COMMENTARY

Neonatal Abstinence Syndrome: Time for a Reappraisal

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The opioid abuse problem in the United States has grown into an epidemic, with an estimated 2.5 million Americans currently dependent on heroin or prescription pain medications.[1] One of the many consequences of this growing public health crisis has been a marked increase in the number of infants born to mothers who used opioids during pregnancy. The rate of neonatal abstinence syndrome (NAS), the syndrome of withdrawal these infants may suffer after birth, quintupled from 2000 to 2012.[2] Often, these infants occupy NICU beds for weeks or even months.[3] Despite these skyrocketing numbers, long lengths of stay, and an enormous strain on the medical system, our standard management of these infants has remained largely unchanged for decades. With a critical reappraisal of our current approach and an eye toward innovation, we can alter our entire paradigm for managing infants with NAS and create opportunities for significant improvements in both patient outcomes and health care expenditures.

The current approach used by many institutions for the management of NAS has its roots in a study published >40 years ago. In 1975, the Finnegan Neonatal Abstinence Scoring System (FNASS) was developed and is now widely accepted as the primary tool to assess infants with NAS. The FNASS is a 21-item tool that lists signs of withdrawal and assigns a point value to each sign. Finnegan and her team developed this score to guide management of infants with NAS and decided, based on their own observations, that infants with scores of ≥8 generally needed pharmacologic treatment.[4] Most institutions have developed protocols that use FNASS scores of ≥8 to trigger the initiation of pharmacologic therapy.

This FNASS-guided approach, though never validated, has gone largely unchallenged since its inception, and it is time to reconsider whether management should be driven by a system that is based so heavily on cataloguing specific signs of withdrawal, many of which may be unrelated to the infant's function or comfort. Is it truly best to give morphine to an infant who yawned 4 times instead of 3, as the FNASS guides us to do? Almost all infants born to mothers dependent on opioids will have some signs of withdrawal, such as hypertonicity or tremors. The FNASS can list the specific signs of withdrawal, but should we not be more concerned with how we manage the infant to allow him or her to function well rather than measuring our success by whether we can reduce the number of sneezes in a given time period?

This reliance on the FNASS to guide our decisions about when to administer medications has also made it difficult to assess the effectiveness of nonpharmacologic interventions, which the 2012 American Academy of Pediatrics policy statement on neonatal drug withdrawal cites as first-line treatment.[5] There is growing evidence that these

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nonpharmacologic interventions, such as creating a low-stimulation environment, swaddling, and feeding on demand, can have a significant impact on clinical outcomes of infants with NAS. Institutions with parental rooming-in models have consistently reported decreases in length of stay and use of medication.[6]

Despite this evidence, most studies of NAS include only infants who receive medications for treatment of withdrawal. This is largely because we are using the FNASS both to diagnose NAS and to guide treatment. If a score of 8 is both the diagnostic cutoff for defining withdrawal and the threshold at which pharmacologic therapy should be administered, how can we ever assess the impact of nonpharmacologic interventions? Looked at another way, if we use intensive nonpharmacologic interventions to reduce the severity of withdrawal signs just enough to decrease the amount of time an infant receives medication, then we can demonstrate a benefit to nonpharmacologic interventions. However, if the effect of nonpharmacologic interventions is strong enough to prevent an infant from receiving medications, then that infant would not be given a diagnosis of NAS, and thus no benefit would be recorded. Although there is some logic in standardizing our assessment of withdrawal severity to allow a better comparison of treatment efficacies and outcomes, we must uncouple this assessment of severity from an automatic initiation of medications if we want to assess the effectiveness of nonpharmacologic interventions.

If we define infants with NAS as only those who receive medication for amelioration of withdrawal signs, only infants who do not benefit from or do not receive first-line, nonpharmacologic interventions actually receive a diagnosis of NAS. This is an unusual approach. Imagine if children with pus behind their tympanic membranes were diagnosed with acute otitis media only after treatment with amoxicillin failed and they were given amoxicillin/clavulanic acid as second-line treatment. That would be ridiculous, yet that is the current approach for infants with evidence of withdrawal. Clearly, nonpharmacologic interventions are not considered to be on the same therapeutic plane as pharmacologic therapy; put simply, it is not thought of as a "real" treatment. In fact, none of the published articles on NAS comparing different drug therapies control for nonpharmacologic interventions, nor are these interventions routinely documented. When a child has a score of $\geq$8, we do not make sure that the mother is at the bedside or review other nonpharmacologic interventions to ensure that they are maximized. We just give morphine.

If we change our definition of NAS back to something closer to the original definition, an infant with prenatal exposure to opioids who develops signs of withdrawal, we may be able to change our perspective on management. Instead of considering only opioid-treated infants as "treated," we can initiate intensive nonpharmacologic interventions for opioid-exposed infants at birth. Thus, all exposed infants can be "treated," although probably only a minority will receive second-line pharmacologic therapy. Once we fully understand the impact of nonpharmacologic interventions on this population, we can create protocols that take full advantage of the power of the maternal–infant dyad. For example, most infants with NAS are managed in NICUs, units that often cannot permit rooming in and have limitations in providing a low-stimulation environment. If we accept that nonpharmacologic interventions are the first-line treatment of NAS, how can we possibly continue to tolerate this practice? Would we ever send a child with asthma to a unit that could not provide albuterol?

There is substantial room for improvement in the care of infants with NAS, and we must start to look at our current approach with a critical eye. Using the FNASS to guide diagnosis and treatment encourages us to treat a number and not the patient. We need to move away from the FNASS to assess these infants and begin to prioritize assessment of the infant's basic ability to function, such as eating, sleeping, and consolability. This change will also uncouple the use of medication from the diagnosis of NAS. Infants with exposure to opioids in utero who develop clear signs of withdrawal, such as hypertonicity or tremors, should be given a diagnosis of NAS. By returning to this definition, we can begin to assess the effectiveness of nonpharmacologic interventions, which can be a powerful therapy and should truly be regarded as first-line treatment. We need innovative approaches to these infants that will help minimize their exposure to additional opioids, reduce hospital stays, decrease costs, and ensure better long-term outcomes.

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