Environmental Conditions and Sincerity affects Cortisol and B-Endorphins Plasma Levels in Young Healthy Subjects Undergoing Dawood's Fast

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Abstract

Background: Prevention of Coronary Heart Disease by identifying risk factors facilitates the planning of prevention interventions. The prevalence of non-communicable disease (NCD) increases with one of the risk factors for NCD being an unbalanced diet. Dawood's fasting is one of the sunnah fastings that can be done at any time except at times that are forbidden to fast. This fast is a combination model of TRF and ADF (modified ADF = MADF).

Objective: To prove that MADF for six consecutive weeks can increase levels of the hormone β-endorphins and reduce levels of the hormone cortisol in peripheral blood circulation.

Materials and Methods: Quasi-experimental research with a comparative design of a non-equivalent control group with a population of PP students. Hidayatullah Surabaya with the purposive sampling method until the number of samples required was met as many as 34 people and divided into two groups, namely control and MADF treatment for six consecutive weeks. Sampling was carried out at the pre-test, at the end of the third week for the middle and at the post-test. All subjects in both groups received the same nutrition twice a day for 42 days. The subject gets spiritual motivation from competent resource persons to give spiritual spark twice.

Result: Dawood's fasting (MADF) for six consecutive weeks did not cause significant differences compared to control on cortisol and β-endorphins ($p > 0.05$). However, Dawood's fasting (MADF) for six consecutive weeks decreased the mean values of cortisol levels due to the effect of fasting, although there was also a significant difference in the control group. Meanwhile the β-endorphins mean values was increased at the middle of study, and then decreased at the end of the study, with a significant difference in the both group before and after treatment.

Conclusion: There was no difference in cortisol and β-endorphins levels in healthy young adult subjects undergoing Dawood's fast due to the influence of the same environmental conditions and a change in the sincerity of the subjects.

Keywords: *Modified alternate day fasting (MADF); Dawood's fasting; atherosclerosis; cortisol; β-endorphin*

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Introduction

The prevalence of death due to Non-Communicable Diseases (NCD) in Indonesia, amounting to 63% of all

deaths[1]. Pusdatin (2018) reports the results of Riskesdas in 2007 and 2013 NCD to tend to increase including heart disease[2]. Of 9.4 million deaths in the world each year due to cardiovascular disease, 45% are coronary heart disease (CHD)[2]. CHD is the seventh-highest NCD in Indonesia. The sample registration system survey results show that the death rate due to CHD is 12.9% of all deaths[3].

Prevention of CHD by identifying risk factors facilitates the planning of prevention interventions. This is following the results of Riskesdas 2017 which stated that the prevalence of NCD increases, NCD risk factors one of which is the diet which is out of balance. The control program on NCD is more focused on prevention efforts[2].

Atherosclerosis is the formation and growth of plaque in the arterial lumen together with loss of elasticity of blood vessels, an inflammatory response in the large arteries that begins with subclinical endothelial dysfunction can turn into life-threatening diseases that manifest as myocardial infarction or stroke. Atherosclerosis is not solely based on balanced lipid metabolism but is mainly driven by chronic inflammation in the walls of blood vessels involving many types of cells[4].

Intermittent fasting (IF) has been shown to increase life span and reduce the incidence of age-related diseases such as diabetes and effectively reduce the risk of heart disease in obesity and reduce risk factors for cardiovascular disease[5]. Ahmet et al (2010) in his study using rats with alternate day fasting (ADF) for six months monitored its echocardiography concluded that increased tolerance of heart muscle to ischemic damage[6]. Other studies on the two-week-old Drosophila fly model that was fasted 12 hours per day (time-restricted feeding = TRF) without reducing its daily calorie intake showed that there was no increase in weight the body from the age of 3 to 7 weeks, where free-eating flies experience the aging process of the heart which is characterized by, among others, an increase in the diastolic and systolic intervals, and arrhythmias[7].

Fasting affects the immune system through hormonal changes associated with the adrenal glands of the kidneys such as cortisol[8]. Several studies have reported that Ramadan fasting induces changes in the circadian rhythm of a number of body hormones including cortisol[9].

