Research Article

The Role of Giving High Dose Calcium for Preventing Preeclampsia

Peran Pemberian Kalsium Dosis Tinggi untuk MencegahTerjadinya Preeklamsia

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Abstract

Objective: Knowing the effectiveness of high doses of calcium in preventing preeclampsia.

Methods: Experimental analytical study with Randomized Controlled design Single-blind trial in the form of survival analysis (survival analysis) in the period June 2018 - May 2019 in fetomaternal outpatients clinic in Mohammad Hoesin Hospital, Palembang

Results: The mean hemoglobin level at the last visit found that the average hemoglobin level between the two groups was 12.81 in the high calcium group and 12.61 in the low calcium group, while the mean hematocrit level between the two groups was 35.17 in the high calcium group and 34.84 in the low calcium group and the respective calcium levels each group is 10.1. In this study, after high calcium intervention, no pregnant women with preeclampsia were found, whereas in the low-dose calcium intervention group it was found that 3 of 17 patients (17.7%) had preeclampsia. With the McNemar test it was found that there was no difference in the incidence of preeclampsia both after high-dose calcium and low-dose calcium interventions (p = 0.250).

Conclusions: High-dose calcium (1.5g - 2g) is effective in preventing preeclampsia and there was no difference in effectiveness between administration of high-dose calcium with low-dose calcium administration to the incidence of preeclampsia.

Keywords: high dose calcium, preeclampsia, randomized control trial.

Abstrak

Tujuan: *Mengetahui efektivitas pemberian kalsium dosis tinggi dalam mencegah preeklamsia.*

Metode: *Penelitian analitik eksperimental dengan desain randomized controlled trial single blind dalam bentuk ujian alias kesintasan (survival analysis) dalam kurun waktu Juni 2018 – Mei 2019 di Poliklinik Fetomaternal Rumah Sakit Umum Pendidikan Mohammad Hoesin, Palembang*

Hasil: *Rerata kadar hemoglobin pada kunjungan terakhir didapatkan rerata kadar hemoglobin antara kedua kelompok adalah 12,81 pada kelompok kalsium tinggi dan 12,61 pada kelompok kalsium rendah, sedangkan rerata kadar hematokrit antara kedua kelompok adalah 35,17 pada kelompok kalsium tinggi dan 34,84 pada kelompok kalsium rendah dan rerata kadar kalsium masing-masing kelompok adalah 10,1. Pada penelitian ini setelah intervensi kalsium tinggi tidak ditemukan ibu hamil yang mengalami preeklamsia, sedangkan pada kelompok intervensi kalsium dosis rendah ditemukan 3 dari 17 pasien (17,7%) menderita preeklamsia. Dengan uji Mc Nemar didapatkan hasil tidak terdapat perbedaan kejadian preeklamsia baik setelah intervensi kalsium dosis tinggi maupun kalsium dosis rendah (p = 0,250). Hal ini berarti kalsium dosis tinggi dan rendah efektif untuk mencegah preeklamsia.*

Kesimpulan: *Kalsium dosis tinggi (1,5g – 2g) efektif dalam mencegah preeklamsia dan tidak ditemukan perbedaan efektivitas antara pemberian kalsium dosis tinggi dengan pemberian kalsium dosis rendah terhadap kejadian preeklamsia.*

Kata kunci: *kalsium dosis tinggi, preeklamsia, randomized control trial.*

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INTRODUCTION

Preeclampsia is a specific multisystem disorder in pregnancy characterized by the development of hypertension and proteinuria after 20 weeks of pregnancy. Preeclampsia is a life-threatening disorder that only occurs during pregnancy, labour, and the postpartum period and is characterized by high blood pressure (hypertension) and protein in the urine (proteinuria). Preeclampsia is stated to have a significant effect on the morbidity and mortality of pregnant women and fetuses.[1]

