



Intramuscular meperidine analgesia at the beginning of active phase shortens labor duration without adverse effects on obstetric lacerations

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Abstract

The primary objectives of this study were to evaluate the impact of intramuscular meperidine on shortening of the active phase of labor, the neonatal outcome and the rate and severity of perineal lacerations in term pregnant women in the first stage of labor. A total of 571 primiparous term pregnant women delivered vaginally were included into this retrospective study. In 437 of them, meperidine (100 mg IM) at the beginning of the active phase was administered and 134 women did not receive any meperidine dose. The length of labor phases, obstetric lacerations, and neonatal outcomes were recorded. The results of this study showed that meperidine could be used safely as an obstetric analgesic with its additional benefit of shortening the active phase of the first stage and second stage of labor without increased risk of obstetric lacerations and perinatal adverse outcomes. In case of limited use of neuraxial analgesia in a busy state maternity hospital, intramuscular meperidine administration as obstetric analgesia seems beneficial in reducing the length of the active phase of the first stage of labor and the second stage of labor without adversely affecting obstetric lacerations and neonatal outcomes.

Keywords: meperidine, neonatal outcome, normal vaginal delivery, obstetric analgesia, obstetric lacerations, stages of labor

1. Introduction

Obstetric analgesia is used to relieve obstetric pain. Effective pain relief has become an essential part of obstetrics. The history of modern analgesia at birth dates back to 1847 with the use of ether and later chloroform (1). Parenteral opioids for labor pain relief are a common option for women worldwide and have been the subject of research for many years. The earliest documents of opioid use in the workplace appear in ancient Chinese scriptures describing the use of opium to relieve pain in the workplace (2). Examples include epidural analgesia and an opioid-based analgesic like meperidine (3). Pain during the first stage of labor is primarily visceral and results from cervical dilation and uterine contractions. Pain during the second stage occurs as the fetus descends through the birth canal, resulting in the stretching and tearing of fascia, skin, and subcutaneous tissue. This pain is somatic and is transmitted through the pudendal nerve; it can be treated with local anesthetics (4). Pain during labor is subjective, and other factors such as anxiety, depression, and neuroticism may contribute to it (4). The patient's age, parity, emotional status, and labor coaching are some other factors influencing labor pain. Pregnant women may benefit from antenatal childbirth training to reduce the

intensity of pain. Physiological changes occurring later in pregnancy are a combination of hormonal factors and mechanical effects from the growing uterus (5).

Epidural analgesia is the most popular method for pain relief during labor. It is effective for both the first and the second stages. Although epidural analgesia is associated with slight prolongation of the second stage and an increased rate of operative vaginal delivery, it does not increase the risk of cesarean delivery or neonatal depression (6). Clinical conditions such as patients' refusal or inability to cooperate, increased intracranial pressure, coagulopathy, infection at the site of needle insertion, maternal fever or sepsis, thrombocytopenia, and hypovolemia preclude its use and leave systemic analgesia as the only option.

Meperidine (pethidine) was synthesized in 1939; it was first used at work in the early 1940s. Since then, it has been the most widely used opioid in the world for pain relief during childbirth (7, 8). Meperidine is generally preferred for labor analgesia; however, concerns about its analgesic efficacy and neonatal respiratory depression have limited its use. Four of five women who deliver by the normal vaginal

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route experience some degree of birth canal lacerations during labor beginning from the cervix to the rectum and anal sphincter (9). The impact of lacerations may range from very superficial to severe long-lasting ones that may deteriorate the quality of life of women of young age. Thus, it is recommended that the occurrence of obstetric lacerations should be prevented by proper management of all phases of labor (9, 10). Though widely used worldwide for many years (11), the role of meperidine use on obstetric lacerations has not been studied much. Based on long-term clinical experience regarding intrapartum analgesia including meperidine, we hypothesized that intramuscular meperidine administration, apart from pain relieving effect, would shorten the active phase of labor without increasing obstetrical lacerations and neonatal morbidity. This study aims to show the impact of meperidine use on the length of the active phase of labor, the rates and severity of obstetric lacerations and neonatal outcomes in term pregnant women delivered vaginally.

