Original Article

A Comparison of Meperidine and Fentanyl for Labor Pain Reduction in Phramongkutklao Hospital

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Objective: To compare the efficacy between meperidine and fentanyl for labor pain reduction.

Materials and Methods: The present study was a randomized controlled trial conducted in term singleton pregnant women planning for vaginal delivery, between August 7, 2017 and January 6, 2018. Women with opioid allergy, addictive substance abuse in the last year, asthma, fetus with anomalies, or cervical dilation more than 8 cm were excluded. The participants were allocated to receive either intravenous meperidine (50 mg every two hours) or fentanyl (50 mcg every hour) during active phase of labor as maternal requested. Pain score was assessed at 0, 30, 60, and 120 minutes by a 10-point numeric rating scale. Maternal and fetal adverse effects, number of opioid administrations, route of delivery, and neonatal outcomes were evaluated.

Results: Ninety-two subjects were allocated to meperidine (n = 46) and fentanyl (n = 46). Pain score at 30 minutes was reduced in both groups (meperidine 0.85±1.38 versus fentanyl 0.89±1.69, p=0.893), and pain scores were similar at 30, 60, and 120 minutes (p=0.779). Women in the fentanyl group experienced less nausea and drowsiness, and a more rapid heart rate but without significant difference. Abnormal fetal heart rate pattern after sedation occurred with similar frequency in both groups (meperidine 19.6% versus fentanyl 17.4%, p=0.788). No newborns required naloxone treatment.

Conclusion: Fentanyl is as effective as meperidine to relieve labor pain with comparable maternal, fetal and neonatal adverse effects.

Keywords: Meperidine, Fentanyl, Pain score, Labor

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Labor causes severe pain for many women and this could be handled by different ways[1]. In the absence of a medical contraindication, maternal request is an adequate indication for pain alleviation during labor. Any choice regarding analgesia should be coordinated closely among the obstetrician, the anesthesiologist, and the patient.

Parenteral analgesia is one of the manners for maternal pain relief[1,2]. Opioids are the most common drug chosen for sedation[3]. They are inexpensive and their use requires no specialized-expertise attention. However, efficacy and adverse effects of each opioid is different in each pregnant woman. All opioids could cross placenta and may have adverse effect on the fetus or the newborn[4]. This may result in loss of fetal heart rate (FHR) variability or a reduction in the FHR baseline. In addition, drug elimination in newborn is longer than in adults, so there might be undesirable effects after delivery such as neonatal respiratory depression or neurobehavioral changes. There remains uncertainty amongst practitioners as to which opioid provides the best pain relief with the least adverse effects[5].

Although a wide variety of opioids available, meperidine is the most commonly used to relieve labor pain worldwide. However, its active metabolite, normeperidine, has a prolonged maternal half-life and about 72 hours half-life in the neonate[6]. Fentanyl, a new synthetic opioid with a greater analgesic potency and a shorter duration of action, is more frequently used nowadays.

The aim of the present study was to compare efficacy between meperidine and fentanyl for labor pain reduction.

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Materials and Methods

The present randomized controlled trial, open label, was approved by the Ethic Committee of the Institutional Review Board of the Royal Thai Army Medicine Department. The authors recruited pregnant women admitted for delivery at the labor room, Phramongkutklao Hospital, between August 7, 2017 and January 6, 2018. All subjects were singleton pregnant women with gestational age between 37 and 42 weeks. Fetus was in cephalic presentation and planned to deliver vaginally. Pregnant women with history of opioid allergy, addictive substance abuse in the last year, asthma, fetus with anomalies, or cervical dilation more than 8 cm were excluded from the study.

Block of four randomization was established by computer-generated random sequence. Women were allocated to either meperidine or fentanyl group according to the assignment in numbered concealed envelopes. Sample size calculation was based on Rayburn et al study[7]. To get power of 80 percent, alpha error of 0.05 plus 10-percent missing data, the authors needed 46 subjects in each group.

