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NEONATAL ABSTINENCE SYNDROME

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ABSTRACT

Sudden discontinuation of drugs during pregnancy can result in neonatal abstinence syndrome (NAS). Both illicit and legal substances can lead to a substance use and addiction disorder and in-utero exposure to substances. The Finnegan scoring system is commonly used to assess the severity of NAS. Neurodevelopmental deficits, cognitive delays, and mood/behavioral disorders often occur in children with a history of NAS. Pharmacological and nonpharmacological treatments for signs and symptoms of infant withdrawal are discussed. NAS is currently not well understood, and more research is required to guide clinicians in the assessment and the long-term effects of NAS on children with prenatal drug exposure.

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Statement of Learning Need

Neuropsychiatric disorders associated with children that have a history of neonatal abstinence syndrome may be difficult for newer clinicians to identify. Once diagnosed with NAS, the child and family members will need consistent clinical follow up and support to address the symptoms and potential complications that may manifest as the child develops.

Course Purpose

To educate health clinicians on neonatal abstinence syndrome, its diagnosis and treatment, as well as the growing incidence of maternal substance use and addiction affecting an unborn fetus.

Target Audience

Advanced Practice Registered Nurses and Registered Nurses

(Interdisciplinary Health Team Members, including Vocational Nurses and Medical Assistants may obtain a *Certificate of Completion*)

Course Author & Planning Team Conflict of Interest Disclosures

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There is no commercial support for this course.

Please take time to complete a self-assessment of knowledge, on page 4, sample questions *before* reading the article.

Opportunity to complete a self-assessment of knowledge learned will be provided at the end of the course.

1. **Which of the following is considered a *primary* cause of the neonatal abstinence syndrome?**

    a. Excessive noradrenergic activity
    b. Dehydration
    c. Decreased adrenergic stimulation
    d. Hypoxia

2. **The onset of neonatal abstinence syndrome can be _____ after birth.**

    a. two to four hours
    b. <24 hours to seven days
    c. two to three weeks
    d. one to two months

3. **Which of the following are *common* signs of the neonatal abstinence syndrome?**

    a. Hypothermia and bradycardia
    b. Seizures and drowsiness
    c. Agitation and sleep disturbances
    d. Respiratory depression and seizures

4. **True or False: In-utero exposure to opioids can be confirmed by laboratory testing.**

    a. True
    b. False

5. **The first-choice therapy for neonatal abstinence syndrome is:**

    a. Clonidine.
    b. Supplemental oxygen.
    c. Morphine.
    d. Supportive care.

Introduction

Neonatal abstinence syndrome results from fetal in-utero exposure to prescription or illicit drugs. The pathophysiology, signs and symptoms of neonatal abstinence syndrome has been a topic of discussion in the literature and continues to be not well understood. The Finnegan scoring system is commonly used to evaluate the severity of neonatal abstinence syndrome. Pharmacological and nonpharmacological treatments for signs and symptoms of infant withdrawal are discussed.

Historical Overview Of Neonatal Abstinence Syndrome

Neonatal abstinence syndrome is the condition of opioid withdrawal that occurs in the immediate postnatal period. Neonatal abstinence syndrome (NAS) was first formally identified in the medical literature in 1975,[1] but it has long been present. Opioids have been used for centuries and there are reports from the late 1800s documenting neonatal abstinence syndrome. This very old problem, however, has become more common in recent years, and there is clear evidence that the incidence of NAS is increasing.[2-4]

Tolia, *et al*., found that from 2003-2014 the number of neonatal intensive care unit (NICU) admissions for treatment of NAS increased from 7 cases/1000 admissions to 27 cases/1000 admissions.[2] Data examined by Patrick, *et al*., showed that from 2002 to 2012 neonatal abstinence syndrome increased by a factor of five,[5,6] and Kozhimannil, *et al*., using data gleaned from National Survey of Drug Use and Health (2005-2014) noted that almost 1% of pregnant women and 2.3% of non-pregnant women reported *non-medical* use of opioids.[7]

Opioids easily transfer across the placenta and the fetal blood-brain barrier, and if a pregnant woman is using or addicted to opioids, or being treated with opioids, this represents a significant risk for the child. Although the data is old, Hudak, *et al*., reviewed the literature and found that 55% - 94% of neonates exposed in utero to an opioid had developed withdrawal symptoms.[8] Most infants do not suffer severe consequences, but seizures, death, and cardio-respiratory compromise have been reported.[9-12] There are long-term effects as well,[10,13] and the length of stay and hospital costs associated with NAS are considerable.[14]

Neonatal abstinence syndrome can be caused by drugs other than opioids, and withdrawal would be a more accurate description of this clinical situation. However, NAS has been the traditional and commonly used term when referring to withdrawal signs and symptoms caused by in-utero exposure to opioids.

