ORIGINAL ARTICLE :

Role of aspirin dose in reducing uterine artery resistance in 16-24 weeks pregnant women with abnormal uterine artery resistance

Muhammad Arief Adibrata, Agus Sulistyono, Ernawati*
Deparment of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga, Dr Soetomo Hospital, Surabaya, Indonesia

ABSTRACT

Objectives: To compare the decrease of resistance index (RI) from uterine artery in pregnant woman receiving low dose aspirin therapy between 80 mg/day and 125 mg/day who had abnormal doppler velocimetry (DV) ultrasound examination at 16-24 weeks.
Materials and Methods: An experimental study using double blind randomized clinical trial design. Subjects were from Mulyorejo and Kalijudan public health service in Surabaya, that included pregnant women with 16-24 weeks of pregnancy with abnormal uterine artery velocimetry ultrasound. The results of ultrasound Doppler examination were divided into four levels; normal (RI<0.58; (-) diastolic notching), level I (RI> 0.58; (-) diastolic notching), level II (RI<0.58; (+) disatolic notching) and level III (RI> 0.58; (+) diastolic notching). Uterine doppler ultrasound examination was performed at Fetomaternal Division, Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo Hospital, Surabaya, Indonesia, by fetomaternal consultants before and after the administration of low-dose aspirin of 125 mg/day and 80 mg/day for four weeks.
Results: Ninety subjects were obtained and randomized into 2 groups, with 45 subject in each group. Before treatment, in 125 mg/day group those with level I were 34 subjects and level III 11 subjects. In 80 mg/day group, level I 41 subjects, level II 2 subjects and level III 2 subjects. After 4 weeks of treatment, a second DV USG was performed in Aspirin 125 mg/day group. Normal were 40 subjects, level I 4 subjects, and level III 1 subject. In aspirin group 80 mg/day, normal 22 subjects, level I 19 subjects and level III 4 subjects. The analysis was performed with Wilcoxon test before and after treatment in both aspirin treatment group 125 mg/day and 80 mg/day with p value respectively, p=0.001 and p=0.005.
Conclusion: Compared with aspirin of 80 mg/day, aspirin of 125 mg/day is more superior to decrease uterine arterial resistance in pregnant women with ultrasound uterine arterial doppler velocimetry at 16-24 weeks gestational age.

Keywords: uterine artery resistance; doppler velocimetry ultrasound; low dose aspirin

ABSTRAK

Tujuan: Menganalisis perbandingan penurunan resistensi pembuluh darah arteri uterina pada ibu hamil 16-24 minggu dengan peningkatan resistensi arteri uterina yang mendapatkan terapi aspirin dosis rendah 80 mg/hari dan 125 mg/hari.
Bahan dan Metode: Penelitian eksprimental dengan desain uji klinis tersamar ganda randomisasi. Subjek penelitian berasal dari Puskesmas Mulyorejo dan Kalijudan Surabaya, yaitu ibu hamil 16-24 minggu dengan DV (doppler velocimetry) arteri uterina abnormal. Hasil pemeriksaan DV arteri uterina dibagi menjadi empat tingkatan yaitu; normal bila RI (Resistance Index) <0,58 notching diastolik (-), tingkat I jika RI >0,58 notching diastolik (-), tingkat II jika RI <0,58 notching diastolik (+) dan tingkat III jika RI >0,58 notching diastolik (+). Pemeriksaan DV arteri uterina dilakukan di Divisi Fetomaternal, Departemen Obstetri dan Ginekologi, Fakultas Kedokteran, Universitas Airlangga, RSUD Dr. Soetomo, Surabaya, Indonesia, oleh konsultan fetomaternal sebelum dan sesudah pemberian aspirin dosis rendah 125 mg/hari dan 80 mg/hari selama empat minggu.
Hasil: Sembilan puluh subyek ikut dalam penelitian. Dilakukan randomisasi menjadi 2 kelompok. Kelompok aspirin 125 mg/hari sebanyak 45 subjek dan kelompok aspirin 80 mg/hari sebanyak 45 subjek. Sebelum perlakuan, pada kelompok Aspirin 125 mg/hari didapatkan hasil kategori DV arteri uterina tingkat I sebanyak 34 subjek dan tingkat III 11 subjek. Pada kelompok aspirin 80 mg/hari didapatkan hasil kategori DV arteri uterina tingkat I sebanyak 41 subjek, tingkat II 2 subjek, dan tingkat III 2 subjek. Setelah mendapatkan terapi aspirin selama 4 minggu, dilakukan USG DV kedua dengan hasil kategori tingkat DV arteri uterina pada kelompok aspirin 125 mg/hari: Normal sebanyak 40 subjek, tingkat I 4 subjek, dan tingkat III 1 subjek. Pada kelompok aspirin 80 mg/hari: Normal sebanyak 22 subjek, tingkat I 19 subjek dan Tingkat II 4 subjek. Dilakukan analisis dengan uji Wilcoxon sebelum dan sesudah perlakuan pada kedua kelompok aspirin 125 mg/hari dan 80 mg/hari dengan nilai p berturut turut p=0,001 dan p=0,005.
Simpulan: Aspirin 125 mg/hari lebih banyak menurunkan resistensi arteri uterina pada ibu hamil dengan USG doppler velocimetry arteri uterina abnormal usia kehamilan 16-24 minggu dibandingkan dengan Aspirin 80 mg/hari.

