

The Effect of Cold Stress on Uterine Artery Blood Flow Velocity Waveforms in Late Pregnant Women with and without Preeclampsia

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KIMURA, Y., OKAMURA, K., WATANABE, T., TAKAHASHI, T., HAGA, I. and YAJIMA, A. *The Effect of Cold Stress on Uterine Artery Blood Flow Velocity Waveforms in Late Pregnant Women with and without Preeclampsia.* Tohoku J. Exp. Med., 1998, 186(2), 71-77 — Cold stimulus, immersing the hand into ice water, was given to pregnant women with and without preeclampsia. The uterine artery blood flow was observed before, during and after the stimulus by Doppler ultrasound. The pulsatility index in the uterine artery blood flow was significantly increased by the cold exposure in preeclampsia from 1.14 to 1.52, whereas it increased in normal control from 0.95 to 1.25. In two of 11 cases of preeclampsia with fetal growth restriction, cold stimulus to the mother elicited a decrease of variability on fetal heart rate monitoring. Cold stimulus induces the constriction of the uterine artery, leading to a decrease of placental blood flow. ——— uterine artery blood flow; cold pressor test; preeclampsia © 1998 Tohoku University Medical Press

Various stresses on pregnant woman have been considered as factors related to preterm labor and delivery (Hedegaard et al. 1993; Luke et al. 1995). However, physiological responses to the stress by the mother are not been fully understood. A strong cold stimulus, such as immersing the hand in ice water, may elicit pain and elevation of blood pressure. Lewis (1929) first described the vascular responses to a cold stimulus and noted that the capillary beds of a given finger tip initially constrict and then periodically dilate for short periods.

One of the objectives of the present study was to assess whether a uterine artery, a medium-sized vessel, constricts in the pregnant woman with an exposure to the cold stimulus. The diminution of placental circulation following a uterine

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artery constriction may lessen the oxygen delivery to the fetus and worsen the fetal state if the fetal basal oxygen supply is low. According to the notion that the decrease of uterine blood flow leads to the impairment of oxygen exchange, a contraction stress test is applied in clinical bases to estimate the fetal capacity in placental insufficiency to endure the transient ischemia during labor. If the cold stimulus to the patient changes uterine arterial blood flow in pregnant woman, the cold pressor test may be clinically applied to predict fetal outcome.

MATERIALS AND METHODS

A cold pressor test was performed in eleven pregnant women with preeclampsia at 32 to 38 gestational weeks. Severe preeclampsia was defined as systolic pressure over 160 mmHg, and mild as over 140 mmHg. Three of the eleven were categorized as severe and the others as mild from the value of the systolic blood pressure in the examination period. Seven pregnant women from 36 to 39 gestational weeks without preeclampsia were selected for the control. Informed consents were obtained from all the pregnant women and their husband before the test.

An ice water bath was prepared at a temperature of 1–4°C. Fetal heart rate monitoring was performed with a Corometrics fetal monitoring system 116 (Corometrics, Wallingford, CN, USA) and the blood pressure was monitored with a Finapres (Ohmeda, Englewood, CO, USA) placed around the third digit of the right hand. The pregnant woman lay in a semi-Farlor position and her left hand was immersed in the ice water for at least three minutes. Velocimetry of uterine artery blood flow was performed by an ultrasound machine connected to a 3.5 or 5.0 MHz Doppler probe (Toshiba SSA-270A, Kawasaki). A Doppler blood flow pattern was obtained three times (before, during and after the immersion into the iced water), when the sampling size of the pulsed Doppler was 2 to 3 mm wide, with the angle of the pulsed Doppler beam to the vessel less than 60° (Fig. 1). A low-cut, 50 MHz filter was also used. Pulsatility index (PI) was defined and calculated according to the installed software.

$$PI = (\text{maximum blood flow} - \text{minimum blood flow}) / \text{mean blood flow}$$

Fetal heart rate variability was interpreted based on visual analysis with subjective judgement of smoothness or flatness of the baseline.

