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Practice Point

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Practice Point

Managing infants born to mothers who have used opioids during pregnancy

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Abstract

The incidence of infant opioid withdrawal has grown rapidly in many countries, including Canada, in the last decade, presenting significant health and early brain development concerns. Increased prenatal exposure to opioids reflects rising prescription opioid use as well as the presence of both illegal opiates and opioid-substitution therapies. Infants are at high risk for experiencing symptoms of abstinence or withdrawal that may require assessment and treatment. This practice point focuses specifically on the effect(s) of opioid withdrawal and current management strategies in the care of infants born to mothers with opioid dependency.

Keywords: *Discharge planning; Management; NAS; NPI; Treatment strategies*

BACKGROUND

For 2016–17, the Canadian Institute for Health Information reported that an estimated 0.51% of all infants born in Canada (approximately 1850/year, Quebec excluded) had Neonatal Abstinence Syndrome (NAS). A large percentage of these cases are attributed to opioid withdrawal (1). The average length of stay in acute care facilities for these infants was 15 days. Recent reports indicate the number of infants requiring observation for withdrawal symptoms is increasing annually and that cases are generally under-reported (2). The costs of hospitalization speak to the significant burden this problem places on the health of mothers, infants and families, along with hospital units, health care providers and other community resources (3).

Opioid use during pregnancy, whether prescribed or illicit, can be associated with negative pregnancy and infant outcomes, including prematurity, low birth weight, increased risk of spontaneous abortion, sudden infant death syndrome and infant neurobehavioural abnormalities (4). Natural compounds include morphine and codeine. Heroin, oxycodone, hydrocodone, hydromorphone and buprenorphine are semi-synthetic. Fentanyl, methadone, normethadone, tramadol and meperidine are synthetic (5). The most significant effects of maternal opioid dependence and prenatal fetal exposure are short-term complications, with NAS predominating. NAS is a set of drug withdrawal symptoms that can affect the central nervous system (CNS), and the gastrointestinal and respiratory systems in the newborn (6). Potential long-term outcomes of prenatal opiate exposure are difficult to predict due to multiple, interrelated variables of maternal-infant risk factors that are known to impact developmental outcomes in this cohort (7,8).

Pregnant women with an opioid dependence should be advised to continue or commence an opioid maintenance therapy program (9). Methadone is often recommended for opioid-dependent pregnant women (10) and some studies suggest buprenorphine as an alternative treatment (11). The literature reports that opioid substitution therapy during pregnancy may lessen the use of other opioids and illicit drugs and improve prenatal care, including access to education, counselling and community supportive services (12,13). Obtaining a comprehensive medication or illicit substance use history and a focused social history are recommended. Other associated health risks include infections (e.g., hepatitis B, hepatitis C, syphilis and HIV), insufficient maternal nutrition or access to antenatal care, as well as social risk factors, and should be screened for, determined and managed appropriately.

CLINICAL PRESENTATION

The presentation of withdrawal symptoms varies, depending on the type of maternal opioid used, the frequency, dose and timing of last exposure, gestational age, maternal metabolism and maternal use of other substances. Approximately 50% to 75% of infants born to women on opioids will require treatment for opioid withdrawal symptoms (14). Symptoms of opioid withdrawal (Figure 1) typically appear shortly after birth, with the majority exhibited within the first 48 h to 72 h postdelivery. Some reports suggest a later symptom presentation, at 5 to 7 days postbirth, after exposure to methadone or buprenorphine (15,16). Initial acute symptoms may persist for several weeks (ranging from 10 to 30 days) while milder symptoms, such as irritability, sleep disorders and feeding problems can persist for 4 to 6 months (17). Preterm infants have been described as being at lower risk for drug withdrawal and symptoms of NAS may not be as apparent as in their term counterparts (18,19). Reasons for this difference include: a shorter in utero exposure time, decreased placental transmission, inability to fully excrete drugs by immature kidneys and liver, minimal fat stores leading to lower opioid deposition and activity, as well as a limited capacity to express classic NAS symptoms by the immature brain (19).

Other neonatal conditions such as hypoglycemia, hypocalcemia, CNS injury, hyperthyroidism, bacterial sepsis or other infections may present with similar symptoms and should be considered as part of the differential diagnosis.