2. Materials and methods

In this retrospective study, 571 primiparous pregnant women with term, singleton, and vertex presented fetuses delivered by the vaginal route at the Samsun Training and Research Hospital, Samsun, Turkey between June 2018, and December 2018, where the annual birth rate was 6500/year and only 17% of deliveries were cesarean sections. This study was conducted after the approval of Human Research Ethics Committee of our Institution.

Multiparous women, women with multifetal gestation, high-risk pregnancy, macrosomia, breech presentation, preterm delivery, intrauterine fetal loss, obstetric analgesia other than meperidine, and operative deliveries were excluded to ensure homogeneity in the study. Patients were divided into two groups: 437 women who received meperidine 100 mg IM at 4-cm cervical dilatation and >70% cervical effacement with compressing head at level 0 and 134 women who did not receive meperidine or any other analgesia.

By convention, labor is divided into three stages (12, 13):

1. First stage: From onset of labor to full dilation of the cervix,

- a) *Latent phase:* from the onset of regular uterine contractions to the beginning of the active phase,
- b) *Active phase:* from the time, at which the rate of cervical dilation transforms at ~ 4 cm to full dilation,

2. Second stage: From full dilation of the cervix to delivery of the infant,

3. Third stage: From delivery of the infant to delivery of the placenta.

In our routine obstetric practice, appropriate time for meperidine use is defined as fetal head engagement at 0 level with 70% cervical effacement and 4 cm cervical dilatation.

All patients in the maternity hospital were followed by ac, and normal vaginal deliveries were performed by experienced midwives. The duration of the active phase, time and dose of meperidine administration and time of delivery were all marked on the cartogram. All primiparous patients who need episiotomy repair, operative deliveries, laceration repairs, and cesarean section were managed by obstetricians. Therefore, all major complications and surgical procedures were recorded whereas minor lacerations were not sutured and recorded.

Obstetric analgesia is offered as opioid-based drug use rather than epidural analgesia in a busy maternity hospital if not otherwise contraindicated. Patients with severe pain who were about to pass the active labor phase at 4 cm with head compression and 70%-80% cervical effacement were given 100 mg meperidine IM for pain relief. Meperidine was not used routinely in patients with mild and moderate pain for obstetric pain relief.

All women who were interned for normal vaginal delivery had an IV line and an induction protocol with 10 IU of oxytocin in 1000 ml of lactated ringer solution beginning with 10 drops/min and an increase of 5 drops every 15 min until regular contractions were recorded in the nonstress test (NST). The maximum induction dose was 40 drops/min. The rectum was emptied by an intrarectal enema in the latent phase, and the bladder was emptied by a disposable catheter at the time of delivery. During delivery, the perineum was supported manually from posterior to anterior to minimize trauma to the perineal body and anal sphincter. Liquid vaseline was used to moisten the labial and vaginal tissues to ease the birth of the fetal head (crowning phase). At the same time, preserving the urethra and periurethral area with the aid of the midwife's other hand is very important to prevent lacerations and bleeding at that anatomical area. A mediolateral episiotomy is almost always added at the third stage of delivery in primiparous women. The second-most important issue to prevent severe lacerations is to warn the mother not to push anymore when the fetal head is out; the rest of the body should be taken out by the midwife. All deliveries of the participating women were conducted in the dorsolithotomic supine position without any extra interventions and abdominal compression to facilitate delivery. All deep and severely bleeding lacerations were recorded according to the ACOG classification (3). Cervical, vaginal, and perineal lacerations were carefully evaluated using bivalves and oval forceps and through rectal examination for anal sphincter damage.

2.1. Statistical analysis

Data were presented as mean, median, and percentage as appropriate. After normality test study variables were compared with Mann-Whitney test or chi-square test. P values below 0.05 were considered statistically significant.

