Analgesia in labour: non-regional techniques

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For many women, labour may be the most painful experience they encounter. A European multicentre study of 611 nulliparous women concluded that the most satisfied were those who not only received effective pain relief, but had expected more pain before their analgesia. The experience of labour, including pain severity, is different for each woman and the measures taken to relieve pain remains the choice of the individual. The provision of clear information about the types of pain relief available has been found to increase feelings of being in control. Local services vary and the advent of midwife-led units for low risk labour may limit the type of analgesia available.

Non-pharmacological methods

A wide variety of non-pharmacological techniques has been used for analgesia in labour, often with little evidence to support their use. It is important for anaesthetists to be aware of such techniques in order that the efficacy and the limitations of such methods can be discussed. We have included a selection of the available techniques. The mechanism of action, advantages, disadvantages, and evidence base of these techniques are summarized in Table 1.

Pharmacological methods

Pharmacological methods include systemic analgesics and inhalational analgesia. Systemic analgesics are still widely used around the world, despite being significantly less efficacious than epidural analgesia. The reasons for this include availability, simplicity of administration and epidural unavailability or contraindications.

Parenteral opioids

Meperidine

Meperidine (pethidine) was made legally available in the UK to midwives for independent use in 1950; it remains the most widely used and investigated opioid in labour. It is a synthetic, weakly basic phenylpiperidine derivative, related to fentanyl and sufentanil. It is ~28 times more lipid soluble than morphine, metabolized to the active metabolite normeperidine and commonly given by midwives in a dose of 1 mg kg⁻¹ (max. 150 mg) intramuscularly. Intravenous administration gives more predictable blood concentrations compared with the intramuscular route and meperidine had been used in patient-controlled analgesia (PCA) devices. Despite widespread use, its efficacy as an analgesic in labour has been questioned, with several studies demonstrating its inferiority compared with other types of analgesia. Midwives have rated the efficacy of meperidine better than the women receiving it; this may be attributable to misinterpretation of sedation for analgesia.

Meperidine can cause confusion, loss of control and sedation. The active metabolite normeperidine has convulsant properties and may be contraindicated in those with severe pregnancy-induced hypertension. In common with all parenteral opioids, meperidine delays gastric emptying and it has been shown to increase gastric volumes in labour. It also causes dose-dependent respiratory depression and hypventilation. Desaturation has been shown to occur between contractions; this is exacerbated when used together with Entonox. It has no major effects on uterine contractility.

Meperidine is principally bound to a_1-acid glycoprotein but readily crosses the placenta by passive diffusion and achieves equilibrium between the maternal and fetal compartments within 6 min. Its effects on the fetus and neonate are dependent largely on the dose and timing of maternal administration. The highest fetal plasma concentration of meperidine occurs 2–3 h after maternal intramuscular administration. Fetal concentrations are higher than maternal because meperidine is a weak base and more ionized in the acidic environment of the fetal circulation. Thus, meperidine accumulates in the fetal compartment, an effect exaggerated in the acidotic fetus.

Respiratory depression is more likely in the neonate than the mother for a variety of reasons including immature respiratory centres, severe respiratory acidosis, and increased sensitivity to meperidine in the neonate. Respiratory depression is more likely at a gestation of 28 weeks or less. The neonate is 2–3 times more sensitive to meperidine. Neonatal meperidine may limit the type of analgesia available. It has no major effects on uterine contractility.

