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The Opioid Exposed Newborn: Assessment and Pharmacologic Management

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Abstract

The infant exposed to opioids in utero frequently presents a challenge to the neonatal care provider in the assessment and treatment of symptoms of Neonatal Abstinence Syndrome (NAS) after birth. This review is intended to provide the health care professional with a brief review of current evidence and practical guidelines for optimal evaluation and pharmacologic management of the opioid exposed newborn.

Introduction

The problem of illicit drug use and abuse of licit drugs among women of child bearing age continues to be a public health concern in the U.S. Illicit opioid use is found in 0.1% of all pregnant women in the US[1], and prescription opioid abuse is an increasing problem due to several reasons, including regulatory shortcomings and lack of public education[2–4]. Methadone is currently the only accepted pharmacotherapy for opioid dependence during pregnancy in the U.S., and it has become the standard of care for this population. Methadone maintenance offers major advantages for opioid dependent pregnant women, including diminished illicit opioid use[5, 6], improved attention to maternal medical conditions and nutrition and the creation of a more stable postnatal environment for the infant[7]. Buprenorphine, a partial opioid agonist, is being used more commonly as an alternative to methadone for treatment of opioid dependency during pregnancy. Buprenorphine may offer advantages, particularly for the neonate in the form of reduced severity of NAS, for this population[8], but has not been approved for use during pregnancy in the US.

Maternal opioid and methadone use during gestation predisposes the infant to signs and symptoms of central and autonomic nervous system regulatory dysfunction, traditionally defined as Neonatal Abstinence Syndrome (NAS), which frequently results in significant morbidity and prolonged hospital stays. Any opioid used by the mother during pregnancy can produce NAS in the infant; a list of some opioids that can cause this syndrome in exposed infants appears in Table 1. It is important to recognize that many opioid exposed infants are in actuality poly-drug exposed, and the contributory effect of other licit and illicit substances, including alcohol and nicotine, to the signs and symptoms of physiologic and behavioral dysregulation after birth must be considered, but is beyond the scope of this discussion. NAS occurs with notable variability, and the variability in NAS expression is not well understood currently. Most researchers agree that NAS severity is not related to maternal methadone dose or cumulative methadone exposure in utero[9, 10]. Presenting symptoms of the disorder occur generally within the first 48–72 hours after birth, but some infants can present with significant symptoms of NAS up to 4 weeks of age[11]. Duration of symptoms is also variable, and infants can exhibit subacute NAS symptoms for many weeks to months after birth[12]. Symptoms of dysregulation and autonomic instability occur with variable severity in different infants, as

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well as in the same infant over the course of time. Most, if not all, opioid exposed infants experience NAS to some degree[13]. Non-pharmacologic therapy should be the standard of care for all opioid exposed infants, regardless of the additional need for medication therapy required by some infants. For a subset of infants with NAS, non-pharmacologic therapy[14] alone is insufficient to prevent significant morbidity, including the inability to sleep, feed, failure to thrive and seizures. For these infants, early identification is warranted for the institution of appropriate pharmacologic management. The longer the delay in initiating medication therapy in such infants, the greater the risk of increased infant morbidity[15].

Evaluation of the Opioid Exposed Newborn

There have been a few scoring scales developed for newborns affected by NAS. The purpose of these scales is to allow a systematic, objective, periodic, and thorough evaluation of the newborn to determine the course of NAS and the need for pharmacologic therapy. It is important to note that these scales are designed for full term infants, as preterm neonates do not possess similar capacities for NAS expression[16]. The three most commonly used tools include:

The Finnegan Neonatal Abstinence Scoring System[17]

The 31 item scale is designed to quantify the severity of NAS and to guide treatment, and is administered every 4 hours. The individual NAS symptoms are weighted (numerically scoring 1–5) depending on the symptom, and the severity of the symptom expressed. Infants scoring an 8 or greater are recommended to receive pharmacologic therapy. The most comprehensive of scales, it is found to be too complex by many nurseries for routine use [18].

The Lipsitz Neonatal Drug-Withdrawal Scoring System[19]

The 11 item scale, with each symptom numerically scored (0–3) based on severity of symptoms, designates a score of 4 as recommended for the institution of pharmacologic therapy. This scale has been recommended by the American Academy of Pediatrics[18]. However, it provides only subjective ratings of gross individual symptoms expressed by affected infants; 4 items only list yes/no outcome responses.