Kata kunci: Bcl-2; folikel antral; cypermethrin

***Correspondence:** Ernawati, Deparment of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga, Dr Soetomo Hospital, Jalan Prof dr Moestopo 6-8, Surabaya 60286, Indonesia. E-mail: ernawati_spog@gmail.com

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INTRODUCTION

Preeclampsia is a major cause of maternal and perinatal morbidity and mortality in the world. The incidence of preeclampsia in the whole world is between 2-8% of all pregnancies.[1] The MMR (Maternal Mortality Rate) in East Java Province in 2015 reached 89.6 per 100,000 live births. In view of the causes of maternal deaths in 2015, East Java Province reported a 31% maternal mortality rate due to preeclampsia and eclampsia and, when compared to the previous year, the figure was relatively constant.[2]

One of the non-invasive preeclampsia screening efforts is the use of ultrasound Doppler Velocimetry in uterine arteries. The way to prevent preeclampsia that has been widely investigated for its effectiveness is the administration of low-dose aspirin. Low-dose aspirin can inhibit platelets from producing thromboxane A2 without affecting prostacyclin production and has the effect of reducing vascular resistance. Therefore, the administration of low-dose aspirin (60-150 mg/day) since the beginning of pregnancy helps improve uteroplacental circulation in pregnant women with abnormal ultrasound doppler uterine artery velocimetry.[3] Until now low-dose aspirin is still recommended to reduce the incidence of preeclampsia in high-risk pregnant women. The provision of this drug is safe for both the mother and the fetus.[4] However, studies conducted by Sciscione and Hayes (2009) proved that low-dose aspirin for low-risk pregnancies with abnormal ultrasound doppler velocimetry did not produce a significant reduction in the incidence of preeclampsia when compared to other low-risk pregnant women who did not receive aspirin low.

In accordance with U.S Recommendations. Preventive Services Task Force, ACOG (American College of Obstetric and Gynecologic), and WHO (World Health Organization), the selection of low-dose aspirin used is the dose of 75 mg/day - 80 mg/day. These doses is optimal in reducing uterine artery resistance and can prevent the occurrence of severe preeclampsia in high-risk pregnant women.[4,5] However, research by Nicolaides et al. (2017) showed that low-dose aspirin which has the best protective effect on the risk of preeclampsia is a dose of 100-150 mg/day.[6] Similarly, a study by Rachmi and Sulistyono (2015) found that giving aspirin in a dose of 125 mg/day to pregnant women of 16-24 weeks gestational age with increased uterine artery resistance could significantly reduce uterine artery resistance.[7]

