

Research Article

Effects of Low-Dose Aspirin in the Prevention of Preeclampsia in Pregnant Women with Abnormal Uterine Artery Doppler at 11 to 14 Weeks of Gestation

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Abstract

Backgrounds: Preeclampsia is one of the most important causes of perinatal morbidity and mortality in pregnant women. To assess the risk for preeclampsia in pregnant women, uterine artery Doppler ultrasound as a useful screening, non-invasive and repeatable method has been introduced. According to the findings of previous studies and controversies in the use of aspirin, To prevent preeclampsia, as well as in most previous studies, to prescribe aspirin versus placebo in women with abnormal uterine artery Doppler in the second half or third trimester of pregnancy had occurred. This study was aimed to investigate the effect of aspirin in reducing the risk and severity of preeclampsia in women with abnormal findings uterine artery Doppler at 11 to 14 weeks of pregnancy.

Methods: The sample included 100 patients referred to the prenatal and pregnancy care center that randomly divided into 2 groups (A) consisted of 50 pregnant women treated daily with 80 mg aspirin and the remaining, 50 cases in the control group (B) were treated with certain medications, also the risk of preeclampsia and its complications was examined.

Results: Among the patients were treated with aspirin in group A (control group), 7 persons (17.5%) developed preeclampsia who 2(5%) had severe preeclampsia criteria. It was while 13(30.9%) of pregnant women in group B (control) also eventually developed preeclampsia and 3(7.1%) were classified as severe preeclampsia (P: 0.03), also significant differences between pregnancy complications between the two studies groups was observed.

Conclusion: Given the significant incidence of preeclampsia and also no significant difference in complications rates between the 2 groups after delivery, It seems that daily treatment until the end of pregnancy and the treatment of women at high risk for preeclampsia, according to the index of ultrasound at 11 to 14 weeks of gestation with low dose aspirin (80 mg) can be effective to reduce preeclampsia.

INTRODUCTION

One of the most important causes of perinatal morbidity and mortality is preeclampsia in pregnant women [1]. The conditions for disease prevention include: [1] the availability of reliable, non-invasive and repeatable screening tests 2- appropriate interventions to correct the underlying pathology [2]. It seems that preeclampsia is due to the lack of fetal-maternal circulation which is associated with impaired trophoblastic invasion and the lack of adequate response of mother vessels to implantation [3]. In these conditions, uterine-placental circulation in this situation would be to have a high resistance and damage to the endothelial cells [4-6]. It is also determined by reducing

the production of prostacyclin through the endothelium and increased thromboxane A2 production by platelets. Prostacyclin is a vasodilator and inhibitor of platelet aggregation inhibitors, vascular and uterine contractions, while the vasoconstrictor thromboxane A2 is driving platelet aggregation and narrowing of the arteries. Cyclooxygenase enzyme is an enzyme that plays a central role in the production of prostacyclin and thromboxane and it can be inhibited by aspirin.

So it seems that oral prescription of aspirin may interfere with the selective inhibition of cyclooxygenase enzyme and prostacyclin / thromboxane A2 in the placenta to prevent or delay preeclampsia. However, the performance of aspirin is in

inhibiting platelet cyclooxygenase only and does not affect the vascular endothelium [7,8]. Several randomized studies of low-dose aspirin in the potential value with high risk in women in terms of preeclampsia have been examined. The use of aspirin in a meta-analysis of 29 studies has reviewed a total of 30,000 pregnancies. The use of aspirin was associated with a mean reduction in preeclampsia [9]. Although these studies have differences in the inclusion criteria, gestational age and dose of aspirin. Some also reported that aspirin has no effect on women with low or moderate risk of preeclampsia and only has effects on women with high risk of preeclampsia, early and severe preeclampsia [10].

To assess the risk for preeclampsia in pregnant women, uterine artery Doppler ultrasound has been introduced as a useful, non-invasive and reproducible screening method [11-13]. During recent 20 years, various studies have shown that this method is useful for screening to identify women who are at high risk for preeclampsia [14]. In a recent study of 8000 pregnant women it was reported that individuals with increased arterial index Pulsatility Index (PI) are more 6 times at risk of developing preeclampsia [15].

In a study on 76 pregnant women at risk of preeclampsia IN 11 to 14 weeks, they conclude that normal resistance (PI, RI) in strong arteries is associated with normal pregnancy outcome in women at risk [16]. Thus, according to the findings of previous studies and controversies in the use of aspirin to prevent preeclampsia, as well as in most previous studies [17-20], prescribing aspirin versus placebo in women with abnormal uterine artery Doppler in the second half or third trimester of pregnancy had occurred, this study had designed to investigate the effect of aspirin in reducing the risk and severity of preeclampsia in women with uterine artery Doppler abnormal findings in 11 to 14 weeks of pregnancy.

