Thai Journal of Obstetrics and Gynaecology
March 2026, Vol. 34, No. 2, pp. 101-112.

OBSTETRICS

Effects of Intramuscular Pethidine on Labor Duration: A Prospective Cohort Study

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ABSTRACT

Objectives: This study evaluated the impact of intramuscular pethidine on labor duration as well as associated maternal and neonatal outcomes.

Materials and Methods: A prospective cohort study at Hatyai Hospital recruited 114 women with singleton, cephalic pregnancies at 37–41 weeks and spontaneous labor in the active phase from May to December 2024. A total of 59 patients chose to receive intramuscular pethidine at a dose of 1 mg/kg, while 41 patients chose not to receive it. Obstetric outcomes, labor characteristics, pain assessment by visual analog scale, and maternal and neonatal drug adverse outcomes were recorded. Multivariable linear regression identified factors associated with labor duration, adjusting for confounders including maternal age, body mass index (BMI), and parity.

Results: The median duration of the active phase of the first stage of labor was significantly shorter in the pethidine group (165 min [interquartile range (IQR) 110, 245]) compared to the non-pethidine group (220 min [IQR 140, 330], p = 0.046). After adjusting for maternal age, BMI, and parity, pethidine administration was found to be associated with a significant reduction in active phase duration by 67.45 minutes (adjusted coefficient = -67.45, 95% confidence interval -118.67, -16.23, p = 0.010). None of birth asphyxia was reported, and no significant differences was observed in neonatal intensive care unit admission. Mild maternal side effects included drowsiness and nausea in the pethidine group, but no severe adverse effects were observed in either group.

Conclusion: Intramuscular pethidine administration significantly shortened the active phase of the first stage of labor compared to the non-pethidine group after adjusting for confounding factors, without increasing adverse maternal or neonatal outcomes.

Keywords: pethidine, intramuscular analgesia, labor duration, obstetric outcomes, neonatal outcomes, pregnancy.

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Received: 7 March 2025, **Revised:** 28 November 2025, **Accepted:** 12 January 2026

ผลของเพทิดีนแบบฉีดเข้ากล้ามเนื้อต่อระยะเวลาการคลอด: การศึกษาแบบติดตามไปข้างหน้า

กันตพงศ์ ไพบูลย์ศิริจิต, พักตร์ประภา ไชยภักดี

บทคัดย่อ

วัตถุประสงค์: *การศึกษานี้ประเมินผลกระทบของเพทิดีนแบบฉีดเข้ากล้ามเนื้อต่อระยะเวลาการคลอดและผลลัพธ์ที่เกี่ยวข้องต่อมารดาและทารกแรกเกิด*

วัสดุและวิธีการ: *การศึกษาแบบติดตามไปข้างหน้าที่โรงพยาบาลหาดใหญ่ได้คัดเลือกหญิงตั้งครรภ์ 114 คนที่เป็นครรภ์เดี่ยว ทารกในครรภ์มีศีรษะเป็นส่วนนำ อายุครรภ์ 37-41 สัปดาห์ และมีการเจ็บครรภ์คลอดเองในระยะ active phase ตั้งแต่เดือนพฤษภาคมถึงธันวาคม 2567 มีผู้ป่วย 59 รายเลือกที่จะรับเพทิดีนแบบฉีดเข้ากล้ามเนื้อในขนาด 1 มก./กก. ขณะที่ผู้ป่วย 41 รายเลือกที่จะไม่รับยา มีการบันทึกผลลัพธ์ทางสูติกรรม ลักษณะการคลอด การประเมินความเจ็บปวดโดยใช้มาตรวัดแบบภาพเปรียบเทียบความเจ็บปวด และผลข้างเคียงของยาต่อมารดาและทารกแรกเกิด การวิเคราะห์ถดถอยเชิงเส้นแบบหลายตัวแปรใช้ระบุปัจจัยที่เกี่ยวข้องกับระยะเวลาการคลอด โดยมีการปรับค่าสำหรับตัวแปรกวน ได้แก่อายุมารดา ดัชนีมวลกาย และจำนวนครั้งที่เคยคลอด เป็นต้น*

