

Usefulness of labor induction in pregnancies complicated by preeclampsia

Shoko Kawano,¹ Rie Kato,² Toshiyuki Okutomi,³ Yoko Ohnishi,¹ Yuji Kanai,¹
Junko Mochizuki,¹ Kan Amano,¹ Nobuya Unno¹

¹Department of Obstetrics, Kitasato University School of Medicine

²Department of Research and Development Center for New Medical Frontiers, Kitasato University School of Medicine

³Department of Anesthesiology, Kitasato University School of Medicine

Objective: The aim of this study is to examine maternal and fetal outcomes of labor induction and to discover desirable conditions for labor induction in pregnancies complicated by preeclampsia.

Methods: We conducted a retrospective study of 195 pregnant women with preeclampsia. We analyzed factors influencing the mode of delivery of preeclamptic patients based on their medical records.

Results: Elective cesarean section was performed in 108 cases among 195 women, and labor induction was performed in 87 cases. Vaginal delivery following labor induction was achieved in 86% of the cases. The incidence of cesarean section in patients of 33–34 weeks' gestation was higher than that in those of 35–36 weeks' gestation (78% vs. 29%, $P < 0.02$). The timing of onset and severity of preeclampsia were not associated with the achievement rate of labor induction. Labor induction was achieved more frequently when the cervical opening was ≥ 1.5 cm than when the cervical opening was < 1.5 cm in primipara women (95% vs. 75%, $P < 0.048$).

Conclusion: Labor induction is a reasonable choice for termination of pregnancy unless absolute indication of cesarean section is present in late preterm and term preeclampsia, in which cases the cervical opening should be considered especially in primipara women.

Key words: labor induction, neuraxial analgesia, preeclampsia, pregnancy outcome

Introduction

A randomized controlled trial shows that induction of labor is preferable for improving maternal outcome in pregnancies with gestational hypertension or mild preeclampsia beyond 36 weeks' gestation.¹ Furthermore, induction of labor has been shown as a reasonable option compared to elective cesarean section in severe preeclampsia which requires preterm pregnancy termination.²⁻⁵ These findings indicate the importance of labor induction in the management of patients with preeclampsia. However, it has been reported that elective cesarean section has been frequently chosen in Japan as well as Brazil, China, the United States of America to prevent further rise in maternal blood pressure and the onset of serious complications including eclampsia,

intracranial hemorrhage, and placental abruption during labor.⁴⁻⁷

During delivery care of pregnancies with preeclampsia, neuraxial analgesia with continuous lumbar epidural analgesia has been recommended.⁸ Advantages of the method include an attenuation of hypertensive response to labor pain, a reduction in circulating levels of catecholamines and stress-related hormones, an increase in intervillous blood flow, and a smooth transition to epidural analgesia in case of emergency cesarean section without general analgesia. In Japan, when termination of pregnancy is indicated due to worsened maternal symptoms of preeclampsia, one of the main reasons for the preference of cesarean section to vaginal delivery is the limited availability of neuraxial analgesia during vaginal delivery in maternity hospitals. In this

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Correspondence to: Shoko Kawano, Department of Obstetrics, Kitasato University School of Medicine
1-15-1 Kitasato, Minami-ku, Sagami-hara, Kanagawa 252-0374, Japan
E-mail: shoko402@hotmail.co.jp

retrospective case-series study, we examined maternal and fetal outcomes of labor induction and attempted to discover desirable conditions for labor induction complicated by preeclampsia.

Materials and Methods

Among 5,538 singleton deliveries at Kitasato University Hospital between January 2008 and December 2013, we examined singleton pregnancies complicated by preeclampsia, in which termination of pregnancy was required due to worsened maternal conditions before the spontaneous onset of labor. The diagnosis and severity of preeclampsia was made based on the criteria of the Japan Society of Obstetrics and Gynecology published in 2004.⁹ The following data were obtained from medical records and analyzed retrospectively: maternal age, number of primipara, indication of pregnancy termination, gestational weeks of onset of preeclampsia, gestational weeks at delivery, severity of hypertension at the decision of pregnancy termination, mode of delivery (induction of labor, elective or emergency cesarean section), cervical dilatation at labor induction, birthweight, amniotic fluid volume, Apgar score, and umbilical arterial pH.