3. Results

As presented in Table 1, the ages, gestational ages, and Apgar score at 1 min, and rates of meconium-stained amniotic fluid, NICU admission, neonatal intubation, cervical laceration, third- and fourth-degree perineal lacerations, vaginal laceration of pregnant women with or without meperidine administration were found comparable ($p>0.05$). The rate of gravidity 1 was significantly higher than the rates of gravidity 2 and 3 in both of the study groups ($p<0.05$); however, there was no significant difference between the rates of gravidity in the study groups ($p>0.05$).

The durations of active phase in the first stage of labor, and second stage of labor in the pregnant women with meperidine administration were significantly lower than those in the pregnant women without meperidine administration ($p<0.05$).

The birth weight and Apgar score at 5 min in the pregnant women with meperidine administration were significantly higher than those in the pregnant women without meperidine administration ($p<0.05$).

4. Discussion

The results of this study show that meperidine can be used safely as an obstetric analgesic with its additional benefit of shortening the active phase of the first stage and second stage of labor without increased risk of obstetric lacerations and perinatal adverse outcomes.

Quality in labor and delivery management should always be judged by the lowest maternal and perinatal morbidity and mortality and not by preset limits on specific interventions. Clinically, good-quality recommendations favor hospital births, delayed admission, support by midwife training birth assistants in developing countries, and upright position in the second stage. These labor and delivery techniques should be performed routinely (14, 15).

Pain is defined as an unpleasant sensory or emotional experience with actual or potential tissue injury. It is closely related to uterine contractions in labor, and patient satisfaction correlates closely to its management, which varies during the phases of labor. Opioids administered intramuscularly or subcutaneously or through repeated IV boluses are widely used in many centers, although they are not recommended in the era of epidural analgesia. In our clinic, meperidine is used as a 100 mg single intramuscular dose in patients with severe obstetric pain. A 2010 Cochrane review reported that parenteral opioids provide some pain relief in labor and were associated with maternal side-effects, including nausea, vomiting, and drowsiness (16). Meperidine may have negative neonatal effects owing to its long half-life (17). However, it has been the drug of choice in the pain relief of labor for years. The half-life of the active metabolite in the newborn may be 2–3 days; this may result in respiratory depression and may affect the consciousness and reflexes of the newborn (18).

Table 1. Baseline and selected obstetric parameters in labor in women received meperidine or not

	Meperidine (n=437)	No meperidine (n=134)	Significance
Age (y)	17-43 (23)	17-44 (24.5)	NS
Gravidity			
1	349 (79.9)	89 (66.4)	p<0.05
2	46 (10.5)	22 (16.4)	
3	42 (9.6)	23 (17.2)	
Gestational age (w)	39.78±1.69	39.50±1.49	NS
Duration			
Active phase of first stage of labor (h)	1-5,5 (3)	1-8 (4,7)	p<0.05
Second stage of labor (min)	5-60 (15)	5-60 (25)	
Birth weight (g)	2550-3990 (3320)	2030-3990 (3255)	p<0.05
Apgar score			
1 min	8.68±0.98	8.79±1.04	NS
5 min	9.74±1.03	9.22±0.75	p<0.05
MSAF (n, %)	41 (9.4)	9 (6.7)	NS
NICU admission (n, %)	41 (9.4)	13 (9.7)	NS
Neonatal intubation (n, %)	23 (5.3)	8 (6.0)	NS
Cervical laceration (n, %)	19 (4.3)	7 (5.2)	NS
Third- and fourth-degree perineal lacerations (n, %)	1 (0.2)	0 (0)	NS
Vaginal laceration (n, %)	45 (10.3)	13 (9.7)	NS

MSAF, meconium-stained amniotic fluid; NICU, neonatal intensive care unit

Most anesthetic drugs are safe for mothers who are breastfeeding and present a low risk to newborns who are breastfed when administered in a single dose. However, high

doses and repeated drug administration significantly increase the risk of side effects in newborns. They should evaluate individual risk / benefit, paying special attention to premature

newborns or infants with concomitant disease, especially as they are more susceptible to side effects (19).