Statistical analysis was performed by paired *t*-test. A $p < 0.05$ was considered statistically significant.

RESULTS

The cold stress elevated the blood pressure in pregnant women and normal controls from 10 to 28 mmHg more than that at rest. The extent of systolic blood pressure elevation was not related to the presence of preeclampsia.

All 11 preeclampsia cases showed an increase in PI from the cold stress in the uterine artery blood flow, whereas 6 of 7 normal control cases showed an increase

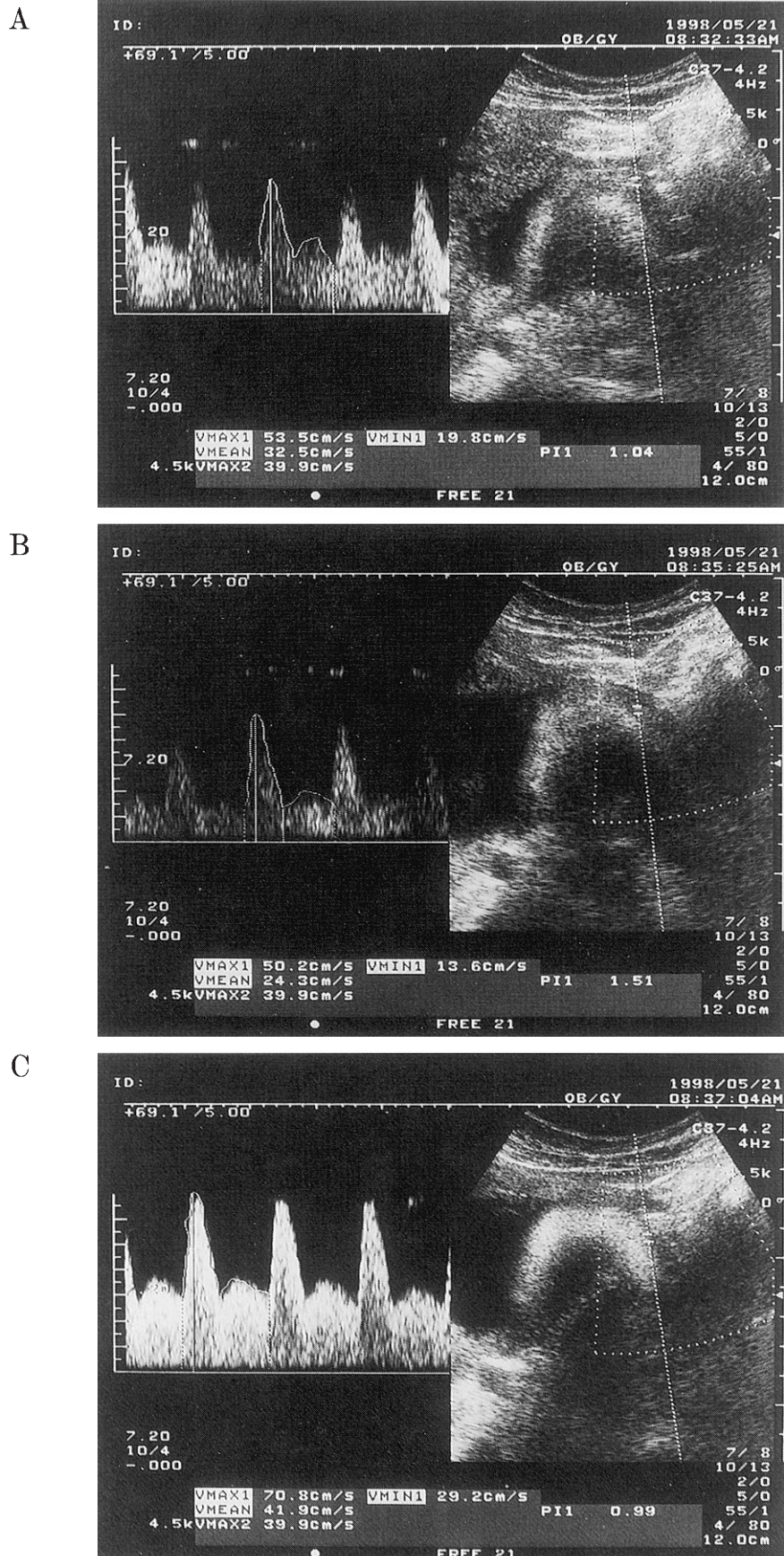


Fig. 1. Doppler flow waveforms in a uterine artery before (A), during (B) and after (C) the cold stimulus in one case.

