ELECTRIC SHOCK INCREASES VCAM AND MCP IN MICE ENDOTHELIAL BLOOD VESSEL

Binti Yunariyah
Health Polytechnique, Ministry of Health Surabaya
Diploma Program in Nurse, Tuban

ABSTRAK

Stroke adalah gangguan saraf yang disebabkan oleh beberapa faktor. Seperti infeksi pada organ tubuh, proses regenerasi sel, masalah genetik, dan sirkulasi darah yang abnormal, kesemuanya menyebabkan aterosklerosis, yang dimulai dengan disfungsi endotel. Dari faktor-faktor tersebut, yang paling dominan adalah stres biologis. Sejauh ini, mekanisme disfungsi endotel pada kondisi stres dalam kehidupan modern belum diuraikan. Penelitian ini dilakukan pada hewan coba, yang terdiri dari 27 sampel dan dibagi menjadi 3 Groups. Untuk membuktikan peningkatan VCAM dan MCP pada mencit stres akibat perlakuan stressor sengatan listrik selama 15 hari, penelitian ini menggunakan pendekatan eksperimental dengan memberikan stres berat, yaitu sengatan listrik, selama 15 hari. Setelah perawatan berakhir, hewan coba dikorbankan dan jantungnya diambil untuk selanjutnya dilakukan pemeriksaan imunohistokimia untuk VCAM dan MCP, serta hematoxylin eosin untuk sel busa. Hasil uji ANOVA menunjukkan bahwa VCAM, yang dibandingkan antara Groups posttest dan pretest, memiliki perbedaan signifikan (p < 0,05). MCP pada Groups posttest dan pretest menunjukkan perbedaan signifikan (p < 0,05). T-test untuk sel busa pada Groups posttest juga menunjukkan perbedaan signifikan (p < 0,05). Penelitian ini telah membuktikan bahwa stressor sengatan listrik meningkatkan VCAM, MCP pada sel endotel dan sel busa pada pembuluh darah pada jantung mencit. Simpulan, sengatan listrik berpengaruh terhadap disfungsi endotel pada VCAM dan MCP pada endotelium pembuluh darah serta pembentukan sel busa pada pembuluh darah arteri jantung pada mencit Balb/c. ***(FMI 2014;50:164-171)***

Kata kunci: *sengatan listrik, disfungsi endotel, VCAM, MCP, sel busa*

ABSTRACT

Stroke is a nervous disorder resulting from several factors, such as infection in body organs, cell regeneration process, genetic problems, and abnormal blood circulation, causing atherosclerosis, which is started with endothelial dysfunction. From those factors, the most predominant is the biological stress. So far, the mechanism of endothelial dysfunction in distress in modern life has not been elaborated. This study was performed to experimental animals, comprising 27 samples, which were divided into 3 groups, in the effort to prove the increase of VCAM and MCP in distress mice due to treatment with stressor of electric shock for 15 days. This study used experimental approach by giving severe stress, presenting as electric shock, for 15 days. After the treatment ended, the animals were sacrificed and the heart was taken and subjected to immunohistochemical examination for VCAM and MCP, and hematoxylin eosin for foam cell. Result of ANOVA test revealed that VCAM, subjected to comparative test between posttest and pretest group, had significant difference (p < 0.05). MCP subjected to comparative test between posttest and pretest group revealed significant difference (p < 0.05). T-test in foam cell in posttest group also showed significant difference (p < 0.05). This study has proved that electric shock stressor increased VCAM, MCP in endothelial cells and foam cell in blood vessel in mice heart. In conclusion, electric shock has effect on endothelial dysfunction in VCAM and MCP in blood vessel endothelium and the formation of foam cell in cardiac arterial blood vessel in Balb/c mice. ***(FMI 2014;50:164-171)***

Keywords: *electric shock, endothelial dysfunction, VCAM, MCP, foam cell*

Correspondence: Binti Yunariyah, Health Polytechnique, Ministry of Health, Surabaya, Diploma Program in Nurse, Tuban. e-mail: bintiners@yahoo.com