The fasting period is often associated with changes in diet, sleep and ritual habits[10], which can change the body's circadian rhythm and become a stressor that the body will respond to[11]. Fasting that is done with a strong intention will give a positive perception, so that it will form an adaptation response to fasting which was originally recognized as a stressor that can reduce the body's immunity to increase the responsiveness of the immune system. One of the causes of this is due to the release of endorphins from the anterior pituitary when a person intends to fast[12]. Ramadan fasting has a positive effect on inflammation by suppressing the expression of proinflammatory cytokines and reducing body fat and the level of circulating leukocytes[13].

Dawood's fasting is one of the sunnah fasts carried out by Muslims at any time except at times that are forbidden to fast. This fast is a combination model of TRF and ADF (modified ADF = MADF). The way to do this is not to eat from sunrise to sunset, and to do with one-day fasting and one-day not fasting[14]. Izzaturrahmi et al (2017) research on the effect of Dawood's fasting on body mass index (BMI) and abdominal circumference in 44 men and women over 50 years old in Yogyakarta, found significant differences in BMI and belly circumference of the Dawood's fasting and non-fasting respondents[15]. Research on students of the Al-Fithroh Islamic Boarding School in Yogyakarta found that perpetrators of Dawood's fasting tend to have a high level of emotional control so that they can withstand anger and lust[16]. This can prevent mental-emotional disorders which are one of the risk factors of CHD. Yatindra et al. (2019) proved that there was a significant decrease in white blood cells in a group of mice undergoing the Dawood's fasting model with a 10-hour fast by taking turns a day after being induced with acetaminophen[17].

Specific research aims to prove that MADF for six consecutive weeks can increase levels of the hormone β-endorphins and reduce levels of the hormone cortisol in peripheral blood circulation. The urgency of this research is to prove that MADF can be used as a model of prevention of cardiovascular disease, especially those related to the process of atherosclerosis associated with

stress and the hypothalamic-pituitary-adrenal (HPA) axis.

Material and Methods

Design

This study was a quasi-experimental study with a comparative pre-test post-test group design. Samples of Hidayatullah Islamic boarding school students in Surabaya 3, 5, and 7 semesters were 134 people with a purposive sampling method until the required number of samples were met.

The experimental protocol of the study was approved by the Medical Faculty of Universitas Airlangga ethics committee with No. 163/EC/KEPK/FKUA/2019, and the research reported here was carried out following the principles of the Declaration of Helsinki as revised in 2000. The research was carried out from August 2019 to June 2020.

Setting

This study was carried out in a young healthy male Indonesian Muslim setting at the Hidayatullah Islamic Boarding School in Surabaya, Indonesia during which fasting was conducted for approximately 14 hours. The participants received some information about Dawood's fasting before they fasted and given a weekly reminder to fast via Short Message Services (SMS), Whatsapp messages, or telephone.

Before the start of MADF (Dawood's fasting) and during the fast, respondents will receive spiritual motivation from a resource person who is competent to give spiritual splash. The aim is for the respondent to maintain a true and sincere intention in following this research until completion.

Participants

The subjects were young healthy male Muslim people divided into two groups, those who observed Dawood's fasting and a group who did not perform the fast. Samples were collected using the consecutive sampling method from January until August 2019. The inclusion criteria were 18-30 years old, Muslim, male, willing and able to do MADF (Dawood's fasting) for six consecutive weeks as evidenced by informed consent, healthy (no history of metabolic disease (HT / DM / CHD as evidenced by history, physical examination and screening Electrocardiogram (ECG) and Random Blood Glucose (RBG)). The number of samples per group required for this study with a correction factor of 30% was 17 samples. The total sample required for this study was 34 samples. Each respondent will fill in the research questionnaire instrument that has been prepared and sign an informed consent.

Intervention

The fasting group precluded any activities that could break the fast (such as eating, drinking, having sexual intercourse) from sunrise to sunset, preceded by the expression of intention to fast on alternate days[14]. This activity lasted for 42 days with 21 days of fasting starting from first following by third, 5th, 7th, 9th, 11th, 13th, 15th, 17th, 19th, 21st, 23rd, 25th, 27th, 29th, 31st, 33rd, 35th, 37th, 39th, and 41st day. The research subjects in both groups were given the same food at dawn and breaking fast (fasting group), and at breakfast and dinner (non-fasting group) and were recommended to always eat the meal before dawn and break the fast immediately after the sunset. During the fasting process, activities of the subjects were observed by the researchers through personal contact with each of them via telephone.

