International Journal of Obstetric Anesthesia (2015) 24, 117–123
0959-289X/$ - see front matter
http://dx.doi.org/10.1016/j.ijoa.2014.11.006

ORIGINAL ARTICLE

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Patient-controlled intranasal fentanyl analgesia: a pilot study to assess practicality and tolerability during childbirth

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ABSTRACT
Background: Intranasal administration of fentanyl is a non-invasive method of analgesic delivery which has been shown to be effective. This pilot study aimed to assess the practicality and tolerability of patient-controlled intranasal fentanyl for relieving pain during childbirth.
Methods: This prospective, non-randomised, clinical trial recruited women with a singleton pregnancy during November 2009 to October 2011. Exclusion criteria included respiratory disease, gestation <37 weeks and pregnancy complications. The device administered fentanyl 54 μg per spray, incorporating a 3-min lock-out. Data collected included demographics, dose, additional analgesia, adverse events, pain relief and delivery outcomes. Follow-up data were obtained within 48 h regarding tolerability of the device.
Results: The final sample included 32 women: mean age was 28.7 years and gestation 39.8 weeks. Mean fentanyl dose was 734 μg and duration of use was 3.5 h. Most women (78.2%) reported satisfactory to excellent pain relief using the nasal device. Four neonates (12.5%) required bag-mask ventilation at birth: three had adequate respiration within 5 min and one required short-term observation in the special-care nursery. For all items, there was a trend towards an adverse outcome, including neonatal respiratory support, as the dose of fentanyl increased. On follow-up, 84.4% reported they would use intranasal fentanyl for their next childbirth experience.
Conclusions: Patient-controlled intranasal fentanyl provides an acceptable level of analgesia during childbirth. It may, however, increase the risk of neonatal respiratory depression. Future, randomised studies should evaluate the safety and efficacy of patient-controlled intranasal fentanyl compared with existing analgesia options.

Keywords: Analgesia; Childbirth; Fentanyl; Intranasal; Obstetric; Patient-controlled

Introduction

Childbirth may be the most severe pain experience for many women. In Australia, various methods of analgesia are available including pharmacologic (systemic and neuraxial analgesia)[1–3] and non-pharmacologic techniques (e.g. continuous birthing support, aromatherapy, intradermal water injections, hydrotherapy, massage, acupuncture, maternal movement and positioning).[2,4] Systemic analgesia includes inhaled nitrous oxide and parenteral opioids. In Australia, pethidine has been the traditional opioid of choice.[5] Opioid administration is associated with maternal side effects including nausea and vomiting, respiratory depression, and delayed gastric emptying. All opioids cross the placenta, and can result in neonatal side effects including respiratory depression, inhibition of suckling, lower neurobehavioral scores, and delay in effective feeding.[6] Doubt has been cast on the suitability of opioid analgesia for pain relief during childbirth because of the high incidence of maternal and neonatal adverse effects and inadequate analgesia.[2] In addition, there are considerable doubts about the effectiveness of pethidine, including the slow onset of action.[7] A recent Cochrane review identified a lack of research regarding the efficacy of opioid analgesia, the most effective opioid, and strategies to minimize adverse side effects.[8] At best, they found moderate maternal satisfaction with opioid analgesia.

Currently, the options for effective analgesia during childbirth are limited. Prolonged and unrelieved pain may cause patient dissatisfaction and is associated with postpartum depression and post-traumatic stress disorder.[9,10] Neuraxial analgesia provides the most effective pain relief without maternal sedation.[2] Following neuraxial block, women may be restricted to bed and have

Accepted November 2014
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limited mobility for a significant period of time which may impact negatively on maternal satisfaction and delivery. Many women choose not to have neuraxial analgesia; for some women it is contraindicated due to medical reasons, for others it is unsuitable due to a fear of needles, or it may be unavailable because of absence of skilled staff (e.g. an anaesthetist to insert the catheter or midwifery staff trained in the management of epidurals). Neuraxial analgesia is associated with an increased risk of instrumental vaginal delivery, prolongation of the second stage of labour and increased oxytocin requirement.[11] Leeman et al.[12] questioned if the high use of epidural analgesia is really the preference among women in the USA or if it is chosen because there is a lack of acceptable options. They recommended further research investigating women's preferences regarding analgesia during childbirth.

