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Comparison between 0.06% and 0.1% Levobupivacaine Combined with 2 μg/mL of Fentanyl for Epidural Labor Analgesia

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ABSTRACT

Purpose: Levobupivacaine is thought to be a good alternative to bupivacaine for epidural labor analgesia because of its pharmacologic profile. However, the optimal concentration of levobupivacaine for labor analgesia has not been adequately studied. The objective of this retrospective study was to compare the analgesic effect of levobupivacaine between 0.06% and 0.1% both combined with 2 μg/mL of fentanyl. **Methods:** Primiparous women (ASA I, II) who delivered their babies to our hospital using combined spinal epidural analgesia and patient-controlled epidural analgesia between August 1, 2011 and September 30, 2011 were included into this retrospective study. The analgesic solution for epidural administration was 0.06% levobupivacaine with 2 μg/mL of fentanyl between August 1 and 31, and 0.1% levobupivacaine with 2 μg/mL of fentanyl between September 1 and 30. Their anesthetic and obstetric charts were reviewed to compare obstetric outcome, anesthetic intervention, and patients' satisfaction. **Results:** There were 46 women fulfilling the inclusion criteria: 23 women in 0.06% group, and 23 women in 0.1% group. The number of patients who needed more than 3 requests for one actual bolus was significantly higher in the 0.06% group ($P < 0.05$). **Conclusion:** Our results revealed that 0.06% levobupivacaine combined with 2 μg/mL fentanyl does not provide sufficient analgesic effects for epidural labor analgesia. It seems that levobupivacaine has not been adequately studied after its withdrawal from the US market. Further studies should be conducted to determine the optimal concentration of levobupivacaine for epidural labor analgesia.

Keywords: PCEA; CSEA; Labor Analgesia; Levobupivacaine

1. Introduction

Levobupivacaine is a pure S(−) enantiomer of racemic bupivacaine, whereas bupivacaine consists of both an S(−) enantiomer and R(+) enantiomer [1,2]. Levobupivacaine is thought to be a good alternative to racemic bupivacaine for epidural labor analgesia because the S(−) enantiomer has less affinity for the sodium channels and thus has fewer depressant effects on the cardiovascular and central nervous systems than the R(+) enantiomer. However, the optimal concentration of levobupivacaine for labor analgesia has not been adequately studied.

At the National Center for Child Health and Development, where combined spinal epidural analgesia (CSEA) followed by patient-controlled epidural analgesia (PCEA) has been adopted as a standard technique for labor analgesia, a combination of 0.1% ropivacaine with 2 μg/mL of fentanyl had been used effectively as a PCEA solution until the end of July in 2011. However, our pharmaceutical department needed to reduce the number of items of local anesthetics, and decided to delete ropivacaine from the list for regular stock. Hence, we had to change the local anesthetic for labor analgesia from ropivacaine to levobupivacaine.

Although levobupivacaine has been used for labor analgesia in some countries [3], we found that an optimal concentration of levobupivacaine has not been well studied by reviewing textbooks and literatures describing levobupivacaine for epidural labor analgesia. Therefore

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we hastened to start with 0.06% levobupivacaine with 2 μg/mL of fentanyl, as it had been reported that minimum anesthetic concentration of bupivacaine and levobupivacaine were similar to each other, and 0.06% of bupivacaine had been successfully used for labor analgesia by combining with fenatnyl.

After one month experience with 0.06% levobupivacaine with 2 μg/mL of fentanyl, we noticed an increased number of patients requiring anesthesiologist's intervention for rescue treatment, and decided to inspissate PCEA solution to 0.1% levobupivacaine with 2 μg/mL of fentanyl. Another one month experience with new solution convinced us that the number of patient with insufficient pain relief decreased. The purpose of this retrospective study was to compare the number of patients with insufficient pain control during their delivery between different concentrations of levobupivacaine (0.1% versus 0.06%), both combined with 2 μg/mL of fentanyl.

