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Oxycodone

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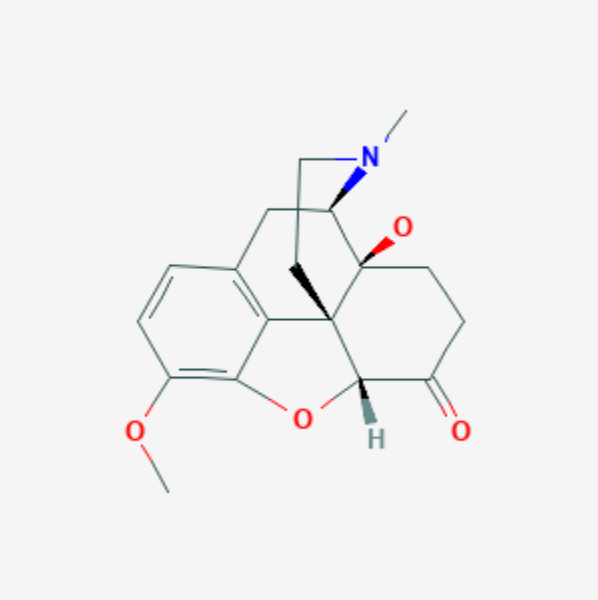

Drug Levels and Effects

Summary of Use during Lactation

Maternal use of oral narcotics during breastfeeding can cause infant drowsiness, central nervous system depression and even death. Infant sedation is common and well documented with maternal use of oxycodone. Newborn infants seem to be particularly sensitive to the effects of even small dosages of narcotic analgesics. Once the mother's milk comes in, it is best to provide pain control with a nonnarcotic analgesic and limit maternal intake of oral oxycodone (and combinations) to a 2 to 3 days, especially in the outpatient setting.[1] A maximum oxycodone dosage of 30 mg daily is suggested, although some sources recommend avoiding oxycodone during breastfeeding.[2][3] Oxycodone elimination is decreased in young infants with much inter-individual variability. Monitor the infant closely for drowsiness, adequate weight gain, and developmental milestones, especially in younger, exclusively breastfed infants. If the baby shows signs of increased sleepiness

(more than usual), difficulty breastfeeding, breathing difficulties, or limpness, a physician should be contacted immediately. Other agents are preferred over oxycodone during breastfeeding.[2]

Drug Levels

Oxycodone is metabolized to the active metabolites, noroxycodone and oxymorphone. Oxycodone has an oral bioavailability of 60% to 87% in adults.[4] Oxycodone elimination is decreased in young infants and much inter-individual variability exists. Oxycodone can be dangerous when used as an analgesic in newborns.[5]

Maternal Levels. Six breastfeeding mothers who were using 1 to 2 capsules containing a combination of 5 mg oxycodone and 500 mg acetaminophen every 4 to 7 hours for post-cesarean section pain had their milk sampled several times after successive doses. Peak oxycodone milk levels reportedly occurred 1 to 2 hours after the first dose and then at variable times after successive doses. The number of hours after a mother's last dose when oxycodone could still be measured in milk was depended on the number of doses taken. Oxycodone could be measured in milk up to 4, 12, and 36 hours after 4, 9, and 11 doses respectively. In all the mothers, measured oxycodone milk levels ranged from undetectable (<5 mcg/L) to 229 mcg/L. The authors estimated that an exclusively breastfed infant would receive a maximum 8% of the maternal weight-adjusted dosage of oxycodone, but active metabolite levels were not measured.[6]

Fifty mothers who delivered by cesarean section and received oxycodone had milk (colostrum) and serum samples measured for oxycodone at 24, 48 and 72 hours postpartum without respect to the time of the previous oxycodone dose. The most common doses received by the mothers during the previous 24 hours (including one 30 mg dose rectally immediately postoperatively in some cases) were 60 mg (range 30 to 90 mg), 40 mg (range 0 to 90 mg), and 20 mg (range 0 to 50 mg), respectively. Mean colostrum concentrations at the 3 collection times were 58 mcg/L (range 7 to 130 mcg/L), 49 mcg/L (range 0 to 168 mcg/L), and 35 mcg/L (range 0 to 31 mcg/L), respectively. Little correlation was found between maternal dosage and colostrum concentrations, although colostrum levels correlated well with maternal serum levels, with a colostrum concentrations 3.2 to 3.4 higher than serum. Ten mothers had colostrum oxycodone concentrations over 100 mcg/L and 5 had detectable oxycodone in milk 37 hours after the last dose.[7]

Infant Levels. In a study of 50 mothers taking oxycodone post-cesarean section, 45 blood samples were taken from 41 breastfed infants at 24, 48 or 72 hours postpartum. Only 1 of the samples had a detectable (>2 mcg/L) oxycodone level of 7.4 mcg/L. Because these infants were in the first 3 days postpartum, their dose was probably limited by the small volumes of colostrum they were ingesting.[7]

A woman who was exclusively breastfeeding her infant was taking 5 to 10 mg of oxycodone every 4 to 6 hours for episiotomy pain. Her 45-day-old infant's urine drug screen showed a concentration of >2000 mcg/L (positive cutoff for opioid metabolites was 5 mcg/L).[8]

