# Should remifentanil patient-controlled analgesia be a routine choice for pain relief in labour?

Patient-controlled analgesia with remifentanil is usually reserved for patients for whom other forms of pain relief are contraindicated. However, remifentanil patient-controlled analgesia reduces the likelihood of needing an epidural and therefore the risk associated with it, provides good pain relief compared to other options, and the risks can be mitigated with appropriate management.

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## Introduction

Remifentanil is a synthetic rapid onset, short-acting mu opioid receptor agonist. Its half life does not depend on the duration of infusion, making it an ideal agent for use in labour where patient bolus and drug onset of action can be timed to coincide with uterine contractions.

Its use as analgesia in labour has been increasing in Europe and has lead to the formation of a Swiss national RemiPCA SAFE Network (Melber et al, 2019), which provides standard operating procedures for the use of remifentanil patient-controlled analgesia in labour. However, it is rarely used in maternity units in the UK.

This article discusses whether remifentanil patient-controlled analgesia should be a routine option for labour analgesia.

## Remifentanil patient-controlled analgesia should be used for pain relief in labour

Proponents of the routine use of remifentanil patient-controlled analgesia for labour argue that the incumbent risks of epidural analgesia are unacceptable when an effective minimally invasive, easily started and stopped alternative is available. The risks of epidurals include infection (risk of epidural abscess is 1 in 47 000), dural puncture and vertebral canal haematoma (where the risk of causing permanent neurological damage is 1 in 140 000 as per the third national audit project of the Royal College of Anaesthetists (NAP3); Cook et al, 2009).

Pethidine is another synthetic opioid used for labour pain, often before epidural analgesia. A multicentre randomised control trial with 401 women (Wilson et al, 2018) compared remifentanil patient-controlled analgesia vs pethidine for labour analgesia. Women who received intravenous remifentanil patient-controlled analgesia had half the proportion of epidural conversions than those who had intramuscular pethidine. Moreover, pethidine can have adverse effects on neonates, such as respiratory depression, up to 72 hours after birth.

There is a reduction in instrumental and caesarean deliveries with remifentanil patient-controlled analgesia compared to epidural analgesia in labour (Murray et al, 2019).

Freeman et al (2015) conducted a multicentred randomised controlled equivalence trial to compare women's satisfaction with pain relief using remifentanil patient-controlled analgesia or epidural analgesia. Interestingly, more women randomised to remifentanil requested and received analgesia, possibly because they perceived that remifentanil is less invasive and more easily available than an epidural. Furthermore, the time between the request for and initiation of analgesia was shorter in the remifentanil group, probably because an anaesthetist is not required. Also, duration of analgesia with epidural was longer than that with remifentanil, possibly because epidural analgesia slows labour.

## Remifentanil patient-controlled analgesia should not be used for pain relief in labour

Epidurals have been described as the gold standard treatment for labour analgesia (Cambic and Wong, 2010). A Cochrane review (Weibel et al, 2017) showed that pain intensity was

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reported to be higher in remifentanil patient-controlled analgesia groups compared to epidural groups (standardised mean difference 0.57, 95% confidence interval 0.31–0.84). Freeman et al (2015) showed that remifentanil patient-controlled analgesia is not equivalent to epidural analgesia with respect to pain relief, with poorer scores in women treated with remifentanil.

Use of remifentanil patient-controlled analgesia in labour analgesia has potential serious adverse events, both maternal (desaturation, cardiac arrest) and neonatal (respiratory compromise). However, among 5740 patients who received remifentanil, there was no need for maternal ventilation or cardiopulmonary resuscitation (Melber et al, 2019). Serious adverse events were shown to 'increase with doses of 40 mcg remifentanil and above or the concomitant use of long acting opioids' (Melber et al, 2019), highlighting the importance of standard operating procedures.

Neonatal concerns may have been overestimated. Murray et al (2019) reported a safer neonatal profile with remifentanil than with epidural analgesia. Compared to the epidural group, the remifentanil group had fewer neonates requiring positive pressure ventilation (remifentanil vs epidural odds ratio of 0.75–0.96), higher APGAR (appearance, pulse, grimace, activity, respiration) scores, and fewer admissions to neonatal intensive care units (remifentanil vs epidural *P*-value 0.00–0.416).

There are limitations to the use of remifentanil. As it can cause respiratory depression, its use may be limited in patients with conditions which can predispose to maternal hypoxia, such as body mass index >40 kg/m$^2$, airway abnormality, concomitant opioid use, use of magnesium sulphate, or cardiac and respiratory disease. However, remifentanil is safe in appropriately selected patients with mature standard operating procedures in place and appropriately trained staff.

The Obstetric Anaesthetists' Association's (2018) recommended one-to-one midwifery care and the intense training required make remifentanil patient-controlled analgesia a very labour-intensive analgesic option, and the additional costs of the required monitoring, such as continuous saturation monitoring and capnography, make its use expensive compared to other labour analgesia such as entonox or pethidine.

Remifentanil may not be a universal option for maternity patients because of its relatively short duration for therapeutic use, and may only be an option for low-risk multiparous women predicted to have a quick delivery. Melber et al (2016) limited the duration of remifentanil patient-controlled analgesia to 2 hours because of tachyphylaxis, whereas the RemiPCA SAFE Network data show a 3.3-hour median duration of use for nulliparous women and 1.8 hours for multiparous women (Melber et al, 2019). Tachyphylaxis can be mitigated against by having pauses in drug administration or by increasing the dose to have the same effect. Problems may arise when the parturient is in a long labour and starts to require additional analgesic options, such as intramuscular pethidine or an epidural.

## Conclusions

An epidural is still the superior method of pain relief for labour, although it has serious potential complications. Remifentanil patient-controlled analgesia can be used safely, provide satisfactory pain relief and superior analgesia to pethidine and entonox, reducing the number of epidurals, instrumental and caesarean deliveries, and can have no long-term consequences for mother and child, as long as safety standards are applied. Maternal satisfaction with remifentanil patient-controlled analgesia is high, so with increased training for staff, and further trials of its use as a labour patient-controlled analgesia, more women can be given a greater choice of effective analgesia during labour.

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