Assessment

Fasting is done from sunrise to sunset (+ 14 hours) and alternating fasting a day and not a day[14]. A blood sample was obtained from each participant before, intermediate, and at the end of Dawood's fasting for 42 days at the Hidayatullah Islamic Boarding School in Surabaya, and was transferred to the Clinical Pathology Laboratory at Dr. Soetomo regional public hospital of Surabaya. Plasma's cortisol and β-endorphin were determined. Venous blood samples were drawn between 0700 and 0900 AM and centrifuged for 15 min at 4ºC. Immediately after centrifugation, the serum samples were frozen and stored at -80ºC. Plasma's cortisol levels were measured with chemiluminescence immunoassay (CLIA) examination using the ADVIA Centaur XPT Immunoassay System tool, Siemens Healthcare Diagnostics, with a ADVIA Centaur® Cortisol (COR) Assay kit by measuring serum range 0.50-75 mg / dL.

β-endorphin levels in serum were measured with an ELISA kit (Elabscience, USA, catalog number

E-EL-H0572). The range access was 15.63-1000 pg/mL. The inside and inter-assay coefficients of variance were less than 5.29% and 4.45%. the measurement of the β-endorphin levels in serum was done in June 2020, because of the trouble in the reagent, so the researcher has to reorder the reagent which takes a time about 6-8 weeks.

Statistical Analysis

The data have been analyzed the normality of distribution using the Shapiro-Wilk test because of the data number below 50. The next step was using the paired T-test (parametric data) or Wilcoxon-signed rank test (non-parametric data) to compare the pre and post-test data both in fasting and non-fasting group. If there were a significant difference, then the test will be continued to two independent samples T-test (parametric) or Mann-Whitney-U test (non-parametric).

Results and Discussion

Of 44 healthy men that volunteered to participate in this study, which were 24 men join the fasting group and 20 men join the non-fasting group. Respondents who entered the inclusion criteria as many as 40 people, 20 from the fasting group, and 20 from the non-fasting group. Before starting the MADF (Dawood's fasting) respondents will be drawn blood for a pre-test examination. At the time of fasting, all respondents both the control group and the treatment will get the same kind of nutrition twice a day for 42 days. At the end of the third-week blood sampling will be done mid, then at the end of the seventh-week respondents will do a post-test blood sampling.

At the end of the study, after 42 days of modified alternate-day fasting, there were only 34 subjects left to finish the study because in the fasting group, there were 2 subjects stopped fasting without any reason and 1 subject stopped fasting due to illness. On the other hand in the non-fasting group, there were 3 subjects could not follow the sampling schedule because of their activity.

The general description of the observed research subjects included age, weight, height, body mass index, and waist/hip circumference, to assess the nutritional status of the study subjects. Complete results can be seen in the table below.

Table 1 Characteristics of subjects based on age, weight, body mass index (BMI), and waist-hip ratio (WHR)

No	Variable	n respondent	
		Treatment n = 17	Control n = 17
1.	Age 18 – 20 years-old 21 – 23 years-old 24 – 26 years-old 27 – 30 years-old	 9 (53%) 7 (41%) 1 (6%) 0 (0%)	 10 (59%) 7 (41%) 0 (0%) 0 (0%)
2.	Body Mass Index (BMI) Underweight Normal Overweight Obesity 1 Obesity 2	 9 (53%) 7 (41%) 1 (6%) 0 (0%) 0 (0%)	 4 (24%) 12 (71%) 1 (6%) 0 (0%) 0 (0%)
3.	Waist – hip rasio (WHR) < 0,95 = low risk of CVD > 0,95 = high risk of CVD	 16 (94%) 1 (6%)	 17 (100%) 0 (0%)

Table 1 above shows the distribution of age, BMI, and WHR in research subjects. The age of the research subjects all met the inclusion criteria which ranged from 18-30 years with the greatest frequency in the treatment group being in the age range 18-20 years-old as many as 9 people (53%), then the age range 21-23 years-old as many as 7 people (41%) and the age range of 24-26 years-old is 1 person (6%). Most of the subjects in the non-fasting group were in the age range 21-23 years-old as many as 10 people (59%) and the age range 18-20 years-old as many as 7 people (41%). This shows that the age distribution in the treatment group is relatively younger than the non-fasting group.

