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THE EFFECT OF MINDFULNESS ON PAIN AND Il-6 LEVEL SERUM IN CANCER PATIENT

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ABSTRACT
Pain is a common symptom experienced by patients of nasopharyngeal cancer. This pain is caused by metastasis, infection and medication. Pain can result in physical, psychological (stress), social, and spiritual impact as well as it causes the emergence of perception about death that can decrease the life quality. Pain response affects changes on psychoneuroimmunology. Integrated treatment on pain is needed. Mindfulness is one form of integrative therapy to relieve pain intensity and reduce pro-inflammatory cytokine activity as a pain response. Objective to show effect Mindfullnes on pain and Il-6 serum level in cancer patient especially nasopharyngeal cancer. Experimental clinical trial one group pre and post test design without control. Sample collected based on consecutive sampling. Pain intensity is measured by using VAS, the neutrophils count is measured by using analyzer packet and IL-6 level is measured with ELISA. The instrument validity test showed r=0.90, while the reability test showed more than 0.90. Data were analyzed using t-test. Average difference of pain intensity before therapy, (mean4,07 + 0,99), there is a difference in the pain level, neuthropyl and IL-6. Mindfulness is proved to give effect on pain intensity, neutrophils count and IL-6 level on patients with nasopharyngeal cancer.

Keywords: IL-6; mindfulness; nasopharyngeal cancer; pain

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INTRODUCTION

The prevalence of nasopharyngeal cancer (NPC) in America ranges from 1-2 cases per 100,000 in men and 0,4 cases in women(clifton P & Titcomb JR, 2001). NPC incidence is malignancy that occupies the first rank in the field of ear, nose and throat (ENT). During the period of 2002 to 2009, NPC ranked second (22,3%) after head-neck lymphoma (26,3%) in RSUP Dr. Kariadi Semarang (General Hospital) (Prasetyo, Udadi, Ika.,2011). Pain is a common symptom experienced by patients of nasopharyngeal cancer that it reaches 90% (van den Beuken-van Everdingen et al., 2007), with a high prevalence on stage III or IV (Keefe FJ., 1986). The pain is neurophatic that gives burning sensation and *allodynia* especially in the sensory nerves on face, head, neck, mouth, ear and shoulder (Bhatnagar & Gupta, 2015). The pain of NPC is caused by metastasis or infiltration, pressure and ulcer as side effects of cancer treatment (radiotherapy, chemotherapy, and surgery), or infection (Teo PM., 1998; Leung, et al.,2000; Chua DT, et al., 2003; Williams JE., 2009).

The acute pain suffered by NPC patients gives many effects such as physical and psychological (stress) effect, perceptions about death, social and spiritual, and it may reduce the quality of life for cancer patients. On stressful condition, there is hormonal and neurotransmitter change. Under chronic stress condition, structure of hippocampus changes and axis activity *hipotalamus pituitary adrenal* (HPA) increases (Blelch et al., 1988)(Dusek et al., n.d.). A series of HPA activity can cause changes on IL-6 level as it becomes proinflammatory cytokines that will intensify the pain response on patients. Neutrophil is one cell that can express IL-6 (Karnen, 2012). The increase of IL-6 level can worsen the disease.

Efforts on pain treatment for NPC patients should be integrative whether physically, psychologically, socially or spiritually. Therefore, it can help to improve cancer patient's quality of life and one of attempts can be done is mindfulness therapy (Kemenkes, 2012). Transpersonal mindfulness therapy takes hold on theory of neuropsychoimmunology. The transpersonal therapy is able to relieve depression and improve life quality of the patients on the aspects of physical/biological, psychological, social, and spiritual (Johanna EP, Thomas DH, 2009). This therapy is a method that shows the improvement on activation of parasympathetic nervous system that leads to the reduction of stress and anxiety (Crewther, 2016). The aim this research to show effect Mindfullnes on pain and Il-6 serum level in cancer patient especially nasopharyngeal cancer.

METHOD

The type of research used in this study is quantitative with the design of experimental clinical trial one group pre and post test design without control. Target of population is stage III and IV NPC patients who came to outpatient clinic and were undergoing radiation treatment. The sampling technique was consecutive sampling that was suitable with inclusion criteria. The process was then followed with measurement of pain intensity, neutrophil count and interleukin 6 level, and the implementation of mindfulness therapy was done afterward. The number of samples was 18 subjects, with inclusion criteria: patients of nasopharyngeal cancer stage III and IV who were experiencing pain with Visual Analog Scale (VAS) 3-6, receiving chemotherapy and or radiation, on the age of over 25 years old.

Measurement device used in this research is VAS questionnaire (Visual Analog Scale) to describe pain intensity and to identify neutrophil count by examining 3 cc of venous blood samples by using a packet analyzer to determine the neutrophil count. Furthermore, the level of interleukin 6 is measured by taking 3 cc of venous blood samples to be centrifuged on 3000 rpm for 10 minutes. It is then stored under temperature of -20 oC and the test is finalized by using enzyme linked immunosorbent assay (ELISA) kit. Data normality test using Saphiro Wilk. T -test was used to determine whether there were differences before and after Mindfulness.