According to WHO, the average incidence of preeclampsia in various countries in 2013 ranged from 0.51-38.4%. In developed countries, the incidence of preeclampsia ranges from 6-7%. The World Health Organization (WHO) estimated that there were 303,000 maternal deaths in the world in 2015. According to the MDG program, there has been a decline of 43% of maternal deaths in 1990. The prevalence of death caused by preeclampsia in 2000 in the world was 12%. In Indonesia itself according to the KIA report of the Directorate of Health Development for the Ministry of Health of the Republic of Indonesia in 2011, the incidence of preeclampsia is around 3.4-8.5%. The number of maternal deaths reported was 2,118. The cause of maternal death due to preeclampsia is around 25%. The maternal mortality rate in Indonesia is still high compared to ASEAN countries. Based on data from the Indonesian Demographic and Health Survey (IDHS) in 2012, the Maternal Mortality Rate (MMR) in Indonesia amounted to 395 per 100,000. The number of maternal deaths in 2015 in the city of Palembang, based on a report of 12 people from 29,011 live births (Profile of Basic Health Services, 2015). The causes were bleeding (41.7%), followed by pulmonary embolism (1 case), suspected cardiogenic shock (1 case), eclampsia (1 case), suspected TB (1 case), hypertension in pregnancy (1 case), and others.[2-5]

In addition to maternal deaths, preeclampsia also affects perinatal delivery, including preterm birth, stunted fetal growth or Intra Uterine Growth Retardation (IUGR), perinatal death and long-term morbidity of cardiovascular disease associated with low birth weight (LBW). The incidence of hypertension in pregnant women is caused by various causes including nutrients or nutrients contained in food. Calcium deficiency contributes to the occurrence of high blood pressure during pregnancy. WHO (2013) states that the administration of calcium to pregnant women is one way that can be used to prevent preeclampsia. Various studies have shown that high-dose calcium supplementation during pregnancy has a beneficial effect to reduce the risk of hypertension due to pregnancy or preeclampsia.[6,7] Therefore, researchers are interested in further analyzing the role of high-dose calcium to prevent preeclampsia at the Mohammad Hoesin General Hospital in Palembang.

METHODS

This study was a randomized control trial conducted in Palembang (Fetomaternal polyclinic / Department of Obstetrics and Gynecology Dr. Mohammad Hoesin Hospital) from June 2018 to May 2019. The population of this study were all pregnant women who performed antenatal care in Palembang (Department / Obstetric Department and Gynecology Hospital Dr. Mohammad Hoesin). The inclusion criteria in this study were pregnant women aged 20 - 35 years, gestational age 20 weeks, pregnant women with blood pressure <140/90 mmHg, pregnant women with blood calcium before the study was low or normal, pregnant women did not suffer from chronic and metabolic diseases, willing to take part in research and sign an informed consent sheet. The exclusion criteria in this study were pregnant women with blood calcium before high research. This study used univariate data analysis to determine the frequency of occurrence of preeclampsia in each sample group. In addition, bivariate analysis was also conducted to determine the role of high-dose calcium in preventing preeclampsia by identifying the effect of high-dose calcium for pregnant women on the incidence of preeclampsia. The bivariate analysis was carried out using McNemar's test. The analysis in this study was carried out using the SPSS 16.0 assistance program.

Works Procedure

First thing first, all women who meet the inclusion criteria were given an explanation of the research that will be conducted. Those who agreed to participate in this study were asked to sign informed consent that had been provided for the study, then all patients included in this study carried out recording complete patient data contained in the patient's medical records, then carried out anamnesis and physical examination

and laboratory support examinations (Hb, Ht and blood calcium). Blood collection was executed by phlebotomy, which was collected from the peripheral blood using a 5 mL syringe. Hematocrit and Hemoglobin were examined by a centrifuge technique using the electrical impedance method that was counting cells from whole blood and separating red blood cells and the returning elements of white blood cells (granulocytes, lymphocytes, and monocytes).

Meanwhile, calcium was carried out by the cresolphtein complex one method. Next up, pregnant women are randomly put into two groups. From 20 weeks of gestation to 35 weeks were assigned to the high-dose calcium group or treatment group who received 1500 mg of oral calcium per day, and the low-dose calcium group or comparison group that received 500 mg of oral calcium per day. This study used a parallel approach which was used as a comparison to use low-dose calcium. Calcium supplementation given was elemental calcium (calcium carbonate) given 1500 mg/day (3 tablets of 500 mg Calos in one meal), given to the treatment group of pregnant women. Then, as a comparison, 3 tablets were given to pregnant women, namely low-dose calcium supplementation which also used 500 mg of Calos / day (1 tablet of 500 mg Calos) and 1000 mg placebo (with the same size, weight, and colour as calcium carbonate) per day in one meal in the comparison group.