Key points

Non-regional analgesia remains the most frequently used method during labour. Anaesthetists need to be aware of non-regional analgesia techniques and their limitations when providing information to women. Meperidine remains the most widely available, used, and investigated opioid for labour despite its side-effects and lack of efficacy. Patient-controlled fentanyl (or more recently remifentanil) analgesia may be useful when an epidural is contraindicated; however, mother and baby require careful monitoring during and after delivery. Entonox can be enhanced by the addition of small quantities of volatile agents, e.g. isoflurane.
a greater free drug concentration caused by lower plasma protein concentrations and ion trapping as described above. This can result in low Apgar scores, depressed fetal oxygen saturations and increased carbon dioxide tensions. The neonatal effects of meperidine are compounded by production of normeperidine, which causes sedation and respiratory depression in addition to its convulsant properties. The half-lives of meperidine and normeperidine are 4 and 20 h, respectively, in the parturient but 13 and 62 h in the neonate. The babies of women who have received meperidine in labour have been shown to be sleepier, less attentive, and less able to establish breast feeding, despite normal Apgar scores at birth. The long-term significance of such changes is unclear although one retrospective study suggested that children of mothers who had been given meperidine may be more likely to develop drug addiction problems later in life.3

### Morphine

Morphine is primarily bound to albumin and rapidly crosses the placenta but rapid maternal elimination results in a low fetal drug load. The dose used for maternal analgesia is 2–5 mg i.v. or 5–10 mg intramuscularly. The side-effects of morphine are dose-related and similar to meperidine; its metabolites do not have convulsant effects but morphine-8-glucuronide is an opioid agonist. It has been argued that both meperidine and morphine merely provide sedation rather than analgesia in labour. A small randomized

### Table 1: Complementary methods of pain relief

<table>
<thead>
<tr>
<th>Method</th>
<th>Mechanism of action</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>TENS</td>
<td>Based on ‘gate’ theory</td>
<td>Non-invasive. Easy to use. Good for back pain</td>
<td>Useful only in early labour. Cost implications</td>
<td>Systematic review of eight RCTs failed to demonstrate analgesic effect</td>
</tr>
<tr>
<td>Immersion</td>
<td>Sensation of warm water inhibits pain transmission and supports gravid uterus</td>
<td>Popular. Backed by Government Health Committee</td>
<td>Cannot use with other methods. Limited accessibility. Temporary</td>
<td>Cochrane review of three trials: No difference in pain relief between immersion and non-immersion groups. Systematic review of seven RCTs: mixed results.</td>
</tr>
<tr>
<td>Massage</td>
<td>Inhibits pain transmission. Provides support and distraction</td>
<td>Perceived as highly effective by those using it</td>
<td>Labour intensive</td>
<td>One RCT with 28 women showed physical and emotional benefits</td>
</tr>
<tr>
<td>Acupuncture (Acupressure, laser acupuncture)</td>
<td>Stimulates specific points on body with fine needles (or pressure or laser); may inhibit pain transmission or produce natural endorphins</td>
<td>‘Drug free’</td>
<td>Invasive. Need trained therapist. Can take 30 min for effect</td>
<td>One RCT of 100 women in Sweden comparing acupuncture with no acupuncture suggested former group needed less analgesia, including epidurals Two double-blind RCTs showed reduction in labour pain but other work showed they were not rated by women as effective as other methods Cochrane review of 15 RCTs involving 12 791 women. Those with continuous support, as opposed to conventional care, were less likely to have intrapartum analgesia, operative birth or be dissatisfied with their experiences</td>
</tr>
<tr>
<td>Waterblocks</td>
<td>Injection of 0.1 ml sterile water in four spots over sacrum. Action similar to TENS</td>
<td>Easy to perform. Good for back pain</td>
<td>Temporary relief only (45–90 min). Initial burning sensation</td>
<td>Two double-blind RCTs showed reduction in labour pain but other work showed they were not rated by women as effective as other methods Cochrane review of 15 RCTs involving 12 791 women. Those with continuous support, as opposed to conventional care, were less likely to have intrapartum analgesia, operative birth or be dissatisfied with their experiences</td>
</tr>
<tr>
<td>Continuous support</td>
<td>Presence of a trained support person can improve the physiological and psychological aspects of labour</td>
<td>Popular. Useful at any stage</td>
<td>None</td>
<td>Cochrane review of three RCTs: one reported less anaesthesia and another less narcotic use, but overall meta-analysis showed no difference in the need for pain relief</td>
</tr>
<tr>
<td>Hypnosis</td>
<td>Entering of a hypnotic state to have better control over the pain</td>
<td>Non-invasive</td>
<td>Not all women susceptible (10–20% are not). Time consuming. Can be harmful</td>
<td>One small (n = 22) RCT compared ginger with lemongrass—no difference in pain scores or pharmacological pain relief</td>
</tr>
<tr>
<td>Aromatherapy</td>
<td>Use of essential oils of plants and flowers for therapeutic effect</td>
<td>Non-invasive</td>
<td>Individual sensation of smell, so oils need to be tested</td>
<td>No RCTs</td>
</tr>
<tr>
<td>Homeopathy</td>
<td>A minute amount of a substance can be used to alleviate symptoms (‘like cures like’)</td>
<td>Needs to be individualized</td>
<td></td>
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</tr>
</tbody>
</table>