This study was approved by the institutional review board of Kitasato University School of Medicine and Kitasato University Hospital.

Decision criteria for pregnancy termination and mode of delivery at Kitasato University Hospital

1. During the preterm period, termination of pregnancy was decided based on deterioration of maternal and/or fetal conditions, such as medically uncontrollable severe hypertension, urine protein of more than 5 g/day, platelet count <100,000/ μ l, presence of maternal pleural effusions, placental abruption, the HELLP syndrome (a life-threatening liver disorder thought to be a type of severe preeclampsia characterized by Hemolysis [destruction of red blood cells], Elevated Liver enzymes [indicating liver damage], and Low Platelet count), eclampsia, and non-reassuring fetal cardiotocogram.
2. After 37 weeks' gestation, we preferred termination of pregnancy by labor induction unless contraindicated. However, conservative management was required in the presence of extremely unfavorable cervical conditions (when the cervix is closed and not ripening at all).

3. Either method was selected based on the following indications.

- A. Absolute indications for cesarean section (CS)
 1. Absolute mechanical indications (elective CS): history of cesarean section and/or uterine surgery, uterine anomalies or abnormal presentation, irrespective of maternal conditions and week of delivery.
 2. Absolute maternal/fetal indications for CS (emergency CS): placental abruption, the HELLP syndrome, eclampsia, maternal disorientation of preeclampsia symptoms, or non-reassuring fetal status. Relative indications: pregnancies with gestational weeks less than 34 weeks and/or estimated fetal body weight less than 2,000 g, and when maternal hypertension and/or renal dysfunction were prominent.
- B. Labor induction was recommended unless there was indication for a CS.

Methods of labor induction at Kitasato University Hospital

1. If the Bishop score was less than 6 points at admission, an intracervical balloon catheter was inserted, and up to 40 ml of saline solution was infused.
2. Following removing the balloon catheter the next morning, a 5 mg of prostaglandin E2 tablet was orally administered at 1-hour intervals up to 3–4 times. Then, with more than 1-hour interval after the final prostaglandin E2 administration, intravenous oxytocin infusion was begun at a rate of 1.7–2.5 mIU/min under continuous cardiotocogram monitoring. The oxytocin infusion was increased (maximum dose of 20 mIU/min) at more than 30-minute intervals until effective uterine contraction was obtained. After amniotomy, when necessary, a scalp lead and an intrauterine pressure catheter were placed.
3. When the patient required pain relief, neuraxial analgesia was given by means of CSEA (combined spinal-epidural analgesia) (an intrathecal dose of 2.0 mg bupivacaine with 20 μ g fentanyl followed by continuous infusion of 0.08% ropivacaine with 2 μ g/ml fentanyl at 8 ml/h via lumbar epidural catheter), or by epidural analgesia (9–12 ml ropivacaine 0.2% followed by infusion of 0.08% ropivacaine with 2 μ g/ml fentanyl at 8 ml/h via lumbar epidural catheter).
4. Anti-hypertensive drugs were administered orally, intravenously, and/or intramuscularly to maintain maternal systolic blood pressure <160 mmHg and diastolic pressure <110 mmHg.

Statistical analyses

Statistical analyses were performed using χ^2 test or Fisher's exact test for categorical data and Student's *t*-test or Welch's *t*-test for continuous data. $P < 0.05$ was considered statistically significant.

Results

During the study period, we extracted 195 cases of singleton pregnancies complicated by preeclampsia (Figure 1). Among them, 108 patients underwent elective cesarean sections (32 cases with absolute mechanical indications, 49 cases with absolute maternal/fetal indications, and 27 cases with relative indications). Labor induction was performed in 87 cases.

Vaginal delivery following labor induction was achieved in 71 of 83 cases (86%) with neuraxial analgesia and 4 of 4 cases (100%) without neuraxial analgesia. There was no statistical difference in the vaginal delivery rate between groups with or without neuraxial analgesia ($P = 0.546$) (Figure 1). Instrumental deliveries were

performed in 23 of 75 cases (31%) who achieved vaginal delivery.