Costs incurred for low-dose aspirin are relatively low and they are widely available in the market with various brands, such as Aspilets(r) 80 mg, Cardioaspirin(r) 100 mg, Miniaspi(r) 80 mg, Aspirin(r) 80 mg, 500 mg, and Acetosal(r) 500 mg. Currently aspirin 80 mg and 100 mg have a price range of IDR 552, - up to IDR 1168, - per tablet, while aspirin 125 mg obtained from a 500 mg preparation costs IDR 155, - per capsule.[8] Based on data available in the 2016 National Formulary Drugs, aspirin categories of doses of 80 mg and 100 mg should be available at level 1 health facilities and the maximum prescription per patient is 30 tabs/month.[9] However, the reality in the field, in this case in Mulyorejo and Kalijudan Public Health Centers, Surabaya, showed that the available aspirin was that of more than 500 mg (Acetosal?) and 80 mg preparation was not available. This study examined the optimal aspirin dosage regimen by taking into account the availability of short and long term preparations, costs, and safety, so that low-dose aspirin can provide maximum results in preventing preeclampsia and decreasing uterine artery resistance in pregnant women with DV ultrasound abnormal uterine arteries. In this study low-dose aspirin was administered in the doses of 80 mg/day and 125 mg/day.

MATERIALS AND METHODS

Data collection was conducted in March and May 2018 after obtaining ethical approval from the Dr Soetomo Hospital Ethics Committee No. 0164/KEPK/IV/2018. This study was an experimental study with randomized double blind clinical trial design. Subjects were taken from Mulyorejo Health Center and Kalijudan Health Center and USG examinations were carried out in the Fetomaternal USG room, Dr. Soetomo Hospital. Inclusion criteria: Pregnant women for 16-24 weeks with abnormal uterine artery velocimetry. Exclusion criteria: multifetal pregnancy, family history of preeclampsia or eclampsia, history of chronic hypertension, obesity, kidney disorders, diabetes in pregnancy, autoimmune diseases and a history of allergies or contraindications to aspirin. Sample size needed for each treatment group was 45 subjects. Sampling was done by consecutive sampling according to the inclusion and exclusion criteria.

The results of measurement of uterine artery Resistance Index (RI) were in the form of data ratio scale. It was regarded as normal if RI <= 0.58 cm/sec and not diastolic notching, abnormal if RI> 0.58 cm/sec and accompanied by diastolic notching (+/-). The results were categorized into 3 levels based on a study conducted by DeVore,[10] ie level I if RI >0.58 cm/sec and diastolic notching (-); level II if RI <=0.58 cm/sec and diastolic notching (+); level III if RI >0.58 cm/sec and diastolic notching (+). The ultrasound machines used was Samsung WS80A and GE Voluson S8 which had been calibrated by the Surabaya Health Facility Safety Agency.

Data normality test was carried out using the Shapiro-Wilk test for each group. If the data were normally distributed for unpaired groups, it was followed by unpaired t test; whereas if the data was distributed abnormally then the test was continued with the Mann Whitney test. To determine the decrease in RI value of uterine arteries before and after treatment in both groups, with a numerical data scale, paired t statistical test was carried out if the data were normally distributed or the Wilcoxon statistical test if the data were not normally distributed. Data calculation used Microsoft Excel(r) 2016 computer program and statistical calculations used IBM SPSS software(r) statistics 23. The results were considered significant if the p value <0.05.

RESULTS AND DISCUSSION

This study was carried out for ± 2 months from the end of March 2018 to April 2018. The study was started by recording women with 16-24 week pregnancy who visited the Mulyorejo and Kalijudan Health centers. They became the study population. They underwent uterine artery Doppler Velocimetry (DV) in the USG Room, Fetomaternal Division, Obstetrics and Gynecology Department, Faculty of Medicine, Airlangga University, Dr. Soetomo Hospital, Surabaya. The population received information about this study and was asked for informed for consent and informed consent if the subject later became a sample according to the inclusion and exclusion criteria. The characteristics of the subjects assessed in this study were the age of the patients (<20 years; 20-35 years; >35 years), gravida status (primigravida; multigravida; grande multigravida), BMI/Body Mass Index (<18.5 kg/cm2 ; 18.5-24.9 kg/cm2; 25-29.9 kg/cm2), gestational age (weeks), and categories of DV ultrasound examination results before and after treatment (Table 1).

