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# The combination effect of brisk walking and relaxation toward hs-crp and anxiety levels in subject with central obesity in Singaraja, Bali



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## ABSTRACT

**Background:** Inflammation and anxiety have reciprocal relationships because low grade chronic inflammation characterized by elevated hs-CRP in central obesity has been proved to induce anxiety. Likewise, anxiety could also induce central obesity and inflammation of peripheral tissue. Brisk walking and relaxation have been proved to have anti-inflammatory effects. However, the effects of their application in central obesity population have not been observed.

**Objective:** The aim of the study is to determine the combination effect of brisk walking and relaxation on hs-CRP and anxiety level.

**Method:** This research is an experimental research with randomized controlled trial design. According to sample size formula, this study required 80 with central obesity which would be selected using purposive sampling. The sample was divided into 4 groups by randomization procedure into control group, brisk walking group,

relaxation group and combination of brisk walking and relaxation group. Each group was given thrice a week treatment for six weeks. Data were analyzed by using SPSS 22.

**Results:** A total of 80 samples with central obesity were enrolled with mean age  $47.66 \pm 7.47$  years old and WHtR  $0.57 \pm 0.04$ . There is no significant effect of brisk walking, relaxation, and their combination to hs-CRP level ( $p = 0.696$ ). On the other hand, all of the interventions were significantly reduce the anxiety level. However, the combination of brisk walking and relaxation had the most significant effect in decreasing anxiety level even when compared to either brisk walking or relaxation group ( $p < 0.05$ ).

**Conclusion:** Both brisk walking and relaxation significantly reduce the level of anxiety but their combination had the most significant effect. However, no intervention had proved to alter the level of hs-CRP.

**Keywords:** Brisk walking, relaxation, combination of brisk walking and relaxation exercises, hs-CRP, anxiety level.

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## BACKGROUND

Central obesity is a widespread health problem which often associated with cardiovascular disease, diabetes mellitus, cancer, osteoarthritis, and psychological disorders.<sup>1</sup> The mechanism involved in central obesity is the induction of low grade chronic inflammation characterized by increased pro-inflammatory cytokines and acute phase proteins such as high sensitive C-Reactive Protein (hs-CRP).<sup>2,3</sup> Central obesity status often determined by measurement of waist-to-height ratio (WHtR).

The psychoneuroimmunology field explain the relationship between the immune system and the nervous system in psychiatric disorders.<sup>4,5</sup> Pro-inflammatory cytokines, such as interleukin (IL) -1 $\beta$ , IL-6, tumor necrosis factor (TNF) - $\alpha$  including CRP, could transverse the blood brain barrier and activate microglia which result in neuroinflammation.<sup>6,7,8</sup> The activated microglia release neurotoxic substances, such as pro-inflammatory cytokines (IL-6, TNF- $\alpha$ , IFN- $\gamma$ , IL-

1 $\beta$ ), *reactive oxygen species* (ROS), *reactive nitrogen species* (RNS) that could affect the neuronal function.<sup>9</sup>

Acute psychological stress activates the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic-adrenomedullary (SAM) system. The activation of HPA and SAM axis will increase the activation and expression of NF- $\kappa$ B.<sup>10</sup> Chronic psychological stress will ultimately lead to HPA fatigue, glucocorticoid resistance, the activation of inflammation related transcription pathway, and negative feedback which would further lead to increased pro-inflammatory cytokines. This processed underlie the reciprocal relationship between inflammation and psychological disorders.<sup>11</sup>

Brisk walking is a moderate intensity of aerobic exercise that has been proved to have anti-inflammatory effects.<sup>12,13</sup> Relaxation could oppose the stress response and alleviate the physiological and psychological alteration induced by stress.<sup>14</sup> However, the physiological effects of brisk walking

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and relaxation on the have not been confirmed especially their effect on chronic inflammation often represented as the level of hs-CRP. Therefore we carry out research by doing a combination of aerobic and relaxation exercises to determine the effect on hs-CRP and anxiety levels.

## METHOD

### Subject Selection and Intervention

A cross-sectional study was conducted at Bhuwana Patra, Singaraja for 6 weeks. According to sample size formula, a total of 80 subjects were required for this study. The inclusion criteria were waist to height ratio  $\geq 0.5$ , age 30-60 years with L-MMPI  $< 10$ , willing to follow the research procedure by not taking anti-inflammatory drugs, not suffering from acute inflammatory diseases, and has sedentary life for the last 3 months. The subjects were divided into four groups, namely control group, brisk walking group, relaxation group, and combination group of brisk walking and relaxation. The group was randomly divided and each treatment was administered thrice a week for six weeks.