The distribution of BMI calculated based on body weight and height of the subject with the formula BW (kg) / BH^2 (m^2) in the most treatment group with underweight BMI was 9 people (53%), followed by normal BMI of 7 people (41%) and BMI overweight as much as one person (6%). The distribution of the control group is different from the treatment group, namely the most normal BMI is 12 people (71%), BMI underweight is 4 people (24%) and BMI overweight is one person (6%). BMI can be used to assess nutritional status so that in general the subjects in the non-fasting group showed better nutritional status than the treatment group.

WHR calculated based on the ratio of waist circumference and hip circumference (in cm) showed that in the treatment group 94% or as many as 16 people had a WHR value < 0.95, and one person had a value > 0.95 (6%). All subjects in the non-fasting group had a WHR value of < 0.95 (100%). A WHR value < 0.95 indicates a low cardiovascular risk, while a value > 0.95 indicates a high cardiovascular risk.

Based on the general description of research subjects, it was found that all research subjects were in a state of nutritional status who were not obese.

The table below shows the results of the research for both cortisol and β-endorphins.

Table 2 Descriptive data of the cortisol (µg / dL) and β-endorphins (pg / mL)

Variable	Group	Pre-test	Intra test	Post-test
		Mean + SD	Mean + SD	Mean + SD
Cortisol	Not fasting	16,72 + 4,16	11,75 + 4,48	12,39 + 2,80
	Fasting	16,01 + 5,09	12,60 + 4,27	11,11 + 3,52
β-Endorphin	Not fasting	473,44 + 249,87	637,32 + 325,38	302,09 + 94,38
	Fasting	529,07 + 286,50	695,32 + 257,71	320,14 + 67,57

Table 1 above shows the descriptive data in the form of cortisol and β-endorphins mean values at the beginning (pre-test), middle (intra-test), and end (post-test) of the study for each group. These results can be illustrated in figure 1 below.