ผลการศึกษา: *ค่ามัธยฐานของระยะเวลาในช่วง active phase ของระยะคลอดที่หนึ่งสั้นกว่าอย่างมีนัยสำคัญในกลุ่มที่ได้รับเพทิดีน (165 นาที [interquartile range (IQR) 110, 245]) เมื่อเทียบกับกลุ่มที่ไม่ได้รับเพทิดีน (220 นาที [IQR 140, 330], p = 0.046) หลังจากปรับสำหรับอายุมารดา ดัชนีมวลกาย และจำนวนครั้งที่เคยคลอด การให้เพทิดีนสัมพันธ์กับการลดลงอย่างมีนัยสำคัญของระยะเวลาในช่วง active phase 67.45 นาที (ค่าสัมประสิทธิ์ที่ปรับแล้ว = -67.45, 95% confidence interval -118.67, -16.23, p = 0.010) ไม่พบภาวะทารกขาดออกซิเจนแรกเกิด รวมถึงอัตราการเข้ารับการรักษาของทารกในหอผู้ป่วยวิกฤตทารกแรกเกิดไม่แตกต่างกันอย่างมีนัยสำคัญระหว่างสองกลุ่ม ผลข้างเคียงที่พบในมารดามีความรุนแรงเล็กน้อย ได้แก่ อาการง่วงซึมและคลื่นไส้ โดยไม่มีรายงานผลข้างเคียงรุนแรงแต่อย่างใด*

สรุป: *การฉีดยาเพทิดีนเข้ากล้ามเนื้อช่วยลดระยะ active phase ของการเจ็บครรภ์คลอดได้อย่างมีนัยสำคัญเมื่อเปรียบเทียบกับกลุ่มที่ไม่ได้รับยา หลังจากได้มีการปรับแก้ผลกระทบของปัจจัยกวนต่างๆ แล้ว โดยไม่เพิ่มอัตราการเกิดผลแทรกซ้อนในมารดาและทารก*

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Introduction

Labor is a critical physiological process that is accompanied by intense pain and marked variability in duration, both features can profoundly affect maternal and neonatal outcomes. The length of labor is influenced by multiple factors, including parity, uterine contractility, fetal weight, and maternal stress levels[1-2]. When labor is prolonged, particularly during the active phase of the first stage, the risks of maternal exhaustion, operative or instrumental delivery, postpartum morbidity, and adverse neonatal outcomes increase substantially[3]. Accordingly, achieving effective pain control and avoiding unnecessary prolongation of labor are not only issues of maternal comfort but key determinants of safe obstetric care, with direct implications for labor progression and the prevention of maternal and perinatal complications[4].

A wide range of options is available for intrapartum pain control, including non-pharmacologic and pharmacologic strategies. Non-pharmacologic approaches such as continuous labor support, hydrotherapy, position changes, breathing techniques, acupuncture, massage, and transcutaneous electrical nerve stimulation aim to improve women's ability to cope with labor pain while allowing them to remain mobile and avoid unnecessary medical interventions. Pharmacologic methods are broadly categorized into inhalational agents, systemic opioids, and regional analgesia. Nitrous oxide/oxygen provides rapid, self-administered analgesia, whereas epidural and combined spinal/epidural techniques are regarded as the most effective options. However, these require anesthetic expertise and substantial resources that are often unavailable in low-resource settings. Consequently, systemic opioids such as pethidine, morphine, fentanyl, and remifentanil remain widely used because they are familiar to clinicians and can be administered quickly and easily where anesthetic capacity is limited[5]. Pethidine's main mechanism is acting primarily on mu-opioid receptors in the central nervous system. Pethidine effectively reduces pain perception and may enhance uterine contractility by alleviating stress-mediated inhibition of oxytocin release[6-7].

Previous studies have documented the analgesic efficacy and labor-shortening duration of pethidine[7–10]. However, such studies vary widely in their assessment of dosage, administration route, timing of pethidine administration, and type of labor augmentation, and evidence regarding its effect on labor progression remains controversial. In addition, there are limited studies in Thailand specifically investigating its primary effect on shortening labor duration. Furthermore, given the high prevalence of pethidine use in the labor room at Hatyai Hospital, where the usage rate reaches 30%, it is essential to assess its safety because of concerns about its potential impact on maternal and neonatal outcomes, such as hypotension and respiratory depression. Therefore, this study aimed to evaluate the impact of intramuscular pethidine on the duration of the active phase of the first stage of labor, along with pain relief and associated maternal and neonatal outcomes.

Materials and Methods

This prospective cohort study was conducted in the labor room at the Department of Obstetrics and Gynecology, Hatyai Hospital, between May 2024 and December 2024. A prospective cohort design was conducted instead of a randomized controlled trial because intrapartum analgesia at Hatyai Hospital is determined by patient request. Random allocation of pethidine would have required overriding patients' choices regarding analgesia, which was considered ethically unacceptable under institutional review board standards and incompatible with respect for patient autonomy. Approval for this research was obtained from the Institutional Review Board of Hatyai Hospital (IRB: HYH-EC 119-66-01) on April 1, 2024. Pregnant women aged 18-40 years, with singleton pregnancies at gestational ages of 37-41 weeks, were recruited. Inclusion criteria included spontaneous labor onset, cervical dilation of 4 cm at admission, a vertex fetal presentation, and good uterine contraction. Exclusion criteria included all high-risk pregnancies,

such as preeclampsia, gestational diabetes, placenta previa, fetal growth restriction, fetal malpresentation, and previous cesarean deliveries.

