ORIGINAL ARTICLE

Opioids in the parturient with chronic nonmalignant pain: A retrospective review

Ibrahim Hadi, MD, FRCPC
Orlando da Silva, MD, FRCPC
Renato Natale, MD, FRCSC
David Boyd, MD, FRCPC
Patricia K. Morley-Forster, MD, FRCPC

ABSTRACT

The purpose of this research was to determine the neonatal outcomes of women who had been taking medically prescribed opioids throughout their pregnancy. A retrospective case study was done of 15 pregnancies associated with maternal opiate use between January 1, 1999, and September 30, 2002. Two cases were excluded due to coaddiction. Neonatal data were collected including gestational age, head circumference, length, birth weight, Apgar score at one and five minutes, details of resuscitation required, and Neonatal Abstinence Score. There were 13 pregnancies, which resulted in 13 live births; opioids prescribed included oxycodone, codeine, meperidine, fentanyl, dilaudid, morphine, and methadone. There were four babies with one-minute Apgar score = 5, and two babies with five-minute Apgar score = 5. It was concluded that neonatal growth markers in this population were within normal limits as plotted on the standard growth and development record of Gairdner-Pearson. Five out of 13 (38.5 percent) neonates were diagnosed with opioid discontinuation syndrome.

Key words: opioids, prescription, pain, pregnancy, neonatal development

INTRODUCTION

The use of opioids for chronic nonmalignant pain is becoming more widely accepted, spurred by evidence from clinical trials and an evolving consensus among pain physicians.[1,2] The appropriate use of these drugs requires skill in prescribing, knowledge of addiction medicine principles, and commitment to perform and document repeated assessments.

Most of the literature on maternal and neonatal effects of opioids has dealt with an addicted population.[3] Commonly abused substances during pregnancy include alcohol, nicotine, opioids, cocaine, heroin, and benzodiazepines. The use of these drugs has been associated with an increased incidence of spontaneous abortion, abruption placenta, congenital malformation, fetal growth retardation, low birth weight, and infections such as human immunodeficiency virus.[4] Problems associated specifically with heroin use during pregnancy include first trimester spontaneous abortion, premature delivery, meconium stained liquor, maternal/neonatal infection, and opioid discontinuation syndrome.[5,6]

The purpose of this study was to review neonatal outcomes of women who had been taking medically prescribed opioids throughout their pregnancy. We are not aware of any previously published study focusing on the use and effects of opioids for chronic nonmalignant pain management in pregnancy.

MATERIALS AND METHODS

The perinatal and neonatal databases from St. Joseph's Health Care, the tertiary perinatal referral center in southwestern Ontario, Canada, were searched from January 1, 1999, to September 30, 2002. Fifteen pregnancies associated with a chronic pain diagnosis and taking of prescription opioids were identified in that time period. On reviewing the chart, opioid use was ascertained by the referral letter from the patient's general practitioner or by the attending physician's notes at the first antenatal visit. Pregnant women with documented coaddiction disorder (e.g., cocaine) were excluded from the study.

The following maternal data were collected: age, height, weight, parity, obstetric and medical antenatal risk factors, smoking/alcohol history, pain syndrome diagnosis, all medication doses including opioids, methods of labor analgesia, and mode of delivery.

Neonatal variables collected were gestational age, birth weight, length, head circumference, Apgar score at