INTRODUCTION

Modern life is full of challenges and tough competition is a stressor conditions that lead to distress in young and productive people. Many young people who are not able to manage the conditions of distress they experienced. It may finally lead to ischemic stroke (Yastroki 2007). Stroke is a serious health problem in modern times it is today. It resulted in the prevalence of stroke increased and resulted in morbidity and mortality of the patients. It is apparently a condition that require special attention. (Wong 2003). Stroke is the third leading cause of death in the UK, accounting for more than 60,000 deaths each year. It is also the single most cases that cause disability. More than 250,000 people are living with disability due to stroke. Stroke is a brain attack which arise due to sudden blockage or rupture of blood vessels of the brain. Stroke is a neurological disorder caused by several things, eg infections in organs, cell regeneration, genetic problems and disorders of blood circulation

resulting in atherosclerosis that begins with endothelial dysfunction (Al Rashid 2007). The most dominant factor for stroke is a biological stress. However, the mechanism of occurrence of endothelial dysfunction in a state of distress in modern life cannot be explained.

Modern society with high living demands further increase the frequency of biological stress. If it is not addressed, it is estimated there will be a positive correlation with the incidence of stroke. From the results of research conducted for 7 years to more than 20,000 people, there were 452 stroke patients and more than 100 were due to stress in their lives (Al Rashid 2007). An estimated 150,000 people in the UK suffer from stroke each year. In Indonesia, the number of stroke patients was 212,000 people. The number of stroke patients is increasing every year, especially in young and productive people. It is estimated that every year as many as 500,000 people have a stroke. Approximately 25%, or 125,000, people died and the rest suffered from mild or severe disability. A proportion of 80% of stroke patients had blockages and 60% of them were due to stress (Yastroki 2007).

In patients who experience stress, hypothalamus releases corticotropin-releasing hormone (CRH) and noradrenergic neuron. Furthermore, CRH stimulates the secretion of norepinephrine through specific receptors and norepinephrine stimulates the secretion of CRH primarily through 1 adrenergic receptors. CRH also stimulates the secretion of corticotropin through anterior corticotrop. Increased pituitary secretion of norepinephrine, epinephrine and dopamine causes vasoconstriction. Vasoconstriction is influenced by shear stress so that endothelial cell nitric oxide synthase is declined, thus decreasing (eNOS) the nitric oxide (NO). A decrease in the formation of NO may result in endothelial dysfunction, although eNOS are constitutively expressed and remains modulated by shear stress, increased low density lipoprotein cholesterol (LDL) also plays an important role in endothelial dysfunction. Endothelial cells would then secrete chemotactic factors, such as monocyte chemotactic protein 1 (MCP-1), monocyte differentiation factors, such as macrophage colony stimulating factor (MCSF) and stimulated to express vascular cell adhesion molecule (VCAM-1). With the monocyte adhesion molecules that would stick to the walls of blood vessels and suppress fat captured by macrophages, accumulation of lipids in the macrophage foam cells will occur, foam cells produce proliferating IL-1 in smooth muscle, resulting in atherosclerosis (Wijaya 2002). Endothelial damage causes changes in endothelial permeability, so that powerful blood flow can cause the release of endothelial cells, resulting in direct relationship between blood components and the walls of the arteries. The affected artery become atherosclerotic, narrowing, causing ischemic blockage, and lack of oxygen that cause stroke.

Because this study could not be applied to humans, since it is impossible to implement a biopsy, this research used experimental animals of the mice *Mus musculus* BALB/C as a model. The mice were stressed with electric shock treatment. The trigger occurs when stress is done for 15 days.