RCT = randomized controlled trial, TENS = Transcutaneous electrical nerve stimulation.
controlled study showed that neither reduced pain scores but did increase sedation with increasing dosage.4

**Diamorphine**

Diamorphine is used in a some units in the UK; the National Birthday Trust survey of 1990 showed that both midwives and parturients rated it better than either Entonox or meperidine. Its proponents claim that it has a more rapid onset of action compared with morphine and it has been shown to be rapidly eliminated by the placenta. In a randomized double-blind comparison of diamorphine and meperidine, neither drug worked well; almost 50% of women reported poor pain relief and ~40% in each group requested rescue analgesia.5 There were more low Apgar scores at one minute in the meperidine group. However, no other differences in neonatal outcome reached statistical significance.

**Fentanyl**

Fentanyl is a very lipid soluble phenylpiperidine derivative, which is highly protein-bound to albumin. It has an analgesic potency 75–100 times greater than morphine and 800 times that of meperidine. Owing to its high lipid solubility, it has a rapid onset of action but its terminal half-life of ~8 h is longer than that of morphine and meperidine. Its advantages for obstetric use include rapid onset and short duration of action, as well as lack of active metabolites. However, repeated doses will result in drug accumulation in both the parturient and fetus.

**Patient-controlled analgesia**

PCA has the benefit of giving the parturient a degree of control. This in itself is associated with increased satisfaction but women need to be instructed in how to use it effectively. Meperidine was the fist opioid to be administered in this way in 1970. Nowadays, patient-administered opioids are an increasingly popular alternative when regional analgesia is contraindicated.

Fentanyl PCA has been described in two case reports for parturients with thrombocytopenia, and in two randomized controlled trials. Niskala and colleagues6 randomized 20 primiparous women to epidural bupivacaine or fentanyl PCA, using a 50 μg loading dose, 20 μg bolus dose and a 5 min lockout time. Although epidural analgesia was more effective, with three out of ten parturients in the PCA group opting for epidural analgesia, overall satisfaction with analgesia was similar in both groups. There were no differences in Apgar scores, umbilical blood gases, neurobehavioural scores or naloxone requirements. However, low (<90%) oxygen saturations were more common during the initial 12 h after delivery in the fentanyl group neonates, and the authors advised monitoring the neonate post delivery.

Morley-Foster and colleagues compared PCA fentanyl with alfentanil in a randomized, blinded study.7 The fentanyl group was given 50 μg loading dose, followed by a background infusion of 20 μg h⁻¹. Boluses of 20 μg were available with a 5 min lockout time. The alfentanil group received a 500 μg loading dose, 200 μg h⁻¹ background infusion, 200 μg bolus and the same lockout interval. Parturients receiving fentanyl PCA were found to have significantly lower pain scores during the later stages of labour compared with alfentanil PCA parturients. Forty-two per cent of the alfentanil group described analgesia as inadequate, compared with 9% of the fentanyl group. Again, there were no significant differences in neonatal parameters.

