Effectiveness of Intravenous Meperidine for Pain Relief in the First Stage of Labour

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Abstract

Objective : To determine the effectiveness and side effects of intravenous meperidine in labour pain relief.

Material and Method : A double blind, randomized controlled trial was conducted in 84 parturients, using normal saline as control. Visual analogue scale, postpartum parturients' opinion of effectiveness, sedative scores, nausea/vomiting, dizziness, delivery method, Apgar scores, and naloxone prescription were assessed.

Result : There were no statistically significant differences between the mean and median of visual analogue scale of meperidine and control group. In addition, the sedative scores, nausea/vomiting and dizziness in the meperidine group occurred more than those in the control group significantly. Even mean of the pain increment in the meperidine group was less than those in the control group ($p < 0.05$). The parturients' opinion on the effectiveness of pain relief during labor within 24 hours of the first postpartum day was only 23.80 per cent in the meperidine group, however, it was statistically significantly different when compared to 7.10 per cent in the control group.

Conclusion : Intravenous meperidine exhibited the effectiveness of pain relief of only 23.80 per cent of the subjects, in addition, it may cause many side effects.

Key word : Meperidine, Pain Relief, Labour Pain

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Pain during the first stage of labour results from cervical dilatation and uterine contraction[1]. More than 50 per cent of the parturients described their pain as sharp, cramping, and intense[2]. There are various techniques for obstetrical pain relief including nonpharmacological methods of pain con-

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trol, systemic opioid analgesia, inhalation analgesia, and epidural analgesia.

Systemic opioid analgesia is still the first choice of treatment in the labour room in general hospitals including Srinagarind Hospital, a medical school hospital. Meperidine is the most preferable opioid in Thai obstetric practice. Four considerations of obstetrical pain relief are effectiveness, simplicity, safety, and preservation of fetal respiration and homeostasis. On account of those principles, systemic meperidine use is simplified, however, there have been inconsistent data regarding the effectiveness in pain relief and safety in both parturients and their fetuses[3-12]. The difference in study design, study population, sample size and outcome measurements might be the reasons for that. The authors, therefore, conducted a double blinded, randomized controlled trial to determine the analgesic effect in addition to side effects of intravenous meperidine during the first stage of labour.

MATERIAL AND METHOD

The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Khon Kaen University and all subjects signed informed consent before entering the study.

Study population

The authors recruited 84 parturients who had been admitted to labour room of Srinagarind Hospital. Inclusion criteria were parturients who 1) were aged 20-35 years 2) had term gestation (37-42 weeks) 3) had cervical dilatation 3-5 centimeters 4) had regular good contractions (interval 2-3 minutes, duration 40-60 seconds) 5) had painful contractions (visual analogue scale 4-10) and 6) required analgesia. Exclusion criteria were 1) complicated pregnancy 2) allergy to meperidine or meperidine analogue 3) had previously received meperidine or other analgesia within 24 hours and 4) refusal to participate in the study.

Eligible subjects were randomly assigned to therapy with meperidine or normal saline by blocks of four. There were 21 boxes and each box contained 4 sealed envelopes, which were labeled with the type of intervention, two were meperidine and the other two were normal saline. After a subject was recruited a sealed envelope was picked up from the box to assign the type of intervention.

Intervention

For the meperidine group, parturients weighing below 75 kg received 50 milligrams of meperidine intravenously and those weighing 75 kg or more received 75 milligrams of meperidine intravenously. For the control group, intravenous injection of normal saline 1.0 milliliter was given for parturients weighing below 75 kg and 1.5 milliliters for parturients weighing 75 kg or more. The cointervention in the study was 25 milligrams of promethazine hydrochloride which was given for parturients who had considerable nausea/vomiting.

Study measurement

Demographic variables, vital signs, fetal heart rates, visual analogue scale (VAS), sedative scores, uterine contraction, nausea/vomiting, and other symptoms were recorded by physicians prior to intervention. After that, vital signs, fetal heart rates, VAS, and sedative scores were recorded by an observer who did not know the type of intervention at 15, 30, and 60 minutes. Subsequently, delivery method, Apgar scores of fetus at 1, 5 minutes, and other interventions including prescription of naloxone for the fetuses were collected. The parturients' opinion on effectiveness of pain relief during labor was assessed within 24 hours of the first postpartum day.