Basic Pharmacology of Opioids

Opioids are a commonly prescribed class of drug that are primarily used for their analgesic properties. The opioids work by binding to opioid receptors located in the brain, the spinal column, and many other areas, subsequently producing an inhibitory effect on the target tissues and organs. The primary effects of opioids are analgesia and sedation, but depending on the location of the opioid receptors they can also cause constipation, cough suppression, miosis, and nausea and vomiting. In high doses, opioids decrease ventilation, can cause coma and hypotension, and may cause hypoxic seizures and acute lung injury.

The commonly used opioids produce a strong feeling of euphoria, and this can be a powerful enticement for people to take the drug again and again.

Unfortunately, opioids also have significant potential for opioid use disorder and addiction, which is an enormous public health problem. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) identifies opioid use disorder as a pattern of use that is problematic. It is accompanied by significant impairment, leads to tolerance, and, if drug use is stopped, causes withdrawal. The adverse effects of opioid use disorder are numerous and severe and include physical, emotional, social, and psychological harm.

Chronic opioid use causes profound alterations in the dopaminergic pleasure center of the brain and downregulates opioid receptors, and these changes cause tolerance and put the user at risk for withdrawal. Tolerance is defined as the need for higher doses to produce the same level of euphoria, and withdrawal is the dysphoric syndrome that is caused when the brain's pleasure center and opioid receptors are not stimulated by an opioid. These are powerful incentives to keep taking the drug.

Pathophysiology Of Neonatal Abstinence Syndrome

The pathophysiology of neonatal abstinence syndrome is not completely understood, but the clinical presentation suggests that it is *primarily* caused by excessive noradrenergic activity and by changes in cholinergic, dopaminergic, and serotonergic transmission.[11,15,16] In addition, two primary effects of opioid drugs, changes in intracellular potassium and an inhibition of cAMP synthesis, are involved as well.[11,15,16]

Changes in Intracellular Potassium

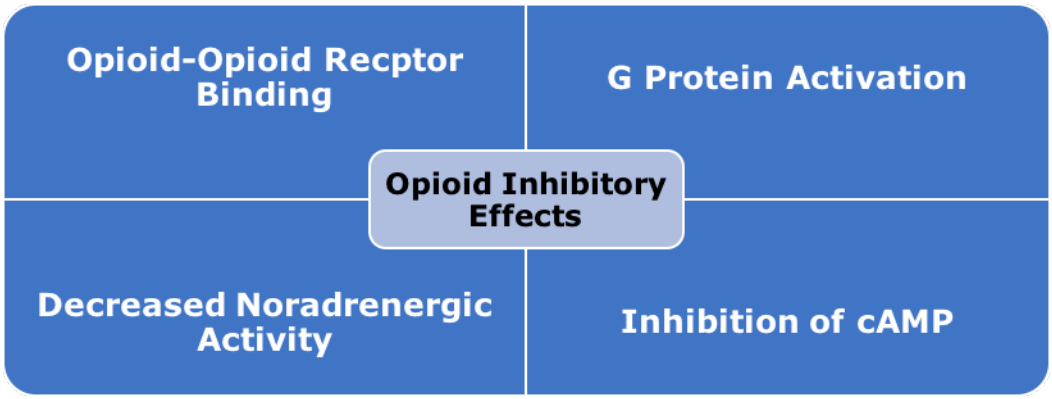
Opioid binding to opioid receptors causes an influx of potassium and increases intracellular potassium concentration. This increases membrane

potential and hyperpolarizes cells, making them less able to initiate or respond to an action potential.

