

Study of the newborn feeding behaviors and fentanyl concentration in colostrum after an analgesic dose of epidural and intravenous fentanyl in cesarean section

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ABSTRACT

الأهداف: مقارنة تأثير عقار الفنتانيل عند حقنه في ابديورال والوريد على تقبل الطفل حديث الولادة للرضاعة الطبيعية.

الطريقة: أجري هذا البحث في مستشفى القصر العيني - جامعة القاهرة في الفترة ما بين مايو 2005م - مايو 2007م. شمل البحث مئة سيدة أجريت لهن عملية قيصرية، وارضعن رضاعة طبيعية من قبل. قسمت السيدات إلى مجموعتين كل مجموعة مكونة من خمسين سيدة، وقد تم التقسيم بصورة عشوائية. تم حقن عقار الفنتانيل في ابديورال للمجموعة الأولى، وحقنه في الوريد للمجموعة الثانية، وقيس نسبة عقار الفنتانيل في لبن السرسوب عند خمسة وأربعين دقيقة وأربعة وعشرين ساعة بعد الولادة القيصرية، وعلاقته بتقبل الرضيع حديث الولادة للبن السرسوب.

النتائج: تم اخذ عينتين من لبن السرسوب من المئة سيدة عند خمسة وأربعين دقيقة وأربعة وعشرين ساعة بعد الولادة القيصرية. ظهرت نسبة عقار الفنتانيل في لبن السرسوب عند خمسة وأربعين دقيقة في المجموعة الأولى أعلى من نسبته في المجموعة الثانية. وكان عدد حديثي الولادة الذين رفضوا الرضاعة الطبيعية أكثر في المجموعة الأولى ولكن دون فارق إحصائي، وقد تساوت النسبتان عند الأربعة والعشرين ساعة.

خاتمة: يمكن بدء الرضاعة الطبيعية مباشرة بعد الولادة القيصرية سواء تم استخدام عقار الفنتانيل في ابديورال أو في الوريد بالرغم من أن نسبة عقار الفنتانيل في لبن السرسوب عند خمسة وأربعين دقيقة كانت عالية نسبياً. وننصح بذلك لأهمية الرضاعة الطبيعية لكلاً من الأم والطفل.

Objective: To compare the effects of epidural and intravenous fentanyl on breast feeding behaviors and fentanyl concentration in the colostrum after an analgesic dose.

Methods: This study was conducted at the Obstetrics Department of Kasr El-Aini Hospital-Cairo University, Cairo, Egypt. The studied mothers were 100 multipara, who have been subjected to cesarean section, and have a previous history of successful

breast feeding. The study was conducted from May 2005 to May 2007. They were divided into 2 groups: group I included 50 patients who received epidural anesthesia with fentanyl, and group II included 50 patients who received spinal anesthesia with intravenous fentanyl, and both groups were observed for initial breast feeding behaviors of newborns, and fentanyl concentration in the colostrum at 45 minutes, and 24 hours after birth.

Results: The study included 100 multipara, 2 samples of colostrum were taken from each patients at 45 minutes, and at 24 hours. The levels of fentanyl concentration were greatest at 45 minutes of the initial sampling time, reaching 0.40 ± 0.059 ng/ml in the epidural group, and 0.19 ± 0.019 ng/ml in intravenous fentanyl group. There was no statistical difference in breast feeding behaviors at birth, or at 24 hours of age in both groups.

Conclusion: Although the levels of fentanyl concentration were greatest at 45 minutes of the initial sampling time, it can be used safely as intravenous or epidural without affecting the initial breast feeding behaviors of the newborn.

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Anesthesia for cesarean section may be regional anesthesia, such as epidural anesthesia, or general anesthesia. Fentanyl is frequently used to provide anesthesia, it can be used either intravenously during general anesthesia or epidurally. Fentanyl is a potent synthetic phenyl piperidine with an extremely high

lipid solubility and high pKa (the acid-base ionization constant). Thus, it should have a propensity for accumulation in breast milk.¹ Epidural fentanyl offers several advantages to patients recovering from cesarean section. These advantages include excellent postoperative analgesia with a decrease in total dose of opioid required, a low level of sedation, minimal accumulation of the drug in breast milk, facilitation of early ambulation, and early return of bowel function. Pruritus is the most common side effect of neuraxial morphine administration, and it is the most frequent cause of patient dissatisfaction with this technique.² The role that intrapartum medications play in preventing effective breast feeding has been debated for many years. Numerous studies have been performed, however, most have been prospective or retrospective observational studies. These studies were not sufficiently well controlled to yield reproducible results. None of the studies, until now, have randomly assigned patients to different doses, and in different routes of administration within a vigorous attempt to determine the impact of intrapartum drugs on breast feeding. The aim of this study was to determine fentanyl concentration in colostrum, after systemic and epidural administration, and its effects on breast feeding behaviors of the neonates.