Accordingly, they were put into capsules of the same colour and different colour wrapping in each group. The next step, pregnant women were examined (follow-up) every 5 weeks until delivery. Supervision of compliance with calcium consumption in patients was done by contacting patients every week on the telephone and every 5 weeks face-to-face. Finally, blood pressure measurements were performed using a tool such as ABN Healthcare System® aneroid sphygmomanometer and Littman® Stethoscope.

RESULTS

Experimental analytical study with a Randomized Controlled Trial Single-blind design to determine the effectiveness of high doses of calcium in preventing preeclampsia has been carried out. The research sample that fulfilled the inclusion and exclusion criteria was 34 people. A total of 17 people received high-dose calcium and 17 others received low-dose calcium.

General Characteristics of Research

The average age of patients who received high calcium was 27.24 ± 2.86 years with a range of 20-31 years while the average age for receiving low-dose calcium was 27.94 ± 2.38 years with a range of 24-32 years. The statistical test showed that there was no age difference between patients who received high-dose calcium and low-dose calcium (p = 0.440). The average gestational age of patients who received high calcium was 22.53 ± 2.07 weeks with a range of 20-25 weeks while the average gestational age who received low-dose calcium was 22.71 ± 2.08 weeks with a range of 20-27 weeks. The statistical test showed that there was no difference in gestational age between patients who received high-dose calcium and low-dose calcium (p = 0.888). Obstetric characteristics of patients receiving high calcium include gravida of 1.92 ± 0.89 with ranges from 1-4, parity of 0.88 ± 0.86 with a range of 0-3 and an average incidence of abortion of 0.06 ± 0.24 with a range of 0-1 while in patients who received calcium dose gravida was obtained at 2.29 ± 1.10 with a range of 1-5, parity of 1.00 ± 1.12 with a range of 0-4 and a mean incidence of abortion of 0.29 ± 0.59 with a range of 0-2. The statistical test showed that there were no gravida differences (p = 0.354), parity (p = 0.940) and abortion (p = 0.145) between patients who received high-dose calcium and low-dose calcium and showed that the two groups were homogeneous.

In the distribution of labour in the study subjects, 58.8% of subjects gave birth spontaneously, 29.4% of subjects gave birth by section caesarean, and 11.8% of subjects who had not given birth in the high-dose calcium group, while there were as many as 52.9 % of subjects who gave birth spontaneously, 29.4% of subjects who gave birth by caesarean section and as many as 17.6% of subjects who had not given birth. From the analysis, there was no significant relationship between labour and calcium groups.

Table 1. General Characteristic of Research

Variable	Calcium		P-value*
	High Dose	**Low Dose**	
Age			
Mean ± SD	27.23 ± 2.86	27.94 ± 2.38	
Median (Min-Max)	27 (20-31)	28 (24-32)	0.440[a]
Gestational Age			
Mean ± SD	22.53 ± 2.07	22.71 ±2.08	0.888[b]
Median (Min-Max)	22 (20-25)	22 (20-27)	
Gravida			
Mean ± SD	1.94 ± 0.89	2.29 ± 1.10	0.354[b]
Median (Min-Max)	2 (1-4)	2 (1-5)	
Parity			
Mean ± SD	0.88 ± 0.86	1.00 ± 1.12	0.940[b]
Median (Min-Max)	1 (0-3)	1 (0-4)	
Abortion			
Mean ± SD	0.06 ± 0.24	0.29 ± 0.59	0.145[b]
Median (Min-Max)	0 (0-1)	0 (0-2)	
Labor			
Spontaneous	10	9	0.881[c]
Sectio Caesarean	5	5	
Have not given birth	2	3	

[a]*Independent T Test, p =0.05*, [b]*Mann Whitney Test, p =0. 05,*
[c]*Fisher's Exact Test, p =0.05*

Characteristics of Blood Pressure

In this study, the research subjects visited 4 times. The parameters examined included systolic and diastolic blood pressure. On the first visit, it was found that the mean systolic and diastolic blood pressure was 116/75 mmHg in the high-dose calcium group, and 112/74 mmHg in the low-dose calcium group. On the second visit, it was found that the mean systolic and diastolic blood pressure was 115/75 mmHg in the high-dose calcium group, and 114/74 mmHg in the low-dose calcium group. On the third visit, the mean systolic and diastolic pressure was 116/75 mmHg in the high-dose calcium group and 116/74 mmHg. On the fourth visit, the mean systolic and diastolic blood pressure was 116/75 mmHg in the high-dose calcium group and 120/76 mmHg in low-dose calcium. From the analysis test, there were no meaningful differences in the two groups each visit.