The details of the modes of delivery by gestational week at pregnancy termination, excluding cases with absolute indications for cesarean section (Table 1)

Elective cesarean section was chosen in 23 of 25 cases (92%) and 4 of 89 cases (4%) in <35 weeks and ≥ 35 weeks, respectively. The actual indications of the 4 elective cesarean section cases in ≥ 35 weeks were maternal pleural effusion (2 cases), fetal growth restriction, the HELLP syndrome, and immature cervical status. The incidence of cesarean section in 33–34 weeks' gestation was higher than that in 35–36 weeks' gestation (78% vs. 29%, $P < 0.02$).

Onset of preeclampsia and mode of delivery (Table 2)

Excluding 81 cases with absolute indication for cesarean section and 2 cases of uncertain preeclampsia onset gestational week, 25 cases demonstrated symptoms of preeclampsia before 32 weeks and were categorized as

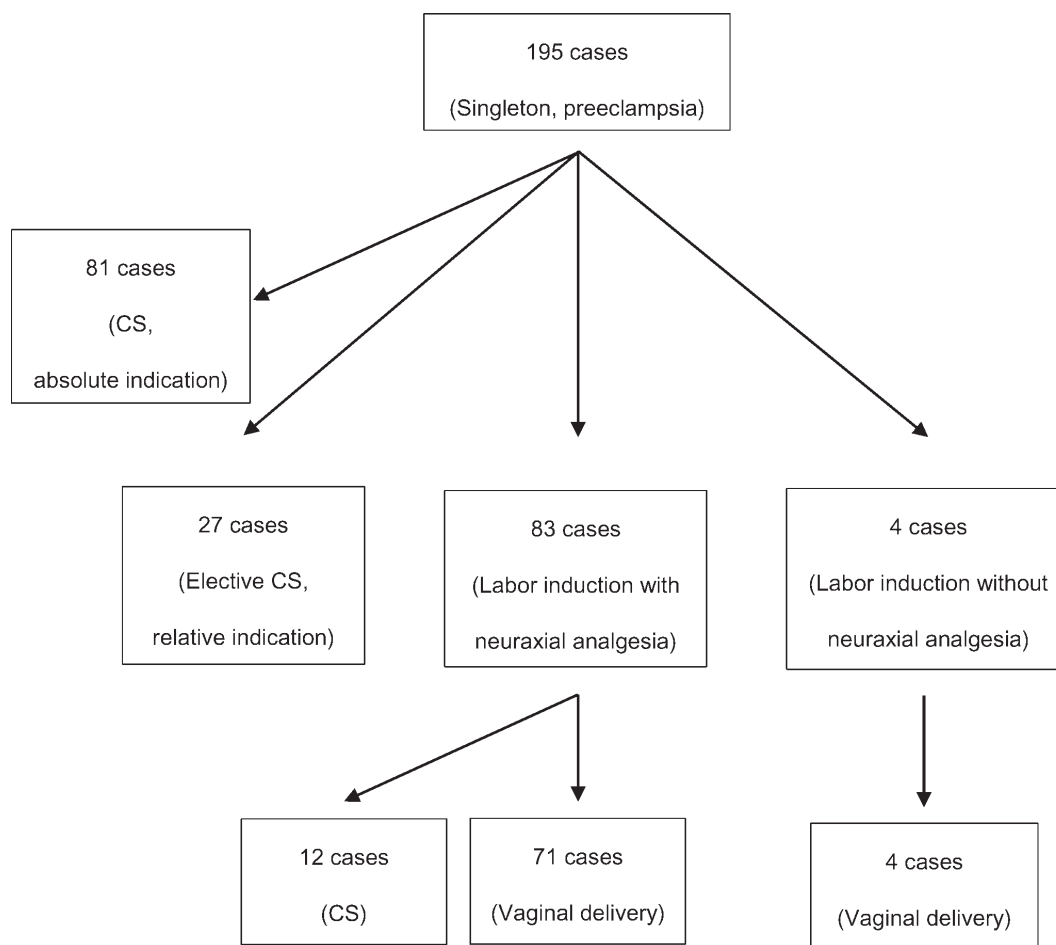


Figure 1. Mode of delivery in 195 cases complicated by preeclampsia
CS, cesarean section