Inhibition of cAMP Synthesis

Endogenous and exogenous substances that are unable to cross cell membranes can influence cellular activity by way of the cAMP second messenger system. A ligand, in this case an opioid, binds to an opioid receptor on the cell and opioid receptors are linked G protein receptors. The G protein receptors act as intracellular switches and, when they are stimulated by opioid binding, they *inhibit* the synthesis of cAMP, which acts as a second messenger by activating intracellular proteins. This, in turn, causes a specific response, and the type of response that occurs depends on the proteins and cells that are targeted. In this instance, the inhibition of cAMP by opioids decreases the activity of noradrenergic neurons that would normally have an excitatory and stimulating effect on the central and peripheral nervous system.

Opioids, G Proteins, and cAMP



These changes in intracellular potassium and cAMP synthesis upsets the normal balance between excitatory and inhibitory neuronal action. The body

responds by upregulating the cAMP signaling pathway and increasing the activity and production of acetylcholine, dopamine, norepinephrine, and serotonin, and these adaptations do effectively offset the inhibitory effect of opioids. However, when opioid use is abruptly stopped - when there is withdrawal - these changes are unopposed. The compensatory increases in neurotransmitters are now the drivers of NAS, and intense over-activity of norepinephrine and the other neurotransmitters, unchecked by the presence of opioids, cause agitation, diaphoresis, GI disturbances, tachycardia, and the other signs and of withdrawal.

The fetus is particularly vulnerable to opioid withdrawal. Opioids easily cross the placenta and the fetal blood-brain barrier. The half-life of opioids is longer in a fetus than it is for a child or an adult; and, as gestation increases so does the movement of opioids across the placenta.[15]

Clinical Presentation And Assessment Of NAS

The timing of the onset of neonatal abstinence syndrome is variable and likely depends on the half-life of the opioid and when the last dose was taken.[10,11,15,16] Infants exposed to heroin, a drug with a short half, will often begin withdrawing a day or two after birth; whereas, methadone has a much longer half-life and the onset of withdrawal has been noted to begin three days or more after birth.[11,15]

These estimates of the time of onset of neonatal abstinence syndrome should be used as basic and imprecise *guidelines*. Withdrawal may occur 24 hours after birth or it may be delayed up to seven days after birth, and there is no way to reliably predict when it will begin.

Signs and Symptoms

Common signs and symptoms of the neonatal abstinence syndrome are listed in Table 1.[9-11,15] Clinicians should, rather than memorizing this list or any other, understand that NAS will primarily cause autonomic nervous system, central nervous system, and gastrointestinal system disturbances.

Table 1: Signs and Symptoms of Neonatal Abstinence Syndrome

Agitation
Excessive crying
Fever
Irritability
Myoclonic jerks
Poor feeding
Sleeping disturbances
Seizures
Tachycardia
Tremors
Vomiting

As mentioned earlier, the onset of signs and symptoms can occur within 24 hours of birth or it may be delayed up to seven days. The intensity of the signs and symptoms ranges from mild to severe, and a more serious clinical presentation *may* be more likely if 1) the fetus had in utero exposure to other drugs, 2) the infant is full-term at birth, 3) the infant is a male, 4) the mother's health and nutrition are poor, 5) drug use during pregnancy is excessive, and 6) the syndrome is not quickly recognized.[10,14,15,17,18]

Assessment of NAS

The Finnegan Neonatal Abstinence Scoring Tool or its modified version appear to be the assessment tools most commonly used for determining the

presence and severity of neonatal abstinence syndrome,[8,10,15,19] and they can be used to monitor the effectiveness of therapy, as well.[15] The modified version can be viewed by referencing Hudak, *et al*.,[8] or D'Apolito.[19]

There are three primary categories in the Finnegan assessment tool: central nervous system, metabolic/vasomotor/respiratory, and gastrointestinal; and, in each category there are specific items the clinician must look for and assess. Examples are provided in Table 2. The scoring for the items is 1 -5 and if the total score is 8 or higher, pharmacologic treatment should be started.[19]

Table 2: Finnegan Neonatal Abstinence Scoring Tool

Central Nervous System
Continuous high-pitched cry – 3 points **Sleeping < one hour after feeding – 3 points**
Metabolic, Vasomotor, Respiratory
Fever > 101° - 2 points **Respiratory rate, > 60/minute with retractions – 2 points**
Gastrointestinal
Projectile vomiting – 3 points **Loose stools – 2 points**

