



ELSEVIER

Contents lists available at ScienceDirect

Midwifery

journal homepage: www.elsevier.com/midw

Subcutaneous administration of fentanyl in childbirth: An observational study on the clinical effectiveness of fentanyl for mother and neonate

Julie Fleet, BA App Sc (Dev Dis), Grad cert (Rehab), BMid (Hons), RM (PhD candidate)*, Meril Jones, RN, BSc (Hons) PhD (Senior Lecturer), Ingrid Belan, BSc, PhD (Senior Lecturer)

School of Nursing & Midwifery, Flinders University, GPO Box 2100, Adelaide, South Australia, Australia

ARTICLE INFO

Article history:

Received 21 February 2012

Received in revised form

19 January 2013

Accepted 22 January 2013

Keywords:

Fentanyl

Pain relief

Labour

Subcutaneous

ABSTRACT

Objective: to explore the maternal and neonatal effects of fentanyl administered subcutaneously to women during labour.

Design: two methods were used: (1) A retrospective audit of the birth register and maternal and neonatal records for the period from January 2000 to December 2007. (2) A pilot study was also conducted on a convenience sample of women between July 2008 and October 2008.

Setting: this study was conducted within a maternity unit at a rural South Australian hospital where approximately 350 babies are birthed each year.

Participants: audit participants included women who had uncomplicated pregnancies and birthed at term (37–42 weeks gestation). Women in the experimental group consisted of those who had utilised only subcutaneous fentanyl for pain relief ($n=75$), or nitrous oxide and oxygen prior to being administered subcutaneous fentanyl ($n=196$). Stratified random selection based on parity and age was used to determine the control group, which consisted of women who used no pharmacological pain relief ($n=196$).

The pilot study involved a convenience sample of women ($n=10$) assessed to have an uncomplicated pregnancy and labour occurring at term (≥ 37 weeks gestation).

Measurements: audit variables examined included the women's age, parity, labour duration, mode of birth (spontaneous or assisted), analgesia used, total dosage, time administered prior to birth, time of birth, neonatal Apgar scores, time to establish breathing, naloxone use, days spent in hospital post-birth and breast-feeding outcomes upon discharge.

The pilot study explored maternal effects assessed pre- and 30 minutes post-administration of subcutaneously administered fentanyl by observing pain scores, vital signs, sedation levels, nausea/vomiting scores and anti-emetic use. To assess possible adverse effects in the neonate Apgar scores, time to establish respiration, naloxone use, transfer to neonatal nursery and breast-feeding outcomes upon discharge were recorded.

Findings: women in the experimental groups were more likely to be induced, experienced a longer duration of labour and had an increased likelihood of an assisted vaginal birth. The average total dose of fentanyl administered was 250 μg . Neonatal outcomes were comparable between groups when examining Apgar scores < 7 at 1 and 5 minutes and time to establish breathing. There was, however, a significant difference with naloxone administration between the groups. There was no significant difference between groups in hospital stay or breast-feeding on discharge.

The pilot study identified a clinically significant reduction in pain scores for 78% of women following the administration of subcutaneous fentanyl, with the average pain score decreasing from 8.4 (± 1.4) to 7.2 (± 1.1) (paired t -test, $p=0.017$). Vital signs were not affected, no anti-emetics were required and all women remained alert with no sedation noted.

Key conclusions: the audit identified fentanyl use was associated with a longer length of labour, but this may be explained by more women in the experimental groups requiring induction of labour than those in the control group. However, length of hospital stay, breast-feeding rates and neonatal outcomes were comparable amongst the three groups.

Results of the pilot study are consistent with those of the audit in relation to the effects on mother and neonate. In addition, the pilot study begins to provide evidence that fentanyl is efficacious in providing pain relief.

* Corresponding author

E-mail address: julie-anne.fleet@flinders.edu.au (J. Fleet).

Implications for practice: results of this study are the first to explore the effects of fentanyl administered subcutaneously to women during labour. This method of analgesia offers women an additional choice of pain relief during childbirth and may be particularly beneficial in remote and rural settings where resources are often limited and access to specialist services difficult. Further research, however, is required to be able to generalise the outcomes and provide further data to support the clinical effectiveness of this route of administration of fentanyl.

© 2013 Elsevier Ltd. All rights reserved.