The Ostrea tool [20] is a 6 item simple ranking (rather than numeric) scale. Despite its relative ease of use, it does not allow for summing of multiple symptoms of NAS, and offers no guidelines for pharmacologic therapy, and is largely viewed as insufficiently comprehensive by treatment providers.

Other tools available are

The Neonatal Withdrawal Inventory[21]—An 8 point checklist of 7 NAS symptoms with a 4 point behavioral distress scale, with pharmacotherapy instituted after the first score of 8.

The Neonatal Narcotic Withdrawal Index[22]—This scale consists of 6 signs of NAS plus an “other” category of 12 additional signs. Items are scored 0–2 points, and a score of ≥5 indicates pharmacotherapy.

Many institutions in the U.S. use some variant of the Finnegan scoring tool despite its complex nature; it is the most comprehensive of scales and the most widely referenced. In general, infants scoring over a certain numerical threshold, representing numbers and/or severity of symptoms presenting, are treated with medication. The goal of medication therapy is stabilization of more severely symptomatic infants, allowing them to eat, sleep, gain weight and interact with caregivers, and then a gradual reduction or weaning of medication to allow hospital discharge.

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Pharmacologic treatment of the opioid exposed newborn

Just as standardized evaluation tools vary from institution to institution, so do medication regimens used to treat NAS. When treating an infant with opioid withdrawal, most U.S. neonatology services use methadone (20%) and opioids other than methadone (63%) [23]. For initial therapy for NAS, many hospitals today use an alcohol free oral morphine sulfate (0.4 mg/mL) preparation; morphine hydrochloride (0.2 mg/mL) solution, has also been found to be effective[24, 25]. Other drugs used for the treatment of NAS that contain the same morphine equivalent as oral morphine solution include diluted tincture of opium and paregoric. Diluted (25-fold) tincture of opium contains a small amount of alcohol, causing many providers to use morphine preparations to avoid unwanted effects of alcohol on the infant. Paregoric was one of the first agents used for treating NAS, but its use has declined due to the potential toxic effects of many of its ingredients, which include camphor (a CNS stimulant), benzoic acid (use associated with acidosis, CNS depression, seizures and death in premature infants) and a high concentration of alcohol (~45%); paregoric is not recommended for use today. Methadone is used by some institutions, but the lengthy and variable half-life in children (range 3.8 to 62 hours; mean(SD) 19.2(13.6) hours)[26] makes this medication's efficacy difficult to gauge in the newborn, for whom changes in status can occur quickly. Diazepam, though used by some treatment centers, has fallen out of use for multiple reasons, including impaired neonatal excretion and late-onset seizures[18].

Due to the variability of NAS itself, which necessarily includes the often underestimated and unknown effects of other licit and illicit drugs, randomized controlled trials for the evaluation of optimal treatment for NAS are difficult, and there is a general dearth of scientific evidence in this arena. Previous comprehensive reviews of pharmacologic management of NAS have been performed[27,28], and these authors, in general, conclude that there exists a lack of strong evidence on the relative efficacy of different pharmacological regimens for the treatment of NAS. Opioid agonist medications are thought to be the most effective agents in the treatment of neonatal neurobehavioral problems related to in utero opioid exposure[28], however, the Cochrane review, a comprehensive review of studies of NAS treatment, fails to identify a specific opioid as optimal for the treatment of infants undergoing opioid withdrawal[29]. Opioid replacement medications for use in the neonate have included morphine, diluted tincture of opium (DTO) and methadone. A 2005 study found that oral morphine was as effective as DTO[30] in treating NAS, with the advantage of avoiding the effects of alcohol present in DTO preparations. A trial comparing methadone to morphine or DTO found that the medications were comparable in terms of length of hospital stay for the neonate[31]. DTO in addition to phenobarbital was effective in reducing the severity of NAS and duration of hospitalization in another study[32]. Buprenorphine, a partial μ-pioid agonist has recently been found to be a safe a novel effective treatment for NAS[33], as has clonidine[34,35], an α_2 agonist, yet both of these agents have undergone little scientific study for efficacy.