Table 1. Maternal and neonatal characteristics

Patient	Diagnosis	Medication	Mode of delivery	Neonatal gestational age (wk)	Neonatal weight (g)	Apgar 1 min	Apgar 5 min
1	Fibromyalgia	Oxycodone/acetaminophen	C/S	39 + 1	2,910	8	8
2	Crohn's disease	Meperidine	C/S	39 + 6	3,180	6	9
3	Crohn's disease	Fentanyl patch/meperidine	C/S	36	2,460	9	9
4	Severe rheumatoid arthritis	Tylenol #3 (acetaminophen 325 mg/codeine 30 mg)	C/S	28 + 1	920	1	5
5	Chronic back pain	Oxycodone/acetaminophen	Vaginal	28 + 4	1,130	7	8
6	Bone pain	Morphine	Vaginal	35 + 6	2,180	9	6
7	Degenerative disc disease	Tylenol #3	Vaginal	38	3,115	5	9
8	Chronic back pain	Oxycodone/acetaminophen	Vaginal	39 + 4	2,665	5	7
9	Chronic pelvic pain	Oxycodone/acetaminophen/ meperidine	Vaginal	38 + 2	4,630	0	5
10	Degenerative disc disease/scoliosis	Oxycodone/acetaminophen/ meperidine	Vaginal	36 + 6	2,475	8	9
11	Chronic hip pain	Codeine oxycodone/ acetaminophen	Vaginal	40 + 3	2,305	8	9
12	Chronic abdominal pain	Fentanyl patch/oxycodone/ acetaminophen	Vaginal	41 + 2	3,965	9	9
13	Chronic osteomy elitis	Meperidine/MS contin	Vaginal	38 + 3	3,675	6	8

C/S, Caesarean section.

one and five minutes, umbilical venous/arterial gases, Neonatal Abstinence Score (NAS), urine/meconium drug screen, administration of naloxone, need for mechanical ventilation, and duration of ventilatory support.

After delivery, NAS was performed using a scale from 1 to 5 (adapted from Finnegan LP, 1986). The NAS score is used to determine when to initiate therapy as well as monitoring therapeutic effects. A NAS of greater than 8 is deemed to be significant, and treatment is usually commenced with oral morphine according to a standardized regime. The scoring system, consisting of 21 signs and symptoms commonly seen in the neonate born to pregnant women who were on opioid treatment, is a comprehensive and precise way of permitting an objective estimate of the withdrawal syndrome. Each symptom is assigned a score based on severity observed over a period of time. Decision to admit to the Neonatal Intensive Care Unit (NICU) was at the discretion of the neonatal team. The duration of admission was recorded.

RESULTS

Two cases were excluded due to coaddiction, leaving 13 for analysis. Table 1 provides demographic information based on maternal data. Opioids prescribed included a range or a combination of the following: morphine, fentanyl patch, meperidine, codeine, and oxycodone.

All opioids were taken throughout the pregnancy; however, the exact doses were difficult to determine because the study is retrospective and doses were missing

Table 2. Mean neonatal growth markers, Apgar, and NAS in study subjects (N = 13)						
Mean gestational age (wk)	**Mean weight (g)**	**Mean head circumference (cm)**	**Mean length (cm)**	**Number of patients with one-min Apgar = 5**	**Number of patients with five-min Apgar = 5**	**Abstinence score > 8 on day one**
37 ± 1	2,739 (920 to 4,630); SD = 1,035	32.8 (26.0 to 35.5); SD = 3.0	46 (31 to 55) SD = 5.7	4	2	5*

* Two patients were intubated and unable to be scored. Numbers in parentheses indicate ranges. NAS, Neonatal Abstinence Score; SD, standard deviation.

from the patient data. The antenatal care was supplemented by psychiatric or psychological counseling and social worker input where necessary. A consult to a pain specialist was often made.

Table 2 summarizes the neonatal data of the 13 live births. Mean gestational age was 37 ± 1 weeks, mean birth weight was 2,739 ± 1,035 g, mean head circumference was 32.8 ± 3.0 cm, and mean length was 46 ± 5.7 cm. After obtaining the mean for neonatal growth markers (length, head circumference and weight), we plotted the results on the standard growth and development record (Gairdner-Pearson 1988). All were within normal limits. Four out of 13 neonates had an Apgar score equal or less than 5 at one minute, two of which required active resuscitation and subsequent NICU admission. Opioid reversal (using Naloxone) was never given during resuscitation because it was not felt to be indicated.