Analysis was carried out on the characteristics of age, gravida status, gestational age, MAP (Mean Arterial Pressure), BMI, and RI uterine artery before treatment to determine whether the two groups were homogeneous before being treated. Data normality test was carried out on all characteristics. The Shapiro-Wilk test showed that all characteristics were abnormally distributed so that to identify whether both groups were homogeneous we used Mann-Whitney test. Table 2 shows that the overall characteristics have a value of p>0.05, which means there are no significant differences in the characteristics of the subjects (maternal age, gravida status, gestational age, MAP, BMI, and uterine artery RI before treatment) between the 125 mg and 80 mg aspirin groups.

Table 1. General characteristics of the subjects

Subject characteristics	Treatment groups	
	125 mg Aspirin n (%)	80 mg Aspirin n (%)
Maternal age (years)		
< 20	3(6.7)	3(6.7)
20-35	33(73.3)	42(93.3)
>35	9(20)	0(0)
Gravida		
Primi	15(33.3)	16(35.6)
Multi	27(60)	29(64.4)
Grande	3(6.7)	0(0)
BMI(kg/cm^2)		
<18.5	3(6.7)	1(2.2)
18.5-24.9	25(55.6)	18(40)
25-29.9	17(37.8)	26(57.8)
Pregnancy age		
16 weeks	7(15.6)	12(26.7)
17 weeks	1(2.2)	8(17.8)
18 weeks	7(15.6)	6(13.3)
19 weeks	5(11.1)	3(6.7)
20 weeks	9(20)	4(8.9)
21 weeks	12(26.7)	2(4.4)
22 weeks	2(4.4)	2(4.4)
23 weeks	1(2.2)	8(17.8)
24 weeks	1(2.2)	0(0)
Pre-treatment uterine artery DV categories		
Level I	34(75.6)	41(91.1)
Level II	0(0)	2(4.4)
Level III	11(24.4)	2(4.4)
Post-treatment uterine artery DV categories		
Normal	40(88.9)	22(48.9)
Level I	4(8.9)	19(42.2)
Level III	1(2.2)	4(8.9)

Table 2. Analysis of subjects' characteristics

Subjects' characteristics	Median (min-max) of the treatment groups		P value
	125 mg Aspirin	80 mg Aspirin	
Age (years)	29(19-39)	28(18-34)	0.121
Gravida Status	2(1-5)	2(1-4)	0.198
Pregnancy age (weeks)	20(16-23)	18(15-23)	0.118
MAP (mmHg)	83.3 (70-96.6)	78 (63-93)	0.091
BMI (kg/cm^2)	24.4 (17.4-36)	27.4 (16.3-29)	0.086
Pre-treatment uterine artery RI (cm/sec)	0.67 (0.0-1.0)	0.65 (0.48-1.0)	0.783

The p value was obtained from Mann Whitney test

After receiving aspirin therapy for 4 weeks, ultrasound examination of Doppler velocimetry was performed again in both groups. During this study, none of the

patients dropped out of the study and none of the study subjects suffered side effects of the aspirin.

Table 3. Analysis of response to aspirin therapy against RI reduction in uterine arteries

During treatment	Median (min-max) RI a uterina (cm/detik)		p value
	Pre-treatment	Post-treatment	
125 mg Aspirin	0.67 (0.00-1.00)	0.51 (0.00-0.83)	0.005
80 mg Aspirin	0.65 (0.48-1.00)	0.58 (0.37-0.78)	0.001

The p value was obtained from the Wilcoxon test.

Table 3 shows the two treatment groups aspirin 125 mg and aspirin 80 mg had a value of p <0.05; which means that there is a statistically significant difference in uterine arteries RI before and after aspirin treatment. Then, to compare between the two groups to find out which one had higher decreased uterine artery resistance, we used the Mann Whitney test. The result showed p=0.006; indicating there was significant difference between uterine arteries RI after treatment between 125 mg aspirin group and 80 mg aspirin group. Mann Whitney test revealed that the mean uterine arteries RI rank in the aspirin group after treatment was higher in 80 mg aspirin group compared to 125 mg aspirin group, so the 125 mg aspirin group had lower uterine artery resistance than 80 mg aspirin group.