Introduction

Although the majority of women in labour choose to use pharmacological pain relief there has been an ongoing debate about efficacy and the clinical effectiveness of each method (Jones et al., 2012). Although epidural analgesia is known to provide effective pain relief, epidurals are associated with adverse effects (Jones et al., 2012), maybe contraindicated or provide inadequate pain relief (Agaram et al., 2009). In addition, not all facilities have access to 24 hour anaesthetic services. In these situations women may be offered an opioid to manage the pain of labour. Recent statistics showed that 19.1% of South Australian (SA) women received a parenterally administered opioid in labour (Chan et al., 2011).

Pethidine remains the most widely used parenterally administered opioid for the relief of labour pain (Bricker and Lavender, 2002; McCool et al., 2004; Althaus and Wax, 2005; Sosa et al., 2006; Douma et al., 2010). However, when multiple doses are administered there are increased risks to the neonate (Kuhnert et al., 1985). This, in part, relates to the active metabolite norpethidine which is only partially antagonised by naloxone. These adverse effects are problematic in rural areas when access to anaesthetic and neonatal services is limited. One alternative to pethidine may be the use of fentanyl. In a study comparing intravenous (IV) fentanyl with IV pethidine for analgesia in labour, it was concluded that fentanyl was preferable, because it was associated with fewer maternal and immediate neonatal adverse effects (Rayburn et al., 1989b). Fentanyl metabolism does not result in the formation of an active metabolite and the terminal elimination half-life in the neonate is 5.3 hours (Koehtop et al., 1986), compared with pethidine's metabolite, norpethidine, which has a half-life of approximately 60 hours (Kuhnert et al., 1985).

Fentanyl administered via intermittent subcutaneous injection, in settings such as palliative, paediatric, and post-operative care, have been reported to provide effective pain relief with few adverse effects (Hunt, 1999; Dietrich and Tobias, 2003; Capper et al., 2010). Over the past 15 years, in an attempt to improve birth outcomes and reduce the number of resources required, several rural South Australian (SA) hospitals have been administering fentanyl via the subcutaneous route when women request pain relief during childbirth. The clinical effectiveness of this method of analgesia during labour, however, has not been examined (Fleet et al., 2011).

The aim of this study was to investigate the practice of administering fentanyl subcutaneously by conducting a retrospective audit of maternal and neonatal records. As data regarding the efficacy of subcutaneously administered fentanyl for pain relief during childbirth was not available in the medical records, a pilot study that examined efficacy and explored possible maternal and neonatal adverse effects was conducted.

Methods

There are two components to this study: a retrospective audit and a pilot study.

Design

1. *Audit:* A non-experimental retrospective audit of medical records conducted during the period from January 2000 to December 2007.
2. *Pilot study:* A non-experimental pilot study was conducted on a convenience sample of women between July 2008 and October 2008.

Setting

This study was conducted in a maternity unit within a SA rural hospital where approximately 350 babies are born each year. Maternity care was provided by four obstetrically trained general practitioners, an obstetric consultant, midwives and physiotherapists.

Ethics

Ethics approval was granted by the Flinders University Social and Behavioural Research Ethics Committee (SBREC) and by the SA rural hospital's Neonatal and Maternal Committee.

Participants

Audit

The participants for the experimental groups were selected from a total of 418 women who had been administered subcutaneous fentanyl for pain relief during childbirth from the dates January 2000 until December 2007. All women birthing in this rural hospital were considered low risk and birthed at term (37–42 week gestation). Women who used fentanyl, in addition to nitrous oxide and oxygen (N_2O+O_2) and/or epidural and/or spinal or pethidine ($n=147$), were excluded from analysis due to confounding factors. This included women who had been administered fentanyl subcutaneously due to ineffective epidural block or while awaiting preparation for theatre. The remaining 271 women were evaluated as follows: a fentanyl only group ($n=75$), who utilised only subcutaneously administered fentanyl for pain relief and a second group of women who utilised N_2O+O_2 prior to the subcutaneous administration of fentanyl ($n=196$). Data for the two subgroups were then compared to a control sample of 196 women who also birthed within this same rural SA hospital during this period, but had not used pharmacological pain relief during labour.

As 657 women met the criteria for the control group, a stratified random selection based on parity and age was used to determine these participants. As more women who birthed without using pharmacological pain relief were of multiparity, the control sample size ($n=196$) was used to match the larger experimental group and enabled the ratio between primiparity and multiparity to be similar between both experimental groups.

The sample size required for the study was estimated for an ANOVA design involving three groups (control and two subgroups) using the software programme G Power 3.1. A total

sample size of 206 was considered appropriate to provide sufficient power ($\beta=0.9$) with a confidence level of 95% and a 5% margin of error.