MATERIALS AND METHODS

The study was conducted as pure experimental study. This study used completely randomized design. Experimental animals were used by criteria: mice of *Mus musculus* BALB/c, gender: male, weight 25-35 grams, aged: 8 weeks. Mice's health can be observed from quite agile movements, lethargy, clean skin and unharmed, bright eyes and not glazed. Type of food: pellet CP 511, with distilled water as drink. Treatment of mice: food pellet was provided 10g/head/day, giving ad libitum drinking 1 liter/3 days to nine mice. Replacement hulls for bedding 2 days. For cage sanitation, the cages were cleaned every day, the temperature was corresponding to the temperature of space, ample ventilation and sunlight, no humidity.

Electric shock was a device made of glass shaped box with a size of 50 x 45 x 25 cm and the base of the copper plate was given with electric current of 0.8 mA to provide treatment in experimental animals for 15 days. The mice were sacrificed by means of decapitation, an act of euthanasia in animals using physical methods. Decapitation with scissors or a knife, this method is effectively done in mice because there are not any chemicals and the method is fast and inexpensive.

Plastic covered wire cage box 27 pieces, 1 box for 1 mice and each equipped with a place to eat and drink bottles, digital scales, copper plates, a set of tools for examining mice's heart, a set of tools that have been calibrated for examination and VCAM levels of MCP on and endothelial cell foam in blood vessels.

The mice *Mus musculus* BALB/c as many as 27 animals were adapted/acclimatization in advance for 1 week to get accustomed to living in a new environment, if there was a sick mice, it was removed from the cage, and then randomly assigned into 3 groups, each group consisting of nine mice, pretest group and the untreated control group while the posttest was given by electric shock treatment for 15 days with the dose increased gradually, after the completion of the trial by a certain time period measured VCAM, MCP and foam cells in the

endothelium of blood vessels of the group pretest (O1), group control (O2), or a group posttest with treatment (O3).

The data were tabulated and analyzed with descriptive statistics to describe the characteristics of variables, homogeneity of variance test to determine the condition before treatment equal to the entire group, the normality test to determine the distribution of the data obtained from the population that is normally distributed. To test the effect of the treatment we performed by one-way ANOVA.

RESULTS

This study was an experimental study using experimental animals mice (*Mus musculus*) Swiss Webster strain (BALB/c) males. The weight mean of males BALB/c mice used in each group are shown in Table 1.

Table 1. Weight Mean and SD of male BALB/c mice (g) (ANOVA)

Groups	n	Berat Badan (gram)		Min	Max	Sig
		Mean	SD			
Pre	9	30.44	2.789	25.000	34.000	
Control	9	29.56	2.698	25.000	34.000	P = 0.722
Pos	9	29.44	3.087	25.000	34.000	

Table 2. VCAM mean and SD in endothelial cells of blood vessels in the heart of BALB/c mice (ANOVA)

Groups	n	VCAM (per endothelial cells)		Min	Max	Sig
		Mean	SD			
Pre	9	1.33[a]	1.000	0	3	P = 0.000*
Control	9	1.67[a]	1.225	0	3	
Pos	9	6.89[b]	1.537	5	9	

Notes: * sig. at α = 0.05
[a, b] Different superscripts mean the column showed significant differences between groups.

Table 3. MCP mean and SD on vascular endothelial cells in the heart of BALB/c mice (ANOVA)

Groups	n	MCP (per endothelial cells)		Min	Max	Sig
		Mean	SD			
Pre	9	1.56[a]	0.882	0	3	
Control	9	2.11[a]	0.782	1	3	P = 0.000*
Pos	9	7.00[b]	1.225	5	9	

Notes: * sig. at α = 0.05
[a, b] Different superscripts mean the column showed significant differences between groups.