The sample size was determined using G*Power 3.1. The expected effect size was derived from Yilmaz et al[11]. Based on the reported mean difference and pooled standard deviation in that study, a standardized mean difference of Cohen's d = 0.57 was obtained. For a two-independent-means comparison with an unequal allocation ratio (N_2/N_1 = 1.39) cited from intrapartum analgesia utilization in Hatyai Hospital's Labor unit throughout 2023, 100 participants (n_1 = 42 and n_2 = 58) were required to achieve 80% power at a two-sided $\alpha = 0.05$. Allowing for an anticipated 14% dropout rate due to emergency cesarean delivery or instrumental delivery, the final sample size was 114 participants.

After informed consent was obtained, baseline demographic data were collected, including maternal age, parity, and body mass index (BMI), and vaginal examination was performed. Labor progress was monitored using standard partographic methods. When cervical dilatation reached 4 cm, pain assessment by visual analog scale (VAS) was recorded at 0, 1, and 2 hours. If uterine contractions were inadequate, augmentation was performed at the physician's discretion. Augmentation methods, based on Hatyai Hospital's standard labor management protocol, included amniotomy, oxytocin infusion, or a combination of both. Oxytocin infusion started at 4 milliunits per minute and was increased by 3-6 milliunits per minute every 15-40 minutes as managed by a registered nurse. The initiation time and dosage of oxytocin (in milliunits per minute) were recorded systematically, along with subsequent dosage adjustments made following established labor room protocols. Uterine contractions were documented at each dosage adjustment, including duration, interval, and Montevideo units. If augmentation was performed using amniotomy, the procedure time was recorded, and cervical assessment, amniotic fluid characteristics, and contraction patterns were documented.

According to Hatyai Hospital's labor room protocol, intrapartum analgesia is provided strictly on a patient-request basis. Participants who requested analgesia, provided that cervical dilation had not exceeded 6 cm, were placed in the pethidine group and received pethidine 1 mg/kg intramuscular. Those who declined analgesia were placed in the non-pethidine group. No randomization or investigator-directed allocation occurred. VAS was reassessed at 0, 1, and 2 hours after drug administration. Before and after pethidine administration, vital signs were recorded at 0, 30, and 60 minutes. Electronic fetal heart rate monitoring was conducted continuously during the intrapartum period, with pelvic examinations performed every 2 hours to assess labor progression.

The primary outcome was the duration of the active phase of the first stage of labor. The duration of the active phase of the first stage of labor was defined for each participant as the time from cervical dilatation of 4 cm with adequate uterine contractions to full dilatation at 10 cm. The secondary outcomes included VAS assessments conducted before and at 1 and 2 hours after pethidine administration, maternal complications such as maternal bradycardia (pulse rate < 60 bpm), hypotension (systolic blood pressure < 100 mmHg or a reduction of ≥ 20% from baseline), nausea-vomiting, deoxygenation (oxygen saturation < 95%) and respiratory depression (respiratory rate < 8 breaths per minute). Neonatal complications assessed were birth asphyxia (APGAR score < 7 at 1 and 5 minutes), neonatal intensive care unit (NICU) admissions, and neonatal latch, audible swallowing, type of nipple, comfort and hold (LATCH) score less than 6 at 8, 16, 24, and 48 hours post-delivery.

All statistical analyses were performed using R software, version 4.2.1, to ensure precision and reproducibility. Continuous variables were presented as mean ± standard deviation (SD) or median and interquartile range (IQR) and compared using independent samples t-tests or Mann–Whitney U tests, as appropriate. Categorical variables were analyzed using chi-square tests or Fisher's exact tests. To identify factors associated with the duration

of the active phase of the first stage of labor, univariable linear regression analysis was performed initially. Subsequently, multivariable linear regression analysis was conducted to identify factors independently associated with active phase duration. The covariates included in the multivariable model were maternal age (≤ 18 and ≥ 35 years), parity (nulliparous vs multiparous), BMI (≥ 30 vs < 30 kg/m²), type of labor augmentation, upright position during labor, and intramuscular pethidine injection (yes vs no), all of which have been identified in previous studies as important determinants of labor progression and first stage duration (12-14). Results were presented as crude and adjusted coefficients with 95% confidence intervals (CI), and a p value < 0.05 was considered statistically significant.