Operational definition

Visual analogue scale was evaluated by parturients themselves and classified as follows: 0 = no pain, 1-3 = mild pain, 4-7 = moderate pain and 10 = severe pain.

Sedative scores was evaluated by the observers and classified as follows: 1 = wide-awake, 2 = drowsy, 3 = intermittent drowsy, 4 = mostly sleeping, 5 = only awakens when aroused.

For this study, both pain and sedative scores were analyzed as continuous variables.

Regarding the parturients' opinion on pain relief, which was evaluated within the first postpartum day, it was classified whether meperidine was able to relieve pain or not. So, it was analyzed as a categorical variable.

Statistical analysis

Previous studies have shown that the placebo effect of pain relief was 0-100 per cent[13] and the meperidine effect of pain relief was 31-47 per cent

(4). To calculate the sample size for this study, the authors assumed that the placebo effect would be 10 per cent and the meperidine effect would be 40 per cent. Finally, the sample size of 84 cases would achieve power of 80 per cent and significance at p-value ≤ 0.05.

The authors calculated mean and SD for continuous variables and percentage for categorical variables. Case-control differences were tested with Student's *t*-test, Kolmogorov-Smirnov test, Chi-square test where appropriate. A difference between groups was considered to have statistical significance if the level of p-value ≤ 0.05.

RESULTS

Table 1 shows that the meperidine and control groups were comparable with regard to subject characteristics. The mean difference of vital signs and fetal heart rate before and after the intervention between the two groups did not differ significantly when comparing the time of 15, 30, and 60 minutes after receiving intervention (Table 2). While the mean of VAS of the two groups increased with the time, there was no statistically significant difference between the mean of VAS of the meperidine and control group at different times. Although, the VAS distribution in the study was not normal distribution, the median of VAS of the two groups was also no statistically significantly different proved by Kolmogorov-Smirnov test (Table 3).

In spite of increasing of VAS, the means of increment in the meperidine group were significantly less than those in the control group at 0-15, 0-30 and 0-60 minutes (Table 4).

Considering the parturients' opinion on the effectiveness of pain relief during labor evaluated within 24 hours of the first postpartum day, only 23.80 per cent of subjects in the meperidine group perceived pain relief but there was statistically significant difference when compared to 7.10 per cent in the control group ($p = 0.0347$).

With regard to side effects, sedation was found in 69.0 per cent in the meperidine group. Nausea/vomiting, and dizziness were significantly

Table 1. Subject characteristics.

Characteristics	Meperidine group	Control group
Age (yr)	26.31 ± 4.05	25.50 ± 4.17
Weight (kg)	63.00 ± 7.46	64.60 ± 8.19
Height (cm)	155.55 ± 5.76	155.96 ± 5.23
GA (wk)	39.24 ± 2.12	39.55 ± 1.49
Cervical dilatation (cm)	3.45 ± 0.74	3.55 ± 0.77
Parity	%	%
Nulliparous	38.10	59.50
Multiparous	61.90	40.50
Uterine contraction		
Mild	0.00	2.40
Moderate	88.10	90.50
Severe	11.90	7.10
Syntocinon infusion	54.76	50.00

Table 2. The mean difference of vital signs and fetal heart rate.

Characteristics	Meperidine group (minutes)			Control group (minutes)		
	15	30	60	15	30	60
Systolic BP (mmHg)	0.45	0.24	0.26	-2.10	-2.29	-1.90
Diastolic BP (mmHg)	2.24	2.00	2.26	2.83	4.05	3.57
Pulse rate (beat/minute)	-2.69	-2.95	-2.43	0.24	0.93	0.86
Respiratory rate (time/minute)	0.45	-0.36	-0.02	0.06	0.74	0.86
Fetal heart rate (beat/minute)	0.95	0.02	-2.36	-3.74	-2.52	-1.95

Table 3. The comparison of the mean and median of pain scores between the two groups at the different times.