Pilot study

During the period of data collection, 12 women utilised subcutaneously administered fentanyl in labour; however, only 10 consented to their observations being included in this study.

Audit variables

Data collected included age, parity, length of labour, mode of birth, (spontaneous, assisted or caesarean section), use of pharmacological analgesia during childbirth and days spent in hospital post-birth. Variables relating to neonatal outcomes also were reviewed, including the time of birth, when fentanyl was last administered prior to birth, the birth outcome (assessed using 1 and 5 minutes Apgar scores), time taken for the baby to establish breathing and whether naloxone was administered. As well, length of hospital stay and breast-feeding outcomes upon discharge were recorded. While it would have been beneficial to examine the efficacy of fentanyl when administered subcutaneously for pain relief during childbirth these data were not available in the medical records. Efficacy and adverse effects, therefore, were examined in a pilot study at the same hospital.

Pilot study measurements

An observation chart was utilised to record maternal pain scores, sedation levels, vomit scores and vital signs including blood pressure (measured as mean arterial pressure), pulse, temperature and respiration rate. Observations were recorded prior to administration of subcutaneous fentanyl and then again half an hour after administration. The Verbal Analogue Scale (VAS) (0–10) also was used during each observation period to enable the woman to self-report their subjective pain score.

Neonatal Apgar scores at 1 and 5 minutes, time to establish breathing, transfer to neonatal nursery, naloxone use and breast-feeding outcomes upon discharge were examined to review neonatal effects.

Hospital standing order and protocol for administration of subcutaneous fentanyl

Fentanyl was administered subcutaneously through a 24 mm IV cannula inserted in the subclavicular or upper pectoral region. Local anaesthetic (1 ml of 1% lignocaine) was administered 1 minute before a loading dose of 200 μg of fentanyl. One hour after administering the loading dose a further 50 μg of fentanyl could be administered every 15 minutes as required, up to 350 μg in a two hour period. The standing order then required a discussion with the medical officer/obstetrician prior to further administration of doses.

Statistical analyses

Audit data were analysed to examine differences in birth outcomes of each group utilising the software package SPSS v 18. Descriptive statistics were used to determine whether the physiological parameters measured for the mother and baby were within the normal range. Chi-square analyses were used for categorical data and ANOVAs were conducted for interval data. Where significant differences were found post-hoc tests were performed (Pearson Chi-square and Tukey HSD). Data are reported as mean (\pm SD), frequency or percentage.

Pilot study data also were analysed utilising the software package SPSS v 18. All statistical analyses were carried out using paired *t*-test unless otherwise indicated. Data are reported as mean (\pm SD), frequency or percentage.

Findings

Audit

Over the eight year study period women who utilised subcutaneously administered fentanyl during childbirth represented 15% of the women who laboured within this rural SA hospital. The demographic characteristics of these women were examined, in particular age, parity, onset of labour and mode of birth. As seen in [Table 1](#), age and parity were comparable between groups, however, significant differences were found amongst groups for onset of labour and mode of birth. Post-hoc tests indicated that there were no significant differences between the two experimental groups when examining either onset of labour ($p=0.838$) or mode of birth ($p=0.331$), but that there were significant differences between the control group and both experimental groups for onset of labour and mode of birth ($p < 0.001$ in all cases) ([Table 1](#)).

The duration of labour also varied significantly between the groups with the control group having a shorter duration of labour than either of the fentanyl groups which did not differ ([Table 1](#)) (Tukey HSD fentanyl only versus control $p=0.007$, and fentanyl + $\text{N}_2\text{O} + \text{O}_2$ $p=0.001$).

Fentanyl dosage was examined between the two study groups, and it was found that the average dose administered was similar in both groups ([Table 2](#)). The standard initial dose of fentanyl (200 μg) was administered to 261 women, with a further 10 women administered a lower initial dose ranging from 50 to 150 μg (practitioners within this setting may prescribe a lower initial dose if birth was believed to be imminent). Cumulative dosages ranged from 50–650 μg . These cumulative doses reflect the number of times women received the drug. There was no consistent time at which fentanyl was last administered before birth, with times ranging from 11 minutes to 10.3 hours.

Apgar scores < 7 , at 1 and 5 minutes resulted in no significant difference between the groups. In addition, there was no significant difference between groups when examining time for neonates to establish breathing ([Table 3](#)).