In this study, uterine arteries RI values were categorized by level (normal, level I, level II and level III), as introduced by DeVore,[10] as listed in Table 1. In the 125 mg aspirin group the Wilcoxon test was performed to determine whether there was an effect of 125 mg aspirin administration to the category of uterine arteries RI level. The results showed p value of 0.001; indicating that there was statistically significant differences between groups before treatment and after treatment, where 42 subjects had decreased uterine arteries RI level, and 3 subjects with constant uterine arteries RI level (Figure 1).

In 80 mg aspirin group, Wilcoxon test was conducted to determine whether there was an effect of 80 mg of aspirin on uterine arteries RI level. The result showed the p value of 0.005, indicating statistically significant differences between groups before treatment and after treatment. Three subjects showed an increase in uterine arteries RI level category, 23 subjects with decreased uterine arteries RI level category and 19 subjects with stable uterine arteries RI level category (Figure 2). Then, Mann Whitney test was performed in both 125 mg and 80 mg aspirin treatment groups. Before treatment 125 mg aspirin group had significantly higher level (p=0.036) than 80 mg aspirin group, while after treatment 80 mg aspirin group was significantly higher (p=0.001) than 125 mg aspirin group. This shows that 125 mg aspirin group experienced higher reduction of abnormal uterine arteries RI level than 80 mg aspirin group.

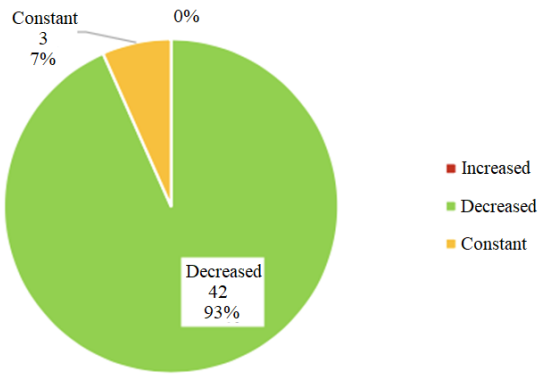

Figure 1. Effect of 125 mg/day aspirin on decreased uterine arteries RI level category

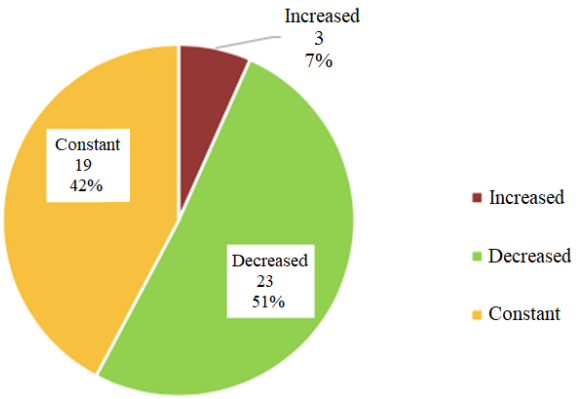

Figure 2. Effect of aspirin 80 mg/day on the decrease of uterine arteries RI level category.

Preeclampsia is a major cause of maternal and perinatal morbidity and mortality in the world. This study used low-dose aspirin at doses of 80 mg and 125 mg. The 80 mg dose was chosen because this preparation was widely available in the market. At the community health centers, the preparation used was 125 mg, which originally was 500 mg Acetosal made into a 125 mg capsule or divided into 4 parts, each 125 mg. The cost for an 80 mg aspirin preparation ranges from Rp. 500 to Rp 1,200 per tablet, depending on the brand of each product, while compounding 125 mg acetosal per capsule requires a cost of Rp. 200 - Rp. 800.[8] A study showed that the effectiveness of aspirin therapy depend-

ed on the dosage of the low-dose aspirin and the time of administration.[6]