Labor induction complicated by preeclampsia

Table 1. Mode of delivery by gestational week in cases with preeclampsia requiring pregnancy termination*

Gestational age at pregnancy termination (weeks)	Elective CS with relative indications (n = 27)	Labor induction → CS (n = 12)	Labor induction → vaginal delivery (n = 75)	Total (N = 114)
25–26	2 (100%)	0	0	2
27–28	3 (100%)	0	0	3
29–30	5 (100%)	0	0	5
31–32	6 (100%)	0	0	6
33–34	7 (78%)	0	2 (22%)	9
35–36	2 (10%)	4 (19%)	15 (71%)	21
37–38	1 (2%)	3 (6%)	44 (92%)	48
39–41	1 (5%)	5 (25%)	14 (70%)	20

*Excluding 81 cases with absolute indications for cesarean section
CS, cesarean section; n, number of patients

Table 2. Onset of preeclampsia and mode of delivery*

Gestational age at onset of preeclampsia	Gestational age at delivery	Elective CS with relative indications (n = 26)	Labor induction → CS (n = 12)	Labor induction → vaginal delivery (n = 74)	Total (N = 112)
<32 weeks	<35 weeks	16 (100%)	0	0	16
	≥35 weeks	0	2 (22%)	7 (78%)	9
≥32 weeks	<35 weeks	6 (75%)	0	2 (25%)	8
	≥35 weeks	4 (5%)	10 (13%)	65 (82%)	79

*Excluding 81 cases with absolute indications for cesarean section and 2 cases of uncertain preeclampsia onset gestational week

Table 3. Severity of hypertension and mode of delivery

Gestational age at delivery	Severity of hypertension	Elective CS (n = 27)	Labor induction → CS (n = 12)	Labor induction → vaginal delivery (n = 75)	Total (N = 114)
<35 weeks	Mild	5 (83%)	0	1 (17%)	6
	Severe	18 (95%)	0	1 (5%)	19
≥35 weeks	Mild	2 (4%)	5 (11%)	39 (85%)	46
	Severe	2 (5%)	7 (16%)	34 (79%)	43

Table 4. Relationship between cervical opening at labor induction and vaginal delivery rate

Number of births	COL ≥ 1.5 cm	COL < 1.5 cm	P value
Primipara (n = 54)	21/22 (95%)	24/32 (75%)	0.049
Multipara (n = 29)	21/21 (100%)	6/8 (75%)	0.070

COL, cervical opening at labor induction

the early onset group, while 87 cases were categorized as the late onset group. In the early onset group, pregnancy was terminated <35 weeks in 16 cases, and all of those were elective cesarean sections. In contrast, in 9 cases, the pregnancy lasted ≥ 35 weeks of gestation, among which there were 7 induced vaginal deliveries (78%) and 2 cesarean sections (22%) after labor induction. In the early onset group, the vaginal delivery rate was significantly higher in cases of pregnancy termination ≥ 35 weeks of gestation ($P < 0.01$). In the late onset group, elective cesarean section was chosen in 75% of the cases who terminated pregnancy <35 weeks, and 82% of the cases who terminated pregnancy ≥ 35 weeks achieved vaginal delivery following labor induction.

Severity of hypertension and mode of delivery (Table 3)

Excluding 81 cases with absolute indication for cesarean section, 52 cases and 62 cases were categorized as "mild" and "severe," respectively. In cases in which pregnancy was terminated <35 weeks, elective cesarean section was chosen in 83% of mild cases and 95% of severe cases. In cases in which pregnancy was terminated ≥ 35 weeks, labor induction was chosen in 96% of mild cases and 95% of severe cases. The achievement rate of labor induction was not significantly different in 39 of 44 mild cases (89%) and 34 of 41 severe cases (83%) ($P = 0.48$). Severity of hypertension was not associated with the achievement rate of labor induction.

