Research Article

Malondialdehyde Levels in Preeclampsia before and after Delivery

Kadar Malondialdehid pada Penderita Preeklamsia Berat sebelum dan sesudah Persalinan

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Abstract

Objective: Determine differences plasma levels MDA in preeclampsia before and 2 hours after delivery.

Methods: This was an analytic cross-sectional study. Subject consists of 23 pregnancies with preeclampsia, where 23 blood samples taken before delivery and 23 were taken 2 hours after delivery. This study was conducted from August 2016 until December 2016 at Department of Obstetrics and Gynecology Faculty of Medicine Universitas Sam Ratulangi / Prof. Dr. R. D. Kandou Hospital Manado and satellite hospital. Samples were taken from plasma and analysed using HPLC method at Prodia clinical laboratory.

Results: In patients with severe preeclampsia before delivery we found average value (1.4796 ± 0.40819 nmol/ml), minimum value (1.03 nmol/ml) and maximal value (2.77 nmol/ml) and 2 hours after delivery with average value (1.2470 ± 0.34324 nmol/ml), minimum value (0.91 nmol/ml), and maximum value (2.47 nmol/ml). by using Wilcoxon test, we found there were significant differences in plasma levels of MDA (p = 0.000).

Conclusion: This significant difference suggests that decreased plasma levels of MDA 2 hours after delivery and gives the sense that there is a relationship between oxidative stress of cells with severe preeclampsia before and shortly after delivery, that MDA is an indicator of oxidative stress.

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Keywords: malondialdehyde, oxidative stress, peroxidation lipid, preeclampsia

Abstrak

***Tujuan**: Menentukan perbedaan kadar plasma MDA pada preeklamsia sebelum dan 2 jam setelah persalinan.*

***Metode**: Penelitian ini merupakan penelitian potong lintang analitik. Subjek terdiri atas 23 kehamilan dengan preeklamsia, di mana 23 sampel darah diambil sebelum persalinan dan 23 sampel diambil 2 jam setelah persalinan. Penelitian ini dilakukan sejak Agustus 2016 sampai Desember 2016 di Bagian Obstetri dan Ginekologi Fakultas Kedokteran Universitas Sam Ratulangi / RSUP. Prof. Dr. R. D. Kandou Manado dan rumah sakit satelit. Sampel yang diambil dari plasma dan dianalisis menggunakan metode HPLC di laboratorium klinis Prodia.*

***Hasil**: Pada penderita preeklamsia berat sebelum persalinan kami menemukan rata-rata nilai (1,4796 ± 0,40819 nmol/ml), nilai minimum (1,03 nmol/ml) dan nilai maksimal (2,77 nmol/ml) dan 2 jam setelah persalinan dengan rata-rata nilai (1,2470 ± 0,34324 nmol/ml), nilai minimum (0,91 nmol/ml), dan nilai maksimum (2,47 nmol/ml). Dengan menggunakan uji non parametrik Wilcoxon, kami menemukan adanya perbedaan bermakna kadar plasma MDA sebelum dan 2 jam sesudah persalinan (p = 0,000).*

***Kesimpulan**: Perbedaan bermakna ini menunjukkan bahwa penurunan kadar plasma dari MDA 2 jam setelah melahirkan dan memberikan arti bahwa ada hubungan antara stres oksidatif sel dengan preeklamsia berat sebelum dan sesaat setelah persalinan, MDA merupakan indikator stres oksidatif.*

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***Kata kunci**: lipid peroksidase, malondialdehid, preeklamsia, stres oksidatif*

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INTRODUCTION

Preeclampsia is a disease characterized by increased blood pressure, proteinuria and oedema that occurs at age 20 weeks to 48 hours postpartum.[1-3] Preeclampsia is associated with the incidence and maternal and perinatal mortality rate both in the world and in Indonesia. Worldwide preeclampsia causes 50000-76000 maternal deaths and 900,000 causes perinatal deaths each year. According to WHO (World Health Organization). The incidence of preeclampsia in pregnancy is ± 5-10%, and became one of the three main causes of maternal mortality after bleeding and infection.[2,3] The incidence in Indonesia is 3.4 to 8.5% of all pregnancies and is still the number two cause of maternal and perinatal mortality rate highest (24%) after bleeding.[1,3]