Table 4. Foam cells mean and SD in the blood vessels of the heart BALB/c mice

Groups	n	Foam Cell (per foam cells)		Min	Max	t-test sample
		Mean	SD			
Pre	9	0	0	0	0	
Control	9	0	0	0	0	P = 0.000*
Pos	9	7.44	1.740	5	10	

Notes: * sig. at α = 0.05

Based on Table 1 it can be seen that the mean body weight of mice BALB/c males (g) in the pretest group was 30.44 ± 2.789 gram; the control group was 29.56 ± 2.698 gram and posttest group were given electric shock treatment was 29.44 ± 3.087 gram. Distribution of normality test weight survey data using the Kolmogorov-Smirnov test was to determine the type of hypothesis test to be used. If a test has a probability value greater than 0.05 ($p > 0.05$) means data distribution was normal. Analysis results obtained that the whole weight of research data were normally distributed ($p = 0.839$; $p > 0.05$). Then we did the homogeneity test weight BALB/c mice males using one way ANOVA test to determine the origin of a sample of the population is homogeneous or not. Results of the analysis found that there was no difference in body weight in all groups ($p = 0.722$; $p > 0.05$). This suggests that the samples come from a homogeneous population.

Figures 1 and 2 can be seen in the results of immunohistochemistry to detect an increasing number of VCAM in endothelial cells in blood vessels of the heart of BALB/c mice, using VCAM monoclonal antibody with 400 x magnification. Positive results are indicated by brown thread. Figure 3 and 4 can be seen the results of immunohistochemistry to detect an increase in the amount of MCP in endothelial cells in blood vessels of the heart of BALB/c mice, using monoclonal antibodies MCP with 400 x magnification. Positive results are indicated by brown thread. Figure 1 shows the results of hematoxylin eosin staining (HE) to detect Foam Cell existing in the arteries in the heart of BALB/c mice, with a magnification of 400 x. Positive results are foam cells (small holes nodes).

