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Case Report

Neonatal Respiratory Depression in the Setting of Maternal Oxycodone Use While Breastfeeding

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Abstract

We report a case of a term male neonate, born via repeat caesarean section (CS), who developed transient tachypnea of the newborn (TTN) shortly after birth followed by two bradycardia/desaturation and apnea/bradycardia/desaturation events on day of life (DOL) three and four, respectively, temporally associated with maternal oxycodone use while breastfeeding. The infant was transitioned from maternal breast milk to donor milk until she was on <40mg/day of oxycodone. This case highlights the importance of close monitoring for respiratory depression and bradycardia in neonates exposed to maternal opioids through breast milk, especially at doses higher than recommended.

Keywords: Neonatal apnea; Maternal opioids; Breastfeeding; Oxycodone; Neonatal respiratory depression; Breast milk exposure

Background

Oxycodone is frequently prescribed to manage moderate to severe postoperative pain after CS, favored for its high oral bioavailability and well-established efficacy in multimodal analgesia regimens [1]. However, its use in lactating women raises concern due to excretion into breast milk and the potential for neonatal exposure [2,3].

Neonates are particularly vulnerable to opioid-related toxicity because of their immature hepatic metabolism and renal clearance, which may prolong drug elimination and amplify central nervous system (CNS) effects [3,4]. Oxycodone is metabolized to active compounds including oxymorphone, which has a significantly higher affinity for μ-opioid receptors and greater potency than the parent drug [5]. Even small concentrations in breast milk can result in meaningful clinical exposure for neonates, especially in the early postnatal period when hepatic enzyme activity is limited [4,5].

Pharmacokinetic studies show that the milk-to-plasma ratio of oxycodone often exceeds 3.0, with modeled neonatal exposures reaching up to 10% of a therapeutic infant dose in worst-case scenarios [1]. In a retrospective study, Lam et al. reported a 20.1% incidence of CNS depression in infants breastfed by mothers taking oxycodone, compared to only 0.5% in those exposed to acetaminophen alone (odds ratio 46.16) [5].

Although oxycodone has been used widely and generally safely, adverse events including sedation, bradycardia, and respiratory depression have been reported, particularly with high maternal doses or concurrent CYP3A4 or CYP2D6 inhibition [6,7]. The LactMed database recommends limiting maternal oxycodone to 60 mg/day for no more than 2-3 days, particularly in exclusively breastfed infants under two months old [2]. Other clinical guidelines, including those from the King Edward Memorial Hospital (KEMH), recommend even stricter thresholds of no more than 40 mg/day and for no longer than three days [3].

The Society for Obstetric Anesthesia and Perinatology (SOAP) acknowledges the risks of neonatal sedation but cautions against switching away from oxycodone entirely due to the limited clinical use and pharmacologic drawbacks of alternative opioids such as morphine and hydromorphone. SOAP supports multimodal analgesia and advises using oxycodone only as rescue therapy at the lowest effective dose for the shortest possible duration [8].

Importantly, a recent cross-sectional study by Ahmadzai et al. found that mothers underreported suspected adverse drug reactions (ADRs) in their breastfed infants, with opioids among the most

frequently implicated medication [9]. These findings underscore the need for greater awareness and monitoring of opioid-related effects in neonates, especially during the early postnatal period when breastfeeding is often most frequent and maternal dosing may be highest.

This case adds to the growing literature suggesting a potential link between high-dose maternal oxycodone use and neonatal respiratory events, warranting further investigation and more cautious prescribing in lactating patients.

Case Presentation

A male neonate was born via repeat CS at 37 weeks and 4 days gestation to a G2P1 mother in her early 30s after she presented to the hospital in early active labor. Mom did not have any complications during this pregnancy and received routine prenatal care throughout. She took a prenatal vitamin with iron, Zyrtec, and a short course of antibiotics for a sinus infection while pregnant. She had a history of marijuana gummy use prior to pregnancy but stopped use once she knew she was pregnant and did not restart while breastfeeding. Syphilis, HIV, GBS, hepatitis B, hepatitis C, chlamydia, and gonorrhoea screenings at the time of delivery were negative.

The neonate weighed 3.76kg at birth and measured 51cm long with a head circumference of 35.5cm. Apgar scores were 8 and 9 at one and five minutes, respectively. However, he required NICU admission for continued respiratory distress, later determined to be secondary to TTN with chest radiograph demonstrating perihilar streaking and fluid in the minor fissure. The neonate was placed on nasal continuous positive airway pressure (5 cmH2O; FiO2-0.21) for DOL 0-2 with supplemental oxygen via nasal cannula (1 lpm; FiO2-0.25) on DOL 0 and was successfully weaned to room air on DOL 2. While in the NICU, he was on gavage feeds of formula and maternal breast milk. After his respiratory distress resolved, he was transitioned to PO maternal breast milk.

Notably, the mother was prescribed 60 mg/day of oxycodone via patient-directed analgesia on DOL 2. She continued to breastfeed either through direct nursing or pumping. On DOL 3, the neonate had an episode of bradycardia/desaturation while stooling that reoccurred the following morning with an associated apneic event. As a result, maternal breast milk was held, and donor milk and formula were initiated. The mother was instructed to discard expressed milk until her oxycodone dosage decreased to 40 mg/day. She ultimately chose to discontinue oxycodone and delay breastfeeding until 48 hours after her last dose. No further apneic events occurred following the transition to donor milk and formula. The neonate was discharged home on DOL 7 weighing 3.41kg and on a formula diet with supplemental poly-vi-sol vitamin drops with iron.

Outcome and Follow-Up

The neonate was well-appearing at his newborn well child check on DOL 8. He weighed 3.4kg, a 9.5% decrease from birth weight. Earlier that morning, his mother reintroduced her breastmilk into his diet as it had been 48 hours since her last dose of oxycodone. He tolerated the maternal breastmilk well and had no repeat episodes of respiratory distress. Review of systems and physical exam were negative for any concerning findings.

The patient appeared to be growing and developing well without any signs of illness. Anticipatory guidance was discussed with both parents and a follow-up appointment was scheduled two days later to closely monitor the patient for excessive weight loss.

Discussion

This case illustrates the potential risk of neonatal opioid exposure via breast milk, particularly in the early neonatal period when hepatic and renal metabolism are immature. Oxycodone is excreted in breast milk, and while levels are generally low, high maternal dosage, as in this case, may result in clinically significant neonatal exposure. Apnea and bradycardia in neonates have multifactorial etiologies, but the temporal association with maternal high-dose oxycodone use, resolution after cessation of breast milk, and absence of other risk factors suggest a causal relationship.

While TTN explains the initial respiratory distress, the subsequent apnea events, particularly on DOL 4, raise concern for opioid-related central respiratory depression. Current guidelines caution against high-dose opioid use in breastfeeding mothers and recommend the lowest effective dose for the shortest duration.

Learning Points/Take Home Messages

- This case underscores the need for caution when prescribing high-dose opioids to breastfeeding mothers.
- Close monitoring of neonates for respiratory depression is warranted, and clinicians should educate mothers on the potential risks of opioid transmission through breast milk.
- Further research is needed to clarify the threshold at which maternal oxycodone use may lead to adverse neonatal outcomes.

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