To this date, even the theory of the etiology and pathogenesis of preeclampsia is still yet to be verified; thereby, preeclampsia is still described as

a "disease of theories".[4] One theory of the etiology of preeclampsia is currently an imbalance between the production of free radicals and antioxidant defense system causes oxidative stress (Hubel et al., 2006).[5] In conditions of oxidative stress, there will be increasing product of lipid peroxidation,[6] which is strongly suspected of instrumental cause endothelial function and the onset of clinical symptoms of preeclampsia.[6-8] Increased lipid peroxidation can be measured with various measurement markers lipid peroxidation in the blood, one using malondialdehyde (MDA),[9] which has been recognised as a clinical marker of lipid peroxidation.[10-12]

Currently, MDA is a marker of oxidative stress and lipid peroxidation in vivo the nicest and most stable, MDA have been found in almost all biological fluids, but the blood (plasma or serum) and urine is a sample of the most commonly used because it is most readily available, least invasive, and gives the same result accuracy and precision of the indices of oxidative stress (Nielson et al., 1997).[13] MDA is a marker of lipid peroxidation measurement of the most widely studied. MDA formed as a compound which is a secondary product or spoilage end of lipid peroxides in the body. Although various studies on the association of lipid peroxidation as a causative factor of preeclampsia has done a lot lately, but there is still disagreement about the increase in lipid peroxidation itself. Most studies of lipid peroxidation in preeclampsia, getting MDA levels were significantly higher in patients with preeclampsia and decreased after delivery. Several studies related, examines the MDA levels in patients with severe preeclampsia before and after delivery, and showed that MDA levels increased up to 24 hours after delivery and decreased significantly 48 hours after the delivery, (Kobe, et al, 2002).[14] (Kressig, et al., 2008) gain of 58 patients of which 20 patients and 38 controls weight preeclampsia found MDA levels at 24 hours after delivery, higher than the control group in patients preeclampsia.[15]

Measurement of markers of oxidative stress and lipid peroxidation is still an interesting study because it deals with prediction, risk, aetiology, and the intervention of preeclampsia. Research to see the differences in levels of MDA as a marker of lipid peroxidation in preeclampsia before and shortly after delivery is still rare in Indonesia, and has never worked at the Department of Obstetrics and Gynecology Faculty of Medicine Universitas Sam Ratulangi Prof. Dr. R. D. Kandou Hospital Manado, although the MDA until now has been recognized as a good clinical marker of lipid peroxidation in vivo.

OBJECTIVE

This study was conducted to determine the plasma levels of MDA in patients with preeclampsia before and shortly after delivery.

METHODS

This study was an analytic cross-sectional study with Wilcoxon test order to compare the plasma levels of MDA in preeclampsia before and 2 hours after delivery. This study was conducted and evaluated since August 2016 to December 2016 at Department of Obstetrics and Gynecology Faculty of Medicine Universitas Sam Ratulangi / Prof. Dr. R. D. Kandou Hospital Manado and satellite hospital in Manado to research subjects who meet the inclusion and exclusion criteria. Inclusion criteria were women with severe preeclampsia who will give birth, intra uterine fetal alive, willing to participate in the study by completing the informed consent form. Exclusion criteria were pregnant women with chronic hypertension, diabetes mellitus and refused to join the study. The subject of this study consisted of 23 pregnancy woman with preeclampsia. After anamnesis, physical examination and has signed informed consent, samples were taken from serum as much as 5 cc before and 2 hours after delivery, and put in a sterile sample container, centrifuged and stored in -20°C and then processed in Prodia Clinical Laboratory with HPLC (High-Performance Liquid Chromatography) analytic. This study also has been approved by the Integrated Health Research Unit of Prof. Dr. R. D. Kandou Hospital Manado. Data were analysed with SPSS version 22.0.

RESULTS

Table 1, shows that majority subject in woman with preeclampsia are most age ≥ 35 years old (12 patients, 52.18%), cases of gravidity 1 (12 patients, 52.18%), nullygravidity (12 patients, 52.18%), high school education (21 patients, 60.87%) and most jobs are housewife for (11 patients, 47.82%).