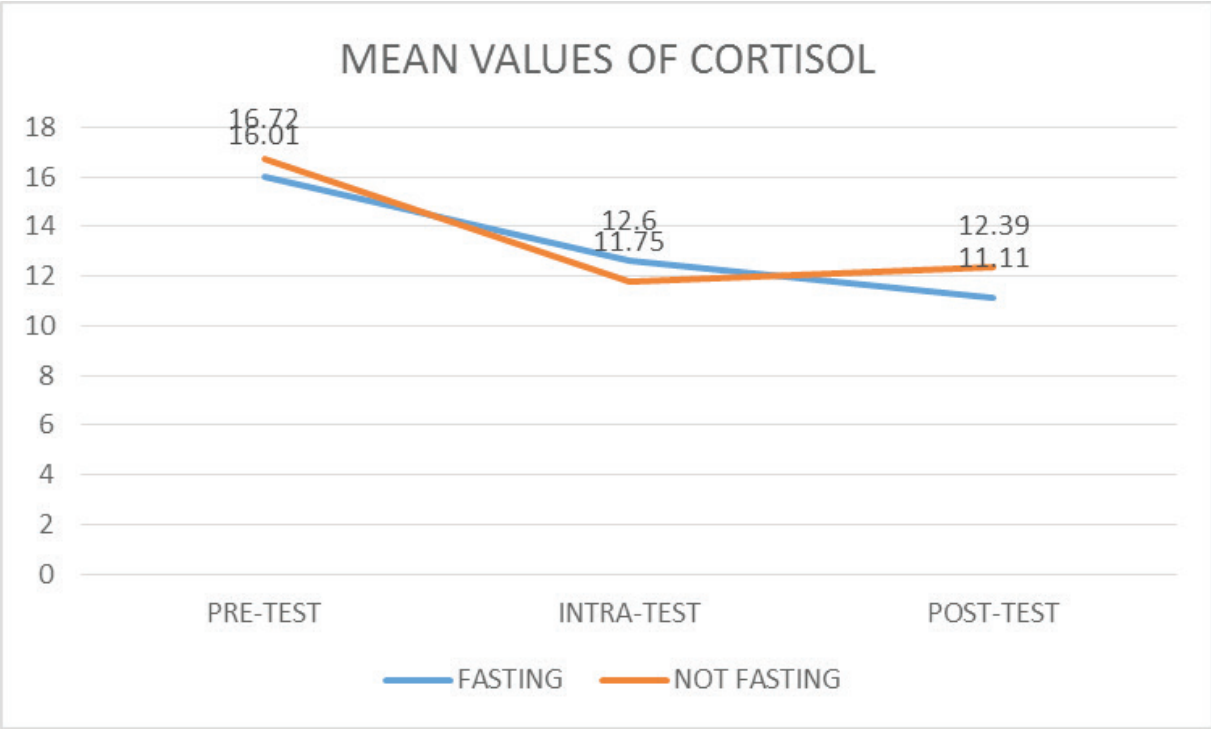

Figure 1 The graph of the cortisol mean values at the beginning, middle, and end of the study for each group.

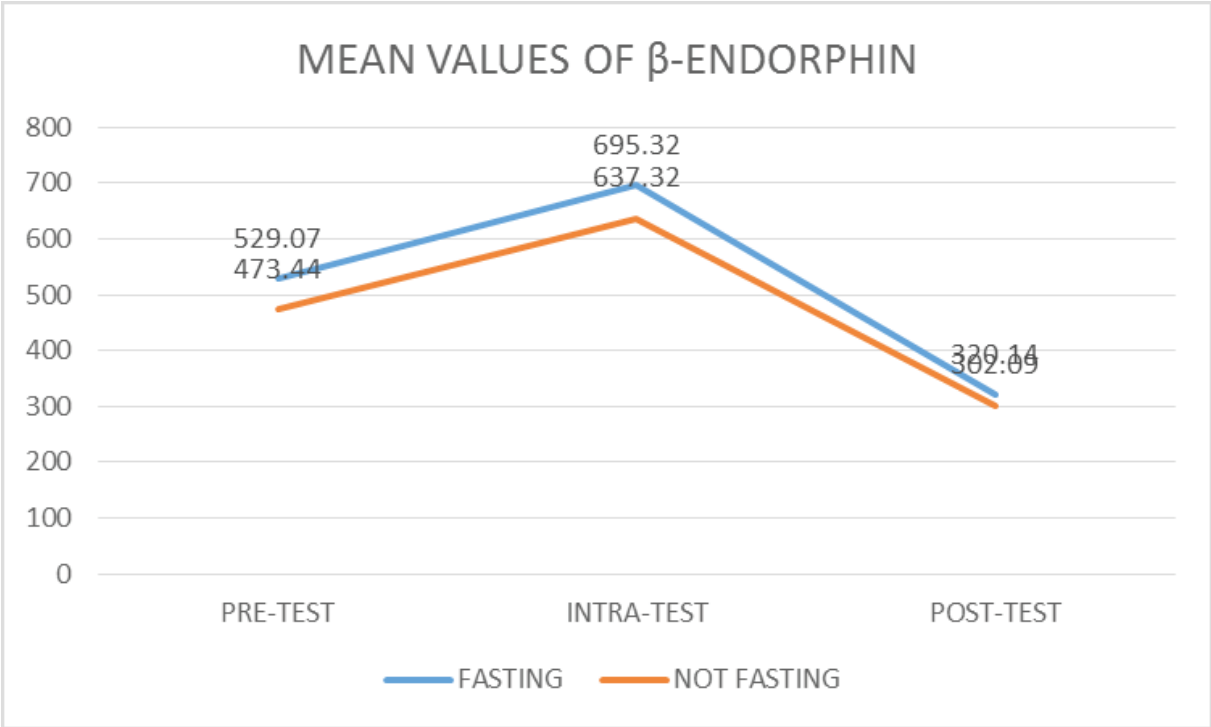

Figure 2 The graph of the β-endorphins mean values at the beginning, middle, and end of the study for each group.