Time (minutes)	Meperidine group				Control group				P-value
	Mean	SD	Median	25th-75th percentile	Mean	SD	Median	25th-75th percentile	
0	6.02	1.87	5.50	5-7	5.91	1.70	5.5	5-7	> 0.05
15	6.33	2.15	6.00	5-8	6.90	1.46	7.0	6-8	> 0.05
30	6.90	2.29	7.00	5-9	7.62	1.81	8.0	6-9	> 0.05
60	7.42	2.34	8.00	6-10	8.28	1.76	8.5	7-10	> 0.05

Table 4. Comparison of the means of pain increment scores between the two groups at the different times.

Time (minutes)	Meperidine group		Control group		P-value
	Mean	SD	Mean	SD	
0-15	0.30	1.54	1.14	1.00	0.004
0-30	0.88	2.10	1.81	1.50	0.022
0-60	1.40	2.17	2.48	1.50	0.010

Table 5. Comparison of the side effects between the two groups.

Side effects	Meperidine group		Control group		P-value
	number	per cent	number	per cent	
Nausea/vomiting	15	36.0	2	4.8	0.001
Dizziness	11	26.4	0	0	0.001
Misc.	2	4.8	2	4.8	1.000
Total	28	67.2	4	9.6	< 0.001

different between two groups (tested by Student *t*-test, $p < 0.05$) (Table 5). However, the method of delivery, Apgar scores, and naloxone prescription revealed no significant difference between the two groups.

DISCUSSION

According to the present study, intravenous meperidine injection was able to reduce the pain increment occurring in the parturients significantly when evaluated at 15, 30, and 60 minutes, but there was no statistically significant difference between the mean and median of VAS of the meperidine and control group. In addition, the sedative scores, nausea/vomiting and dizziness in the meperidine group occurred significantly more often than those in the control group. Postpartum parturients' opinion of pain relief within 24 hours of the first postpartum day was only 23.80 per cent in the meperidine group, but it was statistically significantly different when compared to 7.10 per cent in the control group. Although side effects occurred in parturients of the meperidine group more often than those of the control group ($p < 0.05$), the delivery method, Apgar scores, and naloxone requirement of the newborn were comparable between the two groups.

In 1974 Barnes J reported a study without a control group of 500 cases of meperidine in labour. The result exhibited the effectiveness of pain relief of 55 per cent of the subjects on the first postpartum day[3]. Harper NJN et al also reported a close figure of 65 per cent[7]. However, the treatment effects from an uncontrolled study might be from various factors such as subject characteristics, environment and treat-

ment itself. To avoid bias in the interpretation of treatment effects, a control or comparison group is necessary. There have been many controlled trials regarding the effectiveness of meperidine. For the positive trials, effectiveness of pain relief varied from 18-60 per cent of parturients who received meperidine[4-6,8]. Dosage, route, method to evaluate pain and characteristics of the subjects might affect the outcomes. For the negative trials, control groups in each research were meptazinol[11], morphine[12], epidural block[14], nalbuphine[9,10] and various methods of pain relief[15].

Firstly it was notable that the positive trials for meperidine were conducted from 1947 to 1983, whereas, the negative trials were conducted more recently from 1986 to 1996. Secondly, there has been no research comparing meperidine and placebo, which would be able to discriminate the effect of meperidine itself from placebo effect. Thirdly, the negative trials exhibited the gradual rise of pain even after receiving treatment. According to Melzack R the pain of labour ranks second only to that of causalgia in its severity[16]. In addition, it has the unique properties of being intermittent and increasing intensity over a variable period. These factors combine to make the assessment of analgesic efficacy in labour notoriously difficult[16].

Regarding the side effects of meperidine in the present study, sedative effect was found in 69.0 per cent which was more than that found in the study of Harper NJN et al, 43.5 per cent[7] and Morrison CE et al, 34.6 per cent [11]. Nausea and vomiting was found in 36.0 per cent, which was comparable with other studies, ranging from 13 to 50 per cent[4,5,7, 10,11]. The nausea/vomiting occurring in the present study was not severe enough to receive treatment. For dizziness, the present study found 26.4 per cent which was more than that found in the study of Morrison CE et al, 18.2 per cent[11].