RESULTS

Out of 18 subjects who met the requirements, two of them were excluded because they refused to become respondents reasoning on the impossibility for intervention. Two more patients were drop-out because they were unable to finish the intervention, so it means that the remaining subjects who were able to involve in the research were 14

Table 1.
Respondent Characteristics

Subject Characteristics	f	%
Age		
20 - 30 years old	1	7,1
31 - 40 years old	3	21,4
41 - 50 years old	3	21,4
51 – 60 years old	5	35,7
61 – 70 years old	2	14,3
Gender		
Male	10	71,4
Female	4	28,6
Stage of Cancer		
Stage 3	12	85,7
Stage 4	2	14,3

Table 2.
Score of VAS, Neutrophil Count and Interleukin 6 Level

VAS Score	Mean ± SD	Min	Max	n	Mean Diff	*p value*
VAS pre intervensi						
Mild pain	4,07 ± 0,99	2	6	3	3,50	
Moderate pain						
VAS post intervensi						0,001
Mild pain	3,07 ± 0,91	2	5	11	2,54	
Moderate pain						
Neutrophil Count						
Pre-intervention	4,99 ± 2,31	1,71	9,31	10	3,65	0,004
Post-intervention	3,70 ± 1,34	1,35	6,30	4	2,92	
IL-6 Level						
Pre-intervention	6,81 + 5,40	0,75	17,10	10	3,69	0,021
Post-intervention	4,63 + 3,33	0,62	10,05	4	2,71	

The average pain intensity on a group before mindfulness therapy is higher (*mean* 4,07 ± 0,99) than the average pain intensity after the therapy (3,07 ± 0,91). The result of t-test shows p value of 0,0001 ($p<0,05$). The average level of neutrophil of the group before therapy is higher (*mean* 4,99 ± 2,31) than the average level of neutrophil after the mindfulness therapy (3,70 ± 1,34). The result of statistic examination that applies t-test shows achieved p value of 0,004. The average level of IL-6 on the group before therapy is higher (*mean* 6,81 ± 5,40) than the average level of IL-6 after the mindfulness therapy (4,63 ± 3,33). The p value achieved after t-test statistic examination is 0,021 ($p<0,05$).

DISCUSSION

The research confirms that transpersonal therapy (mindfulness) is one form of Complementary Alternative Medicine which can be used to decrease pain intensity, neutrophil count and interleukin-6 level on advanced patients of nasopharyngeal cancer. Codie R. Rouleau (2015) pointed out that mindfulness is a program that adopts Kabat Zinn theory which includes: meditation, yoga and relaxation that can help patients to understand individual responses toward stress as well as to guide individual in responding the stress response (Rouleau et al., 2015). Mindfulness therapy can also assist the health improvement in its relation with life quality and it can relieve psychological stress under chronic pain condition (Rosenzweig, et al., 2010).

Mindfulness is considered applicable to reduce pain through various mechanisms. Garland et al argued that one mechanism of mindfulness to relieve pain is by decreasing the level of anxiety, stress and emotional reaction (Garland et al., 2012). Factors to increase or decrease pains include distraction, relaxation, stress, belief of hypnosis, belief of mood, and emotional level (Zeidan et al., 2012). Brown concluded that mindfulness therapy can relieve the pain by increasing the cognitive and emotional control as reflection of *Anterior Cingulate Cortex* (ACC)/*ventromedial Pre Frontal Cortex* (vmPFC) activity which leads to the self-acceptance attitude on individuals. When pain attacks, meditator shows greater activation in the brain area which is responsible for the sensory aspect coding of the dangerous stimulation (insular, thalamus, mid cingulate cortex). Respiratory relaxation is assumed as the result of a mindfulness process that can reduce the pain. Chang et al mentioned that the activity of relaxation response is generated from the reduction of autonomic nerve and psychology activity, levels of catecholamines and glucocorticoids that help to reduce blood pressure, metabolism, and respiratory rate (Chang et al., 2011). Respiration is activity of ANS (Autonomic Nervous System) of an individual and PNS activation and it also maintains homeostatis through respiratory.

Relaxation that leads to the pain intensity reduction (Crewther, 2016). Another mechanism that plays role in the mindfulness therapy is stress reduction. Mindfulness helps to relieve the activity of sympathetic nervous system and HPA axis when stress attacks, therefore it helps to relieve the pain (Esch et al., 2003). Mindfulness therapy can also reduce the activity of inflammatory process by diminishing the inflammatory signs and control of pro-inflammatory genes. The relationship between GR and genomic response will activate the anti-inflammatory genes program and regulation of mRNA transcription that includes immune response. Glucocorticoids plays role in the inflammatory response (Stark et al., 2001). Inflammatory protein is produced by immune cell and it works as extracellular communicator during the immune system activity. The improvement on pro-inflammatory protein level can worsen particular disease condition and it can even lead to death (Malarkey et al., 2013; Morgan et al., 2014). Stress is very influential on activity of HPA axis as it can affect immune system. The limitation of this research is the need of controlling group and the necessity to measure stress/anxiety level on patients of nasopharyngeal cancer pre and post mindfulness treatment. Subjects of the study are nasopharyngeal cancer outpatients and it unfortunately causes the researchers unable to identify existing factors that disturb or confound the pain such as stress and anxiety. Next researchers are suggested to conduct the measurement on stress and anxiety level as well as examine the metabolism rate like blood pressure and respiration as a result of stress.

CONCLUSION

Based on the research, it can be concluded that there is a decline in the average pain intensity, the neutrophil count and the level of IL-6 after transpersonal therapy (mindfulness) is given to patients of stage III and IV nasopharyngeal cancer.

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