2. Material and Methods

A list of deliveries between August 1, 2011 and September 30, 2011 was checked to extract primiparous women (ASA I, II) who delivered their baby at our hospital using combined spinal epidural analgesia and patient-controlled epidural analgesia. Their anesthetic and obstetric charts were reviewed to compare obstetric outcome, anesthetic intervention, and patients' satisfaction. Parturient who delivered their babies within 2 hours after the intrathecal administration were excluded from the study because of the potentially limited effects of PCEA.

During the time period of the study, the following standard protocol was used for labor analgesia. When a patient requested pain relief, analgesia was begun with an intrathecal administration of 2.5 mg of hyperbaric bupivacaine and 10 μg of fentanyl. An indwelling epidural catheter was placed simultaneously and connected to PCEA device, which was set as 5 mL for bolus dose, 15 minutes for lockout interval and no background infusion. The analgesic solution for epidural administration was 0.06% levobupivacaine with 2 μg/mL of fentanyl between August 1 and 31, and 0.1% levobupivacaine with 2 μg/mL of fentanyl between September 1 and 30. To make up a transition from spinal analgesia to epidural analgesia smoothly, the first and second epidural bolus administration was instructed by anesthesiologists around 20 and 40 minutes after the intrathecal administration. After these instructed boluses, a PCEA button was given to the patient so that she could request additional pain relief as needed. If the analgesic effect was not sufficient, a rescue dose of anesthetics (PCEA solution, lidocaine, or fentanyl) was administered at the discretion of the anesthesiologist. The postnatal visit was done by an attending anesthesiologist, and the patient's satisfaction was evaluated and classified into 5 grades (very good, good, fair, bad, and very bad).

Patients' background and obstetric outcomes were checked from obstetric charts, whereas number of PCEA request and administered boluses, anesthesiologists' intervention for breakthrough pain and patients' satisfaction were checked from anesthetic charts.

The differences in continuous variables were analyzed by student's t-test, and data were presented as mean ±standard deviation. Differences in categorical variables were analyzed by the chi-square test, and data were presented in real numbers. A P-value of <0.05 was considered to be significant. As the study was conducted retrospectively, an informed consent was not obtained from the patients for this specific study. However, all patients had consented on admission to having their clinical data used for publication as an upfront consent, and our institutional review board approved this consent for publication of the study.

3. Results

There were 46 women fulfilling the inclusion criteria: 23 women with 0.06% levobupivacaine combined with 2 μg/mL of fentanyl (0.06% group), and 23 women with 0.1% levobupivacaine combined with 2 μg/mL of fentanyl (0.1% group).

No significant differences were found between the groups in patient characteristics, duration of labor, mode of delivery, or Apgar-score (**Table 1**). The number of patients who needed more than 3 requests for an actual bolus was significantly higher ($P < 0.05$) in the 0.06%

Table 1. Patient characteristics, duration of delivery, mode of delivery, and APGAR scores.

		0.1% Group (n = 23)	0.06% Group (n = 23)
Patient Characteristics	Age	36.4 (+/− 5.3)	36.9 (+/− 4.2)
	Height	159.5 (+/− 5.1)	160.8 (+/− 5.4)
	Weight	61.4 (+/− 6.7)	60.9 (+/− 7.7)
	Gestational weeks	39.2 (+/− 1.4)	39.4 (+/− 1.2)
Duration of delivery	1st stage	613.5 (+/− 263.9)	747.0 (+/− 297.1)
	2nd stage	149.0 (+/− 61.6)	129.4 (+/− 68.5)
Mode of delivery	Spontaneous	8	8
	Instrument	14	11
	Cesarean section	1	4
APGAR score	1 min	8 (1 - 9)	8 (4 - 9)
	5 min	9 (7 - 10)	9 (8 - 9)

group (**Table 2**). However, there was no difference in patient satisfaction between the groups (**Table 3**).