In this study, it was also found that there were 17 subjects (100%) subjects who had blood pressure <140/90 at the first visit to the fourth in the high-dose calcium group, whereas there were as many as 11 subjects (82.4%) who had blood pressure <140 / 90 on the first to the fourth visit and 3 subjects (17.6%) who had blood pressure> 140/90 in the low dose calcium group on the third visit which was 150/110 and 160/120 fourth visit.

Table 2. Characteristics of Blood Pressure

Blood Pressure	Calcium		P-value*
	High Dose	**Low Dose**	
First Visit			
Mean ± SD (Sistolik)	116.47±4.9	112.94±7.71	0.179
Mean ± SD (Diastolic)	75.29±5.14	74.11±5.07	0.498
Second Visit			
Mean ± SD (Sistolik)	115.88±5.07	114.11±7.12	0.543
Mean ± SD (Diastolic)	75.29±5.14	74.11±5.07	0.498
Third Visit			
Mean ± SD (Sistolik)	116.47±4.92	116.47±9.31	0.939
Mean ± SD (Diastolic)	75.29±5.14	74.70±5.14	0.735
Fourth Visit			
Mean ± SD (Sistolik)	116.47±4.92	120.58±17.12	0.939
Mean ± SD (Diastolic)	75.29±5.14	76.47±7.85	0.848

Independent T-test, p=0.05

Laboratory Characteristics of Research Subjects

In the distribution of hemoglobin levels for the calcium group, the mean haemoglobin level at the first visit between the two groups was 12.32. On the second visit, the mean haemoglobin level between the two groups was 12.46 in the high calcium group and 12.36 in the low calcium group. On the third visit, the mean haemoglobin level between the two groups was 12.64 in the high calcium group and 12.50 in the low calcium group. At the last visit, the mean haemoglobin level between the two groups was 12.81 in the high calcium group and 12.61 in the low calcium group. With statistical analysis, it was found that there was no difference in haemoglobin levels at the first visit (p = 1.000), second visit (p = 0.591), third visit (p = 0.392) and fourth visit (p = 0.279) between patients receiving high-dose calcium and low dose calcium.

In the distribution of hematocrit levels on the calcium group, the mean hematocrit levels at the first visit between the two groups were 34.47 in the high calcium group and 35.29 in the low calcium group, respectively. On the second visit, the mean hematocrit levels between the two groups were 34.47 in the high calcium group and 34.88 in the low calcium group. On the third visit, the mean hematocrit levels between the two groups were 34.76 in the high calcium group and 34.64 in the low calcium group. At the last visit, the mean hematocrit levels between the two groups were 35.17 in the high calcium group and 34.84 in the low calcium group. Based on statistical analysis it was found that there were no differences in hemoglobin levels at the first visit (p = 0.254), second visit (p = 0.305), third visit (p = 0.707) and fourth visit (p = 0.531) between

patients who received high-dose calcium and low dose calcium.

In the distribution of Calcium levels against the calcium group, the mean calcium levels at the first visit between the two groups were 8.81 and 8.68, respectively. On the second visit, the average calcium level between the two groups was 9.26 in the high calcium group and 9.00 in the low calcium group. On the third visit, the average calcium level between the two groups was 9.56 in the high calcium group and 9.35 in the low calcium group. At the last visit, the average calcium level of each group was 10.1. Based on calcium levels, there was no difference in calcium levels at visit-1 (p = 0.512), visit-2 (p = 0.151), visit-3 (p = 0.256) and visit-4 (p = 0.809) between patients who got high-dose calcium and low-dose calcium.