METHODS AND MATERIALS

This study was performed in clinical trial method by using on pregnant women attending in prenatal clinics in Sari Imam Khomeini Hospital from March 2013 to December 2014. The sample size after consulting with statistic adviser by using a statistical formula to achieve a power of 80% and accuracy of 95% among 110 patients was determined (Figure 1). The patients were divided into two groups of 50 persons include A (50 pregnant women treated with aspirin 80 mg daily) and B (50 remaining persons who did not receive any specific medication) based on classification of simple computer, matched and divided numbers randomly (registry number: IRCT17891)

Ethics

All subjects gave their written consent to participate in the study. This study was conducted in accordance with the Declaration of Helsinki and good clinical practice according to International Conference on Harmonisation guidelines. The ethics committee of Mazandaran University of Medical Sciences, Sari, IRAN approved this study. The study was designed as a randomized clinical trial (IRCT:).

Inclusion criteria

Singleton 11 to 14 week's pregnant women and cases with

risk factors for preeclampsia: nulliparity, history of preeclampsia and maternal underlying diseases.

Exclusion criteria

Presence of fetal anomalies-sensitivity to aspirin-history or active peptic ulcer disease, use of prostacyclin-record inhibitors, 10 days before the study of chronic renal failure (CRF), liver (underlying disease liver, liver failure, hepatitis), cardiac (heart failure, congenital heart disease) and systemic lupus - bleeding disorders.