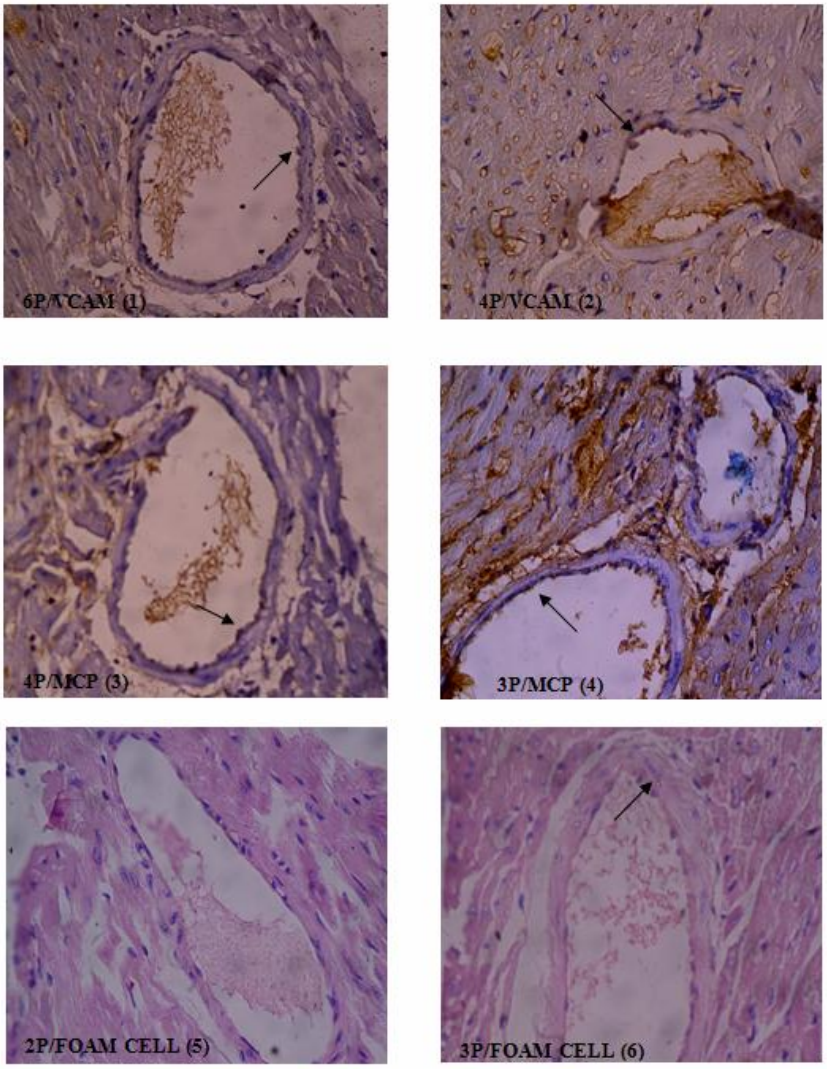

Figure 1. The results of immunohistochemical staining (IHC) and hematoxylin eosin (HE)

Distribution normality test VCAM research data using the Kolmogorov-Smirnov test to determine the type of hypothesis test to be used. If a test has a probability value greater than 0.05 ($p > 0.05$) means the normal distribution of data. Results of analysis obtained that all research data VCAM normal distribution ($p = 0.194$; $p > 0.05$). Then test the homogeneity of variance VCAM in endothelial cells of blood vessels in the heart BALB / c mice. Results of the analysis found that there was no difference VCAM variance in all groups ($p = 0382$; $p > 0.05$). Furthermore, VCAM research data were analyzed using one way ANOVA test to test the difference in the mean number of VCAM in endothelial cells of blood vessels in the heart of mice Balb/c males between groups significant difference ($p = 0.000$; $p < 0.05$), followed by LSD (Least Significant Difference) to determine differences between groups.

Distribution normality test MCP research data using the Kolmogorov-Smirnov test to determine the type of hypothesis test to be used. If a test has a probability value greater than 0.05 ($p > 0.05$) means the normal distribution of data. Results of analysis obtained that all research data MCP normal distribution ($p = 0.070$; $p > 0.05$). Then test the homogeneity of variance MCP endothelial cells in blood vessels of the heart BALB/c mice. Results of the analysis found that there was no difference in MCP variance in all groups ($p = 0.567$; $p > 0.05$).

Furthermore, MCP research data were analyzed using one-way ANOVA to test for differences in the mean number of MCP endothelial cells in blood vessels in the heart of mice Balb/c males between groups significant difference ($p = 0.000$; $p < 0.05$), followed by test LSD (Least Significant Difference) to determine differences between groups.

Based on table 4 it can be seen that the mean number of foam cells in the arteries of heart BALB/c mice in the untreated group pretest is 0; the untreated control group is 0; posttest group were treated (electric shock) was (7.44 ± 1.740). Distribution normality test Foam Cell research data using the Kolmogorov-Smirnov test to determine the type of hypothesis test to be used. If a test has a probability value greater than 0.05 ($p > 0.05$) means the normal distribution of data. Results of the analysis of the data obtained that all research results Cell Foam normal distribution ($p = 0.941$; $p > 0.05$). Furthermore Foam Cell research data were analyzed using a one sample T-test Test to test for differences in the mean number of Foam Cell in the blood vessels in the heart of BALB/c mice between groups and when there are significant differences continued distinguished by 0.

DISCUSSION

Biological stressors may contribute to or even cause physical abnormalities answer. The concept of stress and mental pressure applied in physiological stress also estimates involves various physiological factors, stating that the physical and emotional stressors can lead to stress.

The vascular endothelial cells metabolically responsive. Vascular endothelial layer can adjust the volume of the vascular lumen of smooth muscle cells in blood vessels. It started from the stimulation and activation of vascular endothelial when continuously taking place will result in a condition known as endothelial dysfunction. One of the important components that play a role in endothelial-dependent vascular relaxation is nitric oxyde (NO), NO did not play a role in the relaxation of smooth muscle, but also inhibits the activation, adhesion, and platelet aggregation, as well as the prevention of vascular smooth muscle cell proliferation and adhesion of leukocytes to endothelium layer (Cotran 2002). A stressor may affect some organelles of a cell simultaneously at one time or sequentially, while other stressors may only be able to attack specific to a particular organelle (Constatinides 1994).