Results

During the study period, 1,452 women entered the active phase of labor in the labor unit. Of these, 1,338 did not meet the inclusion criteria and declined to participate, and 114 eligible women were enrolled in the study. Based on their choice to receive or not receive pethidine for analgesia, 66 were allocated to the pethidine group and 48 to the non-pethidine group. However, 7 participants were excluded from the pethidine group; 6 underwent cesarean delivery due to non-reassuring fetal status (n = 1), cephalopelvic disproportion (n = 5), and 1 underwent instrumental delivery due to non-reassuring fetal status. In the non-pethidine group, 7 participants were excluded; 5 participants underwent cesarean delivery due to non-reassuring fetal status (n = 2) and cephalopelvic disproportion (n = 3), and 2 participants underwent instrumental delivery due to non-reassuring fetal status. Ultimately, 100 participants remained in the final analysis, with 59 in the pethidine group and 41 in the non-pethidine group (Fig. 1).

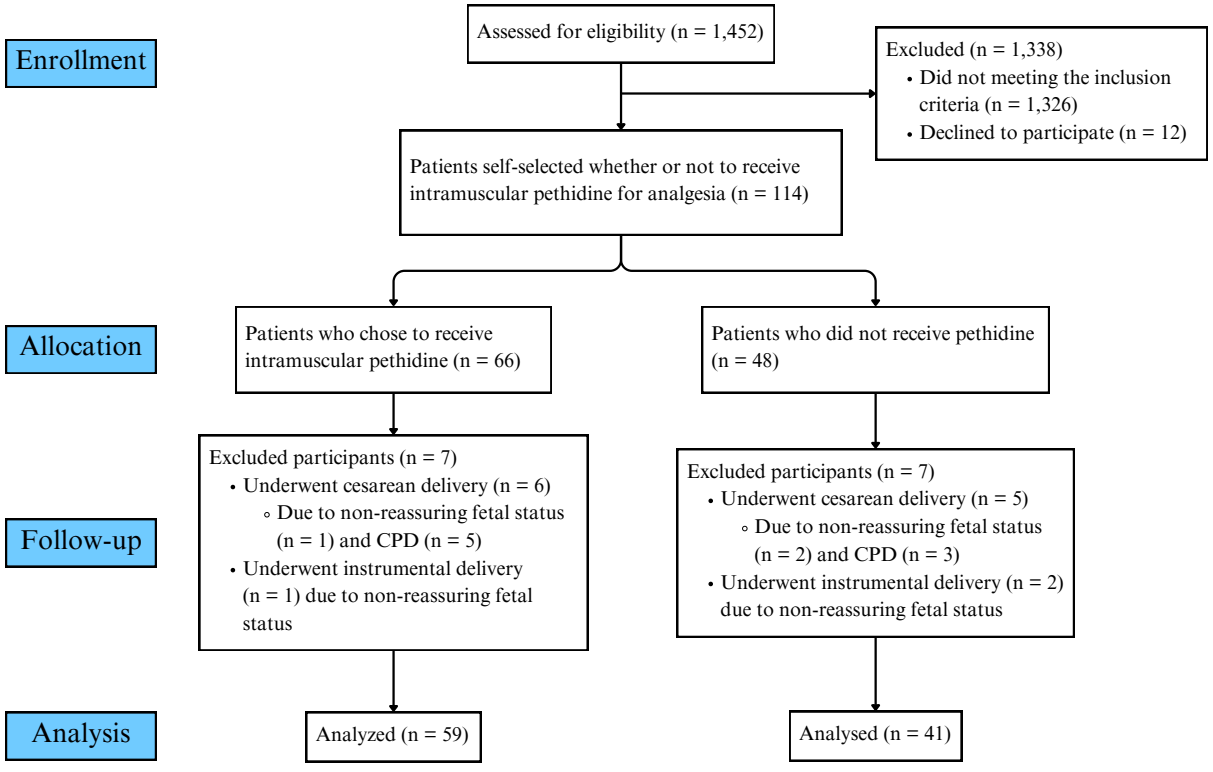

Fig. 1. CONSORT flow diagram of participants recruitment.

The baseline characteristics of the study population revealed no significant differences between the pethidine and non-pethidine groups regarding maternal age (27.3 ± 5.8 vs 26.7 ± 7.1 years, p = 0.655), parity (nulliparous: 54.2% vs 46.3%, p = 0.566), BMI (26.9 vs 26.2 kg/m2, p = 0.710), gestational age (39.4 ± 0.9 vs 39.1 ± 1.0 weeks, p = 0.066) and birth weight (3,047.8 ± 334.1 vs 3,107.8 ± 366.7 grams, p = 0.398). The rate of amniotomy was similar between the groups, with a comparable proportion of patients undergoing this procedure. Additionally, the median VAS score during the active phase was significantly higher in the pethidine group before administration. Oxytocin augmentation was also comparable between the groups, indicating that labor-management approaches were similar across study arms. These findings are detailed in Table 1.