The intervention is determined as follows. Brisk walking was conducted at the speed of 100 steps per minute for 20 minutes in the first two weeks, 30 minutes in the second two weeks, and 40 minutes in the third two weeks. Brisk walking was carried out in the field under the supervision of professional instructors. The intervention and data gathering were conducted at the volunteers' spare time.

The relaxation procedure and assessment was conducted indoors with a combination method of deep breath and guided imagery accompanied

by music. Relaxation takes place 10 minutes in the first two weeks, 15 minutes in the second two weeks, and 20 minutes in the third two weeks. The intervention and data gathering were conducted at the volunteers' spare time.

In the combination of brisk walking and relaxation group, brisk walking was conducted first at the speed of 100 steps per minute, for 20 minutes in the first two weeks, 30 minutes in the second two weeks, and 40 minutes in the third two weeks. Then the participants would do the cooling for 10 minutes and followed by relaxation. Relaxation was conducted by a combination of inner breath, guided imagery, prayer, and accompanied by music. Relaxation takes place 10 minutes in the first two weeks, 15 minutes in the second two weeks, and 20 minutes in the third two weeks. The time of relaxation takes place according to the spare time of each participant.

### Outcome Assessment

The Hs-CRP examination was performed by using immune-turbidimetry method in collaboration with Prodia Laboratory, Singaraja Branch, Bali, Indonesia. The pre-intervention blood test for hs-CRP was performed 24 hours before the study at 10:00 to 12:00 AM. The post-intervention blood test sample for hs-CRP was performed 24 hours after the last treatment at 10.00-12.00 AM. The Anxiety levels were measured using Taylor Manifest Anxiety Scale (TMAS). Pre-intervention examination of anxiety level was performed 24 hours prior to the study while post-intervention examination was carried out immediately after the last intervention.

**Table 1.** The baseline characteristics of research participants

Characteristics	Control	Brisk Walking group	Relaxation group	Combination group	p-value
<b>Gender</b>					
Male	16 (80%)	15 (75%)	16 (80%)	16 (80%)	0.974 <sup>a</sup>
Female	4 (20%)	5 (25%)	4 (20%)	4 (20%)	
<b>Education Level</b>					
High school	7 (35%)	6 (30%)	5 (25%)	6 (30%)	0.997 <sup>a</sup>
Diploma	8 (40%)	8 (40%)	9 (45%)	8 (40%)	
Bachelor	5 (25%)	6 (30%)	6 (30%)	6 (30%)	
<b>Age</b>	47.75 ± 7.74	48.05 ± 8.20	47.20 ± 6.38	47.65 ± 7.96	0.732 <sup>b</sup>
<b>WHtR</b>					
Pre test	0.58 ± 0.04	0.58 ± 0.04	0.58 ± 0.04	0.56 ± 0.04	0.378 <sup>b</sup>
Post test	0.58 ± 0.03	0.58 ± 0.04	0.58 ± 0.04	0.56 ± 0.03	0.344 <sup>b</sup>

<sup>a</sup> Chi Square, <sup>b</sup> Kruskal-Wallis

The effect of each treatment on hs-CRP and anxiety level was analyzed using one way ANOVA or Kruskal-Wallis test depending on the normality of the data. All of the statistical test was performed with SPSS 22.

**RESULTS**

Eighty adults with central obesity were participated in the study, consisting of 63 men and 17 women who divided into four groups. The results of the Fisher's exact test showed no difference of sex in each group ( $p = 1.000$ ). In terms of education, most of the participant had high school, diplomas, and bachelor degrees level of education. The statistical test also showed . The mean age in this study was  $47.66 \pm 7.47$  and no age difference was found among

all groups ( $p = 0.997$ ). The baseline characteristics of the subjects is presented in [Table 1](#).

