ORIGINAL ARTICLE

Management of severe hypertension by nicardipine intravenous infusion in pregnancy induced hypertension after cesarean section

Ayano Matsuura¹, Tamao Yamamoto², Tomoe Arakawa³,
Yoshikatsu Suzuki¹

¹Department of Obstetrics and Gynecology, Nagoya City West Medical Center, Nagoya, Japan,

²Department of Obstetrics and Gynecology, Mammy Rose Clinic, Toyohashi, Japan,

³Department of Pharmacy, Nagoya City West Medical Center, Nagoya, Japan

Reprint request to:

Tamao Yamamoto, M.D., Ph.D.,
Department of Obstetrics and
Gynecology, Mammy Rose Clinic,
Morishita 1, Takasu-Cho,
Toyohashi 441-8006, Japan.
E-mail: tamao-y@outlook.com

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Aim: The aim was to retrospectively investigate whether intravenous administration of nicardipine might be useful for managing blood pressure (BP) after cesarean section in women with severe pregnancy induced hypertension (PIH).

Methods: Fifty-one postpartum women after cesarean section with severe hypertension (systolic BP [SBP] ≥ 160 mmHg) (28 preeclampsia [PE] and 23 gestational hypertension [GH]) were enrolled. According to the modified nicardipine sliding scale procedure, a continuous intravenous infusion of nicardipine at 1 to 6 mg/h was given to goal (SBP 120–140 mmHg) by evaluation every 30 min.

Results: Initial SBPs were 172 ± 10 mmHg in PE and 175 ± 11 mmHg in GH. The stable dose of nicardipine was 1.9 ± 0.8 mg/h in PE and 1.4 ± 0.6 mg/h in GH. The stable dose was greater in PE than in GH. Stable SBPs were 133 ± 11 mmHg in PE and 136 ± 11 mmHg in GH. SBP decrease rates were $23 \pm 6\%$ in PE and $23 \pm 6\%$ in GH.

Conclusion: In this retrospective study, intravenous administration of nicardipine using a sliding scale appeared useful for decreasing BP in both PE and GH.

Introduction

Pregnancy induced hypertension (PIH) is classified according to the severity of hypertension, with mild type (blood pressure [BP] ranges from 140/90 to 159/109 mmHg) and severe type (BP $\geq 160/110$ mmHg), according to the Japan Society for the Study of Hypertension in Pregnancy (JSSH) criteria.^{1,2)} In the 2009 PIH management guidelines of the JSSH, the administration of oral antihypertensive drugs for PIH should be started when the BP is $\geq 160/110$ mmHg to prevent maternal organ damage (cerebrovascular, cardiac, or renal damage) by prompt antihypertensive treatment.³⁾ As the BP goal, systolic BP (SBP) ranges from 140 to 159 mmHg, diastolic BP (DBP) ranges from 90 to 109 mmHg, and mean arterial pressure (MAP) should be

decreased by 15% to 20%.³⁾

The treatment should be switched to intravenous injection therapy, such as nicardipine or hydralazine, when BP control by oral drugs is inappropriate, during labor, and in postpartum women after cesarean section. The guidelines recommend intravenous nicardipine infusion using a sliding scale in both pregnancy and postpartum based on the DBP. In pregnant women, administration should be started when DBP is ≥ 110 mmHg, with a BP goal of DBP from 90 to 109 mmHg. In the postpartum period, administration should be started when DBP is ≥ 90 mmHg, and the BP goal is DBP < 90 mmHg.³⁾

The Japan Society of Hypertension (JSH) Guidelines 2014 for the Management of Hypertension state that the basic treatment for PIH is the interruption of pregnancy,

- If SBP remains ≥ 160 mmHg, Nicardipine stock solution (1 mg/ml) is given intravenously with a syringe pump, starting with an initial dose of 1 mg/h.
- The SBP goal is ranged from 120 to 140 mmHg.
- BP is measured closely and evaluated after 30 min.

SBP (mmHg)	Dose of nicardipine (mg/h)	Evaluation of BP
SBP ≥ 140	The dose is increased by 1mg/h to a maximum dose of 6 mg/h. Call Dr. if the dose is more than 6 mg/h.	Every 30 min
$120 \leq \text{SBP} < 140$	The dose is maintained.	Every 60 min
SBP < 120	The dose is reduced by 1 mg/h or stopped.	Every 60 min

Figure 1. The sliding scale of continuous nicardipine intravenous infusion.

BP, blood pressure; SBP, systolic blood pressure.

and antihypertensive therapy should be given for maternal protection. It recommends that methyldopa, hydralazine, labetalol, and long-acting nifedipine (only after 20 weeks of gestation) should be used as the first-choice antihypertensive oral drugs. Intravenous administration should be selected when a hypertensive emergency (BP $\geq 180/120$ mmHg) occurs.⁴⁾

According to the JSSHP definitions, preeclampsia is present with hypertension and proteinuria, and gestational hypertension is hypertension without proteinuria.¹⁾ The pathogenic mechanisms of preeclampsia and gestational hypertension may differ.