Methods. After approval from the local Ethical Committee, and after informed written consent was obtained, we conducted a prospective, comparative, computerized, randomized, double-blind study in the Obstetric Department of Kaser-El Aini Hospital-Cairo University, Cairo, Egypt. This study included 100 breast feeding mothers. All mothers were healthy multipara who gave birth to full term healthy newborns by cesarean section, using epidural anesthesia or spinal anesthesia with intravenous fentanyl. It was conducted from May 2005 to May 2007. The patients were divided into 2 groups: group I (n=50) patients were randomly assigned to receive epidural anesthesia plus epidural fentanyl, while group II (n=50) patients were randomly assigned to receive spinal anesthesia and fentanyl intravenously. Inclusion criteria were between age 25-35 years old multipara, and had successfully breast fed before. Exclusion criteria were maternal pre-eclampsia, cardiac diseases, placenta previa, fetal distress, prematurity, and congenital neonatal anomalies. After the usual preparation for cesarean section, patients were placed in left lateral position, and a 1500 ml fluid bolus, and a spinal 3-4 ml of 0.5% bupivacaine was administered, supplemented with 50 microgram (microg) of fentanyl given intravenously after delivery of the baby. Epidural anesthesia was initiated with 20 ml bupivacaine 0.5%, epidural fentanyl dose was 100-150 microg, in fractional

increments of no more than 5 ml in 30 seconds, after insertion of epidural catheter. We injected additional drugs as required through the catheter, to obtain sensory level at the fourth thoracic dermatome, and maintained an infusion of 0.25% bupivacaine, and 2 microg/ml fentanyl at a rate of 10 ml/hour. Ephedrine was given intravenously as needed, to keep the systolic blood pressure greater than 100 mm Hg. All cesarean surgeries were attended by neonatology residents, where routine neonatal resuscitation was performed, together with full perinatal history taking, and thorough neonatal clinical examination. Activity, pulse, grimace, appearance, respiration (Apgar) scores of at least 8, at one and 5 minutes, and had no evidence of in-utero or birth asphyxia. All newborns were considered healthy full term neonates, enough to room-in with their mothers, and required no more than standard newborn care. All mothers and newborns were discharged home within 48 hours of delivery without complications. All newborns were exclusively breast fed at the time of hospital discharge. The breast feeding behaviors were recorded using the pre-term infant breast feeding behavior scale (PIBBS) as in Table 1.³ Colostrum samples were taken from each woman at 45 minutes, and 24 hours of labor. Colostrum was simultaneously collected using an electric breast pump, facilitated by gentle manual expression. Two ml of colostrum were collected from the same breast at each sample time, and frozen at -20°C until analysis. Colostrum was taken after the newborn first nursed. The samples were analyzed for fentanyl by Rocky Mountain Instrumental Laboratories of Fort Collins, Colorado. Analysis was by solid phase radioimmunoassay, validated by gas chromatography mass spectrometry.

Statistical method. A type 1 error of .05 was used for all tests of statistical significance. Data were analyzed using SPSS (Chicago, IL, USA). Personal computer program measures of central tendency were calculated for each group. Changes in the mean values for the variables were calculated, and comparisons between groups were made using analysis of variance. Based on the data, analysis of variance for repeated measures was used to analyze the difference between groups over time as well as the differences between individual participants over time. Measures of central tendency were calculated for the variables maternal age, gravida, para, previous breast feeding experience, number of times newborn fed in 24 hours, and newborn gender to evaluate for homogeneity of the sample. These numbers provide an overall significance level of 0.05. Based on 2-tailed test interval and a chi-square test on nominal-level variables to determine if the difference in mean score was significant between the 2 groups.

Table 1 - Assessing a newborn's readiness to breastfeed.

