

Assessment of endothelium: Dependent vasodilation with a non-invasive method in patients with preeclampsia compared to normotensive pregnant women

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Background: To assess the endothelial function via noninvasive method, in pregnant women with preeclampsia compared to normotensive pregnant women. **Materials and Methods:** Brachial artery diameter was measured via ultrasound, in 28 women with preeclampsia in case group and normotensive pregnant women in control group, at rest, after inflation of sphygmomanometer cuff up to 250-300 mmHg, immediately after deflation of the cuff, 60-90 minutes later and 5 min after administration of sublingual trinitroglycerin (TNG). Results of these measurements as well as demographic characteristics of participants in both groups were recorded in special forms. Data were analyzed via Statistical Package for Social Sciences (SPSS) version 16, using *t*-test and repeated measures analysis of variance (ANOVA). *P*-value < 0.05 was considered statistically significant. The results were presented as mean \pm standard deviation (SD). **Results:** The mean of brachial artery diameter at rest in the case and control groups was 4.49 ± 0.39 and 4.08 ± 0.38 mm, respectively (*P* = 0.1). Also the results showed that the brachial artery diameter, immediately after deflation of the cuff, was 4.84 ± 0.4 and 4.37 ± 0.30 mm in the case and control groups (*P* < 0.001), respectively. The mean brachial artery diameter, 60-90 s after deflation of the cuff, was 4.82 ± 0.41 and 4.42 ± 0.38 mm in the case and control groups (*P* < 0.00), respectively. The brachial artery diameter, 5 min after sublingual NO administration, was 4.95 ± 0.6 and 4.40 ± 0.45 mm in case and control groups (*P* < 0.001), respectively. Applying of repeated measures ANOVA showed that the mean difference between case and control groups was statistically significant (*P* < 0.001). **Conclusion:** Current study concluded that there is no difference in endothelium-dependent vasodilation between women with preeclampsia and pregnant women with normal blood pressure.

Key words: Brachial artery diameter, endothelium-dependent vasodilation, Endothelium-dependent vasodilation-Preeclampsia-Nitric oxide (NO), NO, normotensive, preeclampsia

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INTRODUCTION

Preeclampsia, as one of the most important causes of morbidity and mortality in mother and fetus, has prevalence about 6% in general population.^[1,2] In spite of continuous studies for several decades, the mechanism of preeclampsia is still unknown.^[3-5] Endothelial damage is the most recent and powerful theory about the mechanism of preeclampsia which explains that any damage to vascular endothelium, leads to decrease in production of endothelial-derived releasing factors (EDRF), especially nitric oxide (NO), activation of coagulatory pathways, and increase in blood pressure.^[3,5-6] It has been assumed that, NO has a role in normal vasodilation and low blood pressure in maternal-fetal circulations.^[1-3,7,8]

Results of various studies on the endothelial function and effect of NO in preeclampsia, are still controversial.^[2] Some studies found no significant correlation between plasma concentration of NO and preeclampsia; on the contrary, other studies showed marked decrease in NO release and higher concentration of NO inhibitors, in patients with preeclampsia.^[2,3,9] Another study has reported higher concentration of NO in preeclampsia which might be a compensatory effect for the vasoconstriction of preeclampsia.^[8]

It has been proposed that endothelial cell dysfunction is due to an extreme activated state of leukocytes in the maternal circulation. Tumor necrosis factor (TNF) and interleukin may contribute to the oxidative stress associated with preeclampsia. This is characterized

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by reactive oxygen species and free radicals that leads to formation of self-propagating lipid peroxides.^[3]

According to these controversial results, this study was designed to assess the endothelial function via noninvasive method, in pregnant women with preeclampsia compared to control group.

MATERIALS AND METHODS

This case-control study was performed on pregnant women in Isfahan, 2009. Fifty-six nonsmoker pregnant women who were in third trimester of their first pregnancy and did not have any previous history of chronic hypertension, preeclampsia, diabetes, and hypercholesterolemia, were enrolled in this study. Exclusion criteria included twin pregnancy, TNG intolerance, and a lack of cooperation in subjects.

Twenty-eight pregnant women with preeclampsia who met inclusion criteria were selected as case group and 28 healthy women that had not any sign of preeclampsia referred to Alzahra obstetric clinic for routine prenatal care as control group. Both case and control groups were matched by pregnancy time and age.

Written consent was obtained from all of the participants in both case and control groups.