Table 1. Research Subject Characteristics

Characteristics	Severe Preeclampsia	
	n (23)	%
Age		
< 35 years	11	47.82
≥ 35 years	12	52.18
Gravidity		
1	12	52.18
2	4	17.39
3	3	13.04
4	1	4.35
5	3	13.04
Parity		
Nulligravida (0)	12	52.18
Primigravidity (1)	5	21.73
Multigravidity (2-4)	6	26.09
Abortion		
0	21	91.30
≥ 1x	2	8.70
Education		
Bachelor	4	17.40
High School	14	60.87
Junior High school	5	21.73
Occupation		
Government Employee	2	8.70
Student	3	13.04
House wife	11	47.82
Farmer	1	4.35
Privat Employee	6	26.09

Significant results were obtained between the systolic blood pressure in patients with severe preeclampsia before and 2 hours after delivery, with p = 0.000; and diastolic blood pressure in patients with severe preeclampsia before and 2 hours after delivery, with p = 0.008.

Table 2. Distribution of Variables Systolic and Diastolic Blood Pressure in Patients with Severe Preeclampsia before and 2 Hours after Delivery

Variable	Severe Preeclampsia		
	before delivery (n = 23)	two hours after delivery (n = 23)	p
Sistol (mmHg)	170.43 ± 8.779	155.22 ± 9.472	
Mean ± SD	160	0.000	
Minimum	190	140	
Maximum	105.22 ± 5.931	170	
Diastol (mmHg)	100		
Mean ± SD	100		0.008
Minimum	120	102.17 ± 4.217	
Maximum	110		

Table 3. Distribution of Variable Plasma Levels of MDA in Patients with Severe Preeclampsia before and 2 hours after Delivery

Variable	Severe Preeclampsia		
	before delivery (n = 23)	two hours after delivery (n = 23)	p
MDA (nmol/ml)			
Mean ± SD	1.4796 ± 0.40819		
Minimum	1.03 ± 0.91	1.2470 ± 0.34324	0.000
Maximum	2.77	2.47	

Significant results were obtained. Where the value of p = 0.000 for plasma levels of MDA in patients with severe preeclampsia before and 2 hours after delivery.

DISCUSSION

In this study based on the characteristics of the age (Table 1) distribution of the subjects obtained majority were age ≥ 35 years (12 patients, 52.18%). This is consistent with the literature that says that one of the risk factors of severe preeclampsia is age. Age over 35 years is vulnerable age for a pregnancy, because the physiological function of the organs of the body including the reproductive function begins to decline, in addition to the decrease in cardiac output induced contractions of the myocardium, coupled with other degenerative diseases can be debilitating condition of the mother, which can impair blood circulation of the mother to fetus.[2-4] These are the things that show that in women aged over 35 years is essentially a decline in physical conditions coupled with the burden of pregnancy can aggravate the risk factors of pathological conditions in pregnancy, including severe preeclampsia.[11]

The characteristics of parity, gravidity, and abortion (Table 1) is the most severe incident preeclampsia on nullipara (12 patients, 52.18%), and gravidity 1 (12 patients, 52.18%). This is consistent with the literature that explains that primigravid is one other risk factor for the occurrence of preeclampsia occurs preeclampsia.[4,15] In barriers trophoblast invasion into the decidua. As known trophoblast invasion is very important that decidua tissue becomes soft and loose, making it easier dilatation spiral arteries, if this does not happen, then the uteroplacental blood flow decreases, and there hypoxic and ischemic placenta.[6] During pregnancy, the placenta becomes the main source of oxidant and anti-oxidant synthesis endogen.[9,16] Decreased levels of antioxidants in the placenta may be one trigger of abortion, intrauterine growth and preeclampsia.[6,9,10] Data obtained from this study, (21 patients, 91.30%) samples not experiencing abortion.

Based on education and occupation characteristics (Table 1), most cases are high school (14 patients, 60.87%) and house wife (11 patients, 47.82%). It is different with some literature that explains that one of the causes of the high rate of maternal mortality caused by complications during pregnancy, childbirth and the puerperium, including severe preeclampsia. Influenced by education and occupations where there is a lack of knowledge about the whys and control of important complication before and after delivery in preeclampsia.[3,4]