The effects of maternal use of other substances on the course of NAS are variable and unclear. It is likely that infants exposed to multiple illicit or licit drugs in utero may benefit from multiple drug[28] or tailored drug regimens depending on exposures, but this has not been proven. Polydrug withdrawal is primarily treated with opioids alone (52%) and in combination with Phenobarbital (32%) [23]. Most institutions use second line medication therapy, including clonidine or Phenobarbital[21] to treat infants whose symptoms are not well controlled using an opioid. Clearly there is a need for further research in this area.

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An assessment and pharmacologic management algorithm for the opioid exposed newborn

The following is a description of an evaluation tool and medication therapy algorithm to treat infants with NAS. Due to the great variability in NAS presentation, controlled, blinded trials of scale and treatment algorithm efficacy are difficult if not impossible to perform. This tool and treatment schedule is a suggestion for the optimal management of infants with NAS, and has been in use at the Center for Addiction and Pregnancy, an urban multidisciplinary comprehensive care treatment center for drug dependent pregnant and post partum women and their infants and children since 1991[36].

Assessment

Infants identified as prenatally opioid exposed are evaluated, beginning at birth, with vital signs and a modified version of the Finnegan Neonatal Abstinence Scoring System, presented in Table 2. The original scale has been modified in the number of items administered, with some item removed either due to: overlap with other items (i.e. frantic sucking of fists is often an offshoot to hypertonicity or sometimes used by the infant as a self soothing mechanism), items non-responsiveness to medication therapy (i.e. myoclonic jerking, mottling) or consolidation of items (regurgitation and projectile vomiting, watery/loose stools, tachypnea with retractions, and nasal flaring). Two items are added. Irritability was added to encompass those infants who express irritability (i.e. grimacing, discomfort) without crying, and failure to thrive was added to include infants whose hypertonicity or excessive movements caused significant weight loss.

All opioid exposed infants should have continuous monitoring, via a cardiorespiratory monitor or pulse oximetry, due to the potential for respiratory depression secondary to medications and seizures due to NAS[37]. Infants are scored every 3 hours throughout their hospital stay. It is ideal to evaluate and score infants at the third hour after the last score, so that in the event a repeat score need be applied after one hour, the maximal time interval between scores (4 hours) is not breached The NAS score delivered at any point in time should reflect the infant's complete neurobehavioral repertoire for the entire time period since the last score was given. This assessment is ideally done by the caregiver for the infant, usually the assigned nurse, as the symptoms can be variable and the more time spent understanding the infant's signs and symptoms of NAS, the more accurate the scoring and subsequent treatment will be. However, for hospitals caring for mother-infant dyads in a rooming-in fashion information from mothers must be obtained. The nurse should frequently monitor these dyads to ascertain the accuracy of NAS symptom reporting, as some mothers may not be truthful in order to either get medication therapy for their infant, or assure their infant's hospital discharge without medication therapy. Maternal involvement in the infant's care in the postnatal period, however, is an important aspect of non-pharmacologic care for the infant[14].

The scoring items are described below. It is important to recognize the contribution of infant state during each evaluation period:

Excessive cry

is a weighted item that can be scored as either 2 or 3 based on severity. Many infants with NAS cry more often than non-exposed infants, and the cry is high pitched in general. This item should be scored for times when discomfort (i.e. post circumcision, soiled diapers, need for feeding, etc.) has been alleviated. For infants that cry often and are difficult to console, a score of 2 is applied. For infants who cannot stop crying with comfort measures, i.e. are inconsolable even with a pacifier, swaddling and rocking a score of 3 is applied.

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Sleeping

refers to the amount of time that the infant sleeps continuously between feedings and scoring periods. Infants sleeping less than 1 hour at a time are scored 3, sleeping 1–2 hours 2, and 2–3 hours 1, and those sleeping 3 or more hours continuously score 0. The score is based on the longest period of sleeping time during the scoring session. An exception to this scoring is the breastfed infant, particularly the smaller breastfed infant, who may feed every 2 hours in the perinatal period. A breastfed infant feeding every 2 hours consistently would not be scored 1 for awakening at less than 3 hours, but the scale adjusted to the infant's physiologic feeding schedule. Another exception is the older infant, capable of maintaining a quiet alert state. For this group of infants, the time spent in quiet alert (i.e. interacting with mother) can be added to the sleep period to obtain the total sleep for that scoring period. Alternately, the total time spent in the last scoring period fussing or irritably crying may be totaled and subtracted from 4 hours to obtain the amount of sleep time that is scored. Either method serves to allow the infant to spend time in a quiet and organized or interactional state that is not a sleep state without being considered as having sleeping or state control problems as part of his repertoire of NAS expression. Older infants who continue to have distorted sleep/wake patterns should continue to be scored for sleeping less than 3, 2 or 1 hours.