ASSESSMENT

For all opioid-exposed infants, an assessment scoring system should be used to measure the severity of withdrawal symptoms and help determine whether additional monitoring, nursing, medical and pharmacological therapy are required (20). The most widely used scale to evaluate infants for opioid withdrawal is the Finnegan scoring system, which identifies behaviours associated with withdrawal (Figure 1) (21). An initial score is typically obtained within the first 1 h to 2 h postdelivery, then rechecked every 3 h to 4 h thereafter, in conjunction with other nursing assessments. Most guidelines suggest that scoring should be done for a minimum of 72 h and up to 120 h when an infant was exposed in utero to a longer-acting opioid, such as methadone or buprenorphine (19). The scale may also be used to assess the resolution of symptoms after initiating treatment. Accurate, consistent scoring of symptoms is necessary to ensure that the infant receives appropriate

SAMPLE NEONATAL ABSTINENCE SCORING SYSTEM

SYSTEM	SIGNS AND SYMPTOMS	SCORE		AM						PM					COMMENTS
CENTRAL NERVOUS SYSTEM DISTURBANCES	Excessive High Pitched (or other) Cry < 5 minutes	2													Daily Weight
	Continuous High Pitched (or other) Cry > 5 minutes	3													
	Sleeps < 1 Hour After Feeding	3													
	Sleeps < 2 Hours After Feeding	2													
	Sleeps < 3 Hours After Feeding	1													
	Hyperactive Moro Reflex	2													
	Markedly Hyperactive Moro Reflex	3													
	Mild Tremors Disturbed	1													
	Moderate-Severe Tremors Disturbed	2													
	Mild Tremors Undisturbed	3													
	Moderate-Severe Tremors Undisturbed	4													
	Increased Muscle Tone	2													
	Excoriation (Specific area)	1													
	Myoclonic jerks	3													
	Generalized convulsions	5													
METABOLIC/VASOMOTOR/ RESPIRATORY DISTURBANCES	Sweating	1													
	Fever 38°C to 38.3°C	1													
	Fever > 38.3°C	2													
	Frequent Yawning (> 3-4 times/interval)	1													
	Mottling	1													
	Nasal Stuffiness	1													
	Sneezing (> 3-4 times/interval)	1													
	Nasal Flaring	2													
	Respiratory rate > 60/min	1													
	Respiratory rate > 60/min with Retraction	2													
GASTRO-INTESTINAL DISTURBANCES	Excessive Sucking	1													
	Poor Feeding	2													
	Regurgitation	2													
	Projectile Vomiting	3													
	Loose Stools	2													
	Watery Stools	3													
TOTAL SCORE															
INITIALS OF SCORER															

Figure 1. Modified Finnegan scoring system. Reproduced from refs. (15,20,21).

care (22). A variety of instructional videos and "train-the-trainer" approaches are available to ensure that staff education is consistent for proper scoring (23). Priorities are to develop a standardized process to identify, manage and evaluate infants with NAS, then to discharge them as soon as it is safe and appropriate.

MANAGEMENT

Successful supportive management of infants exposed to opioids during pregnancy depends on a number of factors, such as providing appropriate medication(s), correct scheduling, using an accurate tool to measure and evaluate the severity of symptoms, creating a compatible physical environment and having a knowledgeable, experienced health care team. Involving interprofessional team members, (i.e., specialized in nursing, neonatal medicine, social work, pharmacy, nutrition and community resources) is essential for ensuring the seamless management and discharge of these vulnerable infants (15). Treatment goals include preventing complications associated with NAS and restoring normal newborn activities, such as sleep, sufficient feeding, weight gain and environmental adaptation.

In addition to maternal self-reporting, some practitioners conduct urine or meconium toxicology screens for infants born to women with a suspected history of drug abuse during pregnancy. This information may be helpful to identify the substance(s) of abuse and for selecting appropriate pharmacological treatment, when required (16). However, the validity and reliability of toxicology testing is controversial (24). Further, obtaining maternal consent for testing, securing knowledge of who will have access to the results and other legal considerations are important in the decision to conduct or send toxicology screens (25). National neonatal resuscitation guidelines suggest that using naloxone during infant resuscitation should be avoided when an infant is born to a known opioid-dependent mother because it has been associated with seizures in newborns (26). There is no evidence to suggest that a higher than routine level of health care practitioner (HCP) care competency is required at delivery, provided there are no other risk factors present.