There were a total of five neonates who had a NAS equal to or more than 8, which required NICU admission with subsequent initiation of assessment and oral morphine treatment protocol.

DISCUSSION

The results of this small retrospective study of neonatal outcomes in women taking medically prescribed opioids are reassuring in that neonatal growth markers were within normal limits; this is in contradistinction to previous retrospective reviews, which indicated low birth weights and prematurity in heroin-addicted mothers. The exact Canada-wide prevalence of opioid exposure in pregnancy is unknown. However, estimates range between 1 and 3 percent.[7,8] In utero exposure to opioids is associated with abstinence symptoms in 55 to 94 percent of exposed infants.[9]

All infants born to known opioid-dependent women should be initially observed in the high-risk nursery for observation of neonatal abstinence symptoms. Affected infants can require treatment for many days, leading to a prolonged stay in the NICU. This has a major impact not only on maternal and infant bonding but also on bed occupancy. In one institution in Dublin, Ireland, three neonatal beds were always occupied by infants with NAS.[10]

Studies examining growth are frequently difficult to interpret because of high attrition rates and the compounding social factors that contribute to intrauterine growth retardation. In one series, some catch-up growth was demonstrated, but persistent poor weight gain at age one year correlated with methadone usage during pregnancy.[11]

The literature suggests there may be potential risks of maternal exposure to opioids other than intrauterine growth retardation. Infants of pregnant patients taking opioids, particularly methadone, have a two to three times increased risk of unexplained sudden death in infancy,[12] possibly owing to abnormal respiratory control. Sorensen et al. studied the relationship between prenatal exposure to analgesics, both opioid and nonopioid, and the risk of schizophrenia, using data from perinatal cohort and from the Danish Psychiatric Central Register. They concluded that there was a four-fold greater risk of schizophrenia in those children who were exposed to an analgesic in the second trimester.[13]

Developmental outcome may be impaired in infants of women who abuse drugs, as indicated by the wide variety of mild cognitive effects in preschool children reported by researchers using the Bayley scales of mental development.[14] Children born to pregnant patients maintained on methadone have been suggested to be more likely to show poor development, further compounded by factors associated with drug misuse such as smoking; alcohol misuse; and poor nutrition, housing, and education. Examination of children aged 36 months, however, highlighted that some children appear to be resistant to the effects of maternal drug use, as they had developed appropriately.[15]

Lester et al. studied the effects of prenatal cocaine and/or opiate exposure on auditory brain response in infants at one month.[16] Infants with prenatal opiate exposure (n = 477) showed a longer absolute and interpeak latency than control infants matched for race, gender, and gestational age (n = 554). However, the authors concluded that determination of the clinical significance of these effects required a larger sample with control for gestational age, other drugs, and level of cocaine use.

In conclusion, this small study suggests that maternal

use of opioids may be safe for the neonate if medically prescribed. However, opioid discontinuation syndrome is common and usually requires specialized treatment in a NICU. Long-term implications of in utero opioid exposure remain a concern. Further research incorporating a multicenter database with follow-up over five to seven years is necessary to ensure that this modality of treatment is safe for the pregnant woman.

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Ibrahim Hadi, MD, FRCPC, Department of Anesthesia and Perioperative Medicine, University of Western Ontario, St. Joseph Health Care, London, Ontario, Canada.
Orlando da Silva, MD, FRCPC, Department of Paediatrics, University of Western Ontario, St. Joseph Health Care, London, Ontario, Canada.
Renato Natale, MD, FRCSC, Department of Obstetrics & Gynecology, University of Western Ontario, St. Joseph Health Care, London, Ontario, Canada.
David Boyd, MD, FRCPC, Department of Internal Medicine, University of Western Ontario, London Health Sciences, London, Ontario, Canada.
Patricia K. Morley-Forster, MD, FRCPC, Chair, University of Western Ontario Interdisciplinary Pain Program, London, Ontario, Canada.

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