Table 3. Average Hemoglobin Levels per Visit

Laboratory Characteristics	Calcium		P-value*
	High Dose	**Low Dose**	
Hb First Visit			
Mean ± SD	12.32 ± 0.81	12.32 ± 0.44	1.000[a]
Median (Min-Max)	12.6 (11 – 13.5)	12.4(11.3 – 13.0)	
Hb Second Visit			
Mean ± SD	12.46 ± 0.67	12.36 ± 0.35	0.591[a]
Median (Min-Max)	12,5 (11,2 – 13.3)	12.4 (11.5 – 12.8)	
Hb Third Visit			
Mean ± SD	12.50 ± 0.46	12.50 ± 0.47	0.392[a]
Median (Min-Max)	12.6 (11,5 – 13.5)	12.6 (11.5 – 13.1)	
Hb Fourth Visit			
Mean ± SD	12.81 ± 0.42	12.61 ± 0.64	0.279[a]
Median (Min-Max**)**	12.8 (11.9 – 13.6)	12.7 (11.1 – 13.4)	
Hematocrit First Visit			
Mean ± SD	3447 ± 2.50	35.29 ± 1.49	0.254[a]
Median (Min-Max)	35.0 (30.0 – 38.0)	35.0 (33.0 – 38.0)	
Hematocrit Second Visit			
Mean ± SD	34.47 ± 1.06	34.88 ± 1.05	0.305[b]
Median (Min-Max)	34.0 (33.0 – 36.0)	35.0 (33.0 – 37.0)	
Hematocrit Third Visit			
Mean ± SD	34.76 ± 0.97	34.64 ± 1.41	0.707[b]
Median (Min-Max)	35.0 (33,0 – 36.0)	35.0 (32.0 – 38.0)	
Hematocrit Fourth Visit			
Mean ± SD	35.17 ± 1.23	34.94 ± 1.39	0.531[b]
Median (Min-Max)	35,0 (34,0 – 38,0)	35,0 (33.0 – 37.0)	
Calcium First Visit			
Mean ± SD	8.81 ± 0.59	8.68 ± 0.49	0.512[a]
Median (Min-Max)	8.7 (7.8 – 10.1)	8.7 (7.8 – 9.9)	
Calcium Second Visit			
Mean ± SD	9.26 ± 0.59	9,00 ± 0,41	0.888[a]
Median (Min-Max)	9.2 (8.2 – 10.6)	8.9 (8.2 – 9.6)	
Calcium Third Visit			
Mean ± SD	9.56 ± 0,56	9.35 ± 0.47	0.151[a]
Median (Min-Max)	9.5 (8.7 – 10.8)	9.4 (8.4 – 10.2)	
Calcium Fourth Visit			
Mean ± SD	10.1 ± 0.69	10.1 ± 1.04	0.809[b]
Median (Min-Max)	10 (9.1 – 11.2)	9.8 (8.8 – 12.8)	

Independent T-test, p=0.05[a], Mann-Whitney, p=0.05[b]

Comparison of the Effectiveness of High and Low Calcium Doses

In this study, after high calcium intervention, no pregnant women with preeclampsia were found, whereas in the low-dose calcium intervention group it was found that 3 of 17 patients (17.7%) had preeclampsia. With the McNemar test, it was found that there was no difference in the incidence of preeclampsia both after high-dose calcium and low-dose calcium interventions (p = 0.250). This means high and low calcium is effective for preventing preeclampsia.

DISCUSSION

The increasing incidence of preeclampsia in pregnant women is caused by various factors.

Risk factors that can increase the incidence of preeclampsia are hydatidiform mole, nulliparous, age less than 20 years or more than 35 years, more than one fetus, multiparas, chronic hypertension, diabetes mellitus or kidney disease. Preeclampsia is also influenced by parity, genetics and environmental factors.[3]

WHO (2013) states that the administration of calcium to pregnant women is one way that can be used to prevent preeclampsia. A review of 24 studies found that high doses of calcium supplementation (at least 1 g a day) during pregnancy from 13 studies involving 15,730 women were a safe and relatively inexpensive way to reduce the risk of preeclampsia, especially in women with low calcium diets who had increased risk preeclampsia. Women who receive calcium supplements also reduce their risk of dying or experiencing serious problems related to preeclampsia. Premature birth rates also dropped. The use of calcium supplements in pregnant women has no side effects. WHO recommends giving calcium to pregnant women by 1.5 g to 2 g every day for pregnant women who have low calcium intake. But several other studies suggest that administration of low doses of calcium can significantly reduce the risk of preeclampsia, reduce hypertension and reduce the number of babies with low birth weight babies.[2,7]

The average age of patients who received high calcium was 27.24 ± 2.86 years with a range of 20-31 years while the average age for receiving low-dose calcium was 27.94 ± 2.38 years with a range of 24-32 years. The average research subject he got was 27 years old, while the average age of the research subjects Crowther did was aged 24-25 years. This can be different because the study population is not the same. In addition to age, work and education level can affect the incidence of preeclampsia. Low-educated women were 86% more at risk of preeclampsia, while women with secondary education were 72% more at risk of preeclampsia, but the level of education might be a stressor in making decisions. Work was not related to the prevalence of preeclampsia in his study.[8-11]