The attending obstetricians would prescribe opioid analgesia on maternal request during active phase of labor (cervical dilation more than 3 to 4 cm but not exceeded 8 cm). In the meperidine group, the pregnant women received meperidine 50 mg intravenously and additional doses would be repeated every two hours as maternal request, with a maximum of three doses. In the fentanyl group, the pregnant women received fentanyl 50 mcg intravenously and additional doses would be given every hour in accordance with maternal request, with a maximum of five doses.

Pain score was rated by the parturient using a 10-point numeric rating scale (NRS)[8] and recorded by labor nurses at 0, 30, 60, and 120 minutes. Both physicians and nurses knew the drug used while the participants were blinded to the intervention they received.

Primary outcome was compared between meperidine and fentanyl for pain score reduction between 0 and 30 minutes. Secondary outcomes were efficacy for labor pain reduction at 60 and 120 minutes, adverse effects such as nausea, vomiting, itching[9], or drowsiness, and number of opioid analgesia administrations. FHR pattern determined by electronic fetal monitoring, labor course, route of delivery, Apgar scores at 1 and 5 minutes, and need for naloxone therapy. Any breastfeeding problems were also recorded.

Table 1. Demographic data

	Meperidine (n = 46) n (%)	Fentanyl (n = 46) n (%)	p-value
Maternal age (years), Mean±SD	27.8±5.6	27.5±5.0	0.787
Parity			0.450
Nullipara	39 (84.8)	36 (78.3)	
Primipara	5 (10.9)	9 (19.6)	
Multipara	2 (4.3)	1 (2.2)	
Body mass index (kg/m^2)			0.919
<18.50	0 (0.0)	0 (0.0)	
18.50 to 22.99	4 (8.7)	4 (8.7)	
23.00 to 24.99	7 (15.2)	9 (19.6)	
25.00 to 29.99	23 (50.0)	20 (43.5)	
≥30	12 (26.1)	13 (28.3)	
Underlying disease			
Chronic hypertension	3 (6.5)	0 (0.0)	0.078
Overt diabetes mellitus	0 (0.0)	0 (0.0)	N/A
Hyperthyroidism	2 (4.3)	0 (0.0)	0.153
Hypothyroidism	0 (0.0)	0 (0.0)	N/A
Thalassemia	11 (23.9)	7 (15.2)	0.535
Liver disease	0 (0.0)	1 (2.2)	0.315
Pregnancy complication			
Gestational diabetes mellitus	6 (13.0)	3 (6.5)	0.292
Pregnancy induced hypertension	5 (10.9)	5 (10.9)	0.458
Intrauterine growth restriction	0 (0.0)	0 (0.0)	N/A
Oligohydramnios	0 (0.0)	1 (2.2)	0.315

SD=standard deviation; N/A=not applicable

Statistical analysis

The statistical analysis was performed by using SPSS statistical software (version 17.0). The results were reported as percentages and means ± standard deviations (SD). Independent t-test was used to compare continuous data. Chi-square test was used to compare categorical data. Repeated measure ANOVA was used to analyze pain score reduction. The statistical significance was considered at p-value smaller than 0.05.

Results

Ninety-two pregnant women were randomly allocated to receive intravenous meperidine (n = 46) or intravenous fentanyl (n = 46).

Table 1 compares demographic data between meperidine and fentanyl groups. Maternal age, parity,