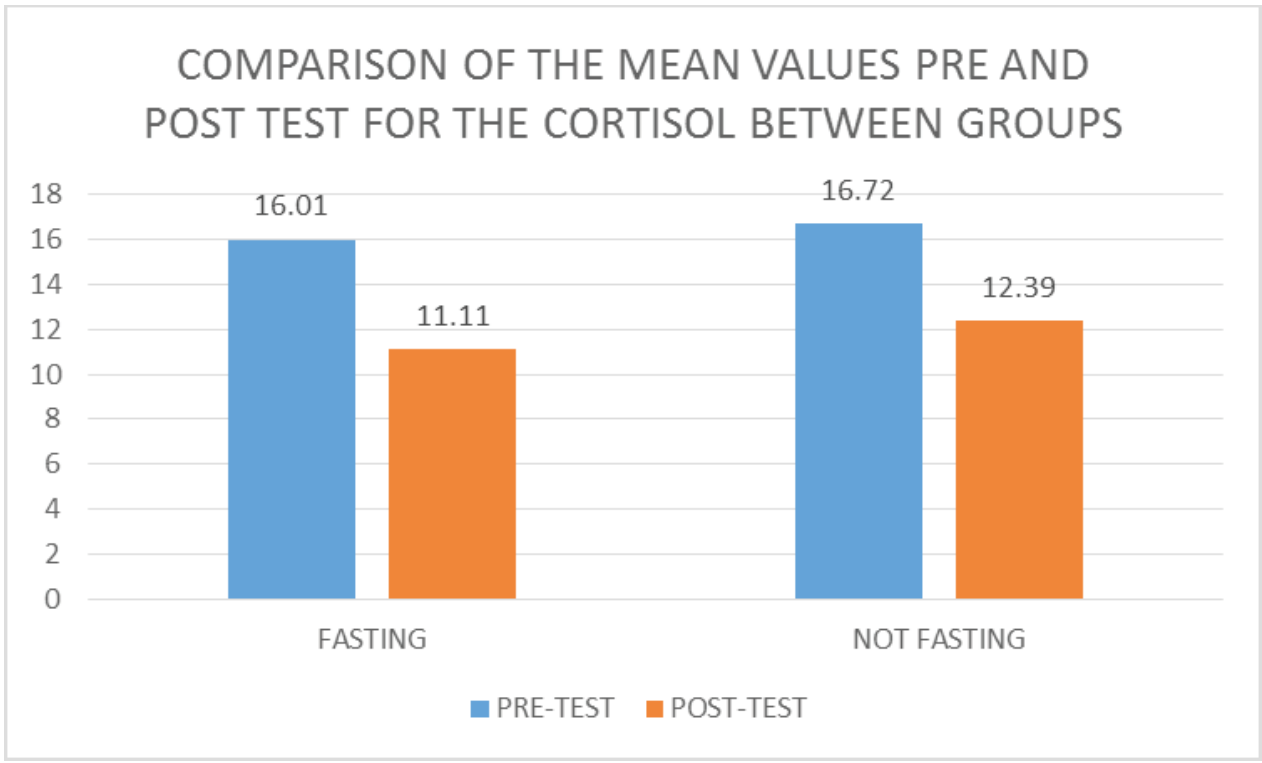

Figure 3 The comparison between mean values of the pre and post-test data for the cortisol