Fentanyl is a synthetic opioid analgesic and may be administered via several routes, most commonly via epidural or intravenous injection, both of which are invasive. Although fentanyl crosses the placenta, serum fentanyl levels in the fetus have been found to be significantly lower than those in the mother. Furthermore, respiratory depression is rare in babies born to mothers receiving fentanyl either parenterally or via an epidural.[13–15]

Maternal satisfaction during birthing has been widely studied. Behaviours that encourage involvement and participation in decision-making during birthing promote feelings of control, coping and feeling supported, facilitating women's assessment of their birth experience as positive.[16] Patient-controlled epidural analgesia has been associated with improved maternal satisfaction and lower volume of local anaesthetic requirement compared with continuous epidural infusion.[17]

Intranasal fentanyl has been proposed as an alternate, fast-acting and non-invasive method of analgesia that is effective in relieving pain for various conditions including acute and chronic pain,[18–21] burns pain,[22,23] postoperative pain,[24–26] and breakthrough cancer pain.[27] Fentanyl administration via an intranasal patient-controlled analgesia (PCA) device has been found to be as effective as intravenous PCA for postoperative analgesia.[26,28] To our knowledge, self-administered intranasal fentanyl has not been reported in the obstetric setting. The administration of patient-controlled intranasal fentanyl (PCINF) may positively affect the birthing experience by virtue of being less invasive and portable, having a short duration of action and being effective in relieving pain during childbirth. This pilot study aimed to assess the practicality and tolerability of PCINF for relieving labour pain.

Methods

This was a prospective, non-randomised, open clinical study registered with the Australian and New Zealand Clinical Trials Registry. Ethics approval was obtained from the Melbourne Health Human Research Ethics Committee. Informed written consent was obtained from all participants in the antenatal period.

Women were recruited from one hospital from November 2009 to October 2011. With over 3500 deliveries per year, it was at the time of the study the third largest obstetric facility in the major metropolitan area. Women who presented to this facility for antenatal care and who fulfilled the study criteria were provided with information about the clinical trial from a midwife during their clinic assessment. To be eligible, women had to be at least 18 years of age and 37 weeks of gestation at the time of presentation and in labour. In addition, they needed to be able to self-administer PCINF and speak and read English. Exclusion criteria included: (1) presence of a pregnancy-related medical condition (e.g. pregnancy induced hypertension, preeclampsia, gestational diabetes); (2) abnormal fetal lie (e.g. breech); (3) placental abnormalities detected during antenatal assessment; (4) non-singleton pregnancy; (5) allergy to opioids; (6) asthma; (7) myasthenia gravis; (8) opioid tolerance (e.g. regular use of methadone, buprenorphine, diamorphine, morphine, oxycodone) and (9) chronic nasal problems (e.g. hay-fever, sinusitis). Eligibility criteria were reassessed by the treating midwife. Women who had previously consented to participate, but when they presented in labour had an exclusion criteria were no longer eligible. Women fulfilling all study criteria were able to request a PCINF device for pain relief. The devices were prepared in advance and available for all women at hospital presentation. Women were informed that they had no obligation to use the PCINF device and that it was available as an analgesic option if, and when, requested.

Fentanyl (300 μg/mL), manufactured and supplied by Orion Laboratories (Balcatta, WA, Australia), was used to fill the Go Medical nasal pump device, purchased from Admedus, Australia (Fig. 1). The single use PCINF devices, as prepared for this study, contained 450 μg of fentanyl (1.5 mL) in total, delivered 54 μg (0.18 mL) per atomised spray thus enabling eight atomised sprays per device. Following demand activation, the device flow control tubing is re-loaded over 3 min. During this refill interval, a partial pro-rata dose can be delivered by pump activation, thus limiting the frequency of full dose administration. At the time of the study, the Western Australian St John Ambulance guidelines recommended a loading dose of 180 μg, followed by 56 μg boluses at 5-min intervals. We proposed 54 μg at 3-min intervals with no loading dose, in lieu of the severity of pain and requirement for more frequent doses, in comparison to patients receiving care in an ambulance for a short time period.

Several safety precautions were exercised including frequent vital sign assessment, restricted volume in a single device and a limit of four devices per participant. To