Of the 271 neonates born to women receiving subcutaneously administered fentanyl during childbirth, 8.1% of neonates ($n=22$) received naloxone. For babies administered naloxone maternal fentanyl dose ranged from 50 to 500 μg and time administered prior to birth was 20–353 minutes. The majority of neonates ($n=17$) administered naloxone established breathing within 1 minute. A further three neonates established breathing within 2 minutes whereas the remaining two established breathing 3 and 5 minutes post-birth.

When length of hospital stay ([Table 1](#)) and breast-feeding outcomes ([Table 3](#)) on discharge were examined no clinically significant differences were found among groups. In all groups the majority of women ($\geq 96\%$) were breast-feeding their neonates at discharge ([Table 3](#)).

Pilot study

The participants' average age was 27 years (± 4.9) with 60% of these women being primigravida. Numerical pain scores were recorded for nine of the ten women who received subcutaneous fentanyl in labour; one woman birthed within 25 minutes of her first dose of fentanyl prior to the post-pain score being recorded.

Table 1

Maternal characteristics, birth details and hospital stay.

	Fentanyl only (N=75)*	Fentanyl+N ₂ O+O ₂ (N=196)	Control (N=196)†	p
Age (year)	27.6 (± 4.7)	28.9 (± 5.5)	29.1 (± 5.1)	0.176
Primiparity (%)	38.7	42.3	42.3	0.839
Multiparity (%)	61.3	57.7	57.7	
Spontaneous onset of labour (%)	70.7	69.4	82.7	0.006
Induction of labour (%)	29.3	30.6	17.3	
Total labour duration(minute)	449.7 (± 204)	486.8 (± 275)	353.8 (± 237)	0.001
Primip labour duration(minute)	563.3 (± 234)	603.2 (± 292)	461.4 (± 261)	0.001
Multiple labour duration(minute)	378.0 (± 145)	401.3 (± 227)	274.8 (± 181)	
Spontaneous birth (%)	82.7	87.2	94.9	0.004
Assisted birth (%)	17.3	12.8	5.1	
Days in hospital post-birth	3.1 (± 1.2)	3.2 (± 1.1)	3.1 (± 1.1)	0.634

Data are mean (± SD) or proportion (%).

* Days in hospital post-birth (n=74).

† Days in hospital post-birth (n=192).

Table 2

Dosage of subcutaneous fentanyl received.

Study group	N	Total dose (µg) mean(± SD)	Dosage range (µg)	Time of last dose to birth (hour ± SD)	Time of last dose to birth range
Fentanyl only	75	251 (± 81)	150–650	2.1 (± 1.5)	18 minutes–8.5 hours
Fentanyl+N ₂ O+O ₂	196	255 (± 84)	50–550	1.8 (± 1.8)	11 minutes–10.3 hours

Data are means (± SD).

Table 3

Neonatal characteristics.

	Fentanyl only (N=75)*	Fentanyl+N ₂ O+O ₂ (N=196)†	Control (N=196)‡	p
Apgar score at 1 minute	7.7 (± 1.4)	7.6 (± 1.4)	8.0 (± 1.2)	0.534
Apgar score at 5 minutes	9.0 (± 0.8)	9.0 (± 0.7)	9.1 (± 0.7)	0.063
Apgar < 7 at 1 minutes	16.0	18.3	11.2	0.136
Apgar < 7 at 5 minutes	1.3	0.5	1.0	0.764
Time to establish breathing (minute)	1.1 (± 0.6)	1.1 (± 0.4)	1.0 (± 0.2)	0.102
Naloxone administration (%)	13.3	6.1	0.0	0.001
Breast-feeding on discharge (%)	98.6	95.9	96.4	0.848

Data are mean (± SD) or proportion (%).

* Breast-feeding on discharge (n=74).

† Breast-feeding on discharge (n=195).

‡ Breast-feeding on discharge (n=194).

It was found that subcutaneously administered fentanyl provided a significant reduction in pain scores for 78% of women with the average pre-dose pain score of 8.4 (± 1.4) decreasing to 7.2 (± 1.1) post-fentanyl administration ($p=0.02$, CI 0.72) (Fig. 1) (Table 4).

In addition to exploring pain scores, other indicators of efficacy were recorded to determine the effects fentanyl administered subcutaneously may have on maternal vital signs. Results from this small sample identified subcutaneously administered fentanyl did not affect the woman's vital signs of respiration rate, body temperature, blood pressure or pulse rate. Statistical analysis of these vital signs showed no differences between measurements pre- and post-administration of fentanyl (Table 4).