In this research using experimental animals with severe stressors administration in the form of electric shock for 15 days by means of an electric current AC (Alternating Current) power supply voltage of 220 Volt and a frequency of 60 Hz via a copper wire in the cage plate treatment of 0.8 mA. The amount of the provision based on the research of electric shock Elyana (2001). This is to determine endothelial dysfunction can be measured by the increase in the number of VCAM and MCP in vascular endothelium which is the number of endothelial cells that express VCAM and MCP by Immunohistochemistry method (CPI) and to determine the formation of foam cells (foam cells) by using hematoxylin eosin (HE) the blood vessels in the heart.

Based on the table 2, after statistically analyzed according to the results of research data distribution normality test VCAM using Kolmogorov-Smirnov test obtained that all research data VCAM normal distribution ($p = 0.194$; $p > 0.05$), so that the truth can be recognized. This means that the animal is not treated stressor electric shock seemed no increase in the amount of VCAM in endothelial cells that react positively on pretest group and the control group. When viewed from the group posttest treated stressor (electric shock) with pretest group significant differences ($p = 0.000$; $p < 0.05$), indicating that the experimental animals were given electric shock treatment stressors may trigger an increase in the number of VCAM vascular endothelial

cells in the heart. VCAM is one important indication to determine endothelial dysfunction. Given the complexity of the stages of formation is needed to produce an optimal bioavailability of NO, then track the formation of NO is very susceptible to vascular events, and can be affected by multifactorial mechanism, which in turn leads to endothelial dysfunction. When vasorelaxation effect caused by endogenous NO could not overcome the effects of vasoconstriction produced by various mediators, resulting in disruption of the endothelium-dependent vasodilation, then this picture is characteristic of endothelial dysfunction (Ganong 2000). VCAM very important role in binding monocytes in the blood vessel wall surface (Kuby 2000). If there is accumulation of monocyte surface of the blood vessel wall, the monocytes will release pro-inflammatory mediators, especially interleukin-1 (IL-1). IL-1 has a very important role in triggering the proliferation of smooth muscle in the walls of blood vessels (Wijaya 2002).

Increased VCAM and ICAM expression in endothelial indicates endothelial dysfunction syndrome. Inflammatory mediators such as TNF, IL-1 will activate an increase in the expression of VCAM in endothelial cells. In a state of distress that can promote activation or endothelial dysfunction, and induces the expression of adhesion molecules VCAM thus spurring the migration of monocytes. In vitro, LDL-ox induce endothelial VCAM, then accumulated into the intima (Libby 2000). Thus, the research hypothesis which states that the stressors of electric shock increases the amount of VCAM in endothelial cells of blood vessels in the heart of BALB/c mice proved.

Based on Table 3, after statistically analyzed according to the results of research data distribution normality test MCP using the Kolmogorov-Smirnov test obtained that all research MCP data had normal distribution ($p = 0.070$; $p > 0.05$), so that the conclusions drawn can be regarded as truth. MCP homogeneity test results in vascular endothelial cells in the heart of mice Balb/c males using one way ANOVA test (analysis of variance) found that there was no difference in MCP in all groups ($p = 0567$; $p > 0.05$), this show that the data is homogeneous, so that the variation in the analysis were as a result of treatment. Under these conditions, followed by using one way ANOVA test to test the difference in the mean number of VCAM in endothelial cells of blood vessels in the heart of BALB/c mice between groups significant difference ($p = 0.000$; $p < 0.05$), followed by LSD (Least Significant Difference) that the mean number of VCAM in endothelial cells that react positively to the group pretest had no differences from that in the control group ($p = 0.241$; $p > 0.05$); as well as in the control group did not differ from group pretest ($p = 0.241$; $p > 0.05$), this means that the animal is not treated stressor electric shock seemed no increase in the amount of MCP in endothelial cells that react positively to the group pretest and the control group. When viewed from the group posttest treated stressor (electric shock) with pretest group significant differences ($p = 0.000$; $p < 0.05$), indicating that the experimental animals were given electric shock treatment stressors may trigger an increase in the amount of MCP in vascular endothelial cells in heart. MCP is one important indication to determine endothelial dysfunction. Given the complexity of the stages of formation, it is needed to produce an optimal bioavailability of NO, then track the formation of NO is very susceptible to vascular events, and can be affected by multifactorial mechanism, which in turn leads to endothelial dysfunction. When vasorelazation effect caused by endogenous NO could not overcome the effects of vasoconstriction produced by various mediators, resulting in disruption of the endothelium-dependent vasodilation, then this picture is characteristic of endothelial dysfunction (Ganong 2000).