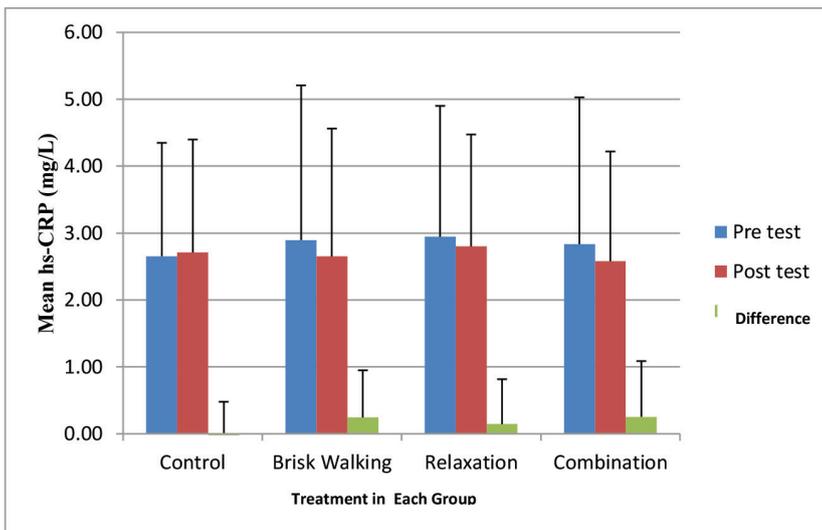
At the beginning of the study, the WHtR measurements were conducted. The data analysis showed no statistical difference in WHtR in each group ( $p = 0, 378$ ). The post-intervention WHtR measurements also showed same result ( $p = 0.344$ ). After intervention, there was an increase in hs-CRP in the control group but decreased hs-CRP level in the brisk walking, relaxation, and combination of brisk walking and relaxation groups (Figure 1). However, the statistical test of delta ( $\Delta$ ) of each group ([Table 2](#)) showed no significant difference ( $p = 0.696$ ).

In contrast, there was decrease trend in anxiety level in brisk walking, relaxation and combination groups (Figure 2). Statistical analysis ([Table 2](#)) showed significant difference ( $p < 0.001$ ) of delta ( $\Delta$ ) for anxiety levels in all four groups. Mann-Whitney test confirmed ([Table 3](#)) that the combination group had the most significant value in decreasing anxiety levels compared with brisk walking group ( $p = 0.004$ ) and relaxation group ( $p = 0.011$ ). But there was no significant difference between brisk walking and relaxation groups in decreasing anxiety levels ( $p = 0.581$ ).

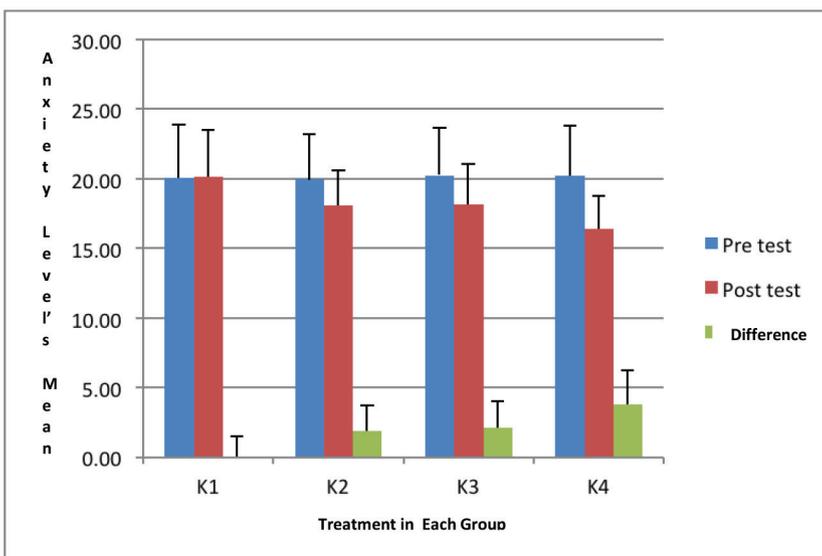
**DISCUSSION**

This study revealed that although brisk walking and relaxation could not change the WHtR, it could significantly affect the anxiety level. Brisk walking increase energy expenditure and negative energy balance which affect the physiological and psychological regulatory processes that support the appetite and energy intake. In addition, there was evidence that exercise will affect the components of energy intake which in turn affect the drive to eat through modulation of hunger (a conscious sensation that reflects the drive to eat) and adjustment in post-prandial satisfaction through interaction with food compositions. Therefore, individual responses to exercise are very difficult to predict and tend to be vary.<sup>15</sup>

In contrast to anxiety level, this study showed no difference of hs-CRP in all four groups. Our finding was contradicted with the fact that hs-CRP level is tend to increase in patients with mobility disorder. It seems that increasing the mobility rate did not have any effect toward hs-CRP or longer intervention period is needed to significantly alter the level of the hs-CRP. The CRP is synthesized in the liver at very low levels. In addition to the liver, CRP is also produced in the vascular smooth muscle, atherosclerosis plaques, and intracardiac tissue. It synthesis often influenced by the level of IL-6, IL-1 and and TNF- $\alpha$ . Induction by IL-6