It is well known that separating infant and mother can be detrimental to early attachment. Recent literature supports practices that keep opioid-dependent mothers and their infants together from birth, such as rooming-in. Such practices have additional benefits, such as lower neonatal intensive care unit (NICU) admissions, higher breastfeeding initiation rates, less need for pharmacotherapy and shorter hospital stays (27–30). A rooming-in model of care—rather than admission to NICU—can be considered for mother–infant dyads at risk for developing NAS symptoms when: infants are term or near term, medically stable, and adequate resources are in place to support both the family and HCPs.

Nonpharmacological interventions

Initial treatment for neonatal withdrawal should be primarily supportive because medical interventions can prolong hospitalization, disrupt mother–infant attachment and subject an infant to drugs that may not be necessary. Nonpharmacological interventions have been shown to reduce the effects of withdrawal and should be implemented as soon as possible following birth (2). Examples of supportive interventions include skin-to-skin contact, safe swaddling, gentle waking, quiet environment, minimal stimulation, lower lighting, developmental positioning, music or massage therapy (31).

Breastfeeding should be encouraged because it can delay the onset and decrease the severity of withdrawal symptoms as well as decrease the need for pharmacological treatment (32). HIV-negative mothers who are stable and on opioid maintenance treatment with either methadone or buprenorphine should be encouraged to breastfeed (9). Breastfeeding provides optimal nutrition, promotes maternal–infant attachment and facilitates parenting competence. Mothers with a dependency who wish to breastfeed may require extra support as they are less likely to initiate breastfeeding successfully and more likely to stop breastfeeding early (33).

NAS infants may show impaired feeding behaviours such as excessive non-nutritive sucking, poor feeding, regurgitation and diarrhea (34). An early study (35) found that opioid-exposed infants had more feeding problems (rejecting the nipple, dribbling milk, hiccoughing, spitting up, and coughing) than nondrug-exposed infants. More recent studies have confirmed these findings and described the challenges caregivers face when feeding infants who show signs of withdrawal (36). Supplementation with concentrate to increase caloric intake or total fluid intake has been suggested for infants with poor weight gain (37).

Pharmacological interventions

Pharmacological therapy is indicated for infants whose withdrawal signs are increasingly severe or whose concurrent NAS scores climb despite supportive measures to reduce and manage symptoms. Infants who require treatment with medications may also require admission to a special care nursery or NICU for cardiorespiratory monitoring and observation while therapy is initiated, particularly if they are medically unstable. A stabilized infant can be transferred back into a care-by-parent area (e.g., rooming-in) provided that assessment, parent education and medication weaning monitoring are ongoing, infant–mother attachment is supported and comprehensive discharge planning can be initiated (29). Rooming-in with mothers on a methadone program and breastfeeding have been shown to reduce the need for pharmacological intervention (30).

Several pharmacological agents have been used to ameliorate symptoms associated with neonatal opioid withdrawal

Table 1. Medications to treat neonatal abstinence syndrome

Medication	Mechanism of action	Dose	Comments
Morphine	Natural m-receptor agonist	If score is ≥ 8 on 3 (or ≥ 12 on 2) consecutive evaluations, start at 0.32 mg/kg/day, divided every 4 h–6 h, orally. If score persists ≥ 8 on 3 (or ≥ 12 on 2) consecutive evaluations, increase by 0.16 mg/kg/day every 4 h–6 h, to a maximum of 1.0 mg/kg/day. Most tapering protocols decrease dose by 10% of the total daily dose, every 48 h–72 h, depending on NAS scores. http://pcmch.on.ca/ClinicalPracticeGuidelines/NeonatalAbstinenceSyndrome.aspx	Most commonly used as first-line treatment in Canada Does not contain alcohol Short half-life (9 h) When NAS scores are stable (< 8) for 48 h–72 h, consider weaning.
Methadone	Synthetic complete m-receptor agonist; N-methyl-D-aspartate receptor antagonist	0.05–0.1 mg/kg/dose every 6 h–12 h, orally Increase by 0.05 mg/kg every 48 h Maximum dose 1 mg/kg/day	Long half-life (26 h) Used in many countries as a first-line treatment (instead of morphine) when mother is on methadone. Available in Canada but requires special dispensing /prescriptive authority Contains 8% alcohol
Phenobarbital	Gamma aminobutyric acid (GABA) receptor agonist	May be used in addition to morphine, especially in poly-substance abuse cases. Loading dose: 10 mg/kg, orally, every 12 h for three doses Maintenance dose: 5 mg/kg/day, orally. Wean by 10% to 20% every day or every two days when symptoms are controlled.	Long half-life (45 h–100 h) Requires blood level monitoring May make GI symptoms worse Sedative effect Contains 15% alcohol
Clonidine	Alpha-2 adrenergic receptor agonist	Alternative therapeutic option in combination with morphine. Especially effective when autonomic symptoms of NAS are present. Start at 0.5 mcg/kg, divided every 4 h–6 h, orally. Wean by 25% of the total daily dose every other day (Q4h to Q6h × 48h, to Q8h × 48h, to Q12h × 48h to HS, then d/c)	Alcohol-free preparation available Long half-life (44 h–72 h) Abrupt discontinuation may cause rapid rise in blood pressure (BP) and heart rate (HR). Gradual weaning is therefore recommended.
Buprenorphine	Semi-synthetic partial m-receptor agonist, k-receptor antagonist	4–5 mcg/kg/dose every 8 h; sublingual route Maximum dose 60 mcg/kg/day	Half-life (24 h–60 h) Sublingual administration of a dilution of buprenorphine solution in ethanol and sucrose Contains 30% alcohol