In this condition, the hypothalamus releases corticotropin-releasing hormone (CRH) and Nor Adrenergic Neuron. Furthermore, CRH stimulates the secretion of norepinephrine through specific receptors and norepinephrine stimulates the secretion of CRH primarily through 1 adrenergic receptors. CRH also stimulates the secretion of corticotropin through corticotrop anterior. The increase of pituitary secretion of norepinephrine, epinephrine and dopamine causes vasoconstriction. Vasoconstriction is influenced by shear stress so that endothelial cell nitric oxide synthase (eNOS) decreased nitric oxide (NO) (Wijaya 2002). A decrease in the formation of NO may result in endothelial dysfunction, although eNOS are constitutively expressed, remains modulated by shear stress, increased low density lipoprotein cholesterol (LDL) also plays an important role in endothelial dysfunction. Endothelial cells would then secrete chemotactic factors such as monocyte chemotactic protein 1 (MCP- 1).

Lipoproteins are modified and will be captured by macrophages and lipid accumulation in macrophages will cause the foam cells. Furthermore, endothelial cells and smooth muscle cells would secrete chemotactic factors such as monocyte chemotactic protein I (MPC-I) and monocyte differentiation factors such as macrophage colony stimulating factor (MCSF). Macrophages, in turn, catch the oxidized LDL via the scavenger receptor and also a variety of factors (growth factors, cytokines, pro-oxidants and others) so that the process of atherogenesis continues (Wijaya 2002).

Nitric oxide (NO) is known to have a role in addition to maintaining vascular rhythm. It can also prevent oxidation of lipoproteins, so it is also an endogenous anti-sclerotic. In the normal state endothelial cells produce NO in considerable numbers to suppress the oxidation of LDL. In contrast to the situation hypercholesterolemia, or in atherosclerotic lesions, NO synthesis remained normal, but most of this nitric oxide will be eaten by superoxide radicals and oxidized LDL, and led to new LDL that were not protected against oxidation (Wijaya 2002).

Through product response of the endothelial cell layer, such as NO, the endothelium can perform its normal function, for setting as aspects of vascular homeostasis, including vascular tone, leukocyte interaction of blood vessels, smooth muscle cell growth and proliferation; as well as local haemostasis-fibrinolysis; redox status. Conversely, the vascular endothelial dysfunction obviously maladaptive result in a series of phenomena which resulted in an unfavorable vascular response. The effects of oxidative stress and redox status changes locally, is profibrinolytic vascular disorder, which resulted in the process of thrombogenesis. Interference modulation of cellular growth resulting in abnormal proliferation of vascular wall, stimulation of molecular adaptation inflammatory oxidant will boost the ability of monocyte adhesion and increased vascular permeability to plasma lipoprotein (Cotran 2002). Endothelial dysfunction is an early atherosclerotic lesions, which alter the inflammatory response homeostasis normal endothelium, into endothelial dysfunction with increased permeability and adhesiveness against lipoprotein, leukocytes, platelets and plasma content of another, mediated NO, spurring migration of leukocytes into the arterial wall is mediated by LDL-ox, MCP-1, MCSF (Ross 1999)