Shnider SM et al found that meperidine would suppress the respiration of the newborn[17], whereas, the present study did not exhibit any significant difference between the two groups. It might be explained by all deliveries occurring after only a single dose of meperidine injection.

Olofsson CH et al described that meperidine acts on the central nervous system but it does not act on the spinal cord. Therefore, at a normal dose, it causes sedation more than pain relief. The parturients would calm down from the sedative effect[12]. At higher dose, it might be able to relieve pain, however, the side effects occurring in parturients and fetuses would also be increased.

The present study was a double blind, randomized controlled trial which is the best study design for determining the treatment effects. On account of the similarity of baseline characteristics of the treatment and control group, the results of the study were solely from the treatment. The authors chose to study the intravenous route because the outcome could be assessed within one hour. There were some limitations of generalizibility of the present study in other circumstances such as in the case of cervical dilatation more than 5 cm and complicated pregnancy. Another limitation was the accuracy of pain evaluation, while assessment during labour might be subjected to misclassification bias due to the sedative effect of the treatment, recall bias might occur when assessing the parturients' opinion on the following day, even within 24 hours of the first postpartum day. Hence, these effects might be the reason for the inconsistent effect of pain relief when evaluated at different times during labour and the first postpartum day.

In conclusion, at present, meperidine is still the first choice of treatment used to provide analgesia and sedation during the first stage of labour. There was inherent inconsistency of the effectiveness of meperidine in pain relief. While, meperidine tended to be able to decrease the pain increment, it also caused many side effects. Thus, physicians should be cautious in the clinical, routine use of meperidine for pain relief in labour. Further study should be done on the appropriate dose and route of meperidine, including other new drugs and other methods for obstetric analgesia.

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ประสิทธิภาพของเมเพริดีนทางหลอดเลือดดำในการระงับปวดในระยะที่หนึ่งของการคลอด

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วัตถุประสงค์ : เพื่อประเมินประสิทธิภาพและอาการข้างเคียงของการใช้เมเพริดีนทางหลอดเลือดดำเพื่อระงับปวดในการคลอด

วัสดุและวิธีการ : แบ่งสตรีที่มาคลอดบุตรจำนวน 84 ราย เป็นสองกลุ่มโดยวิธีสุ่ม กลุ่มควบคุมให้ normal saline กลุ่มทดลองให้เมเพริดีน ประเมินผลโดยการวิเคราะห์คะแนนความเจ็บปวดโดยผู้ป่วย (visual analogue scale) และสอบถามความคิดเห็นในการระงับปวดภายใน 24 ชั่วโมงหลังคลอด อาการข้างเคียงประเมินจากระดับความง่วงนอน อาการคลื่นไส้/อาเจียน อาการเวียนศีรษะ วิธีการคลอด Apgar scores และจำนวนการใช้ยา naloxone ในทารก

ผลการวิจัย : ค่าเฉลี่ยของคะแนนความเจ็บปวดโดยผู้ป่วยทั้งสองกลุ่มไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ และยังพบว่าระดับความง่วงนอน อาการคลื่นไส้/อาเจียน และเวียนศีรษะในกลุ่มที่ได้รับเมเพริดีนมากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ จากการสอบถามผลการระงับปวดภายใน 24 ชั่วโมงหลังคลอดพบว่าเมเพริดีนได้ผลระงับปวดเพียงร้อยละ 23.8 แต่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติเมื่อเปรียบเทียบกับกลุ่มควบคุม ซึ่งได้ผลเพียงร้อยละ 7.10

สรุปผลการวิจัย : การให้เมเพริดีนทางหลอดเลือดดำมีประสิทธิภาพในการระงับปวดในขณะเจ็บครรภ์คลอดเพียงร้อยละ 23.8 และยังอาจก่อให้เกิดอาการข้างเคียงได้หลายอย่าง

คำสำคัญ : เมเพริดีน, การระงับปวด, การเจ็บครรภ์คลอด

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