Doppler velocimetry ultrasonography in uterine arteries is a non-invasive method that is useful for indirectly assessing the initial stages of changes in uteroplacental circulation, so that this can be used as a tool to predict the occurrence of preeclampsia and IUGR (Intra Uterine Growth Restriction).[11] Some studies tried to evaluate the benefits of low-dose aspirin in pregnant women with abnormal uterine artery doppler velocimetry to prevent the occurrence of preeclampsia, but showed mixed results.[12,13]

Some characteristics that are the main risk factors for preeclampsia are maternal age, parity and body mass index.[14] Age is an important factor in the incidence of preeclampsia. The age of mothers over 40 years increases almost 2 times the risk of preeclampsia with OR/Odds ratio 1.96 (CI95% 1.34-2.87).[15] In this study it was found that in 125 mg aspirin treatment group the youngest age was 19 years and the oldest was 39 years, while in 80 mg aspirin treatment group the youngest age was 18 years and the oldest was 34 years. Statistical tests on both age groups showed no significant difference in maternal age between 125 mg and 80 mg aspirin groups.

Some researchers considered preeclampsia a disease in the first pregnancy (primipara).[16] Primigravida with a family history of preeclampsia has 2-5 times more at risk of developing preeclampsia. This happens when the fetus inherits a maternal genetic inheritance with a STOX1 missense mutation at 10q22. Excessive expression of STOX 1 mutations will inhibit trophoblast cell invasion in spiral arteries, resulting in failure of spiral artery remodeling.[17] In this study it was found that most of the patients who took part in the study were multigravida, both in the 125 mg aspirin treatment group and the aspirin 80 mg treatment group. Primigravidas in the 125 mg aspirin group were 15 (33.3%) and in the 80 mg aspirin group they were 16 (35.6%). Analysis carried out in the two treatment groups showed no significant differences in gravida status between both groups.

Obesity is the definitive risk factor for the occurrence of preeclampsia with almost twice the risk in obese pregnant women.[14,15] This study did not get obese patients, because obesity was included in the exclusion criteria. In the aspirin 125 mg group, most pregnant women had a BMI of 18.5-24.9 (normal), which comprised 25 (55.6%) mothers, whereas in the 80 mg group most pregnant women had a BMI of 25-29.9 (overweight) comprising 26 (57.8%) mothers. Analysis of the two treatment groups found no significant difference in the BMI.

The incidence of preeclampsia can also be detected early by calculating mean arterial pressure (MAP). This test has 93% sensitivity and 62% specificity.[1] Positive MAP or MAP> 90 mmHg is stated to increase the probability of preeclampsia as much as 3.5 times.[15] In this study, the patients known to have MAP of $\geq$ 90 mmHg were 11 subjects. Analysis of both treatment groups showed no significant difference in MAP. Analysis was also carried out on gestational age, where the two treatment groups showed no significant difference.

During a normal pregnancy, hemodynamic modification causes a decrease in blood pressure, even though there is an increase in cardiac output and blood volume (a factor that usually causes an increase in blood pressure). The reduction in blood pressure was due to the decrease of peripheral vascular resistance, which is the adaptation of the body of pregnant women to meet the adequacy of blood flow to the uterus.[1,18] The process of remodeling spiral arteries, which mostly occurs after 16 weeks of pregnancy, causes the uteroplacental blood vessels to undergo vasodilation and is unable to respond to vasoactive substances. As a result, uteroplacental vascular resistance will also decrease. Thus, it is not surprising that blood flow to the uterus (uteroplacenta) is abundant to ensure good fetal growth.[14]

One way of identifying the decrease in uteroplacental circulation is by uterine artery examination using doppler velocimetry ultrasound. The principle of this examination is the ability to identify reduced diastolic flow in the uterine arteries as a marker of disruption of placentation process.[11] In ultrasound examination, placentation disorder is characterized by high resistance values in the uterine arteries due to disruption of trophoblast migration in the myometrium and inadequate physiological changes in spiral arteries in women with preeclampsia as evidenced by histopathological examination.[19]

