ORIGINAL ARTICLE

Pre-hypertension predicts pregnancy induced hypertension and its postpartum progression

Shintaro Makino^{1,2}, Atsushi Iwata², Hiroyuki Seki², Satoru Takeda^{1,2}
¹Department of Obstetrics and Gynecology, Juntendo University, ²Department of Obstetrics and Gynecology, Saitama Medical University, Saitama Medical Centre

Reprint request to:

Shintaro Makino, M.D., Ph.D.,
Department of Obstetrics and
Gynecology, Juntendo University,
2-1-1 Hongo Bunkyo-ku, Tokyo,
113-8421, Japan.
E-mail: shintaro@juntendo.ac.jp

Key words:

postpartum progress, pregnancy
induced hypertension, pre-
hypertension

Received: November 22, 2012

Revised: December 18, 2012

Accepted: June 29, 2013

Aim: We investigated incidences of pregnancy induced hypertension (PIH) and prolonged symptoms (hypertension and/or proteinuria) during the puerperal period, focusing on blood pressure in the early second trimester.

Methods: Initial blood pressure data at 16 to 20 weeks of gestation were available from 1,398 women for analysis. Data were classified into the following groups: normal, mild pre-hypertension (preHT), severe preHT, and hypertension, according to JNC-7 criteria. Both the incidence and duration of symptoms were investigated in each group.

Results: PIH incidences significantly increased as initial blood pressure increased. Also, significantly prolonged puerperal periods were observed in cases of severe preHT.

Conclusions: Our data confirmed that initial blood pressure may be a useful predictor of subsequent PIH. Remaining symptoms in the puerperal period may be caused by latent endothelial cell dysfunction seen in preHT before or in early pregnancy.

Introduction

Pregnancy involves substantial changes in vascular function in order to accommodate dramatic increases in blood volume and uteroplacental blood flow for the growing fetus. Despite increased hemodynamics, decreased peripheral resistance results in reduced mean arterial blood pressure mid-pregnancy. Vascular endothelial cells release endothelium-derived relaxing factors and play an important role in the regulation of vascular tone, vascular permeability, and blood coagulation to help maintain circulatory homeostasis.^{1–4)} Endothelial dysfunction has recently been considered a central pathogenic feature of pregnancy induced hypertension (PIH), especially preeclampsia (PE).⁵⁾ Women with a history of PE may exhibit vascular endothelial dysfunction or dyslipidemia and are reportedly more likely to develop ischemic heart disease later in their lives.⁶⁾

Although hypertension and PIH were formerly defined by a blood pressure of 140/90 mmHg or higher, the World Health Organization and US Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure advocated the concept of pre-hypertension (preHT) in 2003 (JNC-7).⁷⁾ The Japanese Society of Hypertension (JSH) defined “high-normal

blood pressure” in the 2009 JSH Guidelines for the Management of Hypertension (JSH2009),⁸⁾ and lifestyle modification is now more aggressively recommended for individuals with a blood pressure formerly regarded as normal or high-normal. If a woman has preHT associated with mild vascular endothelial damage at earlier than 20 gestational weeks, however, pregnancy is believed to increase the vascular load and thus raise incidences of PE and prolonged vascular dysfunction during the puerperal period.

To determine whether preHT is a significant predictor of PIH and its postpartum progression, we classified blood pressure at 16 to 20 weeks of gestation as initial blood pressure according to JNC-7 criteria and investigated the incidence of PIH. Prolonged symptoms of PIH during the puerperal period were also investigated in 4 hypertension groups and by type of PIH.

Materials and methods

Among those who delivered at our hospital between 2001 and 2003, 1,398 women had initial blood pressure data available for analysis and were included in this study. Multiple pregnancies were excluded. Initial blood pressure at 16–20 weeks of gestation was classified according to JNC-7 criteria. In particular, preHT cases

were divided into 2 groups: the mild preHT group, with a systolic blood pressure of 120 to 129 mmHg or diastolic blood pressure of 80 to 84 mmHg, and the severe preHT group, with a systolic blood pressure of 130 to 139 mmHg or diastolic blood pressure of 85 to 89 mmHg. For statistical analysis, the χ^2 test and ANOVA were employed, with a *P*-value less than 0.05 indicating a statistically significant difference.

Comparison of initial blood pressure values

According to blood pressure values measured at 20 weeks of gestation, all cases were divided into the following 4 groups: normal, mild preHT, severe preHT, and hypertension. Incidence of PIH was then investigated in each group.

Investigation of prolonged PIH symptoms during the puerperal period

Excluding those in the superimposed hypertension group, 1,192 cases were examined for duration of symptoms (blood pressure and proteinuria) and type of PIH during the puerperal period.

Results

Comparison of initial blood pressure measurements

The overall incidence of PIH was 8.8%. There were 689 cases (49.3%) in the normotensive group, 363 (26.0%) in the mild preHT group, 218 (15.6%) in the severe preHT group, and 128 (9.2%) in the hypertension group. No differences in age, parity, and body mass index were observed between the groups. The incidence of PIH was 17 (2.5%) in the normotensive group, 25 (6.9%) in the mild preHT group, 36 (16.5%) in the severe preHT group, and 45 (35.2%) in the hypertension group.

the mild preHT group, 36 (16.5%) in the severe preHT, and 45 (35.2%) in the hypertension group, showing significant increases as initial blood pressure increased ($P < 0.05$) (Figure 1).