Table 1. Comparison of demographics and obstetric outcomes between participants receiving or not receiving pethidine.

	Overall (n = 100)	Pethidine (n = 59)	Non-pethidine (n = 41)	p value*
Age (years), mean ± SD	27 ± 6.4	27.3 ± 5.8	26.7 ± 7.1	0.655[t]
Gestational age (weeks), mean ± SD	39.3 ± 1.0	39.4 ± 0.9	39.1 ± 1.0	0.066[t]
BMI (kg/m^2), median (IQR)	26.8 (23.7, 30.1)	26.9 (23.9, 29.9)	26.2 (23.4, 30.2)	0.710[m]
BMI (kg/m^2)				1.000[c]
< 30 (%)	74 (74.0)	44 (74.6)	30 (73.2)	
≥ 30 (%)	26 (26)	15 (25.4)	11 (26.8)	
Parity				0.566[c]
Nulliparous (%)	51 (51.0)	32 (54.2)	19 (46.3)	
Multiparous (%)	49 (49.0)	27 (45.8)	22 (53.7)	
VAS at active phase, median (IQR)	7 (5.0, 8.0)	8 (6.0, 10.0)	6 (4.0, 7.0)	< 0.001[m]
Augmentation				0.445[f]
Amniotomy only (%)	8 (11.8)	6 (14.3)	2 (7.7)	
Oxytocin only (%)	40 (58.8)	22 (52.4)	18 (69.2)	
Amniotomy + Oxytocin (%)	20 (29.4)	14 (33.3)	6 (23.1)	
Birth weight (grams), mean ± SD	3,072.4 ± 346.0	3,047.8 ± 334.1	3,107.8 ± 366.7	0.398[t]

SD: standard deviation, BMI: body mass index, VAS: visual analog scale, IQR: interquartile range
Data are presented as n (%), mean ± SD, or median (IQR).
p value corresponds to t = independent samples t-test, c = chi-square test, m = Mann-Whitney U test, f = Fisher's exact test. * significant at p value < 0.05

Notably, the active phase of labor was shorter in the pethidine group, with a median duration of 165 minutes (IQR 110, 245) compared to 220 minutes (IQR 140, 330) in the control group (p = 0.046), demonstrating a significant reduction in labor duration. The duration of the second and third stages did not differ significantly between the groups. These findings are detailed in Fig. 2.

Maternal side effects were minimal, with drowsiness and nausea being the most frequently reported in the pethidine group (11.8% and 8.5%, respectively). No incidents of hypotension, respiratory distress, or oxygen desaturation were observed. When amniotic fluid was dichotomized as meconium-stained versus clear, meconium was present in 16.9% (10/59) of the pethidine group and 7.3% (3/41) of the non-pethidine group. This difference was not statistically significant (p = 0.23). Neonatal outcomes, including birth asphyxia and desaturation, were comparable across the groups (p > 0.05), although NICU admissions were slightly higher in the pethidine group (n = 5) compared to the non-pethidine group (8.5% vs 2.4%, p = 0.396). Among the five NICU admissions in the pethidine group, two cases were due to early neonatal sepsis, and three cases were attributed to transient tachypnea of the newborn, indicating that the observed increase in NICU

admissions was not associated with pethidine-induced respiratory depression. Additionally, LATCH scores at 8, 16, 24, and 48 hours postdelivery did not differ significantly between the groups, indicating pethidine had no observed impact on the success of early breastfeeding. These findings are detailed in Table 2.

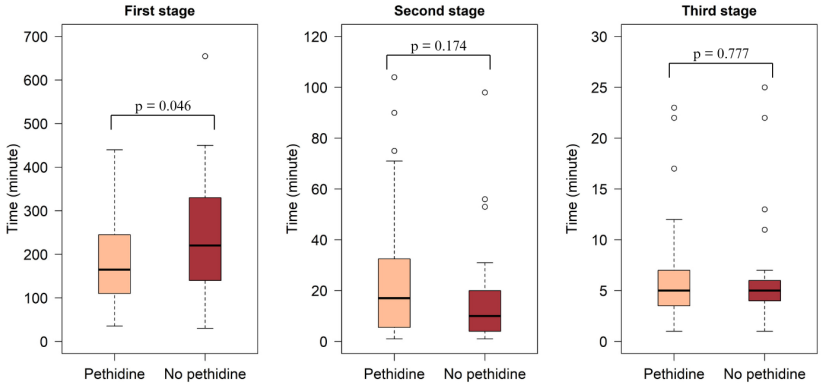

Fig. 2. Comparison of median duration in the active phase of the first, second, and third stages of labor between participants receiving and not receiving intramuscular pethidine.