The average gestational age of patients who received high calcium was 22.53 ± 2.07 weeks with a range of 20-25 weeks while the average gestational age who received low-dose calcium was 22.71 ± 2.08 weeks with a range of 20-27 weeks. The average gestational age for receiving calcium is 20 weeks' gestation, while the average gestational age in the Levine study is a 17-week gestational age range. The WHO recommends that calcium supplements be started for pregnant women at 20 weeks' gestation, based on the reference time used in the WHO meta-analysis. The mechanism of action of these calcium supplements postulates involving modulation of both placental vascularization and systemic vasomotor activity. Although this postulation has not been directly tested, it shows that periconceptional calcium supplementation may be more beneficial, and initiation from the age of 20 weeks of pregnancy.[2,12-14]

Obstetric characteristics of patients receiving high calcium include gravida of 1.92 ± 0.89 with ranges from 1-4, parity of 0.88 ± 0.86 with a range of 0-3 and an average incidence of abortion of 0.06 ± 0.24 with a range of 0-1 while in patients who received calcium dose gravida was obtained at 2.29 ± 1.10 with a range of 1-5, parity of 1.00 ± 1.12 with a range of 0-4 and a mean incidence of abortion of 0.29 ± 0.59 with a range of 0-2. The statistical test showed that there were no gravida differences (p = 0.354), parity (p = 0.940) and abortion (p = 0.145) between patients who received high-dose calcium and low-dose calcium and showed that the two groups were homogeneous.

In the distribution of subjects to the calcium group, at the first visit, it was found that the mean systolic and diastolic blood pressure was 116/75 mmHg in the high-dose calcium group, and 112/74 mmHg in the low-dose calcium group. On the second visit, it was found that the mean systolic and diastolic blood pressure was 115/75 mmHg in the high-dose calcium group, and 114/74 mmHg in the low-dose calcium group. On the third visit, the mean systolic and diastolic pressure was 116/75 mmHg in the high-dose calcium group and 116/74 mmHg. On the fourth visit, the mean systolic and diastolic blood pressure was 116/75 mmHg in the high-dose calcium group and 120/76 mmHg in low-dose calcium. From the analysis test, there were no meaningful differences in the two groups each visit. In this study, it was also found that there were 17 subjects (100%) subjects who had blood pressure <140/90 at the first visit to the fourth in the high-dose calcium group, whereas there were as many as 11 subjects (82.4%) who had blood pressure <140 / 90 on the first to fourth visits and 3 subjects (17.6%) who had blood pressure > 140/90 in the low-dose calcium group on the third and fourth visits.

There were very few samples who

experienced hypertension by consuming calcium supplementation (10 trials, 6634 women, RR 0.81, 95% CI: 0.74 - 0.89), but there were variations in the magnitude of effects across subgroups. The RR channel plot of sample size shows asymmetric plots, with a smaller effect in trials greater than 1000 subjects. The magnitude of the effect is far greater among women who are at high risk of hypertension (4 trials, 327 women, RR 0.45, 95% CI: 0.31 - 0.66), and those with low initial dietary calcium (5 trials, 1582 women; RR 0.49, 95% CI: 0.38 - 0.62).[15]

In the distribution of labour in the study subjects, 58.8% of subjects gave birth spontaneously, 29.4% of subjects gave birth by cesarean section, and 11.8% of subjects who had not given birth in the high-dose calcium group, while there were as many as 52.9 % of subjects who gave birth spontaneously, 29.4% of subjects who gave birth by cesarean section and as many as 17.6% of subjects who had not given birth. From the analysis, there was no significant relationship between labour and calcium groups. There was no significant difference between the types of labour in the calcium group.[15]

The type of labour in cases of preeclampsia found that there were 172 with vaginal deliveries and 21 with planned cesarean delivery. Moreover, women with cesarean delivery after a long period had a 10-fold higher risk of maternal outcomes compared with women with planned cesarean delivery (adjusted odds ratio (AOR) 9.7 (1.2 to 78.6), P = 0.03) or with vaginal delivery ≤ 24 hours (a OR 9.7 (1.4 to 67.4), P = 0.02).[12,16]

From the independent t-test analysis it was found that there was no significant difference in the mean hemoglobin at each visit with a value of p = 1,000; p = 0.591; p = 0.392; p = 0.279. Calcium acts as an inhibitor of iron or iron absorption used to synthesize hemoglobin, but in the study, it was found that there was no decrease in the administration of both high and low doses of calcium. Anne Marie said that there were no changes in the hematological index, including hemoglobin, hematocrit, zinc protoporphyrin, and plasma ferritin produced from calcium supplementation. Anne added that long-term supplementation with calcium does not reduce plasma ferritin concentrations in adults who are still actively consuming iron-containing foods. High hemoglobin concentrations in the first trimester showed risk factors for pregnancy-induced hypertension (OR = 2,462; 95% CI, 1-6,9). But this cannot be proven in this study.