Investigation of prolonged PIH symptoms during the puerperal period

Figure 2 shows cases with prolonged PIH symptoms during the puerperal period. Most cases with prolonged symptoms had hypertension plus proteinuria (HP type). Among 22 cases that developed HP type in the severe preHT group, 9 (40.9%) continued to have symptoms after 12 weeks postpartum. In cases of only hypertension (H type), relatively prompt improvement of symptoms was observed regardless of initial blood pressure status.

Discussion

PIH occurs in 2% to 5% of all pregnant women, and known risk factors include primiparity, history of PIH, obesity, hypertension, increased maternal weight, and twin pregnancy.^{9–11} As early as possible in routine prenatal care, these women should be identified to initiate lifestyle guidance and appropriate treatments to prevent PIH onset and prevent the condition from becoming severe. In this study, we used blood pressure in the early mid-trimester of pregnancy as initial blood pressure to correlate with the incidence of PIH. Blood pressure values measured early in pregnancy or at the initial examination were recently reported to be related to the onset of PIH,^{12,13} which is consistent with the findings of our present study. Odegård et al.¹⁴ reported that the relative risk of developing PE was 3.6 (95% CI, 2.0–6.6), showing a strong correlation with a systolic

Figure 1. Incidence of PIH classified by initial blood pressure.

Initial blood pressure was significantly associated with the incidence of PIH.

* $P < 0.05$, by χ^2 test.

Figure 2. Prolonged symptoms during the puerperal period.

Prolonged symptoms were observed in cases with severe preHT at 6 and 12 weeks postpartum compared to those with normotensive and mild preHT. In cases with continued symptoms after the 12th week postpartum, there was a significant difference between HP type (9 cases, 40.9%) and H type (no cases, 0.0%) ($P < 0.05$).

H type, hypertension only; HP type, hypertension and proteinuria.

* $P < 0.05$, by χ^2 test.

blood pressure of 130 mmHg or more at the initial examination in early pregnancy. The higher incidence of PIH in women with preHT may suggest they were likely to have mild endothelial cell dysfunction before or in the early stages of pregnancy.

Our results also showed that severe preHT following hypertension plus proteinuria involves a higher risk of prolonged symptoms in the puerperal period. It is therefore reasonable to suggest that there may be a subgroup of women who develop PIH due to the involvement of endothelial cell dysfunction before or in early pregnancy. In cases showing persistent symptoms after 12 weeks postpartum, many had suspected latent endothelial cell dysfunction associated with preHT in early pregnancy, advanced age, and past pregnancies.

Conflict of interest

None to report.

References

- Vallance P, Collier J, Moncada S. Effects of endothelium-derived nitric oxide on peripheral arteriolar tone in man. *Lancet*. 1989; 2: 997–1000.
- Moncada S, Palmer RM, Higgs EA. Nitric oxide: physiology, pathophysiology, and pharmacology. *Pharmacol Rev*. 1991; 43: 109–142.
- Kuriyama H, Kitamura K, Itoh T, Inoue R. Physiological features of visceral smooth muscle cells, with special reference to receptors and ion channels. *Physiol Rev*. 1998; 78: 811–920.
- Yamamoto T, Suzuki Y, Kojima K, Suzumori K. Reduced flow-mediated vasodilation is not due to a decrease in production of nitric oxide in preeclampsia. *Am J Obstet Gynecol*. 2005; 192: 558–563.
- Svedas E, Nisell H, Vanwijck MJ, Nikas Y, Kublickiene KR. Endothelial dysfunction in uterine circulation in preeclampsia: can estrogens improve it? *Am J Obstet Gynecol*. 2002; 187: 1608–1616.
- Wikström AK, Haglund B, Olovsson M, Lindeberg SN. The risk of maternal ischaemic heart disease after gestational hypertensive disease. *BJOG*. 2005; 112: 1486–1491.
- Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA*. 2003; 289: 2560–2572.
- The Japanese Society of Hypertension. ed. Guidelines for the Management of Hypertension 2009. Tokyo: Life Science Publishing Co., Ltd., 2009. (In Japanese.)
- Sibai BM, Lindheimer M, Hauth J, et al. Risk factors for preeclampsia, abruptio placentae, and adverse neonatal outcomes among women with chronic hypertension. National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. *N Engl J Med*. 1998; 339: 667–671.
- Eskenazi B, Fenster L, Sidney S. A multivariate analysis of risk factors for preeclampsia. *JAMA*. 1991; 266: 237–241.
- Stone JL, Lockwood CJ, Berkowitz GS, Alvarez M, Lapinski

Pre-hypertension and pregnancy induced hypertension (PIH)

- R, Berkowitz RL. Risk factors for severe preeclampsia. *Obstet Gynecol.* 1994; 83: 357–361.
12. Reiss RE, O'Shaughnessy RW, Quilligan TJ, Zuspan FP. Retrospective comparison of blood pressure course during preeclamptic and matched control pregnancies. *Am J Obstet Gynecol.* 1987; 156: 894–898.
13. Sibai BM, Gordon T, Thom E, et al. Risk factors for preeclampsia in healthy nulliparous women; a prospective multicenter study. *Am J Obstet Gynecol.* 1995; 172: 642–648.
14. Odegård RA, Vatten LJ, Nilsen ST, Salvesen KA, Austgulen R. Risk factors and clinical manifestations of pre-eclampsia. *BJOG.* 2000; 107: 1410–1416.