The Finnegan Neonatal Abstinence Scoring Tool is considered valid, but it is not designed to be used for pre-term (<37 weeks) and older (age > 30 days) infants.[11] It is also relatively complex and because of the subjective nature of several of the assessment items, scoring inconsistencies are

possible.[19] However, D'Apolito points out that if clinicians are well trained in its use and the assessment items are clearly defined, accurate and consistent assessments can be done quickly and easily.[19]

Confirming In-Utero Exposure to Opioids

Neonatal abstinence syndrome is a clinical diagnosis, but it is important for the health of the child and for legal and social issues to have objective confirmation of in-utero exposure to opioids. Confirmation of in-utero opioid exposure can be done by testing an infant's cord blood, hair, meconium, or urine.[10,15] Each test has benefits and limits, and testing meconium and urine appears to be done most commonly.

A urine test will detect opioids within three days of maternal use, and meconium testing will detect opioids from the beginning of the second trimester.[10,15] The initial tests are screening tests and if these tests are positive for opioids, confirmation by more time-consuming and complex procedures should be done.[15] There are natural, synthetic, and semi-synthetic opioids, and not all screening tests can detect all drugs in each of these categories.[15]

Testing a neonate's meconium or urine for opioids is usually done if there is/are 1) indisputable evidence of maternal opioid use, 2) strong indicators of maternal opioid use, or 3) a self-report by the mother of opioid use. However, experience has shown that basing the decision to test on identified use, risk criteria and/or self-reporting by a mother will not identify all cases of maternal opioid use.[20,21] Some researchers have recommended that in areas where opioid use is endemic, universal, consent-based screening for opioid use should be done on all pregnant women.[20]

Treatment Of Infants With NAS

Treatment of an infant who has neonatal abstinence syndrome is symptom-based. If the diagnosis is certain or there is a strong possibility the syndrome is present, an assessment should be done at birth and every three to four hours during hospitalization,[11] and, depending on the score, non-pharmacologic therapy, pharmacologic therapy, or a combination of the two can be used. The orthodox recommendation is that infants who have been exposed in-utero to an opioid should be observed for four to seven days,[8,11,22] but there is little evidence supporting this.[22]

Non-Pharmacologic Therapy

Non-pharmacologic therapy is the first choice for treating infants who have neonatal abstinence syndrome,[11,15] and it should be continued even when pharmacologic therapy is being used.[11] Except for breastfeeding, (discussed later in this section) these treatments have not been well studied[10,23] but they are inexpensive, non-invasive, and simple to implement. In addition, non-pharmacologic treatment may be sufficient for mild cases of NAS and it can reduce the need for pharmacologic therapy.[15] The following table lists the varied non-pharmacological treatments for neonatal abstinence syndrome.[10,11,15,23-26]

Table 3: Non-Pharmacological Treatments for Neonatal Abstinence Syndrome

Breastfeeding
Frequent feeding
Massage
Minimizing excess sensory distraction
Music therapy
Parental presence
Rocking
Rooming in
Soothing
Swaddling

Pharmacologic Therapy

Non-pharmacologic supportive care is the first choice for treating infants who have neonatal abstinence syndrome but in most cases, it is insufficient and pharmacologic intervention is required.[11,15,34,35] However, despite the common need for and use of medications in this situation, there are no standards of care or universally used protocols for what drugs to use, whom they should be used for, or at what dose or for how long.[10,11,15,36] In addition, little research has been done that has compared the drugs (*i.e.*, methadone, morphine) commonly used to treat infants who have neonatal abstinence syndrome.[15]

Standardized protocols for using medications to treat infants who have NAS are often absent in clinical practice,[37] but when they are in place and conscientiously followed, the patient's hospital stay is shortened and less pharmacological intervention is needed.[37-39] Medications are typically started when supportive care is ineffective. Additionally, medications are considered needed when the infant has serious withdrawal complications like fever and seizures, has prolonged diarrhea and vomiting and is dehydrated, and/or the assessment scores are high.[8,10,15] If medications are needed they should be given without hesitation. Treatment delays are associated with increased morbidity and length of hospital stay.[15]

The drugs most commonly used for treatment of neonatal abstinence syndrome are shown in the figure below and discussed in more detail in the following section.