Effects in Breastfed Infants

A 10-month-old, 7.7 kg infant of a prescription drug-dependant mother died of cardiac arrest after a 12- to 24-hour period of lethargy, hypersomnolence and dyspnea. The infant also had a recent history of fever. The mother had reportedly been breastfeeding the infant 3 times a day for several weeks and had taken 180 mg of oxycodone, as well as muscle relaxants, the day prior to her infant's death. A blood oxycodone level of 600 mcg/L was measured on autopsy. The medical examiner considered it unlikely that such a high level of oxycodone in the infant's blood could be due to breastfeeding exposure as reported by the mother and thus considered the death a homicide resulting from either the intentional administration of oxycodone directly to the infant or from a higher dose of oxycodone in breastmilk than that reported by the mother.[9]

In a study of 50 mothers taking oxycodone post-cesarean section, 50 neonates were evaluated for sedation over 48 hours after birth. None was severely sedated and less than 4% had sedation of 3 on a 1 (fully alert) to 5

(difficult to rouse) scale and none more sedated than 3 on the scale. Because these infants were in the first 3 days postpartum, their oxycodone dose was probably limited by the small volumes of colostrum they were ingesting.[7]

An infant was born to a mother taking oxycodone 20 mg 3 times daily, fluoxetine 40 mg daily and quetiapine 400 mg daily. The infant was breastfed 6 to 7 times daily and was receiving 120 mcg of oral morphine 3 times daily for opiate withdrawal. Upon examination at 3 months of age, the infant's weight was at the 25th percentile for age, having been at the 50th percentile at birth. The authors attributed the weight loss to opiate withdrawal. The infant's Denver developmental score was equal to his chronological age.[10]

A woman who was exclusively breastfeeding her infant was taking 5 to 10 mg of oxycodone every 4 to 6 hours for episiotomy pain. Her 45-day-old infant was brought to the emergency department with a temperature of 98.4 degrees F, a heart rate of 154 per minute, 20 breaths per minute, a blood pressure of 71/52, and an oxygen saturation of 60% to 69% on room air. The infant had been constipated since birth, passing one stool every 5 to 8 days. The infant had sluggish movements slow, shallow, and irregular breathing. Her pupils were small, but reactive. Hydromorphone levels in urine were elevated. The patient was intubated and given opiates around the clock for two days before being extubated and discharged. The infant's constipation, CNS and respiratory depression were probably caused by oxycodone in breastmilk.[8]

In a retrospective study, nursing mothers who were taking either oxycodone, codeine or acetaminophen for pain while breastfeeding were contacted by telephone to ascertain the degree of maternally perceived central nervous system (CNS) depression. Mothers taking oxycodone reported signs of CNS depression in 20% (28/139) of their infants, while those taking acetaminophen reported infant CNS depression in only 0.5% (1/184) of their infants. Women who reported infant sedation were taking 0.4 mg/kg daily of oxycodone, and unaffected were taking 0.15 mg/kg daily. Affected infants had more hours of daily uninterrupted sleep than unaffected infants, and 4 of the affected infants reportedly had "irregular breathing". Thirty-eight of 39 mothers reported that infant sedation ceased with maternal oxycodone discontinuation. Mothers of affected infants were also more likely to experience lethargy and other side effects than mothers of unaffected infants. Mothers who took codeine reported a similar rate of infant sedation (17%) compared to oxycodone, but the groups were statistically different in parity and postmenstrual age (PMA), with the codeine group having a slightly higher PMA.[11]

A newborn infant was exclusively breastfed and found to be well by his physician at 2 days of age. At 3 days postpartum, the infant began to be sedated and became difficult to arouse and did not feed from either breast. At 4 days of age, the infant was brought to the emergency department where the infant was found to have lethargy, hypothermia, pinpoint pupils, and a poor sucking reflex. The mother reported that her milk had come in the previous evening. She had taken 10 mg of oxycodone that evening and another 5 mg the next morning in the form of Percocet (oxycodone 5 mg plus acetaminophen 325 mg). The infant was given naloxone 0.34 mg intramuscularly and within 2 minutes, the baby's eyes opened and he drank 45 mL of formula. No further sedation was seen over the next 24 hours.[12] The infant's sedation was probably caused by oxycodone in breastmilk.

A search was performed of the shared database of all U.S. poison control centers for the time period of 2001 to 2017 for calls regarding medications and breastfeeding. Of 2319 calls in which an infant was exposed to a substance via breastmilk, 7 were classified as resulting in a major adverse effect, and three of these involved oxycodone. A 16-day-old infant was exposed to cyclobenzaprine, acetaminophen and oxycodone in breastmilk. The infant was admitted to the hospital in a noncritical care unit for bradycardia, hypotension, and respiratory arrest. A 14-day-old infant was exposed to acetaminophen and oxycodone and developed cyanosis. The infant was treated and released. A one-month-old infant was exposed to fentanyl, morphine, oxycodone, and benzodiazepines. The infant was admitted to the intensive care unit and described as being agitated and irritable and having tachycardia, confusion, drowsiness, lethargy, miosis, respiratory depression, acidosis, and

hyperglycemia. The dosages and extent of breastfeeding were not reported in any of the cases and the infants all survived.[13]

Effects on Lactation and Breastmilk

Oxycodone can increase serum prolactin.[14] However, the prolactin level in a mother with established lactation may not affect her ability to breastfeed.

Alternate Drugs to Consider

Acetaminophen, Butorphanol, Hydromorphone, Ibuprofen, Morphine

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Substance Identification

Substance Name

Oxycodone

CAS Registry Number

76-42-6

Drug Class

Breast Feeding

Lactation

Analgesics, Opioid

Narcotics

Antitussive Agents

Opiates