The biological stress can promote activation or endothelial dysfunction, and induces the expression of adhesion molecules (eg, VCAM-1) and chemokines (eg, MCP 1), thus spurring the migration of monocytes. In vitro, LDL-ox induces the expression of VCAM-1, and then accumulate in the intima, whereas MCP 1 (monocyte chemoattractant potent) induces migration of monocytes into the intima (Libby 2000). Thus, the research hypothesis which states that the stressors of electric shock increases the amount of MCP in the endothelial cells of blood vessels in the heart of BALB/c mice proved to be very significant.

Based on Table 4 statistical analysis appropriate distribution normality test results in Foam Cell research data using the Kolmogorov-Smirnov test obtained that all research data on foam cell had normal distribution ($p= 0.941$; $p < 0.05$), so that the conclusions drawn can be regarded as true. Under these conditions, followed by a test using one sample T-Test to test for differences in the mean number of foam cells in the arteries to the heart of mice Balb/c males between groups significant difference ($p = 0.000$; $p < 0.05$), then compared with the number 0.

Based on Table 4 shows that the mean number of foam cells in the arteries in the group pretest there is no cell foam (0) and the control group there were no cell foam (0). So as to test one sample T-Test on posttest group treated stressor (electric shock) no significant difference after doing different test with zero (0) is ($p < 0.000$; $p < 0.05$), this means that experimental animals which was given electric shock treatment stressor seemed contained foam cells in the arteries to the heart of mice Balb/c males. This occurs because of the monocyte adhesion molecules will stick to the walls of blood vessels and suppress fat then captured by macrophages and accumulation of lipids in the macrophage foam cells will lead to occur, foam cells produces IL-1 so that a proliferation of smooth muscle that causes athero-sclerosis (Wijaya 2002) ,

A decrease in the formation of NO may result in endothelial dysfunction. Although eNOS, an enzyme formation of NO, are constitutively expressed, but his expression is modulated by shear stress, lipoprotein atherogenetik, and cytokines. High LDL is the main injurer of endothelium and myocytes. LDL cholesterol can undergo oxidation, glycation, aggregation, binds to proteoglycans, or fused into immune complexes. LDL particles that enter into the intima may develop into a progressive oxidation of LDL-ox and phagocytosized by macrophages via the scavenger receptor (predators) on the cell surface. Phagocytosis causes the formation of lipid peroxides and facilitate the accumulation of esters cholesterol which results in the formation of foam cells. Thus, the activated foam cell and phagocytosis so happens modification of LDL by macrophages. Modified LDL (ox-LDL, aggregated LDL, LDL by immune complex) is also chemotactic for monocytes and can stimulate gene expression to MCSF and MCP are derived from the endothelium. Thus, a modified LDL can help expand the inflammatory response by stimulating the replication of monocyte-derived macrophages and monocytes new influx into the lesion and was instrumental in the formation of foam cells (Stary et al 2000).

Macrophages in atherosclerotic lesions produce excessive ROS such as O2, and able to induce the oxidation of LDL. Stress can promote activation or endothelial dysfunction, and induces the expression of adhesion molecules (eg, VCAM-1) and chemokines (eg, MCP 1), thus spurring the migration of monocytes. In

vitro, LDL-ox induces the expression of VCAM-1, and then accumulate in the intima, whereas MCP 1 (monocyte chemoattractant potent) induces migration of monocytes into the intima. Distress too, lowers the expression of eNOS, thus promoting the formation of foam cells (Aikawa 2002). In accordance with the results of the research data research hypothesis which states that the stressors of electric shock could prove to be a real can form foam cells in the arteries of the heart BALB/c mice is very significant.

CONCLUSION

In the blood vessels of mice, electric shock stressor increases in endothelial VCAM and MCP, and resulted in the formation of foam cells.

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