Drugs To Treat Neonatal Abstinence Syndrome

Opioids

Opioids are the mainstay of pharmacologic treatment of neonatal abstinence syndrome,[8,10,11,15] and morphine and methadone are the drugs of choice.[8.10,11,15] There is no *proven*, distinct advantage that favors either morphine or methadone for treating NAS,[34,35] and comparative studies of their respective benefits and disadvantages have produced conflicting results.[40-42] Morphine has a shorter half-life than methadone so dose titration would be easier, but it is more likely than methadone to cause respiratory depression. Methadone solutions may contain alcohol. Morphine can provide relief from diarrhea.

Buprenorphine is an alternative to morphine and methadone, but there is comparatively little clinical experience with buprenorphine for this application.[11,15,34] Tincture of opium and paregoric have been used to treat neonatal abstinence syndrome but are no longer recommended,[10,11,15] Dosing the infant can be done using a mg/kg dose or a fixed dose that is determined by the severity of the withdrawal signs and symptoms; the two approaches have not been directly compared.[35] Frequent (every three to four hours) assessments should be done and the dose can be increased, remain the same, or be tapered, or another medication can be added as

needed.[15] Cardiopulmonary monitoring should be in place for the duration of opioid therapy.

Adjunctive Medications

Clonidine is a centrally acting alpha-adrenergic receptor agonist. It is commonly prescribed for adults who are undergoing supervised opioid withdrawal, and it has been used as a single agent or added to opioid therapy to treat infants who have neonatal abstinence syndrome.[11,15] Streetz, *et al*., did a recent (2016) literature review (case studies and clinical trials, involving a total of 272 patients) and the authors concluded that the limited data "... *suggest that clonidine, in combination with other agents or as monotherapy, may be as effective, with minimal adverse effects and reduced treatment time."*[43] Adverse effects of clonidine include bradycardia, hypertension, hypotension, sedation, and respiratory depression.

Phenobarbital is a long-acting barbiturate and it is an excellent sedative.[11,45] It can be helpful if an infant has severe signs of withdrawal and opioids are not effective.[11,15] The use of this drug as an adjunctive treatment or a primary treatment for neonatal abstinence syndrome has been little studied. Some researchers have found that phenobarbital is as effective as morphine as a stand-alone therapy[44] but there is conflicting evidence as to whether adding phenobarbital to an opioid treatment regimen will decrease the duration of hospital stay or reduce the infant's requirements for opioids.[11]

Diazepam, chlorpromazine, and other sedatives should not be used. They have long half-lives and their use is associated with complications.[15]

Opioid antagonists, particularly naloxone, can precipitate a sudden and intense withdrawal and cause seizures. They should not be used for infants who have been exposed in-utero to opioids.[11,15]

Breastfeeding

Literature reviews and single studies have shown that the severity of neonatal abstinence syndrome and the need for pharmacologic treatment are reduced if infants are breastfed,[26-29] and a shorter hospital stay may be possible, as well.[30] Breastfeeding increases mother-child attachment and bonding, and the release of oxytocin may help reduce maternal stress levels. The Academy of Breastfeeding Medicine encourages breastfeeding in women who are on a stable, well-managed program of methadone or buprenorphine.[30]

A small amount of methadone is excreted in breast milk, and breastfeeding appears to be safe if the mother has been taking methadone;[11,31,32] the same may be true of buprenorphine but there is less information about this drug and breastfeeding.[11,31,33] Hydrocodone, and oxycodone are highly concentrated in breast milk.[15]

Breastfeeding may not be safe or acceptable in all cases of neonatal abstinence syndrome, and it should be discouraged if:[11,31]

- The mother is not involved in substance use treatment.
- There are no in-place plans for post-partum substance use treatment.
- The mother has not received prenatal care.
- There has been a relapse and return to illicit drug use or legal substance use.
- The mother shows signs of substance use.

- There is a positive maternal toxicology screen at the time of delivery for illicit drugs or drugs of a substance use disorder.