4. Discussion

Because of its pharmacologic profile, levobupivacaine has been considered to be a suitable anesthetic agent for epidural labor analgesia. However, we could find only one study that compared different concentrations of levobupivacaine for its analgesic effects in epidural analgesia. Tixier and colleagues [4] compared two different concentrations of levobupivacaine (0.0625% and 0.125%) both combined with 5 μg/mL of sufentanil, and found that the 0.125% concentration provided better analgesic effects. However, the use of 0.125% of levobupivacaine was associated with a risk of overdosing, and they insisted that a lower concentration of the agent between the two concentrations they studied should be studied for better analgesic effect and lower risk of overdosing. In the present study comparing two concentrations lower than they suggested, we found that 0.1% levobupivacaine combined with 2 μg/mL of fentanyl provided better analgesic effects than 0.06% levobupivacaine with 2 μg/mL of fentanyl.

Considering an effect of concentration, it is not surprising that 0.1% levobupivacaine provided a better analgesic effect than 0.06% levobupivacaine. However, an analgesic effect of 0.06% levobupivacaine with 2 μg/mL of fentanyl. was somewhat betraying our expectations, as 0.06% bupivacaine, which has a minimum local analgesic concentration (MLAC) similar to that of levobupivacaine [5], has been widely used for epidural labor analgesia in combination with opioid.

The MLACs of various anesthetics have been previously calculated [6]: bupivacaine, 0.081% [5,7-11]; levobupivacaine, 0.083% [5,12,13]; and ropivacaine, 0.11% [8,12-15]. Based on these calculations, 0.1% ropivacaine is assumed to be equipotent to 0.07% levobupivacaine because the MLAC of levobupivacaine is approximately 70% of that of ropivacaine. Therefore, we were aware that the analgesic effect would be decreased to some extent after changing the analgesic for PCEA from 0.1% ropivacaine with 2 μg/mL of fentanyl to 0.06% levobupivacaine with 2 μg/mL of fentanyl. However, the analgesic effect decreased more than we predicted so that after one month, we had to increase the concentration of levobupivacaine to 0.1%. This change was considered enough to provide sufficient analgesic effects for most patients.

Results of a study by Lee and colleagues [16] also suggested that 0.06% levobupivacaine might not provide sufficient analgesic effects even in combination with opioid analgesics. They compared 0.06% levobupivacaine and 0.08% ropivacaine, which were expected to be equipotent [6] (both were combined with 2 μg/mL of fentanyl). Their results showed that the levobupivacaine group required rescue for breakthrough pain significantly more often than the ropivacaine group [16]. Our findings are consistent with their report that 0.06% levobupivacaine combined with opioid could not provide sufficient pain relief for labor analgesia. Recent studies that evaluated the MLAC of levobupivacaine and ropivacaine simultaneously reported very similar values of MLAC [12,13,17,18]. Therefore it seems that levobupivacaine should be used in the same concentration as ropivacaine, not as bupivacaine.

As the study was not a randomized control study, the result might be biased by our expectation and experience. Furthermore, an insufficient analgesic effect of 0.06% ropivacaine could be covered by increasing the bolus dose or shortening the lockout interval. However, we still feel worthy enough to report the result, as few reports exist about the optimal concentration of levobupivacaine for epidural labor analgesia. The scares data of levobupivacaine for labor analgesia may be attributable to the fact that levobupivacaine was withdrawn from the US market [17]. In conclusion, our results revealed that 0.06% levobupivacaine combined with 2 μg/mL fentanyl does not provide sufficient analgesic effects for

Table 2. Number of patients at bad control and unscheduled interventions.

		0.1% Group	0.06% Group
Number of patients needed > 2 requests for one bolus		12	15
Number of patients needed > 3 requests for one bolus		6	13*
Number of intervention by anesthesiologists	0	17	12
	1	2	5
	2	3	2
	3	1	1
	4	0	0
	5 or more	0	3

*P < 0.05.

Table 3. Patient satisfaction.

		0.1% Group	0.06% Group
Patient satisfaction	Very good	4	3
	Good	8	14
	Fair	10	4
	Bad	1	2
	Very bad	0	0

epidural labor analgesia. Further studies should be conducted to determine the optimal concentration of levobupivacaine for epidural labor analgesia.

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