There were two incidents of nausea and vomiting recorded pre-administration of subcutaneous fentanyl and only one incident observed post-administration of subcutaneously administered fentanyl. No anti-emetics were required and all women remained awake and alert with no sedation noted within the study group.

Neonatal respiratory depression was not recorded with all neonates establishing breathing in ≤ 2 minutes. One neonate had an Apgar score < 7 at 1 minute and all neonates had an Apgar

score > 7 at 5 minutes. No neonate required naloxone administration or retrieval to a nursery and all babies were breast-feeding upon discharge.

Discussion

Women are limited in options of pain relief in labour, particularly those who birth within settings where anaesthetists are not readily available to provide specialised analgesia. Therefore, there is a need for further investigation into alternative methods of pain relief that are both safe and effective. The aim of this study was to assess the effect of subcutaneously administered fentanyl for pain relief during childbirth and explore possible maternal and neonatal adverse effects.

All women studied were assessed as low risk and birthed at term. Women who utilised fentanyl were more likely to be induced and experienced a longer duration of labour than the control group. Although all women in the audit birthed vaginally, women who used fentanyl were more likely to require an assisted birth. However, Apgar scores < 7 at 1 and 5 minutes, time to establish breathing and breast-feeding outcomes did not differ

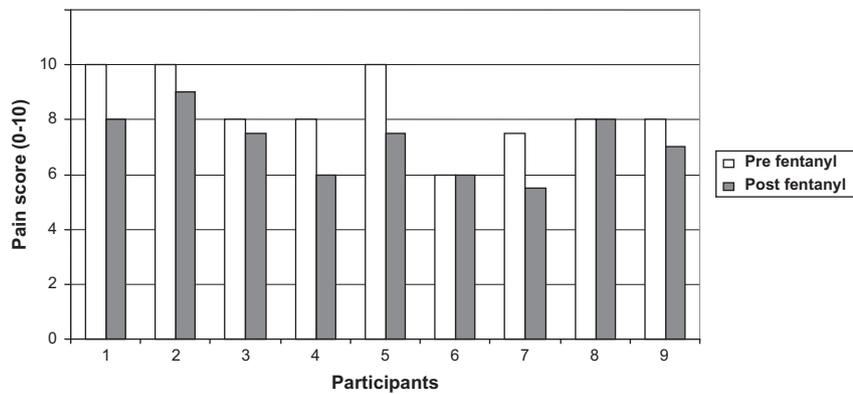


Fig. 1. Numerical pain scores pre- and post-administration of subcutaneous fentanyl in a convenience sample of women in labour.

Table 4

Maternal observations pre- and post-subcutaneously administered fentanyl.

Vital signs	N	Pre-fentanyl (\pm SD)	Post-fentanyl (\pm SD)	p
Body temperature ($^{\circ}$ C)	5	36.5 (\pm 0.6)	36.5 (\pm 0.3)	1.00
Pulse (bpm)	9	82.3 (\pm 12.9)	80.0 (\pm 13.7)	0.24
Respiratory rate (Resp/minute)	8	19.6 (\pm 2.1)	18.5 (\pm 0.9)	0.41
Mean arterial pressure	9	91.0 (\pm 10.4)	94.0 (\pm 9.9)	0.36
Pain score	9	8.4 (\pm 1.4)	7.2 (\pm 1.1)	0.02

Data are mean (\pm SD).

significantly between neonates whose mothers received fentanyl and the control group. In relation to the efficacy of fentanyl, the small pilot study suggested that the majority of women experienced a clinically significant reduction in pain scores.

Although the results of the pilot study need to be interpreted with caution due to the limited sample size, they are consistent with the outcomes of the audit. Overall the findings provide preliminary evidence that suggest fentanyl administered subcutaneously during labour has few adverse, if any, effects on the neonate, but further research is required to determine the clinical effectiveness of this method in the mother.

This study is the first to provide data relating to fentanyl dosage when administered subcutaneously to women during labour. Interestingly, women on average only required approximately 250 μ g of fentanyl, which is significantly less than dosages previously reported in the majority of studies examining fentanyl via IV patient controlled analgesia (PCA) in childbirth (400–1025 μ g) (Kleiman et al., 1991; Rosaeg et al., 1992; Atkinson et al., 1994; Morley-Forster et al., 2000; Nikkola et al., 2000; Castro et al., 2003; Douma et al., 2010). There is limited data available relating to the pharmacokinetics of subcutaneously administered fentanyl, Capper et al. (2010) studied a single 200 μ g bolus dose of subcutaneously administered fentanyl to healthy male volunteers. Their results identified that the median maximum concentration of fentanyl was reached at a median time of 15 minutes (range 10–30 minutes) and the mean terminal half-life was 10 hours (range 5.48–16.37 hours). These results suggest a slower uptake and elimination of fentanyl when administered via the subcutaneous route compared with the IV route (range 1.5–6 hours) (Mather, 1983). This could explain the reduction in the total fentanyl dose required in the present study.