Hemoglobin Hemoglobin levels in the first and second trimesters were associated with adverse pregnancy outcomes such as preeclampsia. An increase in hemoglobin concentration is a vasoconstriction cause in preeclampsia.[15-19]

From the independent t-test analysis it was found that there was no significant difference in hematocrit on each visit with a value of p = 0.254; p = 0.305; p = 0.707; p = 0.531. There were no differences in hematocrit between high-dose calcium and low-dose calcium. There was no significant difference between hematocrit levels in severe preeclampsia both before labour and after delivery with a value of p> 0.05.[17-21]

From the independent t-test analysis, it was found that there was no significant difference in the mean calcium for each visit with a value of p = 0.512; p = 0.151; p = 0.256; p = 0.809. From the McNemar test, it was found that there was no difference in the incidence of preeclampsia both after high-dose calcium interventions and low-dose calcium (p = 0.250). This means high and low calcium is effective for preventing preeclampsia. Calcium supplementation during pregnancy was associated with a significant 45% reduction in the risk of gestational hypertension [Relative risk (RR) 0.55; 95% confidence interval (CI) 0.36-0.85] and 59% in the risk of preeclampsia [RR 0.41; 95% CI 0.24-0.69] in developing countries. Calcium supplementation during pregnancy was also associated with a significant reduction in neonatal mortality [RR 0.70; 95% CI 0.56-0.88] and the risk of preterm birth [RR 0.88, 95% CI 0.78-0.99]. Recommendations for LST to reduce maternal mortality are based on a reduction in the risk of gestational hypertension related to severe morbidity/mortality [RR 0.80; 95% CI 0.70-0.91] and for neonatal deaths based on reduced risk for all causes of neonatal death [RR 0.70; 95% CI 0.56-0.88]. Whereas, who examined calcium administration in cases of recurrent preeclampsia said that there was no significant decrease in recurrent preeclampsia with calcium supplementation before and during early pregnancy. This experiment is fundamentally different from previous calcium trials to prevent pre-eclampsia.[15,22]

Calcium is a nutrient that must be consumed in sufficient proportion in food to ensure adequate serum levels because it is not produced in the body. In pregnancy, serum calcium levels tend to decrease because active transport crosses the placenta to the fetus, which can accumulate up to 25-30 g during pregnancy, especially in the

third trimester. In pregnancy, the absorption of calcium from the digestive tract also increases, mainly because of an increase in 1,25-dihydroxy vitamin D levels and increased urinary calcium excretion. Parathyroid hormone and calcitonin levels increase which subsequently impacts on serum calcium levels. Calcium intake needed in pregnancy is 1000 mg per day, however, it is recommended that only 6% of pregnant women reach this daily amount. The maternal risk of calcium deficiency in pregnancy includes osteopenia, osteoporosis, tremor, paresthesia, muscle cramps and tetany. Calcium also has a role in fetal bone mineralization and in preventing fetal growth restriction. Serum calcium levels have been found to be reduced in patients with preeclampsia and calcium deficiency that is also associated with other pregnancy morbidity such as preterm labor. Potential pathological mechanisms behind calcium deficiency and potential preeclampsia through parathyroid hormone and renin release, increase intracellular calcium levels and lead to vasoconstriction through contraction of smooth muscle blood vessels.[20-23]

The limitations of this study are limited sample size and research time. In addition, this study only compared the administration of high doses of calcium and low doses without knowing whether there were other calcium intake such as milk for pregnant women used by the research subjects. However, the basic data from this study can be used as data for further research.

CONCLUSION

The administration of high-dose calcium, in this study used calcium carbonate in accordance with WHO recommendations (1.5-2 g), effective in preventing the occurrence of severe preeclampsia and there was no difference in effectiveness between administration of high-dose calcium with low-dose calcium administration to the incidence of preeclampsia with a value of p = 0.250.

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