Table 2. Comparison of obstetric outcomes, maternal adverse drug effects, and neonatal outcomes between participants receiving and not receiving intramuscular pethidine.

	Pethidine (n = 59)	Non-pethidine (n = 41)	p value
Maternal adverse drug effect (%)			
Drowsiness	7 (11.8%)	-	
Nausea vomiting	5 (8.5%)	-	
Dizziness	2 (3.4%)	-	
Meconium-stained amniotic fluid (%)			0.229[f]
Present	10 (16.9)	3 (7.3)	
Absent	49 (83.1)	38 (92.7)	
Fetal heart rate pattern (%)			0.351[f]
CAT 1	54 (91.5)	35 (85.4)	
CAT 2	5 (8.5)	6 (14.6)	
Birth weight (grams), mean ± SD	3,047.8 ± 334.1	3,107.8 ± 366.7	0.398[t]
APGAR score, median (IQR)			
1 min	9 (9,9)	9 (9,9)	0.092[m]
5 min	9 (9,9)	9 (9,9)	0.242[m]
NICU admission (%)	5 (8.5)	1 (2.4)	0.396[f]
Neonatal desaturation (%)	3 (5.1)	3 (7.3)	0.687[f]
LATCH score, median (IQR)	3 (5.1)	3 (7.3)	0.687[f]
At 8 hours	8 (8.0, 9.0)	8 (8.0, 9.0)	0.818[m]
At 16 hours	8 (8.0, 9.0)	8 (8.0, 9.0)	0.979[m]
At 24 hours	8 (8.0, 9.0)	8 (8.0, 9.0)	0.975[m]
At 48 hours	8 (8.0, 9.0)	8 (8.0, 9.0)	0.992[m]

CAT: category of electronic fetal monitoring by the National Institute of Child Health and Human Development (NICHD), LATCH: latch, audible swallowing, type of nipple, comfort, and hold.
Present meconium includes both thin and thick meconium, absent indicates clear amniotic fluid. p value corresponds to m = Mann-Whitney U test, f = Fisher's exact test, or t = independent samples t-test.

The study results indicated that the initial VAS scores were significantly higher in the pethidine group before administration (median 8, IQR 6, 10) compared to the non-pethidine group (median 6, IQR 4, 7) ($p < 0.001$), reflecting the fact that women with more severe pain were more likely to request intramuscular pethidine for pain relief. Median VAS scores before and 1 hour after pethidine administration were 8 (IQR 7, 10) vs 8 (IQR, 7, 10) ($p = 0.109$). It showed that, although some patients experienced pain relief, the overall median pain score did not show a statistically significant reduction post-administration. Subsequently, median VAS scores increased significantly from 8 (IQR 7, 10) to 9 (IQR 8, 10) ($p = 0.004$) between 1 and 2 hours after injection. When comparing the initial VAS scores with those at 2 hours, the change from 8 (IQR 6, 10) to 9 (IQR 8, 10) did not reach statistical significance ($p = 0.724$). These temporal changes in pain scores in the pethidine group are illustrated in Fig. 3.

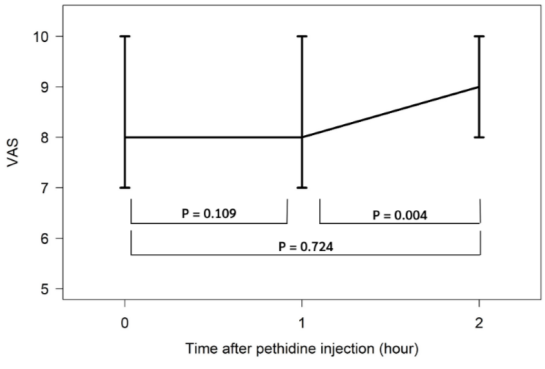

Fig. 3. Changes in visual analog scale (VAS) scores before and after pethidine administration.

In the multivariable linear regression model, maternal age, parity, BMI, type of labor augmentation, upright position during labor, and intramuscular pethidine injection were included as potential determinants of active phase duration. Maternal age was not significantly associated with the duration of the active phase, with non-significant coefficients both for women aged ≤ 18 years (–91.59 minutes; 95% CI –184.36, 1.19; $p = 0.053$) and for those aged ≥ 35 years (–48.11 minutes; 95% CI –120.18, 23.96; $p = 0.188$). Multiparity and obesity (BMI ≥ 30 kg/m^2) were not significantly associated with the duration of the active phase (adjusted coefficients –23.71 minutes; 95% CI –76.59, 29.16; $p = 0.375$ and 2.65 minutes; 95% CI –52.38, 57.68; $p = 0.924$, respectively) (Table 4). Therefore, the coefficients represent mean differences in active phase duration compared with the reference categories, with positive values indicating longer and negative values indicating shorter duration.