In the audit, labour duration and parity was examined as it is recognised that primigravida women are more likely to have longer labours than multigravida women (Albers et al., 1996). The results of this study are consistent with this observation. In determining the effects of an opioid, it is also important to

understand whether it has an effect on the labour process, such as on uterine tone and subsequent labour duration. In studies reviewing placental passage and uterine effects of IV fentanyl, no significant changes to uterine blood flow or tone were reported (Craft et al., 1983; Atkinson et al., 1994). In our audit, length of labour was significantly longer for the fentanyl groups than the control group even when parity was taken into consideration. Likewise, mode of birth was also significantly different between groups with the fentanyl groups resulting in more assisted births.

A limitation of the audit was that both experimental groups had a significantly larger proportion of women requiring an induction of labour (IOL) (Table 1). Kelly et al. (2009) conducted a systematic review and reported IOL resulted in a risk of uterine hyper-stimulation, increased need for analgesia and a higher incidence of assisted vaginal births. The results from this review may account for the observations that more women in the experimental groups were induced, required pharmacological pain relief, and had an increased need for an assisted birth (Table 1).

Despite the above result, there were no statistical differences between the experimental and control groups in neonatal outcomes when comparing Apgar scores $<$ 7 at 1 and 5 minutes. Respiratory depression was rarely seen in neonates associated with fentanyl use, with 98% of neonates establishing breathing \leq 2 minutes. However, 8.1% of neonates were administered naloxone despite the majority of these neonates establishing breathing within 1 minute (Table 3). The high incidence of naloxone use may reflect the individual practice of the rural setting rather than provide a true measure for respiratory depression given that the onset of action for IM administration of naloxone is 2–5 minutes in (Lehne, 2010). No neonates in the fentanyl groups suffered prolonged respiratory depression $>$ 5 minutes. These results are consistent with a similar study that compared IV fentanyl to a control group using no pain relief, as no difference was seen in neonatal outcomes including, respiratory depression, Apgar scores and neurological and adaptive capacities at 2 and 24 hours (Rayburn et al., 1989a).

Opioid analgesia, in particular, pethidine has also been associated with adverse neonatal effects including drowsiness and irritability which impacts on the commencement of breast feeding at birth (Ransjo-Arvidson et al., 2001). However, few studies have explored neonatal effects past the newborn period. In a review by Jones et al. (2012), only two out of 57 trials of opioids even reported breast feeding as an outcome. The audit and the pilot study both showed that, breast-feeding outcomes upon discharge were not significantly different between either fentanyl groups or the control.

When reviewing efficacy it should be noted that not all women want to be pain free. Instead, as one study identified, women

want to be able to cope with the pain of labour (Ross, 1998) and even severe pain is not always reported as having negative effects (Rowlands and Permezel, 1998). Several studies have examined the clinical significance of reported changes to pain severity measured using the VAS (Todd et al., 1996; Kelly, 1998; Gallagher et al., 2001; Powell et al., 2001). These studies report that a score change in pain severity between 0.9 cm and 1.3 cm is clinically important. Therefore, an average score reduction of 1.2 in the pilot study suggests that subcutaneously administered fentanyl provided a significant decrease in pain scores for the majority of women. In addition, findings of the pilot study are consistent with studies that have examined the analgesic effects of IV administered fentanyl when administered during childbirth (Rayburn et al., 1989a, 1989b; Atkinson et al., 1994; Nikkola et al., 1997; Douma et al., 2010).

In the few studies that have compared the effects of fentanyl with pethidine, fentanyl was identified to produce fewer adverse effects. For example, Douma et al. (2010) conducted a randomised control trial (RCT) that examined efficacy when pethidine, remifentanyl, and fentanyl were administered via patient-controlled analgesia (PCA) to women in labour. Interestingly, there was no significant difference in the proportion of women who crossed over to an epidural in the remifentanyl and fentanyl groups (13% and 15%, respectively). In contrast, 34% of the pethidine group crossed over to epidural analgesia. Furthermore, 85% of women utilising PCA fentanyl resulted in a spontaneous vaginal birth whereas only 69% of the pethidine group and 62% of the remifentanyl group achieved a spontaneous vaginal birth (Douma et al., 2010).