Table 2. Intrapartum period

	Meperidine (n = 46) n (%)	Fentanyl (n = 46) n (%)	p-value
Gestational age (weeks), Mean±SD	38.8±1.1	39.2±0.9	0.082
Intrapartum period			0.456
Spontaneous labor	34 (73.9)	37 (80.4)	
Induction	12 (26.1)	9 (19.6)	
Cervical dilation when maternal request (cm)			0.741
3	16 (34.8)	13 (28.3)	
4	15 (32.6)	17 (37.0)	
5	6 (13.0)	8 (17.4)	
6	9 (19.6)	7 (15.2)	
7	0 (0.0)	1 (2.2)	
Meconium stained amniotic fluid	6 (13.0)	8 (17.4)	0.689
Route of delivery			0.262
Vaginal delivery	34 (73.9)	29 (63.0)	
Cesarean section	12 (26.1)	17 (37.0)	
Side effects on pregnant women			
Nausea	6 (13.0)	4 (8.7)	0.503
Vomiting	2 (4.3)	2 (4.3)	1.0
Tremor	1 (2.2)	1 (2.2)	1.0
Itching	1 (2.2)	0 (0.0)	0.315
Slow heart rate	8 (17.4)	7 (15.2)	0.778
Rapid heart rate	4 (8.7)	7 (15.2)	0.335
Drowsiness	26 (56.5)	19 (41.3)	0.144
Side effects on fetus			
Abnormal fetal heart rate pattern*	9 (19.6)	8 (17.4)	0.788
Subject requiring additional dose	6 (13.0)	15 (32.6)	0.025**
Duration of labor in vaginal delivery@			
Active phase in first stage of labor (hours)	3:37±2:07 (0:30 to 9:00)	3:43±1:49 (1:00 to 8:20)	0.845
Second stage of labor (hours)	0:38±0:34 (0:01 to 2:17)	0:38±0:32 (0:06 to 1:44)	0.991
Third stage of labor (hours)	0:07±0:03 (0:02 to 0:19)	0:08±0:04 (0:03 to 0:20)	0.096
Last dose to delivery (hours)	3:01±2:03 (0:45 to 9:47)	3:02±1:54 (0:43 to 7:01)	0.979

SD=standard deviation

* Loss of fetal heart rate (FHR) variability or decrease in FHR baseline, ** Significant at the 0.05 level

@ Data are recorded as mean±SD (min-max), meperidine (n = 34) vs. fentanyl (n = 29)

body mass index, underlying disease, and pregnancy complication did not differ statistically.

Mean gestational age in meperidine and fentanyl groups was 38.8±1.1 weeks and 39.2±0.9 weeks, respectively (p=0.082). Less pregnant women were admitted due to spontaneous labor in meperidine group (73.9% versus 80.4%). These two groups were similar regard to cervical dilation when maternal requesting parenteral analgesia, meconium stained amniotic fluid, and route of delivery, as shown in Table 2.

Women in the fentanyl group experienced less nausea and drowsiness, more rapid heart rate, but no significant difference between groups was detected. Other maternal side effects were similar between the two groups.

The time interval among women delivered vaginally did not significantly differ between both groups in terms of first, second, and third stage of labor. Time of active phase in first stage of labor was 3:37±2:07 and 3:43±1:49 hours in meperidine and fentanyl groups, respectively (p=0.845).

Table 3 illustrates similar mean pain score before opioid injection in both groups (meperidine 9.17±1.30 versus fentanyl 8.83±1.43; p=0.227). Pain scores apparently decreased but the difference between groups did not achieve statistical significance.

Table 3. Maternal pain scores

	Meperidine (n = 46) Mean±SD	Fentanyl (n = 46) Mean±SD	p-value
Pain score (numeric rating scale; 0 to 10)	9.17±1.30	8.83±1.43	0.227
Pain score reduction			0.779*
After 30 minutes	0.85±1.38	0.89±1.69	0.893
After 60 minutes	1.02±2.70	0.35±2.47	0.215
After 120 minutes	2.57±4.20	2.13±4.79	0.645

SD=standard deviation

* Repeated measure ANOVA

Table 4. Neonatal outcomes

	Meperidine (n = 46) n (%)	Fentanyl (n = 46) n (%)	p-value
Apgar score, Median (min-max)			
At 1 minutes	8 (3 to 9)	8 (7 to 9)	0.238
At 5 minutes	9 (8 to 10)	9 (8 to 10)	1.0
Birth weight (g), Mean±SD	3,138.59±460.01	3,200.54±408.18	0.496
Naloxone treatment	0 (0.0)	0 (0.0)	N/A
Breastfeeding in 24 hours postpartum	28 (60.8)	25 (54.3)	0.324