Moro reflex

An exaggerated Moro reflex is scored 1, and consists of a hyperactive response with excessive abduction at the shoulder and extension at the elbow, with or without tremors. Score of 2 is applied for the response above plus marked adduction flexion at the elbow with arms crossing to the midline. The Moro reflex can be scored in all states, but it is optimal to score this item in a drowsy or quiet awake state.

Tremors

are involuntary movements that are rhythmical in nature and generally of equal amplitude. Tremors that occur in the absence of stimulation are deemed undisturbed, those that occur with any stimulation (including unwrapping a swaddled infant), disturbed. Tremors are generally bilaterally symmetrical, but mild asymmetries can be noted, particularly if the head is not in the midline. A score of 1 is applied for mild tremors, occurring frequently in fussy or crying states and occasionally in quiet alert states. A score of 2 is applied for moderate to severe tremors, occurring occasionally in drowsy states, often in quiet alert states, and consistently in fussy or crying states, or consistently and repeatedly in all states. Myoclonic jerks are involuntary rapid muscle contractions that occur during sleep, and may be asymmetrical. These are not tremors, and are not included in the scoring of this item.

Increased muscle tone

Tone is the resistance of parts of the body to passive movement, and can be observed with the infant at rest and assessed by testing the infant's motor resistance with gentle handling. The infant's arms and legs are passively extended and released to assess recoil. Hypertonia is increased resistance to extension or flexion; the extremity returns to its prior position spontaneously. Infants scoring 1 for hypertonia have generalized increased resistance to extension or flexion of the limbs (slight flexion or extension is possible) which is palpable on handling, and head lag on pull to sit. Infants with exaggerated increased tone, or those infants whose increased tone can be visualized without handling, and/or have increased resistance to extension of their limbs with difficulty in straightening or bending the arms with or without head lag (or alternatively have chin tuck) on pull to sit, score 2. Infant tone should be evaluated at rest and with gentle handling, in quiet alert and mildly fussy states, but not when the infant is rigorously crying or overstimulated. Infants experiencing NAS may have fluctuating tone, i.e. tone may be increased during handling, but normal at rest – this is also deemed hypertonia.

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Asymmetries in tone are not uncommon, but should be brought to the attention of a provider for full assessment to rule out neurological complications. Assessment of the infant with the head in midline will avoid the contribution of the asymmetric tonic neck reflex to any asymmetrical response.

Excoriation

is redness of the skin or broken/bleeding skin that is the result of rubbing an extremity or face on a linen covered surface and is generally found on elbows, knees, nose and/or chin due to excessive and uncontrolled movements of the extremities (tremors) and/or head (rooting). Facial excoriations may occur due to the neonate clawing at his face. Infants with excoriation are scored for this as long as the excoriation is present. A score of 1 is applied if the skin is red, but intact or is healing. A score of 2 is applied if the skin is broken. Excoriations in the diaper area (scored as excoriations) should be distinguished from diaper dermatitis (not scored as excoriations) due to loose stools. Diaper dermatitis is a red, irritated rash that starts from the anus and gradually spreads outward. Diaper area excoriation is red, irritated or broken skin on either side of the gluteal folds, and is due to excessive motor movements of the infant.

Generalized seizure

Infants exhibiting any seizure activity should be brought emergently to the attention of a neonatal provider. The incidence of seizures as a symptom of NAS is low, but if present, are scored 8.

Hyperthermia

Elevations in body temperature should be assessed by a provider to rule out infection, and if no infection is present are scored as long as fever is present. A score of 1 is applied for any axillary temperature of 37.3 C (99.0 F) or higher.

Yawning, sweating, nasal stuffiness and sneezing

These symptoms represent alterations in autonomic nervous system regulation. A score of 1 is applied for an infant yawning 4 times or more within the 3–4 hour testing period. Sweating can be defined by dampness of the infant's forehead or upper lip, taking care that the infant is not overbundled. A score of 1 is applied for any nasal noise on breathing, and may or may not be associated with coryza and is not associated with illness. Stuffiness can result from overzealous nasal suctioning, and this should be avoided if possible to accurately assess the infant. If the infant sneezes 4 or more times within the 3–4 hour assessment period, either individually or continuously, a score of 1 is applied. Autonomic dysregulation symptoms may be subtle, with or without stimulation, and assessed in any state.