Cervical opening at labor induction (COL) and vaginal delivery rate (Table 4)

Excluding 4 cases, in which records of COL were unavailable, relationship between COL and vaginal delivery rate was analyzed in 83 induced cases (primipara 54 cases, multipara 29). Labor induction was achieved more frequently when $COL \geq 1.5$ cm (95%, 21 in 22 cases) than $COL < 1.5$ cm (75%, 24 in 32 cases) in primipara women ($P = 0.048$). In multipara women, labor induction was achieved in all 21 cases with $COL \geq 1.5$ cm and 6 of 8 (75%) with $COL < 1.5$ cm. The difference in vaginal delivery rate between cases with $COL < 1.5$ cm and $COL \geq 1.5$ cm in multipara women did not reach a statistically significant level in this study ($P = 0.07$).

Maternal and neonatal characteristics by delivery mode after labor induction with neuraxial analgesia (Table 5)

Among 83 labor induction cases with neuraxial analgesia, 71 cases achieved vaginal delivery (86%, the vaginal delivery group), and 12 cases required cesarean section (14%, the cesarean section group). Between these two groups, there was a significant difference in maternal age and rate of $COL < 1.5$ cm.

The details of the 12 cases that required cesarean section after labor induction (Table 6)

The indications were 5 cases of non-reassuring fetal status and 7 cases of arrested labor. In the non-reassuring fetal status cases, 2 of 5 were diagnosed as oligohydramnios and arrest of fetal growth. In the arrested labor cases, 6 of 7 had cervical openings at labor induction < 1.5 cm.

Table 5. Maternal and neonatal characteristics by delivery mode after labor induction with neuraxial analgesia in preeclamptic women

	Vaginal delivery (n = 71)	Cesarean section (n = 12)	P value
Maternal age (years; mean \pm SD)	32 \pm 6	36 \pm 5	0.03
Number of primipara	45 (63%)	10 (83%)	0.15
Gestational age at delivery (weeks; mean \pm SD)	37.8 \pm 1.5	38.1 \pm 1.5	0.44
Severe hypertension	31 (44%)	7 (58%)	0.35
Oligohydramnios	3 (4%)	1 (8%)	0.90
Birthweight (g; mean + SD)	2,509 \pm 433	2,683 \pm 642	0.38
Light for date ^a	23 (32%)	3 (25%)	0.44
Cervical opening < 1.5 cm ^b	28 (41%)	10 (91%)	0.002

SD, standard deviation

^aBased on Japanese standards of birth weight and height in 1998

^bExcluding cases with unknown COL (2 cases from the vaginal delivery group and 1 case from the cesarean section group)

Table 6. Cases requiring cesarean section after labor induction, n = 12

Para	Gestational age at delivery (weeks)	Ultrasound finding	Cervical opening (cm)	Indication for CS	Birth weight (g)	Apgar score (1 min)	Apgar score (5 min)	UA pH
0	36	OH, DA	Unclear	NRFS	1,674	8	9	7.26
0	37	OH, DA	1.0	NRFS	1,846	8	9	7.30
0	36	NP	0	NRFS	2,174	8	9	7.23
0	37	NP	1.0	NRFS	2,566	8	8	7.33
1	39	NP	1.0	NRFS	3,230	3	8	7.11
0	39	NP	0	AL	2,524	8	9	7.17
0	40	NP	0	AL	3134	8	9	7.23
0	40	NP	0.5	AL	2,806	8	8	7.30
0	37	NP	1.0	AL	3,470	2	6	7.12
2	36	NP	0	AL	1,914	9	9	7.32
0	36	NP	1.5	AL	2,422	8	9	7.29
0	39	NP	0	AL	3,278	9	9	7.31

UA, umbilical arterial blood; OH, oligohydramnios; DA, developmental arrest; NRFS, nonreassuring fetal status; AL, arrested labor; NP, not particular

Table 7. Comparison of neonatal outcomes between cesarean section for absolute mechanical indications and labor induction with neuraxial analgesia after 35 weeks of gestation