In this retrospective study, whether intravenous administration of nicardipine using a sliding scale might be useful for the management of preeclampsia and gestational hypertension was investigated, focusing on changes in SBP.

Methods

Fifty-one postpartum women after cesarean section with SBP ≥ 160 mmHg, 28 with preeclampsia and 23 with gestational hypertension, were enrolled. They included 14 patients (4 with preeclampsia and 10 with gestational hypertension) with a hypertensive emergency (≥ 180 mmHg).

If SBP remained ≥ 160 mmHg, a continuous intravenous infusion of nicardipine at 1 to 6 mg/h using a sliding scale was given. The SBP goal was < 140 mmHg. The sliding scale procedure is shown in Figure 1.

The decrease in SBP was observed during drug administration. When SBP reached the appropriate SBP (< 140 mmHg) for more than 30 min, this was considered a stable BP. Initial SBP, stable SBP, stable dose of nicardipine, and the SBP decrease rate (stable SBP/initial SBP) were evaluated.

This study was retrospectively conducted in the Department of Obstetrics and Gynecology at Nagoya City West Medical Center from 2011 to 2014. The protocol of

this study was approved by the Clinical Investigation Ethics Committee of Nagoya City West Medical Center. Informed consent was obtained from each patient. PIH was retrospectively diagnosed 3 months after delivery according to the JSSHP criteria.³⁾

Statistical analysis

Data are expressed as mean $\pm$ SD. Statistical analysis was performed using Excel Toukei 2012 (SSRI Co., Ltd., Tokyo, Japan). The data were evaluated using the unpaired *t*-test, the Mann-Whitney *U* test, and the chi-square test comparing the preeclampsia and gestational hypertension groups. The level of significance was set at $P < 0.05$.

Results

Decrease in SBP with drug administration

Initial SBPs were 174 ± 10 mmHg in all patients, 172 ± 10 mmHg in preeclampsia, and 175 ± 11 mmHg in gestational hypertension (Table 1). All patients reached a stable SBP within 6 h (107 ± 63 min in all patients, 108 ± 66 min in preeclampsia, 106 ± 60 min in gestational hypertension). Stable SBPs were 134 ± 11 mmHg in all patients, 133 ± 11 mmHg in preeclampsia, and 136 ± 11 mmHg in gestational hypertension (Table 1). The SBP decrease rates were $22 \pm 7\%$ in all patients, $23 \pm 6\%$ in preeclampsia, and $23 \pm 6\%$ in gestational hypertension (Table 1). Stable SBP > 140 mmHg was seen in 10 patients overall (6 with preeclampsia and 4 with gestational hypertension).

The severity of SBP was divided into two levels, with level I SBP from 160 to 180 mmHg and level II SBP at more than 180 mmHg (hypertensive emergency). Level I was present in 24 of 28 preeclampsia cases and in 13 of 23 gestational hypertension cases. The severity of SBP differed between the preeclampsia and gestational hypertension cases ($P = 0.015$, chi-square test).

Stable SBPs were similar between the preeclampsia

Table 1. Decrease in systolic blood pressure (SBP) with drug treatment

	Number	Initial SBP (mmHg)	Stable		
			SBP (mmHg)	dose (mg/h)	Rate of decrease (%)
PE	28	172 ± 10	133 ± 11	1.9 ± 0.8*	23 ± 6
Level I	24	170 ± 7 [†]	132 ± 11	1.9 ± 0.7	22 ± 6
Level II	4	187 ± 10	139 ± 8	2.3 ± 1.0	25 ± 8
GH	23	175 ± 11	136 ± 11	1.4 ± 0.6	23 ± 6
Level I	13	168 ± 7 [†]	136 ± 5	1.2 ± 0.4 [†]	19 ± 4 [†]
Level II	10	186 ± 5	136 ± 16	1.7 ± 0.7	27 ± 9
Total	51	174 ± 10	134 ± 11	1.7 ± 0.7	22 ± 7

Level I ranges from 160 to 180 mmHg, Level II is ≥ 180 mmHg. Data are expressed as mean ± SD. * $P < 0.05$ vs GH;

[†] $P < 0.05$ vs. Level II.

SBP, systolic blood pressure; PE, preeclampsia; GH, gestational hypertension.

Table 2. Stable doses and reduction rates

	Stable dose of nicardipine		
	1 mg/h (n)	2 mg/h (n)	3 mg/h (n)
PE			
Level I (n = 24)	24 ± 7% (8)	21 ± 4% (11)	21 ± 8% (5)
Level II (n = 4)	19% (1)	24% (1)	29 ± 10% (2)
GH			
Level I (n = 13)	20 ± 4% (10)	16 ± 1% (3)	—
Level II (n = 10)	27 ± 9% (4)	27 ± 11% (5)	24% (1)

Case numbers are in parentheses. Data are expressed as mean ± SD.