Tachypnea

(respiratory rate > 60 breaths per minute) should be scored 2 if the infant is tachypneic at rest (sleep, drowsy or quiet alert states) and not in fussy or crying states. Assessment of these infants to rule out other medical conditions is essential.

Poor feeding

When present, poor feeding is scored 2. Infants who feed poorly may do so for a variety of reasons, and the infant exhibiting this symptom requires additional and careful assessment. Poor feeding does not always imply a suck/swallow incoordination problem, and can be due to positioning difficulties due to hypertonia, sensory integration difficulties, etc. Infants displaying suck/swallow incoordination difficulties can be recognized by an inefficient suck, inefficient sucking pattern (short bursts of relatively weak sucks, despite excessive or strong

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sucks before the feed), maladaptive tongue positioning, including tongue thrusting or placing tongue above or to the side of the nipple, formula loss at the sides of the mouth (can be secondary to ineffective lip closure around nipple), gulping or clicking noise with sucking, and often take frequent breaks from feeding to breathe, burp or spit up. These infants typically require long periods of time and nursing intervention for every feed.

Vomiting

Defined as the effortless return of mouth, esophageal and/or stomach contents from the mouth. Small amounts of formula or milk lost during burping ("wet burp") do not constitute vomiting. A score of 2 is applied for infants that vomit either a whole feed or two or more times during a feed, not associated with burping or vomits large amounts with burping. Projectile vomiting may indicate other pathology and should be referred to a provider for assessment.

Loose stools

A ½ liquid, ½ solid stool or a liquid stool with or without a water ring on the diaper is assigned a score of 2.

Failure to thrive

should be scored at any scoring time the infant's weight is less than 10% below his birth weight, which may occur continuously over several scoring periods and several days.

Irritability

There are infants with NAS who manifest irritability or fussiness, particularly with light touch or handling despite attempts to console, but may not cry excessively or at all. Irritability can be otherwise expressed as grimacing or appearing sensitive to touch, light or sound, displaying symptoms such as gaze aversion, pull down, , etc. and can occur distinct from, or in conjunction with, crying. This sensitivity can be expressed in various ways depending on the infant. Dysregulated behaviors in response to any internal or external stimuli or rapid changes of state (termed poor state control, defined as moving rapidly between sleep/wake and quiet/fussy periods with little modulation between states) would constitute irritability. Minor irritability is defined as an infant that calms/whose behaviors become more regulated only with intervention and displays 1 symptom of irritability. A score of 2 is applied for an infant that displays 2–3 signs of irritability and is consoled only with intervention after time. A score of 3 is applied for an infant in whom no amount of consoling reduces the symptoms of irritability.

Infants are scored in this fashion, and the total score (the tally of all individual scores for that 3–4 hour time period) recorded. The total score should reflect the category of NAS, 0 to V, that the infant currently resides in, which are outlined at the top of Table 2.

Pharmacologic management

Infants requiring medication therapy should always receive such therapy in a hospital setting for three reasons. First, most medications used to treat NAS can cause respiratory depression in infants and require inpatient monitoring. Second, the infants are born to opioid dependent individuals. For this population, access to an opioid, even one that is accessible in small amounts that would not yield any appreciable effect for an adult, may be a trigger for relapse to substance abuse or put them in danger of other people with addictions who may desire the medication. Third, symptoms of NAS can provide the infant with significant morbidity, and the variability in course puts infants not being frequently assessed by trained providers at risk for either over- or under-medication. Premature hospital discharge can place affected newborns at significant risk for ensuing morbidity, maternal relapse and infant abuse. While it is true that infants treated with medication frequently require lengthy inpatient hospital stays, this period

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of time can be used to provide parenting assessment and intervention, assessment of maternal post partum medication requirements and psychiatric status of the mothers, as well as the facilitation of post partum drug abuse treatment.