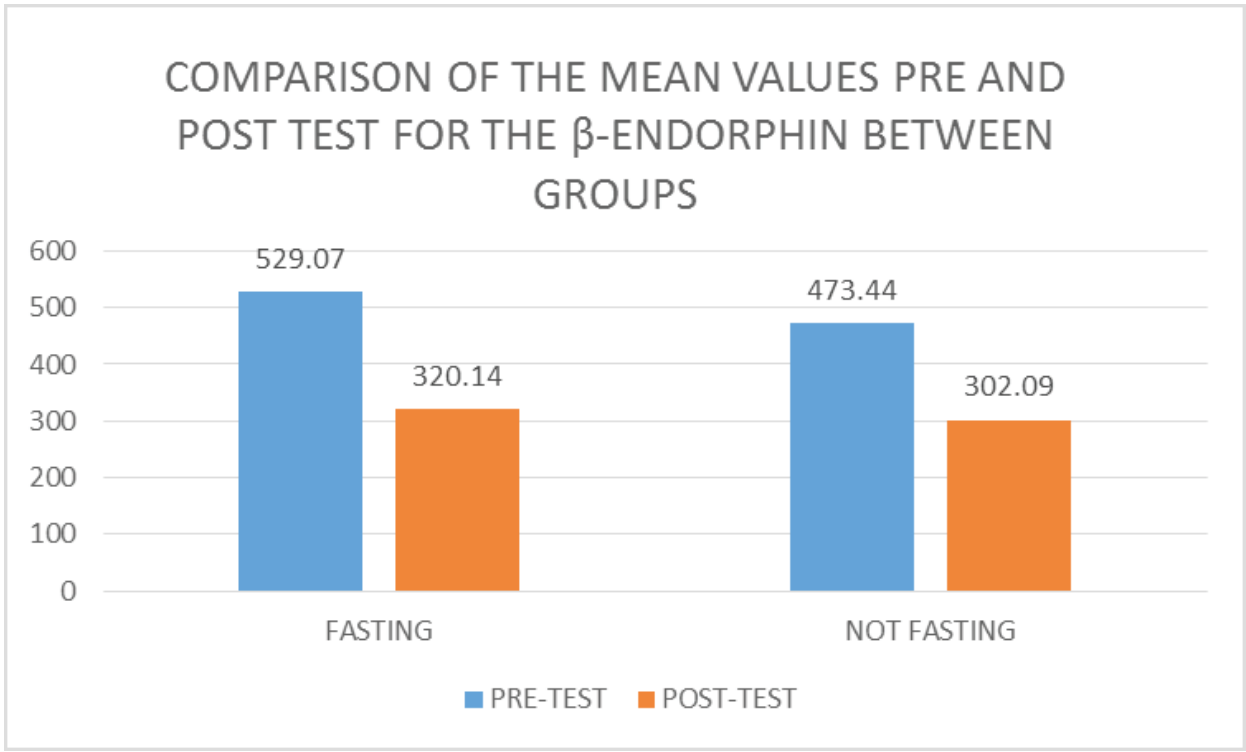

Figure 4 The comparison between mean values of the pre and post-test data for the β-endorphins

The mean values of the cortisol in figure 1 show that the mean values of the post-test cortisol level in the fasting group were lower than the non-fasting group, while figure 3 shows that in both groups the mean values were decreased at the end of the study.

The β-endorphins mean values in figure 2 show that the post-test β-endorphins mean values in the fasting group were higher than the non-fasting group, while in figure 4 it shows that in both groups the mean values were also decreased at the end of the study.

Table 3: The comparison between-time (pre and post-test) and between-group (fasting and non-fasting) for the mean values of the cortisol and β-endorphins

Variable	Group	p Between-time	p Between-group
Cortisol	Fasting	0,01[a]	0,71[c]
	Not fasting	0,01 [a]	
β-endorphin	Fasting	0,03[b]	0,67[d]
	Not fasting	0,01 [b]	

Note : signicantly different, if p < 0,05; a : paired-T test; b : Wilcoxon signed-rank test; c : two independent samples T-test; d : Mann-Whitney-U test.

Data from the normality test of the cortisol variable showed that all data were normally distributed (p>0,05) in all control and treatment groups. This caused the test to be continued for a paired-T test to compare pre and post-test cortisol data for both groups. The results of the paired T-test were showed significantly different with p = 0,01 in both groups. Therefore the test to be continued with the two independent samples T-test, because the normality test of the delta pre and post-test was normally distributed. The result of the two independent samples T-test showed p = 0,71, which means there was no difference between groups.

Meanwhile, the data from the normality test of the β-endorphins variable showed that not all data were normally distributed (p>0,05) in all control and treatment groups, the test to be continued for non-parametric Wilcoxon-signed rank test to compare pre and post-test β-endorphins data for both groups. The results of the non-parametric Wilcoxon-signed rank test showed that there was a significantly different both in fasting (p=0,03) and non-fasting group (p=0,01). Therefore the test to be continued with the Mann-Whitney-U test, because the normality test of the delta pre and post-test was not normally distributed. The result of the Mann-Whitney-U test showed p = 0,67, which means there was no difference between groups.

The aim of this study was that Dawood's fasting for six consecutive weeks resulted in lower cortisol levels and higher β-endorphins levels than non-fasting. The results of this study found that the post-test mean values of cortisol levels in the fasting group were lower than the pre-test mean values, with a significant difference in comparison test as shown in table 3 using the paired T-test. The non-fasting group also showed the same results that the post-test mean of cortisol levels was lower than the pre-test mean, with a significant difference of comparison test as shown in table 3 using the paired T-test. Because of the significant differences between both groups, the test was continued with the comparison test between groups using two independent samples T-test. The result of two independent samples T-test was p = 0,71 (p<0,05), which was not found the difference between groups.