Fentanyl PCA can be summarized as follows:

(i) It is not as effective as, but a useful substitute for, regional analgesia.
(ii) The ideal loading dose, bolus dose, lockout time and maximum hourly dose are still unknown.
(iii) Both the parturient and neonate require careful monitoring during and after delivery.
(iv) Absence of active metabolites is an advantage.

Remifentanil is an ultra-short-acting opioid derivative of fentanyl and, uniquely amongst the opioids, is rapidly hydrolysed by red blood cell and tissue esterases. These are non-saturable; thus, remifentanil does not accumulate, even after prolonged infusions. Remifentanil has a terminal half-life of <10 min and a context sensitive half-life, after a 3 h infusion, of ~3 min, compared with 44 min for an equipotent infusion of alfentanil. (Context sensitive half-life is the time for the plasma concentration to fall by 50% after terminating an i.v. infusion.)

To date, there have been four small case series using remifentanil PCA in labour, two larger dose-finding studies and two randomized studies. Initial reports of remifentanil PCA appear promising when used as analgesia in the first stage of labour, in two small series of thrombocytopenic parturients. Adverse maternal and fetal effects were noted when large doses were used, but these responded promptly to a reduction in the bolus dose.

Blair and colleagues carried out a feasibility study in 21 women using increasing bolus doses, with and without a background infusion.8 Nineteen obtained a significant reduction in pain scores with a bolus of 0.25–0.5 μg kg⁻¹ and a 2 min lockout time. No adverse neonatal sequelae were reported, but maternal side-effects occurred when a background infusion was used. Another study by Volmanen and colleagues9 in 20 parturients identified a median effective PCA dose of 0.4 μg kg⁻¹, but overall consumption showed large individual variation. In both studies, desaturation episodes occurred in a proportion of women, and some transient fetal heart rate abnormalities were seen.

Two studies have compared remifentanil with meperidine: Thurlow and colleagues randomized 36 women to PCA remifentanil (20 μg bolus and a 3 min lockout) or intramuscular meperidine 100 mg and a phenothiazine antiemetic.10 Pain scores were lower in the remifentanil group but seven parturients went on to choose regional analgesia compared with three from the meperidine group. However, this study was not blind, and the PCA device itself proved popular, with most of the women appreciating the controllability of this technique.

One double-blind randomized controlled trial by Volikas and colleagues,11 compared PCA remifentanil 0.5 μg kg⁻¹ with a 2 min lockout time with PCA meperidine 10 mg and a 5 min lockout...
time. The trial was terminated early because of poor Apgar scores in the meperidine group. However, of the 17 patients recruited, the nine given remifentanil had significantly lower pain scores at 1 h and after delivery.

Remifentanil PCA can be summarized as follows:

(i) It can provide useful, although not complete, analgesia.
(ii) Bolus doses of 0.25–0.5 μg kg⁻¹ with 2 min lockout times seem to be the most successful PCA regimen to date.
(iii) Close monitoring is required.
(iv) Supplemental oxygen may be required.
(v) The ideal dose is still unclear.
(vi) There is a need for large studies to ascertain adverse fetal and maternal effects.

Other drugs
A variety of other opioids has been used in labour, including some with both agonist/antagonist properties. A summary of the characteristics of these drugs is given in Table 2.

Inhalational methods

Entonox
Nitrous oxide/oxygen mixtures have been used in obstetric practice since 1880. Entonox (50% nitrous oxide in oxygen) was available in 99% of units and used by 60% of parturients in the UK in 1990. Nitrous oxide has a low blood-gas solubility coefficient (0.47) so it equilibrates rapidly with blood. There is minimal accumulation with intermittent use in labour, as it is rapidly washed out of the lungs. Technique of use is important; ~10 breaths or 50 s are required to achieve near-maximum effect. The parturient can be trained to use Entonox effectively by timing maximum effect to peak contraction pain. There are conflicting reports concerning the efficacy of this type of analgesia, from providing no or slight analgesia in 25–48%, to being more efficacious than meperidine or TENS. Other factors apart from effective blood-gas concentration may be involved—the distraction, relaxation and sense of control derived from self-administration may explain why a small randomized controlled trial by Carstoniu and colleagues showed no difference between Entonox and compressed air in early labour.¹²