This algorithm for the treatment of infants with NAS uses a symptom-based, as opposed to a weight-based treatment protocol. Many pediatricians are most comfortable using a weight-based approach to any medication in newborns. However, the presentation of the NAS spectrum of physiologic and behavioral symptoms is very variable, much more variable than infant birthweight, as are the frequent changes in infant withdrawal status that occur in such infants. This makes applying increasing doses of opioid replacement medication for increasing severity of NAS symptoms, until a manageable plateau of symptom expression is reached, a more feasible way to treat this disorder. Additionally, the application of medication dosing based on infant weight is presumably done to attain a specific plasma level of drug to appease the symptoms of NAS. Plasma methadone levels in infants with and without NAS are generally not defined. There is no simple relationship between maternal or neonatal plasma methadone concentrations and the occurrence or severity of NAS[38].

Infants scoring in category 0 (a total NAS score of less than 9) continue to be monitored and receive supportive care. Any infant having a score greater than 8 is rescored in one hour. Rescoring after a short time interval allows more accurate assessment of the infant and disallows pharmacologic intervention for a temporary fussy state, i.e. an infant experiencing overstimulation due to an external stimuli such as a wet diaper. If the infant continues to score in a category other than 0 after one hour, medication therapy is instituted based on the severity of symptoms and category of NAS. Infants scoring between 9 and 12 receive 0.04 mg morphine sulfate solution, those scoring 13–16 receive 0.08 mg, those scoring 17–20 receive 0.12 mg, and so on. The higher of the two scores greater than 8, if they are in different categories, is the one used to determine initial treatment. Once medication therapy has begun, it can be adjusted upwards as needed to allow the infant to regain some self-regulatory control, which will be expressed as a reduction in NAS scores to 8 or less. For persistent scores in Category I, morphine is increased by 0.02 mg, for category II 0.04 mg, and so on. It is important to medicate infants at an interval no longer than every 4 hours, as longer dosing intervals have been found to be associated with longer hospital stays[39]. Medication is delivered with infant feeding, and sleeping infants should be awakened and medicated at 4 hours to avoid rebounding increases in NAS scores and unnecessary increases in medication dose. The goal of medication is to keep the infant stable in category 0. The infant is then maintained on the dose of medication that allows him to remain in category 0 with all NAS scores below 9 for a 48 hour period.

After the 48 hour period of stabilization, the infant may then be gradually weaned from medication. Morphine can be weaned by 0.02 mg every 24 hours as long as NAS scores remain in category 0. The weaning process is deferred for one score in category I. Should the infant receive a score in category I, he should be rescored in one hour. If the infant has 2 NAS scores in category I, then treatment must be reescalated. It is important to recognize that some infants have a biphasic course of NAS, with two rather than one peak NAS severity. In general, re-escalation doses are half of the initial doses, as increased NAS severity after an initial period of stabilization is generally of reduced symptom intensity. To reescalate treatment, increase morphine by 0.01 mg every 3 – 4 hours for 2 scores in category I. For two scores in category II, increase morphine 0.02 mg, for 2 scores in category II, 0.04 mg, and so on. A plateau of scores below 9 for 48 hours is required for reweaning, which occurs as above.

While most infants can be maintained in a newborn nursery that allows for continuous monitoring, some may require NICU admission for a peak of NAS that is unable to be controlled or of unique presentation. Infants receiving greater than 0.20 mg of morphine every three hours may require NICU admission and a secondary medication strategy. Infants that appear

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somnolent or difficult to arouse should be evaluated by a practitioner, keeping in mind that some infants may exhibit symptoms of pull down[14].

In an ongoing study of fetal development in methadone maintained women[40], neonatal outcomes of 88 methadone exposed newborns were analyzed to evaluate the efficacy of the described model (Table 3). Subjects were enrolled at 32 weeks of gestation, and this sample of infants was not exposed to illicit drugs after enrollment as determined by random maternal toxicology testing. Women with alcohol dependence, as determined by the Addiction Severity Index, were excluded from participation. Additionally, women who were non-program compliant, or who either refused to provide a urine specimen for testing or appeared intoxicated were presumed to be clinically positive and were disenrolled from the parent study at any point after study enrollment. All subjects provided informed consent, and the protocol was approved by the governing IRB. Infants were followed from birth until hospital discharge. Infant data was abstracted from the medical record after birth.

No infant was born prior to 37 weeks gestation, none had significant medical complications other than NAS, and none were readmitted to the hospital once they were discharged for symptoms of NAS. There were no significant relationships between infant birth weight and dose of medication required for NAS treatment or length of hospital stay. Put simply, larger babies did not display more severe NAS symptomatology, and therefore did not require larger doses of opioid replacement medication for NAS treatment, as would occur with weight-based medication strategies.

