Remifentanil during labour could halve the number of women needing an epidural

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Half as many women in labour who were given a drug called remifentanil to help manage their pain needed a subsequent epidural, compared to the women given pethidine—the current standard of care, according to an open-label randomised controlled trial of 400 women from 14 maternity units in the UK published in *The Lancet*.

Epidurals—injections of pain relief drugs around the spinal cord—provide effective pain relief but increase the risk of needing instrumental delivery (forceps or vacuum) during birth, which in turn can increase the risk of trauma and long-lasting problems for the mother, such as incontinence and sexual dysfunction.

Pethidine is given to more than a quarter of a million women in labour each year in the UK, and many more worldwide. In the UK and Europe, remifentanil is rarely offered routinely in labour and its use restricted to women who cannot receive an epidural for medical reasons (such as blood clotting disorders). The authors suggest that using remifentanil instead of pethidine could reduce the need for epidurals, instrumental deliveries, and consequent morbidity for large numbers of women worldwide, but recommend more research to understand the effects of low maternal oxygen levels it can cause.

"Previous studies have shown that at least one in three women given pethidine to manage pain during labour require a subsequent epidural as the drug is not always effective. It also has unwanted side effects such as sedation and nausea for the mother, and it may pass into the baby's

bloodstream through the placenta," says lead author Dr. Matthew Wilson, University of Sheffield, UK. "Our findings challenge the routine use of pethidine for pain relief during labour. Remifentanil reduced the need for an epidural by half and there were no lasting problems for the mothers and babies in our trial, although the effect of remifentanil on maternal oxygen levels needs to be clarified in further studies."

The study included 400 women aged over 16 years old who were giving birth after 37 weeks and had requested opioid pain relief. The participants were told about the trial in antenatal visits or when admitted to hospital to have labour induced, and could sign up to take part when they were in active labour.

Half of the women were allocated to receive remifentanil and half were allocated to pethidine. Remifentanil was given as a patient-controlled drip and women could receive 40μg of the drug every two minutes by pressing a hand held device, whereas pethidine was given as an injection of 100mg of the drug into a muscle up to every four hours with a maximum of 400mg in 24 hours. Because of the difference in how the drugs were given, participants and healthcare professionals knew which drug was being used.

All women in the trial received one-to-one care from a midwife, with checks on the mother's breathing rate, sedation, pain ratings and oxygen levels every 30 minutes. The women could request an epidural at any time, and other pain relief was stopped if an epidural was given.

In the remifentanil group 93% (186/201) of women received the drug, and in the pethidine group 77% (154/200) of women received the drug. The main reasons for not receiving the allocated drug were women giving birth before it could be administered (12 women in the remifentanil group and 17 women in the pethidine group) or the mother deciding to immediately request an epidural after randomisation, without

receiving the allocated opioid, which only occurred in the pethidine group (in 22 women).

Half as many women in the remifentanil group went on to have an epidural (19% [39/201]) than in the pethidine group (41% [81/199]) and this remained the same even when the women who did not receive the drug they were meant to were excluded.

On average, women in the remifentanil group rated their pain as less severe than women in the pethidine group.

Women given remifentanil were also less likely to need forceps and vacuum during labour than women given pethidine (15% [31/201] vs 26% [52/199]).

However, remifentanil was associated with twice as many mothers having low oxygen levels than pethidine (14% [26/189] vs 5% [8/154]), and more women in the remifentanil group were given supplementary oxygen. Despite this increase it did not cause any negative effects for the mother or baby, but more research in larger groups will be needed to confirm this.

Breathing problems and sedation in the mother were rare in both groups.

The authors note some limitations, including that the higher number of women in the pethidine group opting for an epidural immediately could be because they had preconceptions about pethidine's effectiveness. Once a women requested an epidural, it would have been unethical to withhold it. However, excluding these episodes from analysis made little difference to the findings so they had no effect on the result.

Women whose labour was induced were more common in the study than in the general population as this provides extra time before labour and

meant they were more easily recruited into the study. However, being induced is very common so the authors believe their findings are still relevant.

Writing in a linked Comment, Professor Peter Kranke, University Hospitals of Wuerzburg, Germany, says: "In returning to the initial question of whether remifentanil is better than pethidine, we can carefully say yes in view of the efficacy data by reducing the epidural progression rate by 50%, with the proviso that the reported effect for this conversion to epidural might have been overestimated by an unknown magnitude, and providing that safety issues are thoroughly addressed. For all those who would want a more precise answer, this finding gives impetus to further studies, particularly with regards to the selection of women with contraindications or those who express the explicit desire not to have an epidural analgesia. In this scenario, at least the prospect of the gold standard cannot bias the treatment effect."

More information: *The Lancet* (2018). www.thelancet.com/journals/lan … (18)31613-1/fulltext

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