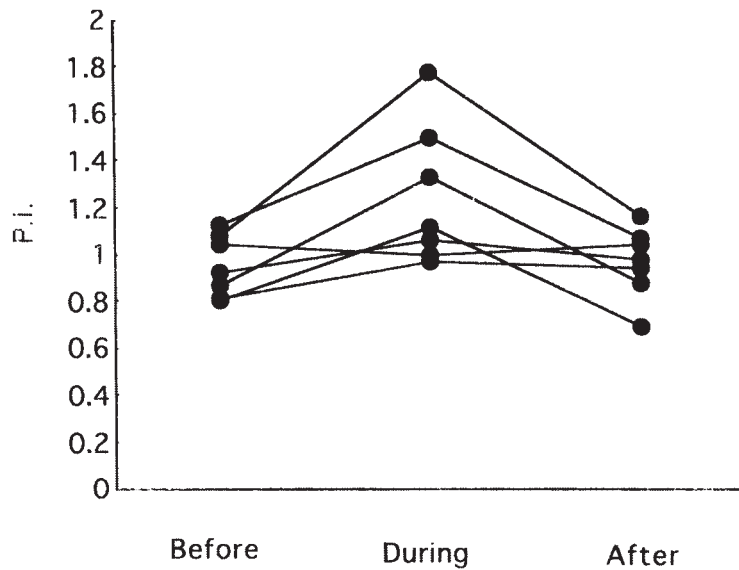


Fig. 2. Change of PI in pregnant women without preeclampsia from the cold pressor stimulus.

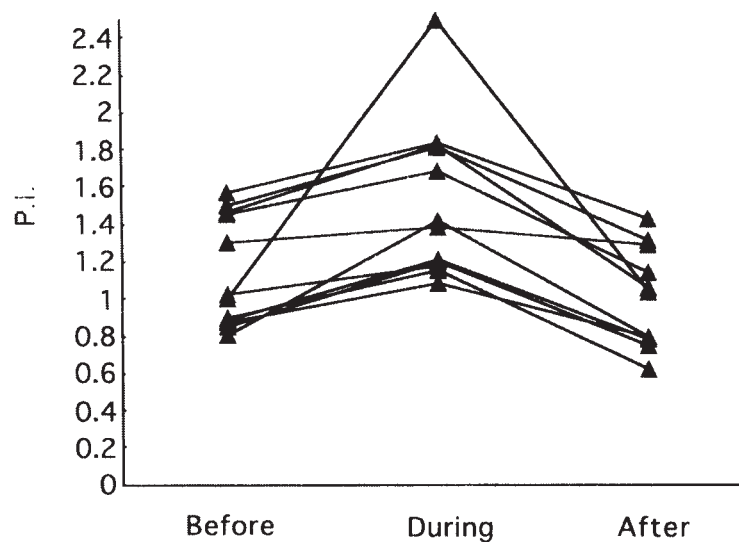


Fig. 3. Change of PI in pregnant women with preeclampsia from the cold pressor stimulus.

in PI (Figs. 2 and 3). The mean PI in preeclampsia was 1.14 ± 0.30 (mean \pm s.d.) before the cold stimulus, significantly increased to 1.52 ± 0.42 during, and returned to 1.00 ± 0.27 after the completion. The index in normal controls also changed from 0.95 ± 0.13 before, to 1.25 ± 0.30 during and 1.00 ± 0.15 after the cold exposure (Table 1). The PI value was not statistically different in either before or during the cold exposure between preeclampsia and normal controls, although the mean values were higher in preeclampsia than in normals.

