



# Does pethidine still have a place in the management of labour pain?

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## Summary

**Pethidine can provide short-term relief of acute pain, but it is not effective for everyone. During labour, intramuscular or intravenous pethidine sedates women, but may not give them adequate analgesia. Pethidine and its active metabolite, norpethidine, can have adverse effects on the neonate as well as the mother, especially if repeated doses are given during labour. There is little evidence to show that other drugs have greater efficacy than pethidine, so epidural analgesia may be a more effective option.**

Key words: analgesia, breastfeeding, epidural.

(*Aust Prescr* 2004;27:34–5)

## Introduction

Many women prefer to experience birth actively and as naturally as possible. Their preferences for analgesia should be discussed and reviewed regularly. If required, adequate analgesia during labour is beneficial to the mother, has a positive influence on the course of labour and improves neonatal outcome. The ideal obstetric analgesic should provide potent analgesic efficacy with minimal maternal and neonatal adverse effects.

Pethidine was first introduced in Germany in 1939 and was first used in labour in 1940. Since then pethidine has been the most widely used systemically administered opioid for obstetric analgesia<sup>1</sup>, perhaps because it is cheap and easily given by midwives. While pethidine relieves acute pain for 2–4 hours<sup>2</sup>, there are concerns about its efficacy in labour. There is also the potential for maternal and neonatal adverse effects from pethidine and its active metabolite norpethidine.

## Efficacy of pethidine in labour

Early studies reporting that pethidine had good analgesic effects in labour were unfortunately flawed because efficacy was evaluated by an independent observer rather than the patient. If the patients were interviewed it was 24 hours post-delivery.<sup>3</sup>

A double-blind randomised controlled trial compared intravenous pethidine with placebo in 84 women during labour. Pethidine provided effective pain relief in only 23.8% of patients compared to 7% of those given placebo. Although this difference is significant ( $p < 0.05$ ), there was no difference

between the median or mean visual analogue pain scores in the pethidine and placebo groups. Pethidine significantly increased the sedation scores, dizziness, nausea and vomiting.<sup>4</sup>

## Comparison with other analgesics

In a randomised controlled trial involving 20 patients in labour, pethidine (up to 1.5 mg/kg) and morphine (up to 0.15 mg/kg) given intravenously produced no significant change in pain scores over time with three doses. Following treatment with opioids 15 of the patients requested an epidural. Nausea was more common with pethidine (6/10) than with morphine (1/10). Patients receiving pethidine were calmer and more euphoric, but both drugs caused similar significant sedation (mean sedation scores 8/10 after three doses). The patients were therefore all significantly sedated and fell asleep during labour, but were awakened by pain during contractions. The researchers concluded that labour pain was not sensitive to systemically administered pethidine or morphine and that it was unethical to treat requests for pain relief by giving sedation.<sup>5</sup>

Pethidine has also been compared with intravenous fentanyl<sup>6</sup>, remifentanyl<sup>7</sup> and tramadol in randomised controlled trials. Fentanyl given as an intermittent intravenous infusion was equianalgesic to pethidine, but caused less nausea, vomiting and sedation. Remifentanyl given as patient-controlled analgesia produced significantly lower pain scores than pethidine. However, the study was terminated early due to low Apgar scores in the pethidine group. In one study tramadol 100 mg intramuscularly had no greater efficacy than pethidine 75 mg.<sup>8</sup> Tramadol has its own safety issues.

A Cochrane review of the available studies has concluded that there is not enough evidence to evaluate the comparative efficacy and safety of the various opioids used for analgesia in labour.<sup>9</sup> Despite antenatal ambivalence about a specific analgesic choice, 65% of nulliparous women in one Australian tertiary unit chose epidural analgesia. Nearly 60% of women given intramuscular opioid 'crossed over' to epidural analgesia, confirming the inadequacy of systemically administered opioids.<sup>10</sup>

## Pharmacology

There are pharmacokinetic reasons why systemically administered opioids are ineffective in controlling the pain of labour. Following injection into the gluteal muscle, plasma concentrations of pethidine are significantly lower than after intravenous administration or injection into the deltoid muscle. This suggests that drug absorption from the gluteal muscles

is impaired in pregnant women.<sup>11</sup> Another study of women in labour compared intravenous, intramuscular and epidural administration. Epidural absorption of pethidine was rapid with a plasma concentration similar to intravenous administration. However, the analgesia provided by the epidural route was far superior to that of intravenous and intramuscular administration.<sup>12</sup>

This suggests that for pethidine to be effective in labour its concentration must be sufficient at central opioid receptors. This view is supported by an experimental animal model of noxious distension of the cervix which induces reflex abdominal muscle contraction. Morphine produced a dose-dependent inhibition of this reflex activity, which was reversed by naltrexone, but not by methyl naltrexone, suggesting a central site of inhibition.<sup>13</sup>

Pethidine given intramuscularly or intravenously does not appear to achieve concentrations that are sufficient to inhibit the visceral pain of noxious cervical stimuli. However, the concentration is high enough to produce significant maternal and neonatal adverse effects.

### **Norpethidine and adverse effects**

Norpethidine is the active metabolite of pethidine. It accumulates in both the mother and fetus with a half-life of 20.5 hours and is thought to be responsible for adverse neonatal effects<sup>14</sup> including respiratory depression. Newborns exposed to pethidine have significantly impaired normal infant behaviours such as hand and mouth movements, nipple touching before suckling, and licking movements. Half of the infants exposed to pethidine fail to breastfeed and cry more in the neonatal period.<sup>15</sup> In addition to the maternal sedating effects of pethidine, there is also the theoretical risk of maternal delayed gastric emptying, aspiration and respiratory depression. Norpethidine can also induce seizures.

### **Conclusion**

Pethidine administered systemically has little place in the management of labour pain because it is minimally effective, has significant adverse effects for mother and baby, and does little more than sedate the patient. There is limited evidence supporting the use of any systemically administered analgesic in labour; epidural analgesia is a better option.

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*Conflict of interest: none declared*

### **Self-test questions**

*The following statements are either true or false (answers on page 51)*

1. Analgesia is effective in 60% of women given intravenous pethidine.
2. The active metabolite of pethidine, norpethidine, does not cross the placenta.