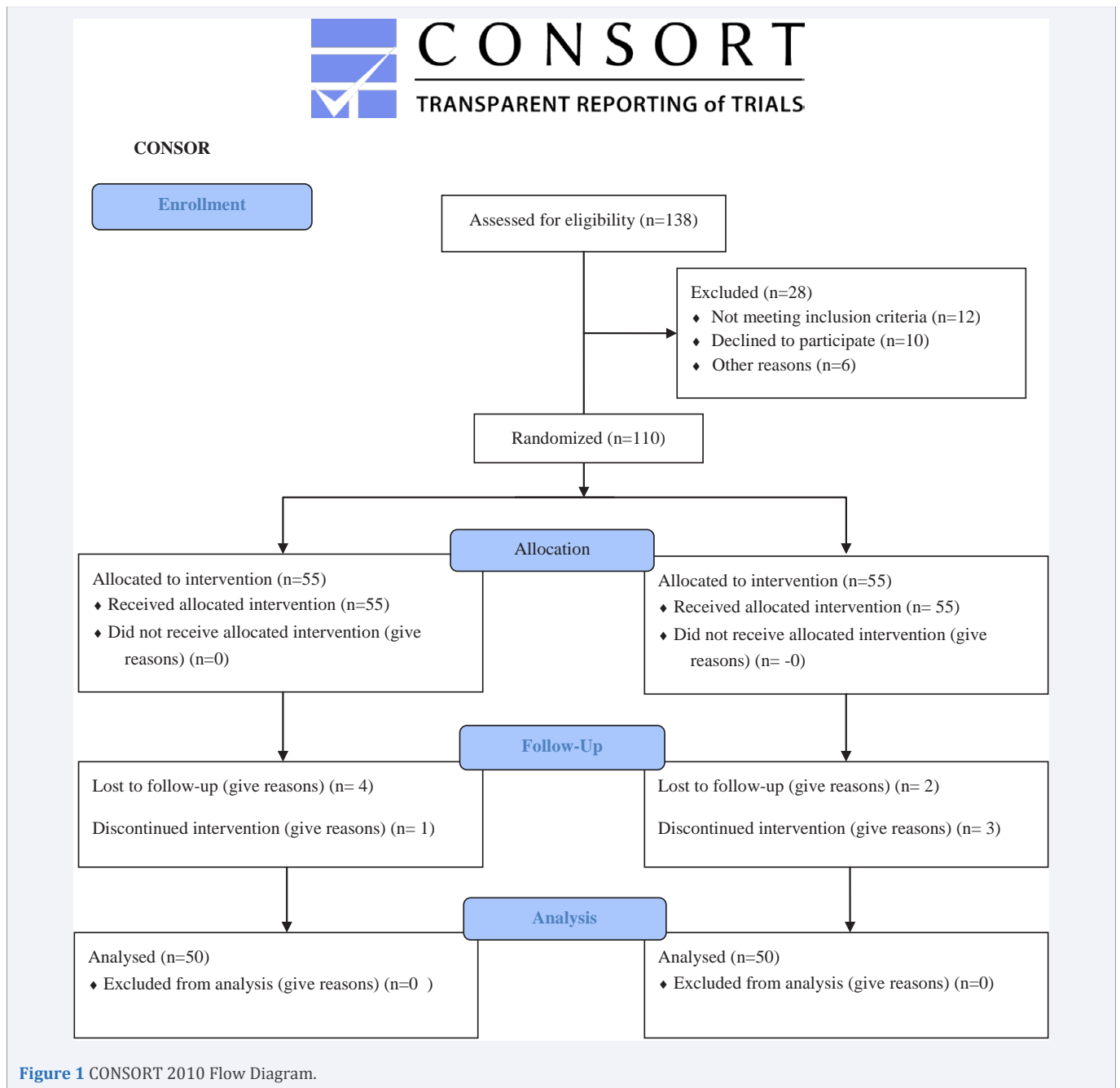
Patients, treatment and evaluation

Patients were enrolled based on inclusion and exclusion criteria. Objectives and implementation of the study was explained to pregnant women and their written consent was obtained.

Gestational age based on LMP and or ultrasound baseline was calculated at the beginning of inclusion for all nulliparous and / or multiparous women with a history of preeclampsia and underlying disease, in addition to routine prenatal ultrasound for evaluation of pregnancy, uterine artery Doppler Velosymmetry as a trans-abdominal artery IVF was performed by transvaginal ultrasound. Doppler ultrasound was performed by Siemens ultrasound G50 and probe spherical Lynar 3.5-5 MHZ by standard methods. Abdominal and pelvic ultrasound was performed to evaluate uterine artery using a sagittal view of the uterine cervical canal and internal os and its location was identified. The transducer is moved slowly from one side to another side and simultaneously color Doppler was also used to identify uterine artery on each side parallel to the surface of the cervix on internal os. Pulsatility Index (PI) and Resistance index (RI) was evaluated. Patients with RI> 0.6 increase in uterine artery waveforms and / or PI> 1.6 (95% percentile) (15) come into the main phase of the study. Demographic characteristics of patients included maternal age, gestational age, parity and gravidity was recorded. Risk factors for preeclampsia, such as a history of preeclampsia in a previous pregnancy, underlying vascular disease, chronic hypertension, first pregnancy, diabetes, or a history of gestational diabetes, age below 20 years or older than 40 years were also recorded.

Pregnant women with abnormal findings in uterine artery Doppler and by using computer generated numbers randomly divided into two groups. Case group is a group that would be under treated by the end of pregnancy with aspirin 80 mg daily. The control group consisted of individuals who didn't receive the drug. All of routine prenatal examinations, blood pressure and urinary protein excretion were examined in terms of the length of time of the examination that depending on the circumstances of each individual was different.

Routine ultrasound was performed to confirm the health and growth of the fetus [20]. The remaining capacities of patients with pill counts at each examination period were reviewed. Patients who do not take their daily dose, as well as those who were not present at periodic visits and had not suitable following-up, were excluded from the study. Data obtained in the statistical software Spss-15 was recorded. Parametric data as mean and standard deviation and non-parametric data were expressed in descriptive



terms. The student-t test and the sum of the two squares for data analysis in two groups were used. $p < 0.05$ was considered as significant level.

RESULTS

The demographic characteristics of study population were summarized in (Table1).The mean± sd age of Group A (treatment with aspirin) and Group B (control) were 27.3 ± 3.6 , 26.1 ± 4 respectively (p value: 0.6). There were no significant differences between demographic features of these two groups (Table 2).

Among the patients were treated with aspirin in group A (control group), 7 persons (17.5%) developed preeclampsia who 2 (5%) had severe preeclampsia criteria. It was while 13

(30.9%) of pregnant women in group B (control) also eventually developed preeclampsia and 3 (7.1%) were classified as severe preeclampsia, also significant differences between pregnancy complications between the two studies groups was observed. There was significant differences in prevalence of Preeclampsia in Group A (treatment with aspirin) and Group B (control) (Table 2).

Also, there was significant notice that late preeclampsia (>34week) was observed in 11 cases in Group B and 6 patients in Group A (Table 2).