In two cases with preeclampsia, variability of fetal heart rate monitoring decreased during the cold exposure and recovered after ending the stress. These cases turned out to be growth-restricted babies weighing 1986 g at 37 and 1504 g at 36 weeks of gestation, delivered by cesarean section.

TABLE 1. *Pulsatility indices of uterine artery blood flow before, during and after the cold stimulus to the pregnant women*

	Before	During	After
Preeclampsia ($n=11$)	1.14 ± 0.30	1.52 ± 0.42	1.00 ± 0.27
Normal ($n=7$)	0.95 ± 0.13	1.25 ± 0.30	1.00 ± 0.15
Mean \pm S.D.			

DISCUSSION

This study clearly demonstrated that cold stimulus brought about an increase of resistance in the uterine artery following the decrease of blood flow. Changes in the blood flow by a cold pressor stimulus in medium-sized vessels other than the uterine artery, such as the radial and intracerebral arteries, have been already demonstrated (Perret et al. 1989; Miceli et al. 1994). It is especially important to note that in preeclampsia, where the vascular change leading to placental insufficiency may develop, the fetus may deteriorate from the constriction by cold stimulus and suffer from hypoxia.

Vasoconstriction from the cold exposure is thought to come through an increase in the sympathetic efferent input to the adrenal, without a significant effect on the autonomic efferent cardiac signals. It has been controversial whether chemical mediators would be involved in the sympathetic activation by the cold exposure (Goldstein et al. 1994; Grojec et al. 1996; Ceresini et al. 1997). From an old study by Reilly et al. (1935), irritation of the autonomic nervous system may break down microcirculation in the peripheral arterioles and eventually elicit organ failures. This phenomenon is thought to be secondary to the vasospasms in a hyperstimulated sympathetic nervous system. If the exposure of the stress, which induces the irritation of sympathetic activity to pregnant women, is frequent, uterine artery blood flow should diminish with the constriction and lead to a decrease in the placental blood supply, followed by a growth restriction of the fetus.

The etiology of preeclampsia has been discussed for a long period and various physiological and hematologic factors have been reported to be involved. Recently, angiospastic phenomena occurring in the hepatic artery were demonstrated by angiography in HELLP syndrome (Matsuda et al. 1994), and in the cerebral artery in eclampsia by MR angiography (Kanayama et al. 1993). Since preeclampsia is etiologically regarded as an angiospastic syndrome, based on the fact that both of HELLP syndrome and eclampsia are closely associated with preeclampsia and that the serum factor(s) responsible for the vascular changes that occur in preeclampsia was demonstrated (Tulenکو et al. 1987), it is likely that vessels in pregnant women with preeclampsia may be changed to be more sensitive to the stress inducing angiospasmus. In this study, there were no differences

between preeclampsia and normal controls in terms of how much the blood pressure rises or how much the uterine artery blood flow diminishes from the cold stress. However, the extent of the response seems to be different among those with preeclampsia.

The contraction stress test has been clinically used to forecast fetal health. In this test, uterine contraction, pharmacologically or physically induced for brief periods, impairs the oxygen exchange. It was demonstrated that the uterine artery flow resistance increased significantly during contractions in the contraction stress test (Olofsson et al. 1996). The disadvantage of this test is the time lapse and it can not be used on pregnant women in jeopardy of premature delivery. In order to reduce the uterine blood flow to examine the critical threshold of the fetus, the cold pressor test may be a substitute to the contraction stress test.

During the cold exposure, two of the 11 pregnant women with preeclampsia showed a diminished variability of fetal heart rate. Although the outcome of these two fetuses was favorable, they were little-for-date babies compared to the Japanese standard. Loss of variability induced by the cold stimulus to the mother implied that these babies in utero were vulnerable to the impairment of oxygen exchange. From our experience, the cold pressor stimulus may be used as one of the clinical tools to examine the vascular response in preeclampsia and the presence of placental insufficiency.

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