Conclusion

It is important to characterize this evaluation and treatment protocol as a suggestion for optimal management of the opioid exposed newborn as no clinical trials evaluating various aspects of this evaluation exist. Limitations of the study presented include relatively small numbers and the use of a convenience sample; particularly a sample devoid of illicit drug exposure after 32 weeks gestation, which may impair applicability to other populations of poly-drug exposed infants. However, this data does suggest that a symptom-based treatment algorithm for NAS in affected infants might allow the use of less replacement medication therapy for the infant than would be used with a weight-based protocol. Clearly, more research, including blinded, randomized trials comparing symptom-vs weight-based treatment algorithms are needed. It is also important that each institution treating this high risk population of women and infants have a standardized assessment and treatment protocol for the early identification and appropriate treatment for opioid exposed infants. Principally due to the poorly understood pathophysiology of NAS, optimal evaluation and treatment for this disorder continues to evolve. More research is required to determine the optimal management for infants with NAS.

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Table 1

Opioids causing NAS in exposed infants include:

Agonists
Diamorphine (Heroin)
Fentanyl
Hydromorphone
Meperidine (Pethidine)
Methadone
Morphine (including prodrug Codeine)
Oxycodone
Propoxyphene
Mixed agonists-antagonists
Buprenrophine
Butorphanol
Nalbuphine
Pentazocine

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Table 2

NAS Scoring and treatment form*

NAME:_____ **MR#:**_____

Nursing Instructions

1. If infant scores >8, rescore in one hour
2. Notify physician if two scores, 1 hour apart, >8
3. Give medication as prescribed by physician every 3-4 hours. Do not exceed 4 hours in dosing.

Initiation of morphine sulfate therapy:

CATEGORIES	SCORE	Morphine	= Morphine Sulfate oral solution
0	0-8	0	0.4 mg/ml
I	9-12	0 .04 mg	
II	13-16	0.08 mg	
III	17-20	0.12 mg	
IV	21-24	0.16 mg	
V	>=25	0.20 mg	

SIGNS AND SYMPTOMS	SCORE	Date /time	Date /time	Date /time	Date /time	Date /time	Date /time	Date /time	Date /time	Date /time	Date /time	Date /time	Date /time
Excessive Cry	2 - 3												
Sleeps < 1 hour after feeding Sleeps < 2 hours after feeding Sleeps < 3 hours after feeding	3 2 1												
Hyperactive Moro Reflex Markedly Hyperactive Moro Reflex	1 2												
Mild Tremors: Disturbed Moderate-Severe Tremors: Disturbed	1 2												
Mild Tremors: Undisturbed Moderate-Severe Tremors: Undisturbed	1 2												
Increased Muscle Tone	1-2												
Excoriation (specific area)	1 - 2												
Generalized Seizure	8												
Fever > 37.2 C	1												
Frequent Yawning	1												
Sweating	1												
Nasal Stuffiness	1												
Sneezing	1												
Tachypnea (Respiratory Rate> 60/min)	2												
Poor Feeding	2												
Vomiting	2												
Loose Stools	2												
Failure to Thrive (weight gain ≥ 10% below birth weight)	2												
Excessive Irritability	1 - 3												
TOTAL SCORE / CATEGORY													
INITIALS													

Morphine sulfate solution (0.4 mg/ml) dosing schedule:

Time morphine												
Dose morphine (in mg.)												
Route												
Initials												

* Adapted from Finnegan, 1975[17]

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Table 3

Maternal methadone dose during pregnancy and perinatal outcomes N=88*

Methadone dose (mean, range)	**77.1 mg (20 – 120 mg)**
Pediatric outcomes	
Gestational age at delivery (mean, sd)	39.5 (1.3) weeks
Birth weight (mean, sd)	3,137.0 (528.2) gr
Pharmacologic treatment for NAS	56%
Average modified Finnegan score day1(mean,sd)	4.0 (2.7)
day 2	6.1 (2.7)
day 3	6.0 (2.7)
day 4	5.7 (2.6)
Highest Finnegan score (mean, sd)	11.6 (5.0)
Total mg morphine used to treat NAS (mean, sd)	7.8(10.7)
Total days treated for NAS (mean, sd)	16.1 (11.2)

* data abstracted from Jansson, 2005[40]