Meperidine, also called pethidine, is an opioid that is around one-tenth as potent as morphine; it can be prescribed and administered by midwives. The side-effects are similar to those of other opioids, namely, respiratory depression of the mother and neonate, delayed gastric emptying, nausea, vomiting, sedation, and hypotension (20). Meperidine crosses the placenta, and fetal exposure to this drug is maximal at 2-3 h after maternal intramuscular administration. Thus, the use of intramuscular meperidine at the right time will shorten the active phase and may prevent maternal and neonatal complications. This is the key issue of meperidine use in our setting for patients with severe pain who may react to the drug with pain relief and faster termination of the active phase of labor, which is beneficial to the mother and the newborn. The optimal time for the delivery of the baby following a dose of meperidine is within 1-4 h of dosing. Our time-range for the active phase of labor and delivery is consistent with this literature. Therefore, our neonatal results are good. Delayed delivery after meperidine use, which is not encountered commonly, necessitates consultation with a pediatrician to attend the delivery for possible neonatal respiratory distress. Meperidine use is not recommended in settings without pediatric support during labor (6, 20, 21, 22, 23). In a trial involving 407 women, 100 mg IV meperidine was used in women with term, singleton pregnancies who required oxytocin because of dystocia at 4-6 cm. The authors concluded that meperidine use does not worsen operative delivery rates and neonatal outcomes compared with placebo as in our study. Although many studies have investigated neonatal outcomes with meperidine use during labor, to the best of our knowledge, our study is the first to present the effect of meperidine use on the duration of labor.

In our maternity hospital with a high rate of daily deliveries, only operative procedures such as episiotomy and suturing for lacerations that were managed by obstetricians were recorded. That is why minor cervical, vaginal, and perineal lacerations were not found in the files for evaluation. This is the limitation of our study. Because minor lacerations have no severe effect on the quality of life of patients and our main outcome measure was shortening the duration of labor, this limitation was not a big bias. In a recent study, Mizrahci et al. argued with our results of obstetric lacerations. They studied all lacerations including minor ones, which were their primary objective. However, our primary objective was shortening the active phase of labor, and obstetric lacerations and neonatal outcomes were secondary outcomes. Another limitation is the retrospective nature of this study (9).

In conclusion, in case of limited use of neuraxial analgesia, meperidine use as an obstetric analgesic drug remains a safe, cheap, and noninvasive analgesic choice that reduces the duration of labor. Obstetric lacerations and

neonatal outcomes are not different from those in patients not using meperidine. Thus, timely meperidine use affords benefits such as shortening the duration of the active phase of labor, pain relief, and good neonatal outcomes. Therefore, it can be an advantageous modality in obstetric analgesia where neuraxial analgesia is contraindicated or not available. Further prospective and large-scale studies are warranted.

Conflict of interest

None to declare.

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None to declare.