Aspirin can interfere with platelet aggregation by irreversible inactivation of cyclooxygenase (COX-1) enzymes, while the effect of dose-dependent aspirin on endothelial cells quickly restores COX-1 activity, so it is less important than the antiplatelet effect in platelets. Therefore, the administration of low-dose aspirin can improve the ratio of PGI2 and TXA2 relatively increases, decreases vascular resistance and improves uteroplacental circulation. It has been proven that the administration of low-dose aspirin (60-150 mg/day) specifically inhibits thromboxane production without significantly affecting prostacyclin production.[6,20] Ana-

lysis of thromboxane (TBX2) and prostacyclin (6-keto-PGF-1α) metabolites in maternal urine showed that low-dose aspirin reduced thromboxane metabolites 61-87%, while prostacyclin metabolites had no effect.[21]

This study showed that low-dose aspirin 60-150 mg in pregnant women of 16-24 weeks gestation age with abnormal uterine artery doppler velocimetry resulted in an improvement of uterine artery resistance level, so the administration of low-dose aspirin in pregnancy still has protective effect against poor pregnancy outcomes such as preeclampsia.[22] However, some literatures say that the administration of low-dose aspirin in women at high risk should start from <16 weeks' gestation. This is related to the start of transformation of the spiral arteries at 8 weeks gestation which ends at 24 weeks gestation,[23,24] so that pregnancy complications, such as preeclampsia, severe preeclampsia and IUGR, can be prevented.

The size of the aspirin dose affects the output of the DV ultrasound level in this study, where the dose of 125 mg was better to reduce abnormal ultrasound DV level of the uterine artery to become normal again compared to the dose of 80 mg. These findings are in line with previous studies, where large doses of aspirin (100-150 mg) had a more significant effect on improving uterine artery resistance and reduced maternal and neonatal adverse outcomes compared with aspirin doses of 60-80 mg.[6,10]

A study by Caron et al. (2006) assessed low-dose aspirin responses using PFA-100 (Patelet Function Analyzer). The results of the study showed that for most pregnant women 80 mg aspirin therapy had less effect on platelet function than doses of 100-150 mg. In this study it was also foundthat 28.7% of the patients who received 80 mg aspirin showed no change.[25]

The difference in the effect of 125 mg aspirin and 80 mg aspirin on DV ultrasound levels of abnormal uterine artery can be attributed to various other factors which are the limitations of this study. First, we did not monitor the compliance of the pregnant women in taking the drug. Second, the absorption of aspirin in gastrointestinal tract is reduced. Aspirin absorption will decrease if consumed with other foods because aspirin is extensively hydrolyzed by esterase in the gastrointestinal mucosa, so that active metabolites that arrive at the liver port system will decrease and reduce the effectiveness of thromboxane inhibition. Third, this study used two different brands of ultrasound machines to measure uterine artery DV, which might affect the outcome of RI measurement of uterine arteries. However, in this study the evaluation of each subject was carried out with the same machine and examiner. The USG machines had been monitored by the Surabaya Health Facility Safety Agency (Badan Pengaman Fasilitas Kesehatan, BPFK). In this study the ultrasound parameter assessed was RI uterine arteries with a ratio measurement scale, which would not significantly affect the results of RI measurements, using 2 different ultrasound machines. Fourth, this study did not measure the impact on platelet aggregation ability in the two treatment groups. The study of a Collaborative Low-dose Aspirin Study in Pregnancy (CLASP) shows that low-dose aspirin consumption (75-150 mg/day) is safe for the fetus and does not increase the risk of bleeding in pregnant women (post saline bleeding, placental abruption and complications from using regional anesthesia).[26]

CONCLUSION

Aspirin doses of 80 mg/day and 125 mg/day can significantly reduce uterine artery resistance in mothers of 16-24 week gestational age with abnormal uterine artery resistance, where 125 mg/day aspirin decreases uterine artery resistance more than 80 mg/day. Similar study can be done at an earlier gestational age (> 12-16 weeks) as an effort to detect and prevent secondary preeclampsia. This study can also be followed up by considering maternal and neonatal outcomes in both treatment groups at the end of the pregnancy period. All mothers with a gestational age of 16-24 weeks are advised to check their pregnancy to a health center so that early detection and prevention of poor pregnancy outcomes can be carried out, including ultrasound examination of uterine artery doppler velocimetry and the administration of low-dose aspirin to those at risk.

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