Adverse effects of Entonox include drowsiness, disorientation and nausea, which results in actual loss of consciousness in 0.4% of cases after prolonged use. Some women may try using it continuously to improve analgesia and hyperventilate, resulting in maternal hypocapnia, alkalosis and vasoconstriction. This reduces uterine blood flow and causes fetal desaturation. When Entonox and meperidine are used, the risk of maternal hyperventilation, diffusion hypoxia and desaturation, is increased. Lastly, there is the theoretical risk of bone marrow suppression through the inhibition of methionine synthase, as nitrous oxide inactivates co-factor B₁₂.

Halogenated agents
Isoflurane has been administered intermittently for labour pain and, although concentrations of 0.75% produced better analgesia than Entonox, this was at the expense of increased maternal sedation. When given continuously for the second stage of labour, in concentrations of 0.2–0.7%, analgesic efficacy and patient satisfaction were no better than for Entonox. In an attempt to improve efficacy, 0.2–0.25% isoflurane added to Entonox was studied by Aurora and colleagues and Wei and colleagues.¹³ ¹⁴ The addition of isoflurane produced superior analgesia than entonox alone, and maternal sedation was not significantly increased.

In the UK, the Health and Safety Executive introduced occupational exposure standards limiting ambient concentration of nitrous oxide and isoflurane to 100 and 50 p.p.m., respectively. Regular monitoring of exposure of health-care workers, and active scavenging in delivery suites may be required for compliance.

Desflurane has a low blood-gas partition coefficient (0.42), allowing rapid onset and offset of action. Concentrations of 0.1–4.5% in oxygen have been used for the second stage of labour and compared with 30–60% nitrous oxide. Both were found to be

| Table 2 Some characteristics of opioid agonists/antagonists used in labour |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Opioid                          | Usual dose      | Onset           | Efficacy         | Other notes     |
| Nalbuphine (Nubain)             | 10–20 mg i.m. every 4–6 h; PCA dose 1–3 mg with 10 min lockout | Within 15 min or 2–3 min i.v | Similar to 100 mg meperidine i.m. | Kappa-mediated sedation. May cause dysphoria but less vomiting |
| Meptazinol (Meptid)             | 100–150 mg i.m. every 2–4 h |                   | 1/10th potency of morphine, similar to meperidine | May cause dysphoric effects in high doses, increased nausea and vomiting compared with meperidine |
| Pentazocine (Talwin)            | 40 mg i.m. every 2–4 h | Within 15–60 min after i.m. | 1/3rd potency of morphine, similar potency to meperidine | May cause dysphoric effect but less nausea compared with meperidine |
| Butorphanol (Stadol)            | 1–2 mg i.m. or i.v. | Within 10 min of i.v. | Five times more potent than morphine, 40 times more potent than meperidine | Ceiling effect of respiratory depression, lack of active metabolites |
| Tramadol (Zydol)                | 50–100 mg i.m. or i.v. |                   | Similar to meperidine and morphine | Fewer maternal side-effects and neonatal respiratory depression |

i.m. = intramuscular.
effective but desflurane resulted in a higher incidence of amnesia (23% vs 0%). In a pilot study by Toscano and colleagues, sevoflurane 2–3% in oxygen and air was given intermittently to 50 parturients, aiming for an end-point of FET (Fraction of end tidal concentration) of 1–1.5. This significantly reduced pain scores when given 1 min before the start of contractions. However, an anaesthetist was required to administer the sevoflurane. The Apgar score was unaffected.

References


See multiple choice questions 5–9.