References

1. Aburel E. L'anesthésie locale continue (prolongée) en obstétrique. *Bull Soc Obstet Gynecol.* 1931; 20:35-37.
2. Wood A. Treatment of Neuralgic Pains by Narcotic Injections. *Br Med J.* 1858 Aug 28;1(87):721-3.
3. ACOG Committee Opinion #295: pain relief during labor. *Obstet Gynecol.* 2004 Jul;104(1):213.
4. Lang AJ, Sorrell JT, Rodgers CS, Lebeck MM. Anxiety sensitivity as a predictor of labor pain. *Eur J Pain.* 2006 Apr;10(3):263-70. doi: 10.1016/j.ejpain.2005.05.001.
5. Zakowski MI, Herman NL. The Placenta: Anatomy, Physiology, and Transfer of Drugs. In: *Chestnut's Obstetric Anesthesia: Principles and Practice.* 2009; 4:55-68.
6. Munro A, George RB. *Chestnut's Obstetric Anesthesia Principles and Practice, Fifth Edition.* *Can J Anesth Can d'anesthésie.* 2015; 62:1027-1028.
7. Latta KS, Ginsberg B, Barkin RL. Meperidine: a critical review. *Am J Ther.* 2002 Jan-Feb;9(1):53-68. doi: 10.1097/00045391-200201000-00010.
8. Caton D. The History of Obstetric Anesthesia. In: *Chestnut's Obstetric Anesthesia: Principles and Practice.* 2009; 114:1326-1331.
9. Mizrachi Y, Leytes S, Levy M, Ginath S, Bar J, Ezri T, et al. Does meperidine analgesia affect the incidence of obstetric lacerations at vaginal delivery? *J Matern Fetal Neonatal Med.* 2018 Mar;31(5):586-590. doi: 10.1080/14767058.2017.1292500.
10. Viktrup L. The risk of lower urinary tract symptoms five years after the first delivery. *Neurourol Urodyn.* 2002;21(1):2-29. doi: 10.1002/nau.2198.
11. Macarthur AJ, Macarthur C. Incidence, severity, and determinants of perineal pain after vaginal delivery: a prospective cohort study. *Am J Obstet Gynecol.* 2004 Oct;191(4):1199-204. doi: 10.1016/j.ajog.2004.02.064.
12. Leduc D, Biringer A, Lee L, Dy J. Induction of labour: SOGC Clinical Practice Guideline. *J Obs Gynaecol Can.* 2013; 35:840-857. doi: 10.1016/S1701-2163(15)30842-2
13. Kominiarek MA, Zhang J, Vanvelhuisen P, Troendle J, Beaver J, Hibbard JU. Contemporary labor patterns: the impact of maternal body mass index. *Am J Obstet Gynecol.* 2011 Sep;205(3): 244.e1-8. doi: 10.1016/j.ajog.2011.06.014.
14. Berghella V, Baxter JK, Chauhan SP. Evidence-based labor and delivery management. *Am J Obstet Gynecol.* 2008 Nov;199(5):445-54. doi: 10.1016/j.ajog.2008.06.093.
15. Millen KR, Kuo K, Zhao L, Gecsi K. Evidence-based guidelines in labor management. *Obstet Gynecol Surv.* 2014

- Apr;69(4):209-17. doi: 10.1097/OGX.0000000000000057.
16. Smith LA, Burns E, Cuthbert A. Parenteral opioids for maternal pain management in labour. *Cochrane Database Syst Rev.* 2018 Jun 5;6(6):CD007396. doi: 10.1002/14651858.
 17. Nissen E, Widström AM, Lilja G, Matthiesen AS, Uvnäs-Moberg K, Jacobsson G, et al. Effects of routinely given pethidine during labour on infants' developing breastfeeding behaviour. Effects of dose-delivery time interval and various concentrations of pethidine/norpethidine in cord plasma. *Acta Paediatr.* 1997; 86(2):201-8. doi: 10.1111/j.1651-2227.1997.tb08869.x.
 18. Shnider SM, Moya F. Effects of meperidine on the newborn infant. *Am J Obstet Gynecol.* 1964; 89:1009-15. doi: 10.1016/0002-9378(64)90292-3.
 19. Oliveira MRE, Santos MG, Aude DA, Lima RME, Módolo NSP, Navarro LH. Anestesia materna deve atrasar a amamentação? Revisão sistemática da literatura [Should maternal anesthesia delay breastfeeding? A systematic review of the literature]. *Rev Bras Anesthesiol.* 2019 Mar-Apr;69(2):184-196. Portuguese. doi: 10.1016/j.bjan.2018.11.006.
 20. Allman KG, Wilson H, and O'Donnel A. Chapter 41 Regional anaesthesia. In: *Oxford Handbook of Anaesthesia.* 2006:1120.
 21. Pillai A, Bogod D. Chestnut's Obstetric Anesthesia: Principles and Practice. *Br J Anaesth.* 2015; 114:861.
 22. Maronge L, Bogod D. Complications in obstetric anaesthesia. *Anaesthesia.* 2018 Jan;73 Suppl 1:61-66. doi: 10.1111/anae.
 23. Tita ATN, Rouse DJ. Obstetric Management of Labor and Vaginal Delivery. In: *Chestnut's Obstetric Anesthesia: Principles and Practice.* 2009:223-245.