Similarly, the method of labor augmentation (amniotomy only, oxytocin only, or amniotomy and oxytocin) and upright position did not significantly influence active phase duration (adjusted coefficient 46.50 minutes; 95% CI –2.48, 95.49; $p = 0.063$). In contrast, intramuscular pethidine injection remained an independent predictor of a shorter active phase when compared with non-pethidine management, with an adjusted coefficient of –67.45 minutes (95% CI –118.67, –16.23; $p = 0.010$), corresponding to a reduction of approximately 67 minutes in the active phase after adjustment for all other covariates (Table 3).

In the pethidine group (n = 59), most women received a dose of 50 mg (31 women, 52.5%), followed by 75 mg (26 women, 44.1%) and 100 mg (2 women, 3.4%). The mean weight-adjusted dose was 0.92 ± 0.17 mg/kg per dose. The median interval from pethidine administration to delivery was 139 minutes (IQR 90.8, 221.0), and cervical

dilatation at the time of injection had a median of 4 cm (IQR 4, 5), indicating that pethidine was typically administered in the early active phase of labor (Table 4).

Table 3. Univariable and multivariable linear regression identifying factors associated with the duration of the active phase of the first stage of labor.

	Crude Coeff. (95% CI)	p value	Adjusted Coeff. (95% CI)	p value
Maternal age*		0.410		0.082
≤ 18	-41.91 (-123.78, 39.97)	0.312	-91.59 (-184.36, 1.19)	0.053
≥ 35	-33.15 (-98.77, 32.47)	0.319	-48.11 (-120.18, 23.96)	0.188
Multiparity	-13.33 (-59.89, 33.24)	0.571	-23.71 (-76.59, 29.16)	0.375
BMI ≥ 30 kg/m^2	-2.05 (-55.21, 51.11)	0.939	2.65 (-52.38, 57.68)	0.924
Augmentation		0.884		0.831
Amniotomy	-9.25 (-102.08, 83.58)	0.844	22.63 (-77.58, 122.83)	0.655
Oxytocin	14.57 (-41.12, 70.27)	0.605	25.43 (-31.85, 82.72)	0.380
Amniotomy and oxytocin	20.5 (-46.44, 87.44)	0.545	25.73 (-58.5, 109.95)	0.545
Upright position	36.05 (-11.44, 83.54)	0.135	46.5 (-2.48, 95.49)	0.063
Pethidine injection	-48.72 (-95.11, -2.33)	0.040	-67.45 (-118.67, -16.23)	0.010

CI: confidence interval, BMI: body mass index

Crude Coeff. (β): crude regression coefficient from univariable linear regression examining each factor individually, Adjusted Coeff. (β): regression coefficient from multivariable linear regression including maternal age, parity, BMI, augmentation method, upright position, and intramuscular pethidine injection.

Table 4. Data on pethidine used in the pethidine group.

	Overall (n = 59)
Pethidine dosage (%)	
50 mg (%)	31 (52.5)
75 mg (%)	26 (44.1)
100 mg (%)	2 (3.4)
MKdose, mean ± SD	0.92 ± 0.17
Pethidine-to-delivery time (minutes), median (IQR)	139 (90.8, 221.0)
Cervical dilatation at pethidine injection, median (IQR)	4 (4, 5)

MKdose: milligrams per kilogram per dose, SD: standard deviation, IQR: interquartile range

Discussion

At Hatyai Hospital, intrapartum analgesia is provided strictly on a patient-request basis, and women demonstrate a strong preference for determining whether they wish to receive pethidine. Enforcing a randomized allocation would require withholding or mandating analgesia against patients' expressed preferences, which directly conflicts with patient autonomy. Such an approach was deemed ethically inappropriate and would not comply with the hospital's IRB standards. Therefore, a prospective cohort design was the only feasible and ethically acceptable design instead of a randomized control trial.

