns of leukocytes, neutrophils, platelets and serum

proteins (Jim & Andersen 2007). Breast and ovarian cancer patients with changes in cortisol rhythm showed chaos circulation patterns of leukocytes, neutrophils, platelets and serum proteins (McDaniel et al 1995). Dysregulation of cortisol response may lead to tumor resistance. Glukorticoid have implications in tumor growth, both in animal and in vitro studies (Lointier et al 1992). When cortisol profiles are affected, there is also the activity of immune dysregulation and immune cell trafficking (Kronfol et al 1997).

EQM and Immunity response (TNF-α IL-2)

Several lines of psychological variables directly related to immune function, including behavioral, neurological and endocrine mechanisms. In the first case, positive emotions affect immunity through healthy lifestyle habits, such as better quality of life, quality of social relationships better and better health prakek (Ader2007). When environmental challenges exceed the individual 's coping abilities, the endocrine system is activated, particularly the HPA system and the sympathetic -adrenal medullary system (SAM), resulting in activation of receptors for cortisol and catecholamines on leukocytes, which alter cellular trafficking, proliferation and differentiation, and cytokine production (Blalock 1994). According Ah et al (2007), stress has adverse effects on the immune function of breast cancer patients, interventions to reduce stress and improve optimism help improve output breast cancer. Cytokines are signaling molecules that mediate and regulate immunity, inflammation, and is an important component of biological hematopoesis associated with breast cancer. Cytokines used as a biomarker for prognosis in research and has been accompanied by symptoms and adverse outcomes in a variety of conditions including breast cancer.

In this study, no differences in the levels of TNF-α (α = 0705), and IL-2 (α = 0.600) in patients with breast cancer after training EQM. This lack of difference is due to the effects of antineoplastic drugs suppress immunity by decreasing the number and function of immune cells and/or increase the active immunosuppressive mechanisms (eg regulatory T cells) (Dhabhar 2009), which also acts as a stressor induces adaptive signal which limits the clinical value. Implementation EQM for 4 times is not enough to restore the immune response as a result of chemotherapy in breast cancer patients. These results require replication sample larger and more representative in breast cancer patients. According Ah & Kang (2009) type adjuvant therapy of breast cancer chemotherapy has inhibitory effect recovery immunosuppressive cytokine responses (IFN-γ, IL-2, IL-4, IL-6, and IL-1β) Until 12 months after

chemotherapy and in children with malignant immune changes persist 9-12 months after chemotherapy is stopped (Mustafa et al 1998). Even according to Harris et al. (1976), in the course of chemotherapy experienced sustained suppression of immune function next 2-3 years in certain groups of patients, ie patients who recovered normal or nearly normal. Effects of chemotherapy, such as a decrease in the number of leukocytes (immunosuppressive), platelets and hemoglobin, nausea, vomiting, and decreased appetite, also affects the immune system of breast cancer patients who have an impact on the clinical value of the cytokines examined. Other factors, namely low socioeconomic status, also affect the nutritional status of patients who participate in the formation of the immune system of breast cancer patients, although the study was not done and not controlled in this study.

However, in patients who receive training EQM mean changes in levels of TNF-α increased and, conversely, decreased in the group of patients who did not get EQM. These findings suggest that training EQM fix marked trend of increased macrophage TNF-α. Increased TNF-α will stimulate/activate TH1 in breast cancer patients, although statistical analysis was not significantly different. In response to the threat, the hypothalamus secretes corticotropin-releasing hormone, triggers systemic glucocorticoid and catecholamine secretion, which inhibits leukocyte memperoduksi TNF-α (Elenkov & Chrousos 2002). Glucocorticoids decrease cytokine expression by binding to and activating the negative regulation of gene promoter element in the production of cytokines and the induction of IB -, a protein that binds to and neutralizes cytokine transcription factor nuclear factor-B (NF-B) (Scheinman et al 1995). If distress and pessimism can activate a biological response to stress, on the contrary, a decrease in distress (eustres) and optimism fixing biological stress response during the diagnosis and treatment of cancer. TNF-α is an important cytokine that accompany tumor regression, a potent proinflammatory and increased survival time in cancer patients (Nakamoto et al 2000). At the location of the tumor, TNF-α induces apoptosis in angiogenic vascular cells, leading to hemorrhagic necrosis (Andersen et al 2004). With the induction of tumor permeability, TNF-α facilitate the uptake of chemotherapeutic drugs such as doxorubicin (reviewed restaurants in Eggermont et al 2003) cytotoxic effect on breast cancer cells (Weitsman et al 2003) and is a key factor induction of CTL (Sasiain et al 1998).

Although there was no statistical difference (Table 3), a decrease of changes in IL-2 in control patients was greater than the treatment group. These findings suggest that training could inhibit cell depletion EQM CTL and

NK cells by inhibiting IL-2 due to a decrease in immunosuppressive caused neoadjuvant chemotherapy. IL-2 plays a fundamental role in the generation of immune cells capable of mediating tumor regression. IL-2 is an activator of NK cells and CTL (Lissoni et al 1991). Research Lissoni et al (1991) showed IL-2 were found to be lower in breast cancer patients compared to healthy people who do not respect and response to therapy. IL-2 is a predictor of lower shorter survival time and increased risk of cancer recurrence (Arduino et al 1996). The decrease in IL-2 could be due to the presence of excessive production of prostaglandin E2 in breast cancer can decrease the production of IL-2 (Baxevanis et al1993).

Cytokines are like IL-2 and IFN-γ can increase NK cell cytotoxicity and lymphocyte-activated killer (LAK) to kill. Interferon is a major regulator of NK cells, stimulate growth and differentiation also increases his ability destroy target cells, including cancer cells (Kiecolt-Glaseret al 2002). In breast carcinoma cell lines were different, IFN-γ induces growth cessation in mid-G1 (García-Tuñón et al 2007). Cytokines, IL-2 and interferon are known to increase NK cell activity (Sinkovics & Horvath 2005). The tendency of increased levels of TNF-α and IL-2 in breast cancer patients undergoing chemotherapy in the treatment group showed a training effect is still in the process of adaptation. EQM training proved beneficial for breast cancer patients to deal with pain and more effective immune system. Reduction of stress can reduce immune decline on strong negative emotions that weaken the immune response over time.

CONCLUSION

Emotional Quality Management repairing stress perception that converts into eustres distress in breast cancer patients. Decrease stress modulates the activity of the HPA axis resulting in decreased cortisol levels, followed by a trend of increased TNF-α, IL-2, and both of these cytokines is an indicator of improved cellular immunity that is necessary for the patient's body resistance against breast cancer cells.

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