Long-term Effects Of In-Utero Opioid Exposure

Neonatal abstinence syndrome can be severe but serious morbidity with lasting harm and/or deaths are uncommon. The average duration of stay for treatment of neonatal abstinence syndrome has been reported to be three weeks, but it can resolve in a week or the infant may need to be hospitalized for over a month.[6,36] As mentioned, deaths are uncommon, although some older research has reported a relatively high mortality rate.[46-48] Unfortunately, the immediate effects of NAS may not be the only harmful outcome caused by in-utero exposure to opioids.

Organ System Damage

Although the A-D and X pregnancy classification system is no longer used to describe the teratogenic effects of drugs, the commonly used opioids were categorized as category C - no adequate and well-controlled studies of these drugs during pregnancy - and prenatal exposure to opioids was thought not to be harmful to the fetus.[49] However, current drug information databases (*i.e.*, Lexicomp®) for drugs such as oxycodone and expert sources suggest that the opioids are teratogenic. In addition, opioid use during pregnancy has been associated with an increased risk for early delivery, poor fetal growth, and stillbirth.[50]

Unfortunately, there is comparatively little research that has been done examining what, if any, organ system damage may be caused by in-utero exposure to opioids, but what is available is not reassuring. Stover, *et al.,* note that prenatal opioid use has "... *been associated with numerous*

obstetrical complications including intrauterine growth restriction, placental abruption, preterm delivery, oligohydramnios, stillbirth..."[16] and there is evidence that in-utero exposure to these drugs negatively affects the development of the nervous system and cognitive and psycho-social functioning.

Results from human cell cultures, animal studies, and relatively small scale studies on infants and children suggest that prenatal exposure to opioids can have many adverse effects on neural tract development, including but not limited to, decreased brain volume, decreased myelin formation, changes in neurotransmitters, decreased white matter maturation, and an increased rate of programmed neuron death.[51-54] Further, Broussard, *et al*., in a study done for the National Birth Defects Prevention Study found an association between maternal therapeutic opioid use and atrioventricular septal defects, conoventricular septal defects, gastroschisis, and hypoplastic left heart syndrome.[55]

Research has suggested an association between in utero exposure to opioids and visual pathologies including (but not limited to) anterior chamber defect, decreased visual acuity, delayed visual maturation, glaucoma, and strabismus.[49] *Viteri, et al*., from their 2015 review of the literature, indicated that "*Altogether, it appears that there might be grounds to reconsider the long-held view that opioids are not teratogenic*."

Cognitive and Behavioral Effects

There is evidence that both in-utero exposure to opioids and neonatal abstinence syndrome can cause cognitive and behavioral abnormalities and social issues,[11,13,56-61] problems that begin in childhood and persist into adolescence and beyond.

Table 4: Cognitive/Behavioral Effects of In-Utero Opioid Exposure and Neonatal Abstinence Syndrome

Attention problems
Behavioral disorders
Decreased cognitive functioning
Decreased social functioning
Hospitalization due to maltreatment and trauma
Low IQ
Mental disorders

The evidence however shows association not causation, and there are many prenatal and postnatal factors (*i.e.*, economic, parental, social) that could explain why these infants are at risk for developing cognitive and behavioral problems.[15]

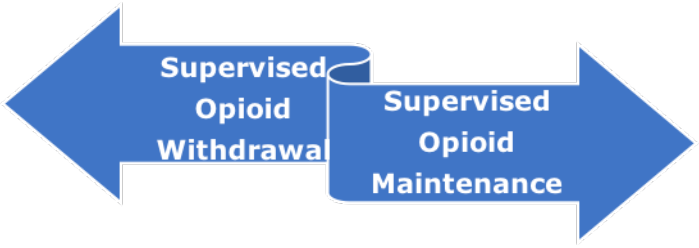
Treatment Of Pregnant Women With Opioid Use Disorder

Allowing a pregnant woman who has an opioid use disorder to continue her drug-taking pattern is obviously not acceptable, as the opioids are potentially very harmful for her physical and psychological health and the health of her child. And sudden withdrawal, commonly called going *cold turkey*, is inadvisable as this can cause serious fetal harm and fetal death.[62,63] The treatment then of a pregnant woman who has opioid use disorder presents clinicians with a choice, a choice that reduced to its simplest terms is this: prescribe supervised opioid maintenance *or* supervised opioid withdrawal.