This study examined the impact of intramuscular pethidine on labor duration, with a particular focus on its effect on the active phase of the first stage of labor. Elevated adrenaline levels can inhibit the effectiveness of oxytocin by stimulating β-adrenergic receptors in the uterus, leading to weaker or disorganized contractions[15-16]. By reducing adrenaline, pethidine may indirectly diminish this inhibitory effect, allowing oxytocin to function more efficiently and promote coordinated uterine contractions[11]. The physiological

mechanisms underpinning the efficacy of pethidine in labor progression are multifaceted. Its analgesic properties reduce pain perception and lower circulating catecholamine levels, thereby enhancing uterine contractility and promoting cervical dilation. At the molecular level, pethidine is implicated in enzymatic pathways involving urokinase, plasmin, and collagenase, which facilitate the degradation of cervical collagen[17]. The sedative effects of the drug may also alleviate maternal anxiety, indirectly supporting labor progression[4], reducing maternal anxiety and risk of complications from prolonged labor, such as unrecognized intraamniotic infection in patients with premature rupture of membranes[18]. The findings of this study demonstrated that pethidine administration significantly shortened the duration of the active phase by an average of 67.45 minutes without adversely affecting maternal or neonatal outcomes, similar to previous studies[17, 19-23]. Recent randomized trials from Thailand have shown that other intrapartum interventions can also shorten the active phase of labor, similar to this study, but with different mechanisms. For example, the study by Puttakul et al[24] demonstrated that 5% dextrose in half-strength normal saline infused at 120 mL/h significantly reduced total labor time and the duration of the active phase, as explained by the optimization of myometrial energy supply. Additionally, the study by Kamkong et al[25] similarly reported that a single 20-mg intravenous dose of hyoscine butylbromide shortened the active phase of the first stage of labor due to the reduction of uterocervical spasms. In contrast, other studies reported no significant reduction in labor duration following pethidine administration. This discrepancy may be due to differences in patient selection criteria, labor augmentation methods, pethidine dosage, timing, and administration route[26-27]. These findings emphasized the importance of tailoring pethidine use to individual patients, including patient selection, dosage, timing, and route of administration.

A minimal increase in VAS scores between 1 and 2 hours after pethidine administration was observed, consistent with previous studies[28], indicating that its effectiveness diminishes after 2 hours, although pain should be reduced 1-4 hours after intramuscular pethidine injection using its pharmacological mechanism[29]. However, intramuscular pethidine injection seemingly did not help to reduce VAS pain scores in this study, which can likely be explained by the fact that most women requested pethidine only when their pain was already severe (median VAS 8), so the efficacy of pethidine for their pain relief may be obscured by severe pain during labor progression, thus potentially leaving little margin for a visible numerical decrease in pain score. Moreover, labor pain is highly subjective and influenced by psychological factors, so improvements in uterine activity or stress response may not be fully captured by VAS at fixed time points. In contrast, other studies found that pethidine helped to reduce pain score, which may be due to different baseline pain scores in those populations; the women in those studies had lower pain scores before being given pethidine when compared with this study[22, 30] in higher dosage of pethidine[27, 31], via other routes such as intravenous[26, 32], or with different pain assessment methods[19, 27], which may contribute to patients reporting reduce pain levels. Moreover, pethidine was provided on a patient-request basis. Thus, women who had more severe pain were more likely to request analgesia, resulting in higher baseline VAS scores in the pethidine group. Pethidine can readily cross the placenta and has the potential to induce neonatal respiratory depression, particularly if the neonate is delivered more than 4–5 hours post-administration. Previous research suggests that delivery within 1–4 hours of maternal dosing maintains neonatal pethidine concentrations at levels unlikely to cause significant respiratory suppression[20]. This finding supports the confidence of this study, as the median pethidine-to-delivery time in the cohort was 139 minutes, aligning with the optimal window to mitigate neonatal respiratory risks.

A key strength of this study is that it was one of the few studies from Thailand to examine the

association between intrapartum pethidine and the duration of the active phase of labor. The use of multivariate regression further enhanced the robustness of the findings by adjusting for potential confounders, ensuring a more precise evaluation of the drug's impact. However, the observational nature of the study precluded definitive causal inferences. Additionally, the single-center setting used in this study may limit the generalizability of the findings. While sufficient for primary outcomes, the sample size may not have been large enough to detect rare adverse events. Future multicenter randomized controlled trials are necessary to validate these findings and establish standardized dosing protocols.

Conclusion

Intramuscular administration of pethidine in pregnant women with spontaneous labor in the active phase of the first stage of labor significantly shortened the duration of the active phase by an average of 67.45 minutes compared to the non-pethidine group after adjusting for confounding factors, without increasing obstetric or neonatal risks, and may indirectly alleviate maternal stress related to labor pain.

Acknowledgements

The authors would like to acknowledge the support provided by the Department of Obstetrics and Gynecology at Hatyai Hospital in Songkhla, Thailand.

Potential conflicts of interest

The authors declare no conflicts of interest.

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