**Figure 1** hs-CRP before and after treatment in each group



**Figure 2.** Levels of anxiety before and after treatment in each group

**Table 2. Comparison of hs-CRP and Level of anxiety before and after treatment in each group**

	Control	Brisk walking	Relaxation	Combination	P
hs-CRP					
Before	2.66 ± 1.69	2.89 ± 2.31	2.95 ± 1.96	2.84 ± 2.19	
After	2.71 ± 1.69	2.65 ± 1.91	2.80 ± 1.96	2.58 ± 1.64	
Delta (Δ)	-0.06 ± 0.54	0.25 ± 0.70	0.15 ± 0.67	0.26 ± 0.83	0.696 <sup>a</sup>
Anxiety Level					
Before					
After	20.05 ± 3.87	19.95 ± 3.25	20.25 ± 3.38	20.20 ± 3.59	
Delta (Δ)	20.15 ± 3.35	18.10 ± 2.53	18.15 ± 2.94	16.40 ± 2.39	
	-0.10 ± 1.59	1.85 ± 1.87	2.10 ± 1.89	3.80 ± 2.46	< 0.001 <sup>a</sup>

<sup>a</sup> Kruskal-Wallis**Table 3. Mann-Whitney test of anxiety level in each group**

Grup	P
Control dan Brisk walking	0.001
Control and Relaxation	0.001
Control and Combination	< 0.001
Brisk walking and Relaxation	0.581
Brisk walking and Combination	0.004
Relaxation and Combination	0.011

usually mediated by STAT3 and C / EBPβ which alter the transcription of CRP.<sup>16</sup> On the other hand, exercise had been proved to decrease TNF-α and IL-6 level. Exercise results in reduced infiltration of macrophages and T cells into adipose tissue and induce a phenotypic shift of macrophages from pro-inflammatory M1 to anti-inflammatory M2.<sup>17,18</sup> The activity of anti-inflammatory exercise is also due to the decrease of TLR4 and ICAM-1 expression as well as increase Treg differentiation.<sup>19,20</sup>

Downregulation of TNF-α expression by relaxation is allegedly obtained via the inhibition of NF-κB pathway and MAPK pathway. Psychological stress will result in the activation of the HPA and SAM axes activation which enhance the production of the adrenocorticotrophic hormone from the pituitary gland and lead to glucocorticoid hormone secretion.<sup>10</sup> Meanwhile, the activation of the SAM axis will increase the secretion of catecholamines like epinephrine and norepinephrine. Glucocorticoids and catecholamines are thought to have immunomodulation properties through receptors present in immune cells.

Psychological stress also leads to an increase in TLR-4 expression, which increases the sensitivity to internal stressors relay proteins such as *pathogen-associated molecular patterns* (PAMPs) and *damage-associated molecular patterns*

(DAMPs).<sup>10</sup> The combination of the HPA axis and glucocorticoid resistance in the activation of the NF-κB and MAPK pathway.<sup>11</sup> All of these processes will lead to the activation of the NF-κB and MAPK pathway which will further increase the production of pro-inflammatory cytokines including TNF-α. Relaxation significantly reduce psychological stress so that the activation of the NF-κB and MAPK pathway can be prevented and, thus, prevent inflammatory activation. Unfortunately, there were no measurements of pro-inflammatory cytokines in this study. However, there are two possibilities why there was no change in hs-CRP. First, there is probably no alteration of cytokines level. Secondly, even if there was a decrease level of pro-inflammatory cytokines, the change was not sufficient to alter the hs-CRP level due to multifactorial nature of hs-CRP expression. Thus, further research is needed to understand and elucidate the molecular and physiological reason behind this phenomenon.

On the other hand, brisk walking lower the anxiety level mainly due to the decrease in pro-inflammatory cytokines which caused neuroinflammation responsible for the anxiety. Exercise has also been known to increase β-endorphin, BDNF, and serotonin in CNS.<sup>21</sup> Relaxation works to lower anxiety through its anti-inflammatory activity. Relaxation can also prevent neuroinflammation by preventing the migration of monocyte to the CNS especially during psychological stress.<sup>22,23</sup> Relaxation is also known to increase β-endorphin, BDNF, and serotonin in the CNS.<sup>24,25,26</sup>

## CONCLUSION

The combination of brisk walking and relaxation is the most effective way in lowering the anxiety levels, but could not significantly alter the hs-CRP and WHtR. Further research with more biomarkers is needed to find out the beneficial effects of the combination of brisk walking and relaxation.

## FUNDING

This study is self-funded with no third party contribution involved

## CONFLICT OF INTEREST

Authors declare that there is no conflict of interest regarding this article

## ETHIC APPROVAL

This study has been approved by Ethic Committee with Ethical Clearance number 128/IV/HREC/2017

## AUTHOR CONTRIBUTION

All authors contributed equally. The first author established the concept and wrote the draft of the article. The second, third, and fourth authors revised the concept and added many improvements in method, result and discussion.

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