Brachial artery diameter in all of the participants, was measured in a distance about 5-15 m above the elbow, at rest, via ultrasound by a radiologist who was unaware of case and control groups. After that, in all of the subjects, sphygmomanometer cuff was inflated on the forearm up to 250-300 mmHg for 5 min and then immediately after deflation of the cuff and 60-90 s later, brachial artery diameter was measured again. This method was used for assessment of artery response to flow-mediated dilatation (FMD) mechanism.^[7,8]

After resting for 15 min, brachial artery diameter was measured for the fourth time, after administration of one sublingual trinitroglycerin (TNG)-exogenous NO, at the same point above the elbow. This latter method was used for assessment of artery vasodilation, independent of endothelium.^[7,8]

Results of these measurements as well as demographic characteristics of participants in both groups were recorded in specific forms.

Data were analyzed via Statistical Package for Social Sciences (SPSS) version 16, using *t*-test and repeated measure analysis of variance (ANOVA). *P*-value < 0.05 was considered statistically significant.

RESULTS

Twenty-eight pregnant women with preeclampsia as case group and 28 healthy pregnant women as control group were evaluated in this study. The mean \pm standard deviation (SD) of age control and case group was 21.9 ± 1.7 and 22.1 ± 2.2 years, respectively ($P = 0.74$).

The mean \pm SD of brachial artery diameter at rest in the case and control groups was 4.49 ± 0.39 and 4.08 ± 0.38 mm ($P = 0.1$), respectively. The mean \pm SD of brachial artery diameter, immediately after deflation of the cuff was 4.84 ± 0.4 and 4.37 ± 0.30 mm in the case and control groups ($P < 0.001$), respectively. The mean brachial artery diameter, 60-90 s after deflation of the cuff, was 4.82 ± 0.41 and 4.42 ± 0.38 mm in the case and control groups ($P < 0.00$), respectively. The mean \pm SD of brachial artery diameter, 5 min after sublingual NO administration, was 4.95 ± 0.6 and 4.40 ± 0.45 mm in case and control groups ($P < 0.001$), respectively. According to repeated measures ANOVA there is a statistically difference among follow-up time within both groups ($P < 0.001$) and there is a statistical difference between two groups ($P < 0.001$). Also according to results of this study, no significant interaction was seen between groups and follow-up time ($P = 0.23$). The trend of brachial artery diameter changes has been shown in [Figure 1].

DISCUSSION

Our study results showed that brachial artery diameter was significantly increased, after increase in blood flow (endothelium-dependent vasodilation) and use of exogenous NO (endothelium-independent vasodilation) in women with preeclampsia and normotensive pregnant women, compared to baseline and this increase in participants with preeclampsia was significantly higher compared to control group.

These results suggest that NO as a potent vasodilator has an important role in both mechanisms and shows its effect

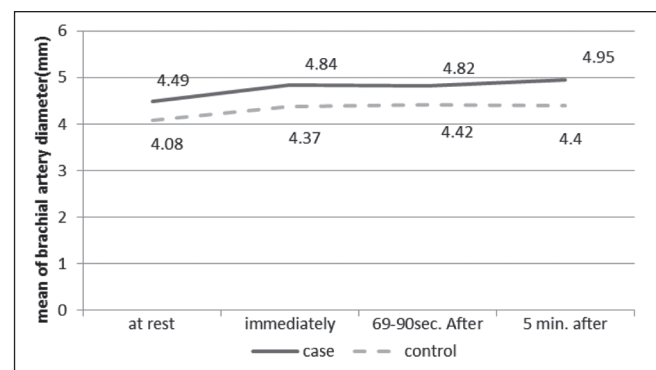


Figure 1: Trend of brachial artery diameter between two groups, during different times

in decrease of vascular resistance and vasodilation. As a result, both women with preeclampsia and normotensive pregnant women have no difference in endothelial function.

Chamber and Fusi in an invasive study showed that blood flow is an important factor in NO release, only in normotensive pregnant women, not in women with preeclampsia;^[10] which is different from our results which reported that increase in blood flow leads to more increase in NO release.

Silver *et al.*, reported no correlation between plasma concentration of NO and severe preeclampsia.^[11] In our study, we did not measure NO concentration in women with preeclampsia.

Dorup *et al.*, study showed that no activity is enhanced during a normal pregnancy and leads to decrease in vascular resistance and vasodilation.^[7] Our study showed that both in normal pregnancy and preeclampsia vascular resistance decreased after increase in brachial artery diameter, following exogenous NO which somewhat resembles to results of Dorup *et al.*

Current study concluded that there is no difference in endothelial function between women with preeclampsia and pregnant women with normal blood pressure.

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