	CS for absolute mechanical indications (n = 17)	Labor induction with neuraxial analgesia (n = 81)	P value
Gestational age at delivery (weeks; mean \pm SD)	37 \pm 0.9	38 \pm 1.4	0.047
Severe hypertension	6 (35%)	37 (46%)	0.43
Birthweight (g; mean \pm SD)	2,461 \pm 410	2,567 \pm 478	0.4
Light for date	3 (18%)	26 (32%)	0.23
Apgar score (1 min) <7	1 (6%)	6 (7%)	0.65
Apgar score (5 min) <7	0	3 (4%)	0.56
Umbilical arterial pH <7.2	1 (6%)	10 (12%)	0.39

Neonatal outcomes in labor induction with neuraxial analgesia (Table 7)

We compared neonatal outcomes between cesarean section for absolute mechanical indications (17 cases, the absolute mechanical C-section group) and labor induction with neuraxial analgesia (81 cases, the labor induction group) after 35 weeks' gestation. There were no significant differences in severity of preeclampsia, birthweight, light for dates, Apgar score, and umbilical arterial pH between the two groups. The cases of Apgar score <7 at 5 minutes were not in the absolute mechanical C-section group, and 3 cases (4%) were in the labor induction group. Two of 3 cases were light for date, and 1 case was complicated by diabetes mellitus. Fetal acidemia indicated by umbilical arterial pH < 7.2 was observed in 1 case (6%) of the absolute mechanical C-section group, and 10 cases (12%) in the labor induction

group, among which 5 cases were light for dates, and 1 case was found to be placental abruption after delivery.

Discussion

In the present study, we discovered some interesting findings in the labor management of pregnancies complicated by preeclampsia. Labor induction is more successful after 35 weeks' gestation, including early-onset preeclampsia. Although there are limited cases before 34 weeks' gestation in this study, our results are comparable with the studies of Koopmans et al.¹ (86% achievement rate in ≥ 36 weeks' gestation) and Shibata et al.⁵ (66% achievement rate in ≥ 34 weeks' gestation).

As one of the conditions for favorable results, a cervical opening of ≥ 1.5 cm at labor induction is an important indicator in primipara women. Our results are

basically consistent with previous reports of the relationship between the Bishop score at induction and the cesarean section rate after labor induction in preeclampsia.^{10,11} In the present study the reasons for the cesarean section after labor induction were arrested labor and nonreassuring fetal status. The cases of arrested labor were COL < 1.5 cm except for 1 case. Because preeclampsia is a disorder that affects not only mothers but also fetuses and uteroplacental circulation, many factors affect the achievement of labor induction. COL and fetal wellbeing appear important factors for vaginal delivery in preeclamptic patients.

We also found that the timing of preeclampsia onset and the severity of preeclampsia were not related to the achievement rate of labor induction in the present case-series study. There were no reports on the relationship between the preeclampsia onset timing and the mode of delivery. If it is possible for pregnancy with early onset of preeclampsia to maintain to late preterm period by treatments, the probability of vaginal delivery must be increase.

The achievement rate of labor induction was independent of the hypertension severity level in the present study. We could not find any reports on the relationship between the preeclampsia level and the achievement rate of labor induction. When patients develop uncontrollable hypertension by labor pain, emergency cesarean section may be necessary due to the elevation of blood pressure. However, there were no cases of cesarean section due to uncontrollable hypertension in the present study. It is possible that the pain control by neuraxial analgesia had a beneficial effect on stabilizing blood pressure. Since there were only a few cases without neuraxial analgesia in the present study, so we could not compare the achievement rate of labor induction with and without neuraxial analgesia. Previous studies provided supportive findings of the effectiveness of neuraxial analgesia in managing vaginal delivery with preeclampsia. Neuraxial analgesia blocks the sympathetic nerves resulting in stable maternal blood pressure in the presence of the stress responses caused by labor pains⁸ without affecting cardiac output.¹² Neuraxial analgesia also maintains uteroplacental blood flow¹³ by reducing serum epinephrine levels¹⁴ and has the effect of increasing intervillous blood flow.¹⁵ The previous findings⁸ and the results in the present study may support the idea that pain control by neuraxial analgesia has beneficial effects in managing blood pressure during labor.

Labor induction is a reasonable choice for termination of pregnancy in late preterm and term preeclampsia, unless there is maternal-fetal absolute indication for

cesarean section, and size of the cervical opening should be considered especially in primipara women.

Conflicts of Interest

None

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