In (Table 2), we found in the systolic blood pressure in patients with severe preeclampsia before delivery (170.43 ± 8.779 mmHg) and 2 hours after delivery (155.22 ± 9.472 mmHg), with p = 0.000; and diastolic blood pressure in patients with severe preeclampsia before delivery (105.22 ± 5.931 mmHg) and 2 hours after delivery (102.17 ± 4.217 mmHg), with p = 0.008. which means there were significant differences in the systolic and diastolic blood pressure before and 2 hours after delivery in severe preeclampsia. Increased systolic and diastolic blood pressure and correction proteinuria levels are an important consideration to determine prognosis in patients with preeclampsia/eclampsia.[1,2,17] (Llurba et al., 2004) suggests that 78 patients with severe preeclampsia as much as 33.4% showed an increase in blood pressure, mentions one theory that placental trigger preeclampsia, preeclampsia which will only happen if there is a placenta and improvement in the state began after the release placenta.[18] These results are supported by previous studies carried out by (Lumban Raja et al., 2013) which suggests that there was an increase systolic blood pressure at a time before and a decrease in systolic blood pressure after 24 hours of labor from 174.91 + 2.619 mmHg become 150.09 + 2.994 mmHg (p <0.001). Diastolic blood pressure also showed an increase before delivery and significantly decrease 24 hours after delivery from 107.27 mmHg become 93.36 mmHg (p <0.001). There are significant differences in systolic and diastolic blood pressure in preeclampsia before and after delivery.[19]

In the process of delivery, oxygenation comes from mother to fetus undergoing a process of oscillation, which causes unstable respiratory of the mother.[16] This instability caused by a weak period and shallow breathing during labor, where the conditions are like this will decrease the partial pressure CO2 in the arteries, when the uterus contracts, will cause changes in blood pressure in the blood vessels of the uterus, it is compounded by the response of pregnant women to pain and stress during birth, this response will lead to a state of

tissue hypoxia and ischemic tissue resulting in increased stress oxidative and produce free radicals that will influence the delivery process.[12] The lipid peroxide as oxidants or free radicals are highly toxic, will circulate throughout the body in the bloodstream and will damage the endothelial cell membrane, causing dysfunction endotel.[5] Been estimated previously that the release of certain factors from the placenta and increased resistance utero placental response to ischemia results in endothelial dysfunction in the maternal circulation (KM Sowinski, 2000).[20] Lipid peroxidation also induced in the placenta during pregnancy. The lipid peroxide generated from the trophoblast and villi chorealis be secreted into the mother's blood circulation, resulting in increased concentration in the mother's blood circulation which will cause an increase in plasma levels of MDA.[8,9] Previous studies provide data, plasma levels of MDA will decrease after delivery, (Nakai, et al, 2000) suggests these results show that the greatest possible placenta is a source of increased lipid peroxidation in pregnant women with preeclampsia, with the release of the placenta after delivery will provide an overview of the decrease in the levels of lipid peroxidation on the first day to the third day after delivery, there is no research has been conducted to assess the presence of lipid peroxide levels decrease shortly after delivery.[12]

In this study, we examined plasma levels of MDA in patients with severe preeclampsia before and 2 hours after delivery (Table 3), in patients with severe preeclampsia before delivery we found average value (1.4796 ± 0.40819 nmol/ml), minimum value (1.03 nmol/ml) and maximal value (2.77nmol/ml) and 2 hours after delivery with average value (1.2470 ± 0.34324 nmol/ml), minimum value (0.91 nmol/ml), and maximum value (2.47 nmol/ml) by using the non-parametric Wilcoxon test, we found there were significant differences in plasma levels of MDA (p = 0.000). This significant difference suggests that decreased plasma levels of 2 hours after delivery and gives the sense that there is a relationship between oxidative stress of cells with severe preeclampsia before and shortly after delivery.

This study has a relationship with some of the research that has been done before, where the research done by (Santoso et al, 2012) to get the plasma levels of MDA in patients with severe preeclampsia before delivery seem higher, and decreased after the 8th day after delivery with average levels of plasma MDA in pregnant women with severe preeclampsia amounted to 0.883 mol/ml, and amounted to 0.284 in women of severe preeclampsia 8th day after the delivery.[21] (Kressig et al., 2008) gain of 58 patients of which 20 patients severe preeclampsia and 38 controls found MDA levels at 24 hours after delivery, higher than the control group in severe preeclampsia.[15] (Kobe et al., 2002) suggests an increase in MDA levels were significantly non enzymatic accompanied by a decrease in antioxidants, such as Vitamin E, Vitamin C, and Vitamin-A in pregnant women who develop severe preeclampsia.[14] It may consider granting antioxidants in patients with severe preeclampsia, according to research conducted by (Roberts JM et al., 2010) that the provision of anti-oxidants such as vitamins A, B6, B12, C, E, FE, and folic acid, can lower blood pressure can reduce the risk of preeclampsia.[22]

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