DISCUSSION

Preeclampsia is a syndrome of pregnancy created by impaired

Table 1: Demographic features of these series.

variable	Group A (treatment with aspirin)	Group B(control)	P value
age	27.3±3.6	26.1±4	0.64
More than 40 yr	(7.5)3	(7.1)3	0.72
Less than 20 yr	4 (10)	(7.1)3	0.42
BMI (KG/M ²)	24.2±4.8	23.8±5.2	0.34
nully parity	28 (70)	32 (76)	0.54
Multi parity	12 (30)	10 (24)	0.82
Number of pregnancy	1±2	1.5±0.5	0.71
Systolic blood pressure	112±8.1	110±7.1	0.63
Diastolic blood pressure	83.2±4.1	81.1±4.2	0.25
Mean age of pregnancy(weeks)	12.1±0.8	11.8±0.9	0.37
Diabetes mellitus	(7.5)3	(14.2)6	0.38
Chronic hypertension	(22.5)9	(16.6)7	0.56
History of preeclampsia	(17.5)7	5 (12)	0.71
PI Index(cm/s)	1.72±1.1	1.75±0.9	0.26
RI index(cm/s)	0.76±0.6	0.75±0.3	0.36

Table 2: The outcomes of treatment in both groups in this research.

variable	Group A (treatment with aspirin) N	Group B(control) N	P value
Preeclampsia (<34 week)	1	2	0.36
Preeclampsia(>34week)	6	11	0.03
Preeclampsia (minor)	5	10	0.03
Preeclampsia (severe)	2	3	0.32
Weight of infant (PE)	3094±218	3101±368	0.74
Weight of infant (NL)	3178±234	3160±412	0.71
NVD(PE)	4	6	0.27
NVD(NL)	20	13	0.36
C/S(PE)	3	7	0.31
C/S(NL)	13	16	0.28
IUGR(PE)	2	0	0.4
IUGR(NL)	1	2	0.45
TT< 37 (PE)	2	3	0.48
TT< 37 (NL)	1	2	0.46
TT >37 (PE)	5	10	0.52
TT>37 (NL)	32	27	0.56
still birth	0	0	0
Bleeding > 500 cc after delivery	1	0	0.6

PE=Preeclampsia; TT: Termination Time; NL=Normal; C/S: Caesarian Section; NVD: Normal Vaginal Delivery

perfusion of organs after a severe vasospasm (1) and generally by using ultrasound and calculated analysis index can examine a lot of blood flow uterine arteries.

However, as noted, several studies have shown that to assess the risk for preeclampsia in pregnant women, uterine artery Doppler ultrasound can be a useful and repeatable method for screening in preeclampsia and its complications in pregnancy [11-13].

Today in different articles, various drugs and therapies to reduce the incidence of this syndrome (preeclampsia) are used in high risk women. However, the clinical significance of this disease maternal and neonatal outcomes, it seems logical step in this direction.

Different and conflicting studies about the effects of aspirin in the prevention of preeclampsia has been done the present study was conducted with the objective to present most significant results in accordance with this objective.

The present findings indicate that about 5/82% of those who were treated with low-dose aspirin (80 mg daily), did not show preeclampsia and the chance of preeclampsia in women treated with aspirin is less than 85 / 1.

Our study is in line with research conducted by Baschut and colleagues through reporting similar results, so that low-dose aspirin can reduce blood flow resistance in pairs and prevent the onset of preeclampsia [21].

In a study conducted by Ebrashy, also the incidence of preeclampsia in patients treated with aspirin has been 35% (versus 65% of control group) [22].

In a study by Harrington et al, among 216 women who were at high risk for preeclampsia based on ultrasound findings, patients were divided into 2 groups of 103 persons treated with a daily dose of 100 mg of aspirin in control group [23].

The results didn't reveal significant differences between the 2 groups in the incidence of preeclampsia and IUGR in birth time. But other problems during pregnancy were also significantly different between the 2 groups.

Perhaps we can justify the cause of no reduction in the incidence of preeclampsia among patients based on higher gestational age (23-17 weeks) at this time to begin later ultrasound and aspirin compared with our study.

However other studies report different results of the overall therapeutic effect of aspirin on the incidence of preeclampsia.

Perhaps we can express existing contradictions between gestational age and the ratio of aspirin.

The findings of this study indicate that in group A, (the) average birth weight of babies and gestational age at delivery time, there is no significant difference with the control group (B). Also, in terms of delivery, it is not found a statistically significant association with aspirin, which is in line with other studies by other researchers including Golding.

CONCLUSION

Therefore, considering the significant incidence of preeclampsia, there is no significant difference in complication rates between the 2 groups after delivery, It seems that daily use and treatment, until the end of pregnancy of women at high risk for preeclampsia, according to the index of ultrasound at 11 to 14 weeks of gestation with low dose aspirin (80 mg) significantly reduce the incidence of preeclampsia, and consequently has a significant role in reducing costs and adverse clinical effects on the mother and newborn and somehow reduce the social effects. Although the further studies with a larger sample size to achieve the result of a Multicenter and the same scientific result seems logic.

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