Supervised Opioid Withdrawal

For many years, supervised opioid withdrawal for pregnant women was thought to be dangerous for the fetus and potentially harmful for the

mother, as this therapy was thought to cause fetal death and increase the rate of relapse of opioid use.[62] Current thinking is that supervised withdrawal does not increase the risk of fetal death, but it is associated with a high rate of relapse, and by itself it does not decrease the incidence of neonatal abstinence syndrome.[63-65]



Supervised Opioid Maintenance

Supervised opioid withdrawal with methadone is the treatment recommended by the American College of Obstetricians and Gynecologists,[63] and this approach has been successfully used since the 1970s. The dose should be sufficient to prevent withdrawal signs and symptoms and craving, but not so high that the patient becomes excessively drowsy. Pregnancy affects the bioavailability and pharmacokinetics of methadone, so close monitoring of the patient is necessary.[62]

Buprenorphine is a partial mu opioid receptor agonist and it has been successfully used for supervised opioid maintenance therapy in pregnant women.[62,63,66] Buprenorphine is often combined with naloxone and although naloxone is usually not recommended in these situations because of the risk of fetal withdrawal, there is some evidence that the combination can be safely used for supervised opioid maintenance.[62] Methadone and

buprenorphine have the same mechanism of action and there is no consensus as to which is more effective for supervised opioid maintenance in pregnant women. However, prescribing one or the other involves more than the consideration of effectiveness. There are important differences between these drugs including, but not limited to, adverse effects, drug interactions, how and where they can be prescribed, and potential adverse effects on the fetus.[62]

Summary

Along with the increased use of opioids in the United States, the incidence of opioid use during pregnancy has also increased and consequently, neonatal abstinence syndrome has become more common, as well. NAS is typically a clinical diagnosis, but laboratory confirmation of in-utero opioid exposure should be done.

Commonly seen signs of neonatal abstinence syndrome include, but are not limited to agitation, excessive crying, fever, poor feeding, sleep disturbances, and tachycardia. Serious complications such as seizures are uncommon and if the syndrome is quickly detected and promptly treated, death is very unusual.

There are three primary categories in the Finnegan assessment tool: central nervous system, metabolic/vasomotor/respiratory, and gastrointestinal; and, in each category there are specific items the clinician must look for and assess. The scoring for the items is 1 -5 and if the total score is 8 or higher, pharmacologic treatment should be started.[19]

Treatment of NAS should begin with symptomatic and supportive care. Unless there are specific contraindications, breastfeeding is encouraged and it has been shown to be an effective treatment. If symptomatic and supportive care are not sufficient, morphine or methadone are the first-choice drugs. Clonidine and barbiturates can be used as adjunctive therapies.

Research is limited but there is evidence that the opioids may be teratogenic and that in-utero exposure to opioids may cause physical damage to the fetus. There is also evidence that suggests that in-utero exposure to opioids and NAS may cause cognitive and behavioral problems that persist through childhood and adolescence.

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Completing the study questions is optional and is NOT a course requirement.

1. **Which of the following is considered a *primary* cause of the neonatal abstinence syndrome?**

    a. Excessive noradrenergic activity
    b. Dehydration
    c. Decreased adrenergic stimulation
    d. Hypoxia

2. **The onset of neonatal abstinence syndrome can be _____ after birth.**

    a. two to four hours
    b. <24 hours to seven days
    c. two to three weeks
    d. one to two months

3. **Which of the following are *common* signs of the neonatal abstinence syndrome?**

    a. Hypothermia and bradycardia
    b. Seizures and drowsiness
    c. Agitation and sleep disturbances
    d. Respiratory depression and seizures

4. **True or False: In-utero exposure to opioids can be confirmed by laboratory testing.**

    a. True
    b. False

5. **The first-choice therapy for neonatal abstinence syndrome is:**

    a. Clonidine.
    b. Supplemental oxygen.
    c. Morphine.
    d. Supportive care.

6. **A first-choice drug for treating neonatal abstinence syndrome is:**

    a. Morphine.
    b. Phenobarbital.
    c. Clonidine.
    d. Diazepam.