Findings of this pilot study demonstrated that fentanyl was well tolerated by the participants with few adverse effects recorded. Although two women reported nausea and vomiting prior to administration of subcutaneous fentanyl there was only a single report of nausea and vomiting post-administration of fentanyl; no anti-emetic treatment was required. Although this study did not provide a comparative group that either used no analgesia or an alternative opioid, findings from RCTs that compared IV fentanyl with IV pethidine for analgesia in labour, concluded that fentanyl was preferable, because it was associated with fewer maternal and immediate neonatal side effects (Rayburn et al., 1989b; Douma et al., 2010). In the systematic review conducted by Jones et al. (2012), they reported that more women who received pethidine, experienced adverse effects such as, drowsiness and nausea when compared to women who received other opioids.

Our study is the first to examine maternal and neonatal outcomes when fentanyl was administered subcutaneously to women in childbirth. Further, the results of the study begin to provide evidence for an alternative option for pain relief in labour. This method of administration is particularly beneficial for remote and rural settings where resources are often limited and access to specialist services problematic.

Although this study provides useful data relating to the use of subcutaneously administered fentanyl for women during labour, it is noted that there are a number of limitations to such a design. Therefore, a multicentred randomised control trial [ACTRN12609001027202] is currently being conducted to address these limitations.

Acknowledgements

The authors would like to acknowledge the dedicated practitioners working within remote and rural areas who undertake innovative practices to enable women more choice, especially when specialist services are limited. In particular to the doctors,

midwives and allied health staff working throughout Country Health SA.