PE, preeclampsia; GH, gestational hypertension.

and gestational hypertension cases. The SBP decrease rate was greater for level II than for level I in only gestational hypertension.

Dose of nicardipine with stable SBP

The stable dose of nicardipine was 1.7 ± 0.7 mg/h overall, 1.9 ± 0.8 mg/h in preeclampsia, and 1.4 ± 0.6 mg/h in gestational hypertension. It was greater in preeclampsia than in gestational hypertension ($P = 0.0146$, unpaired t -test and $P = 0.0018$, Mann-Whitney U test; Table 1). The dose of nicardipine was greater in level II (1.9 ± 0.7 mg/h vs. 2.3 ± 1.0 mg/h in preeclampsia and 1.2 ± 0.4 mg/h vs. 1.7 ± 0.7 mg/h in gestational hypertension) than in level I in only gestational hypertension (Table 1).

In preeclampsia, the dose of nicardipine was greater even though most patients belonged to Level I (24 of 28). Seven patients needed a dose of nicardipine of 3 mg/h. In gestational hypertension, only one of the 10 level II patients needed a dose of nicardipine of 3 mg/h (Table 2).

Discussion

JSH Guidelines for the Management of Hypertension 2014 state that antihypertensive drug therapy for PIH should be started at a BP ≥ 160/110 mmHg. However, if SBP is greater than 180 mmHg or DBP is greater than 120 mmHg in pregnant or postpartum women, antihypertensive treatment should be started under a diagnosis of hypertensive emergency using drugs for intravenous injection.⁴⁾

The 2009 guidelines of PIH management by the JSSHP state that the treatment should be switched to intravenous injection therapy when BP control by oral drugs is inappropriate, during labor, and postpartum after cesarean section. Intravenous nicardipine infusion using a sliding scale in both pregnancy and postpartum based on the DBP has been recommended.²⁾

In our previous study, just before eclampsia, all patients had a SBP ≥ 160 mmHg, while few had DBP ≥ 110 mmHg. Furthermore, eclamptic women tended to have a higher SBP than non-eclamptic women, while both

DBP and MAP were similar to those in non-eclamptic patients.⁵⁾ Thus, we focused on SBP. If SBP was ≥ 160 mmHg, a continuous intravenous infusion of nicardipine at 1 to 6 mg/h using a sliding scale was given, with an SBP goal of less than 140 mmHg. Another study might be done by using DBP in the future.

Using the revised nicardipine sliding scale, in most PIH patients with severe hypertension, SBP could be kept under 140 mmHg, and it took 2 h to reach a stable SBP.

The concentration of nicardipine hydrochloride solution is 1 mg/ml. In a hypertensive emergency, administration at $0.5 \mu\text{g/kg/min}$ is started, and it ranges from 0.5 to $2 \mu\text{g/kg/min}$. In women weighing 50 kg, the starting dose of nicardipine is 1.5 mg/h, and it is increased up to 6 mg/h according to this equation. In the present study, nicardipine was administered at an average dose of 1.7 mg/h and ranged from 1 to 3 mg/h.

It is well known that there are differences in pathogenesis between preeclampsia and gestational hypertension. As for severity, preeclampsia is more severe than gestational hypertension, and management of preeclampsia is more difficult than that of gestational hypertension. The NICE guidelines thus recommended different management strategies for preeclampsia and gestational hypertension.⁶⁾

In the present study, in postpartum women given intravenous administration, the more severe the hypertension was, the higher dose of nicardipine was needed in gestational hypertension. In preeclampsia, even though most patients had Level I hypertension, the dose of nicardipine was greater than in gestational hypertension. Postpartum, after interrupted pregnancy, strict management of preeclampsia should be needed. In a previous study, oral administration of labetalol, β -receptor, and a selective α_1 -receptor blocker effectively decreased BP during pregnancy. However, the effectiveness of labetalol was greater in patients with gestational hypertension (58%) than in those with preeclampsia (27%). This confirmed that labetalol would be more effective in gestational hypertension than in preeclampsia.⁷⁾ Thus, the pathogenesis of preeclampsia might not be simple. Furthermore, it may be difficult to control BP in preeclampsia compared with gestational

hypertension. From our results, it is suggested it might be necessary to terminate the pregnancy earlier in preeclampsia than gestational hypertension. However, it is often difficult to discriminate the two in the clinical course.

In this retrospective study, intravenous administration of nicardipine using a sliding scale appeared useful for the management of both preeclampsia and gestational hypertension.

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Conflict of interest

None.

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