SD=standard deviation; N/A=not applicable

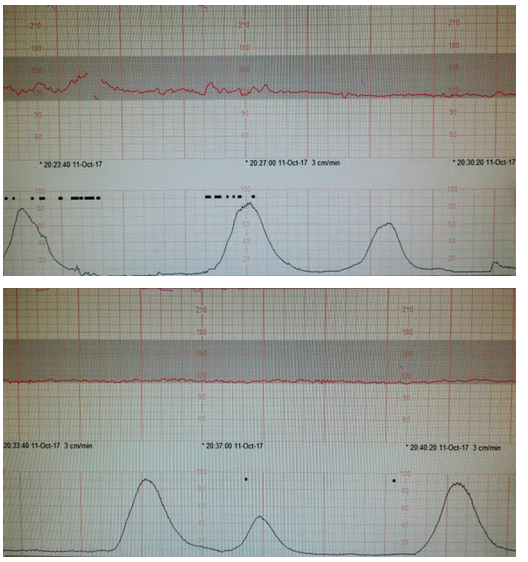

Figure 1. (A) Electronic fetal tracing before opioid administration. (B) After opioid injection, loss of fetal heart rate variability occurred about 40 minutes and returned to normal subsequently.

Abnormal FHR pattern after sedation occurred with similar frequency in both groups (meperidine 19.6% versus fentanyl 17.4%, p=0.788). These included loss of FHR variability or decrease in FHR baseline about 15 to 45 minutes as shown in Figure 1.

Neonatal outcomes are shown in Table 4. Newborns in both groups did not require naloxone treatment. More than half of the newborns in each group could establish breastfeeding 24 hours after delivery.

Discussion

Epidural analgesia that provides better pain relief is not accessible to all women during labor, and throughout the world, parenteral opioids are still widely used. However, there are some concerns about their use including analgesic effectiveness and the sedative effects on women and newborns.

The present study showed that fentanyl is as effective as meperidine in labor pain relief and results in slightly lower rate of some maternal side effects i.e., nausea and drowsiness, which was consistent to previous studies[5,7,10,11].

At present, the choice of opioid for analgesia in labor depends on what is available in the hospital. Meperidine has the virtue of familiarity and low cost[12]. On the other hand, there are substantial concerns about its potential maternal, fetal, and neonatal adverse effects due to its active metabolite and long neonatal half-life (18 to 20 hours)[1]. Result from the present study supported that fentanyl appears to be suitable option to meperidine when providing

pain relief to laboring women especially those with advanced labor owing to its faster action, shorter half-life, and lack of active metabolites.

Neither duration of labor nor route of delivery was affected by both opioids in the present study. Shoorab et al[13] compared labor course between fentanyl and placebo and revealed that active phase period after fentanyl injection was statistically significant shorter than placebo.

Due to the differences in dosing frequencies, fentanyl was repeated more often than meperidine in the present study. Nevertheless, Apgar scores at 1 and 5 minutes were comparable between both groups and no naloxone therapy was required, which was similar to the previous report by Douma et al[14]. However, Fairlie et al[15] conducted the study comparing meperidine with diamorphine and noticed that there were more newborns with low Apgar scores that needed neonatal resuscitation and naloxone administration in the meperidine group.

More research should be carried out to determine which medication provides not only labor pain reduction but also greatest satisfaction to pregnant women with acceptable adverse effects for mothers and their newborns. Regarding to the shorter half-life, cost-effectiveness of fentanyl compared with other analgesics should be further analyzed.

Conclusion

Fentanyl is as effective as meperidine to relieve labor pain with comparable maternal, fetal, and neonatal adverse effects.

What is already known on this topic?

Opioids are relatively inexpensive, and the use of opioid drugs in labor is common in obstetric practice in Thailand. Pethidine is the most commonly administered opioid for labor pain, but has the potential adverse effects. Obstetricians continue to debate which opioid is most effective.

What this study adds?

Fewer maternal side effects are anticipated with fentanyl because of the drug's rapid onset, short duration, and lack of active metabolites. Easing discomfort and minimize any maternal side effects and neonatal depression are desirable. Confirmation of these impressions through well-designed trial is encouraged.

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Conflicts of interest

The authors declare no conflict of interest.

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