Pre-term Infant Breast-feeding Behavior Scale	Score
<i>Behavior related to rooting</i>	
Did not root	0
Showed some rooting behavior	1
Showed obvious rooting behavior	2
<i>Areolar grasp: How much of the breast was inside the baby's mouth?</i>	
None, the mouth only touched the nipple	0
Part of the nipple	1
The whole nipple, not the areola	2
The nipple and some of the areola	3
<i>Latching and fixing to the breast</i>	
Did not latch on at all so the mother could feel it	0
Latched on for 5 minutes	1
Latched on for 6–10 minutes	2
Latched on for ≥11–15 minutes	3
<i>Sucking</i>	
No sucking or licking	0
Licking and tasting, but no sucking	1
Single sucks, occasional short sucking bursts (2–9 sucks)	2
Repeated short sucking bursts, with occasional long bursts (≥10 sucks)	3
Repeated (≥2) long sucking bursts	4
<i>The longest sucking burst</i>	
1-5 consecutive sucks	0
6-10 consecutive sucks	1
11-15 consecutive sucks	2
16-20 consecutive sucks	3
21-25 consecutive sucks	4
>26-30 consecutive sucks	5
<i>Swallowing</i>	
Was not noticed	0
Occasional swallowing was noticed	1
Repeated swallowing was noticed	2
<i>Other parameters</i>	
Assess what the infant looked like during feedings	
Good perfusion versus diaphoretic	
Normal respirations versus tachypnea or apnea	
The milk-ejection reflex (letdown)	
Present	
Absent	

Adapted from Nyqvist KH et al,³ with permission of the International Lactation Consultant Association

Table 2 - Patients' demographic data.

Patients Parameters	Group I	Group II
Age (years)	30 (19-37)	31 (15-43)
Height, (cm)	160 (149-179)	165 (144-179)
Weight (kg)	70 (52-93)	70 (53-102)
Data are expressed as number and (mean)		

Table 3 - Breast feeding behaviors of the neonates in both groups.

Breast feeding behaviors of the neonates	Group I (n=50)	Group II (n=50)	P-value
No response to breast	12	10	0.18
No response to breast	13	11	0.49
Infant slips off breast	10	8	0.15
No rooting occurs	15	7	0.47
Mouth closed, points forward	14	13	0.36
Lower lip turned in	10	4	0.70
Cannot see infant's tongue	3	2	0.9
Cheek tense or pulled in	12	9	0.94
Rapid sucks	8	3	0.67
Can hear smacking or clicking	5	6	0.11
Infant does not latch on	20	29	0.89
Infant falls asleep	8	7	0.97
Infant not sucking well	9	9	1.0

Table 4 - Concentration of fentanyl in colostrum, Apgar score, and supplemental bottle feeding in both groups.

Parameter	Group I (n=50)	Group II (n=50)	P-value
Concentration of fentanyl in colostrum at 45 minutes (mean±SD)	0.40±0.059 ng/ml	0.19±0.019 ng/ml	-
Concentration of fentanyl in colostrum at 24 hours (mean±SD)	0.08±0.018.	0.05±0.018.	-
Apgar score at one minute	6 (7-8)	8 (7-9)	0.51
Apgar score at 5 minutes	9 (7-10)	9 (8-10)	0.61
Supplemental bottle feeding (%)	20	14	0.63

Results. This study included 100 multiparous patients. They are divided into 2 groups, and 2 colostrum samples were taken from each patient, one at 45 minutes, and the other at 24 hours. Table 2 shows the demographic data of both groups, and there was no significant statistical difference. Infant slips off breast, mouth closed point's forward, and infant falls asleep were higher in group I than in group II, we found a difference based on the amount of epidural fentanyl received. There was a significant difference in the pre-term infant breast feeding behavior scale (PIBBS) at 24 hours, with median scores of 35 in the epidural fentanyl, and 34 in the intravenous fentanyl ($p=0.03$,

Table 3). The clinical significance of these differences is not clear. We found an association between the pediatricians' evaluation of difficult breast-feeding at 24 hours, and PIBB scale ($p=0.0003$). Radioimmunoassay showed that fentanyl appeared in colostrum. The highest concentration at 45 minutes was in group I, at 0.40 ± 0.059 ng/ml, and in group II, at 0.19 ± 0.019 ng/ml. Fentanyl concentrations were greater in group I than in group II. Fentanyl became undetectable in the blood at 24 hours after administration (Table 4). We did not find any difference in Apgar score between the 2 groups, one or 5 minutes (median score of 9 in the 2 groups at one and 5 min). In the maternal overall assessment at 24 hours after delivery, 10 women reported problems with breast-feeding in group I. Eight of these problems were mild, and 2 were moderate. No one had severe problems. Women randomly assigned to the intravenous dose of fentanyl reported a problem in breast-feeding in 7 women, less often than those randomly assigned to the epidural fentanyl.