7. A first-choice drug for treating neonatal abstinence syndrome is:

a. Lorazepam.
b. Fluoxetine.
c. Methadone.
d. Amitriptyline.

8. True or False: Breastfeeding is absolutely contraindicated for infants who have neonatal abstinence syndrome.

a. True
b. False

9. Long-term effects of neonatal abstinence syndrome may include

a. susceptibility to infection.
b. cardiac arrhythmias
c. liver disease.
d. cognitive deficits

10. Pregnant women who have opioid use disorder should be treated with

a. supervised opioid maintenance therapy.
b. abrupt withdrawal.
c. supervised opioid withdrawal.
d. medical monitoring.

Correct Answers:

1. **Which of the following is considered a *primary* cause of the neonatal abstinence syndrome?**

    a. Excessive noradrenergic activity

    "*The pathophysiology of neonatal abstinence syndrome is not completely understood, but the clinical presentation suggests that it is primarily caused by excessive noradrenergic activity and by changes in cholinergic, dopaminergic, and serotonergic transmission.*"

2. **The onset of neonatal abstinence syndrome can be _____ after birth.**

    b. 24 hours to seven days

    "*Withdrawal may occur 24 hours of birth or it may be delayed up to seven days after birth, and there is no way to reliably predict when it will begin.*"

3. **Which of the following are *common* signs of the neonatal abstinence syndrome?**

    c. Agitation and sleep disturbances

    "*Commonly seen signs of neonatal abstinence syndrome include, but are not limited to agitation, excessive crying, fever, poor feeding, sleep disturbances, and tachycardia. Serious complications such as seizures are uncommon and if the syndrome quickly detected and promptly treated, death is very unusual.*"

4. **True or False: In-utero exposure to opioids can be confirmed by laboratory testing.**

    a. True

    "*Confirmation of in-utero opioid exposure can be done by testing an infant's cord blood, hair, meconium, or urine.*"

5. The first-choice therapy for neonatal abstinence syndrome is:

d. Supportive care.

"*Non-pharmacologic supportive care is the first choice for treating infants who have neonatal abstinence syndrome but in most cases, it is insufficient and pharmacologic intervention is required.... Treatment of NAS should begin with symptomatic and supportive care.*"

6. A first-choice drug for treating neonatal abstinence syndrome is:

a. Morphine.

"*Opioids are the mainstay of pharmacologic treatment of neonatal abstinence syndrome, and morphine and methadone are the drugs of choice.*"

7. A first-choice drug for treating neonatal abstinence syndrome is:

c. Methadone.

"*Opioids are the mainstay of pharmacologic treatment of neonatal abstinence syndrome, and morphine and methadone are the drugs of choice.*"

8. True or False: Breastfeeding is absolutely contraindicated for infants who have neonatal abstinence syndrome.

b. False

"*Literature reviews and single studies have shown that the severity of neonatal abstinence syndrome and the need for pharmacologic treatment are reduced if infants are breastfed, and a shorter hospital stay may be possible, as well.... Treatment of NAS should begin with symptomatic and supportive care. Unless there are specific contraindications, breastfeeding is encouraged and it has been shown to be an effective treatment.*"

9. Long-term effects of neonatal abstinence syndrome may include

d. cognitive deficits.

"*Unfortunately, there is comparatively little research that has been done examining what, if any, organ system damage may be caused by in-utero exposure to opioids, but what is available is not reassuring. [...] there is evidence that in-utero exposure to these drugs negatively affects the development of the nervous system and cognitive and psycho-social functioning.... There is evidence that both in-utero exposure to opioids and the neonatal abstinence syndrome can cause cognitive and behavioral abnormalities and social issues, problems that begin in childhood and persist into adolescence and beyond.*"

10. Pregnant women who have opioid use disorder should be treated with

a. supervised opioid maintenance therapy.

"*The treatment then of a pregnant woman who has opioid use disorder presents clinicians with a choice, a choice that reduced to its simplest terms is this: prescribe supervised opioid maintenance or supervised opioid withdrawal.... Supervised opioid withdrawal with methadone is the treatment recommended by the American College of Obstetricians and Gynecologists, and this approach has been successfully used since the 1970s.*"

References Section

The References below include published works and in-text citations of published works that are intended as helpful material for your further reading.

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