References

- Agaram, R., Douglas, M.J., McTaggart, R.A., et al., 2009. Inadequate pain relief with labour epidurals: a multivariate analysis of associated factors. *International Journal of Obstetric Anesthesia* 18, 10–14.
- Albers, L., Schiff, M., Gorwoda, J., 1996. The length of active labor in normal pregnancies. *Obstetrics and Gynecology* 87, 355–359.
- Althaus, J., Wax, J., 2005. Analgesia and anesthesia in labour. *Obstetrics and Gynecology Clinics of North America* 32, 231–244.
- Atkinson, B.D., Truitt, L.J., Rayburn, W.F., et al., 1994. Double-blind comparison of intravenous butorphanol (Stadol) and fentanyl (Sublimaze) for analgesia during labor. *American Journal of Obstetrics and Gynecology* 171, 993–998.
- Bricker, L., Lavender, T., 2002. Parenteral opioids for labor pain relief: a systematic review. *American Journal of Obstetrics and Gynecology* 186, S94–S109.
- Capper, S.J., Loo, S., Geue, J.P., et al., 2010. Pharmacokinetics of fentanyl after subcutaneous administration in volunteers. *European Journal of Anaesthesiology* 27, 241–246.
- Castro, C., Tharmaratnam, U., Brockhurst, N., et al., 2003. Patient-controlled analgesia with fentanyl provides effective analgesia for second trimester labour: a randomized controlled study. *Obstetrical and Pediatric Anesthesia* 50, 1039–1046.
- Chan, A., Scheil, W., Scott, J., et al., 2011. Pregnancy Outcome in South Australia 2009. *Pregnancy Outcome Unit, SA Health, Government of South Australia, Adelaide*.
- Craft, J.B., Coaldrake, L.A., Bolan, J.C., et al., 1983. Placenta passage and uterine effects of fentanyl. *Journal of Anesthesia and Analgesia* 63, 894–898.
- Dietrich, C.C., Tobias, J.D., 2003. Pediatric pain: case reports subcutaneous fentanyl infusions in the pediatric population. *American Journal of Pain Management* 13, 146–150.
- Douma, M.R., Verwey, R.A., Kam-Endtz, C.E., et al., 2010. Obstetric analgesia: a comparison of patient-controlled meperidine, remifentanyl, and fentanyl in labour. *British Journal of Anaesthesia* 104, 209–215.
- Fleet, J., Jones, M., Belan, L., 2011. Non-axial administration of fentanyl in childbirth: a review of the efficacy and safety of fentanyl for mother and neonate. *Midwifery* 27, e106–e113.
- Gallagher, J.E., Liebman, M., Bijur, P.E., 2001. Prospective validation of clinically important changes in pain severity measured on a visual analog scale. *Annals of Emergency Medicine* 38, 633–638.
- Jones, L., Othman, M., Dowswell, T., et al., 2012. Pain management for women in labour: an overview of systematic reviews. *Cochrane Database Systematic Reviews* 3, CD009234.
- Hunt, R., 1999. A comparison of subcutaneous morphine and fentanyl in hospice. *Journal of Pain and Symptom Management* 18, 111–119.
- Kelly, A.J., Malik, S., Smith, L., et al., 2009. Vaginal prostaglandin (PGE2 and PGF2a) for induction of labour at term. *Cochrane Database of Systematic Reviews*, <http://dx.doi.org/10.1002/14651858.CD003101.pub2>, Issue 4. Art. No.: CD003101.
- Kelly, A.-M., 1998. Does the clinically significant difference in visual analog scale pain scores vary with gender, age, or cause of pain? *Academic Emergency Medicine* 5, 1086–1090.
- Koehntop, D., Rodman, J., Brundage, D., et al., 1986. Pharmacokinetics of fentanyl in neonates. *Journal of Anesthesia and Analgesia* 65, 227–232.
- Kleiman, S.J., Wiesel, S., Tessler, M.J., 1991. Clinical report patient-controlled analgesia (PCA) using fentanyl in a parturient with platelet function abnormality. *Canadian Journal of Anaesthesia* 38, 489–491.
- Kuhnert, B.R., Kuhnert, P.M., Phillipson, E.H., et al., 1985. Disposition of meperidine and normeperidine following multiple doses during labor. *American Journal of Obstetrics and Gynecology* 151, 410–415.
- Lehne, R.A., 2010. *Pharmacology for Nursing Care*, 7th edn. Saunders Elsevier, Missouri, USA.
- Mather, L.E., 1983. Clinical pharmacokinetics of fentanyl and its newer derivatives. *Clinical Pharmacokinetics* 8, 422–446.
- McCool, W.F., Packman, J., Zwerling, A., 2004. Obstetric anaesthesia: changes and choices. *Journal of Midwifery & Women's Health* 49, 505–513.
- Morley-Forster, P.K., Reid, D.W., Vandenberghe, H., 2000. A comparison of patient-controlled analgesia fentanyl and alfentanil for labour analgesia. *Canadian Journal of Anaesthesia* 47, 113–119.
- Nikkola, E., Ekblad, U., Kero, et al., 1997. Intravenous fentanyl PCA during labour. *Canadian Journal of Anaesthesia* 44, 1248–1255.
- Nikkola, E., Jahnukainen, T.J., Ekblad, U.U., et al., 2000. Neonatal monitoring after maternal fentanyl analgesia in labour. *Journal of Clinical Monitoring and Computing* 16, 597–608.
- Powell, C.V., Kelly, A., Williams, A., 2001. Determining the minimum clinically significant difference in visual analog pain scores for children. *Annals of Emergency Medicine* 37, 28–31.
- Ransjo-Arvidson, A.B., Matthiesen, A., Lilja, G., et al., 2001. Maternal analgesia during labor disturbs newborn behavior: effects on breastfeeding, temperature, and crying. *Birth* 28, 5–12.
- Rayburn, W.F., Rathke, A., Leuschen, M.P., et al., 1989a. Fentanyl citrate analgesia during labour. *American Journal of Obstetrics and Gynecology* 161, 202–206.

- Rayburn, W.F., Smith, C.V., Parriott, J.E., et al., 1989b. Randomized comparison of meperidine and fentanyl during labor. *Journal of Obstetrics and Gynecology* 74, 604–606.
- Rosaeg, O.P., Kitts, J.B., Koren, G., et al., 1992. Clinical reports maternal and fetal effects of intravenous patient-controlled fentanyl analgesia during labour in a thrombocytopenic parturient. *Canadian Journal of Anaesthesia* 39, 277–281.
- Ross, R., 1998. Maternal satisfaction with labour analgesia. *Bailliere's Clinical Obstetrics and Gynaecology* 12, 499–512.
- Rowlands, S., Permezel, M., 1998. Physiology of pain in labour. *Bailliere's Clinical Obstetrics and Gynaecology* 12, 347–360.
- Sosa, C.G., Buekens, P., Hughes, J.M., et al., 2006. Effects of pethidine during the first stage of labor on the acid–base status at birth. *European Journal of Obstetrics and Gynecology and Reproductive Biology* 129, 135–139.
- Todd, K.H., Funk, K.G., Funk, J.P., et al., 1996. Clinical significance of reported changes in pain severity. *Annals of Emergency Medicine* 27, 485–489.