Discussion. Breast milk is considered the ideal nutrition for new-borns. Early contact between mother and infant is important for the establishment of breast feeding. This initial contact should occur, if possible, during the first hour postpartum. There are many factors that are thought to influence breast feeding including, type of anesthesia, general or epidural anesthesia multiparty, and supplemental bottle feeding.⁴ Also, breast-feeding problems can be due to infant issues (namely, infant does not latch onto the breast or suck well, palate structure), or maternal issues (such as inverted nipples, lack of education, or incentive). The use of regional anesthesia has become increasingly popular for labor analgesia, however, its effect on breast-feeding has been questioned. Our study was designed to compare the fentanyl concentration in colostrum after either systemic or epidural administration of fentanyl, or the relation between these levels and the neuro adaptive score of the neonates. The limitations of our study were that the number of the samples and their timing, the peak colostrum fentanyl levels may have been missed due to the first, and second samples being taken 45 minutes and 24 hours, after fentanyl administration. This may be due to an ethical point, agreement with the patients, and the lack of financial support for more samples. Our study compared large epidural dose with the small dose of intravenous, we found that the concentration of fentanyl was higher in the colostrum group I, than in group II (intravenous fentanyl) and it was statistically insignificant. Infant slips off breast, mouth-closed point's forward, and infant falls asleep were higher in group I than in group II, and it was statistically insignificant. The study also

showed that fentanyl does appear in colostrum after an analgesic dose. Our study agrees with a prospective cohort study by Chang and Heaman.⁵ They found no significant difference between the epidural fentanyl and intravenous fentanyl groups in breast feeding effectiveness or infant neuro behavioral status at 24 hours, or in the proportion of mothers continuing to breast feed up to 4 weeks. Therefore, epidural fentanyl and intravenous fentanyl did not appear to inhibit effective breast feeding. On the other hand, in a study by Dewey et al⁶ they found that breast feeding behavior on the first day was lower among those whose mothers received regional anesthesia during labor, and was lower among those whose mothers received intravenous (IV) or intra-muscular (IM) analgesia during labor on the third day, and delayed onset of lactation was more common in mothers who received both regional, and IV/IM labor medications.⁷

Other studies have shown an association between the age of the mother, use of epidural analgesia, and the problem of not having enough milk.⁸ Therefore, the influence of labor pain medications on breast feeding has been controversial considering the large number of women receiving pharmacological care, and so, the investigation of drugs in breast milk remains unexplored. However, Beilin et al⁹ noted that initiation of breast feeding should be considered distinctly from duration. Several physiological factors combine to make the neonate more vulnerable to drug toxicities. Metabolic and elimination pathways at birth, are functioning at only a fraction of adult capacities. Protein binding of drugs is diminished quantitatively and qualitatively in the neonate, which permits more drugs to be free for action at its receptor site. The respiratory chemoreceptors have a decreased sensitivity to carbon dioxide and hypoxia at birth. Considering these factors, if any doubt exists concerning the safety of breast feeding, the mother should be advised to pump her breasts to maintain lactation and resume nursing at a later time.¹⁰ Principal factors which determine neonatal effects from drug exposure through breast milk include the maternal dose, the volume of milk consumed, and the child's post-conceptual age.¹¹ However, considering the small and fleeting amount of fentanyl detected in colostrum, full-term infants should not be restricted from breast feeding. Neonates consume very little colostrum in the first few days of life, and gradually increase their intake to an average of 150 ml/kg/day.¹² Taking the worst example, the amount of fentanyl a neonate is likely to receive is extremely small. If one assumes a concentration of fentanyl as high as one ng/ml in colostrum, and if the baby ingests as much as 100 ml, the neonate could receive 100 ng of fentanyl. Assuming 49% bioavailability, and a 3-kilogram infant, this represents a dose of 0.016 mic/kg. It would be surprising if such

a low dose would produce any deleterious effects.¹² No scientifically based interval between surgery under general or regional anesthesia, and resumption of breast feeding can be recommended. Instead current opinion is that breast feeding can be resumed as soon as the mother feels physically and mentally capable to do so.

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Related topics

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