For β-endorphins levels, it is shown in table 2 that the post-test mean values of β-endorphins levels in the fasting group were lower than the pre-test mean values, with a significant difference in comparison test as shown in table 3 using the non-parametric Wilcoxon signed-rank test on both groups. Because of the significant

differences between both groups, the test was continued with the comparison test between groups using the Mann-Whitney-U test, and the result was p = 0,67 (p<0,05), which was not found the difference between groups.

This means that there are no differences between people who did the Dawood's fast (MADF) and did not on cortisol and β-endorphins levels in this study. This is presumably because research subjects come from the same environment, a boarding school dormitory where their activities are almost the same for all subjects. Apart from that, motivation by the source is also thought to be the cause of the absence of significant differences between the fasting and non-fasting groups.

Cortisol is a steroid hormone from the glucocorticoid class which is produced by cells in the fasciculate zone of adrenal glands in response to the stimulation of the ACTH hormone secreted by the anterior pituitary gland. Cortisol is a hormone that responds to stress received by the body[18,19]. The high production of adrenal hormones and catecholamines will result in a narrowing of the heart blood vessels and an increased heart rate and ultimately will result in disrupted blood supply to the heart. Prolonged stress can increase the production of the cortisol hormone in large quantities by the body, which has been shown to cause decreased endurance and decreased cognitive function. Coronary heart disease sufferers usually tend to have higher stress levels[20]. Hypertension, mental-emotional disorders, and diabetes mellitus (DM) are the dominant risk factors for CHD in Indonesia[3]. Adult stress appears to have a more influential role in triggering cardiovascular events[21].

The Dawood's fast (MADF) ought to change a person's stress perception by increasing the stress threshold value, which results in people who undergo Dawood's fast not easily complaining of stress. Although from the comparison test between-groups there was no significant difference, it can be seen in figure 3 that the difference between pre and post-test mean values in the fasting group was greater than in the non-fasting group. This shows that although the statistical results did not differ significantly between groups, the decrease in cortisol levels in the fasting group was greater than the non-fasting group.

β-endorphins are neuropeptide hormones derived from proopiomelanocortin (POMC) neurons which are mostly produced in the anterior pituitary and the brain. β-endorphins have been identified in human plasma, and their release to the circulation in response to stress and pain is well known, but β-endorphins are rapidly degraded by blood proteases. β-endorphins can increase with exercise and increase more if accompanied by loud music but decreased if excessive exercise[12]. β-endorphins are mainly used in the body to reduce stress and maintain homeostasis. This is corresponding with the research conducted by Lahdimawan, et al. (2013)[12] which showed an increase in β-endorphins levels after Ramadhan fasting in healthy humans and PBMC.

Levels of β-endorphins are positively related to feelings of pleasure or happiness and sincerity. The greater the feeling of happiness, the higher the level of β-endorphins in the peripheral blood, the greater the sense of sincerity, the greater the feeling of happiness. So the greater the sense of sincerity, the higher the β-endorphins levels in plasma. Although the results of the statistical test in table 3 showed that there was no difference between the fasting and non-fasting groups, it can be seen in figure 2 that the pattern of changes in plasma β-endorphins levels was similar in both groups. This is presumably duet o the motivation given by the informants as well as similar conditions to subjects who live in the same environment (the dormitory) and have almost the same activities. The pattern of changes in the mean values of β-endorphins levels was seen to increase up to 3rd week in both groups, then decreased after 3rd week until the end of the study. The possibility that what happened is that there was a change in the sincerity that occurred after the 3rd week of the study that affected the plasma β-endorphins levels until the end of the study. The changes of sincerity can be related to increased activities or other things that can not be predicted. This is one of the limitations of the study, which was unable to measure the levels of happiness or sincerity of the subjects.

Conclusion

There was no difference in cortisol and β-endorphins levels in healthy young adult subjects undergoing Dawood's fast due to the influence of the same environmental conditions and a change in the sincerity

of the subjects. A longer fasting time may be needed to make a meaningful difference between groups, in addition to that is necessary to conduct a study on people who did Dawood's fasting for over 1 year compared to people who have never fasted at all.

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