Data taken from ref. (19). d/c, discontinue; HS, bedtime.

(Table 1). Few studies have examined pharmacotherapy efficacy. The American Academy of Pediatrics recommends matching drug selection to the type of agent causing withdrawal (19). Morphine and methadone remain the most common first-line medications, with lack of evidence for which agent is superior (38). Compared with oral morphine, sublingual buprenorphine has recently been shown to reduce length of stay in hospital by 42% in symptomatic infants born to mothers on methadone (39). Adjunctive use of phenobarbital or clonidine therapy to treat opioid withdrawal has been studied and implemented in some guidelines (40,41). Published guidelines provide information on initial dosing, dosing increments, initiating additional treatments and weaning, to assist in a consistent approach to management (42).

DISCHARGE CONSIDERATIONS

Length of stay in hospital varies depending on prenatal drug(s) exposure, severity of withdrawal, symptoms, treatment and social factors (42). Observe for a minimum of 72 h. If the treatment threshold is not reached within that time, the infant becomes eligible for discharge (43). The key to successful transition home is to ensure continuity of care by an interprofessional team, with anticipatory planning for when the infant meets criteria for discharge.

Individualized discharge planning should include appropriate referral to a primary health care provider familiar with pharmacological treatments for opioid withdrawal, nutritional and family supportive resources and infant neurodevelopmental assessment. Communicating with the infant's biological (or where necessary, foster care) family and the primary HCP about the discharge plan and follow-up is essential. In some situations, when adequate medical and social follow-up is available, infants may be discharged home on pharmacological support (44,45). There are a few studies, for a select group of infants, which have demonstrated that infants can be managed safely in an outpatient setting without increasing treatment time (46). Benefits of home-based detoxification include: decreasing length of hospital stay and associated health care costs, promoting infant–caretaker attachment and increasing breastfeeding rates (47). Of course, these benefits must be weighed against possible risks. Before discharge, the infant should be demonstrating tolerance of pharmacological tapering, with consistent withdrawal scores < 8. Also, a clear, documented medications weaning plan should be in place for the HCP and family to follow. Other community referrals to consider may include ongoing maternal substance abuse treatment programs, public health and child and youth services, a community support worker, infant development programs and/or parenting support groups. Also, the families and/or guardians must show they can provide a supportive and safe home environment (48).

Summary

Opioid-dependent mothers should be informed that their infant, who has been exposed to natural, semi-synthetic or synthetic opioids during pregnancy, will require observation for symptoms and signs of neonatal withdrawal following birth. Antenatal consultation by perinatology, paediatrics and/or neonatology is encouraged.

All infants at risk for developing neonatal opioid withdrawal should be evaluated using a reliable, valid neonatal withdrawal score instrument.

Information and guidelines for HCPs on managing infants born to opioid-dependent mothers should outline the continuum of care. Strategies to support keeping mothers and infants together and breastfeeding are essential. Providing nonpharmacological interventions, such as skin-to-skin contact, developmental positioning, comfort measures, minimizing environmental stimuli, ensuring adequate nutrition and providing pharmacological treatment when indicated, are key components of a comprehensive plan.

An effective and well-coordinated discharge plan that involves an interprofessional health care team and outlines a comprehensive medications weaning schedule, is essential to ensure seamless transition from hospital to community, and for maintaining continuity of care.

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