PERSPECTIVES

Optimal Care for NAS: Are We Moving in the Wrong Direction?

Lauren M. Jansson, MD, Martha L. Velez, MD

The growing numbers of infants born to women with opioid use disorder (OUD) and experiencing neonatal abstinence syndrome (NAS), and the increasing costs of their care,[1] has led to a reassessment of prevailing approaches to clinical treatment. Emerging protocols that reduce assessment to limited domains of infant functioning are being adopted and advanced, raising several concerns.

NAS is a "generalized multisystem disorder"[2] causing a dysregulation of the central and autonomic nervous systems that manifests in a variety of physiologic and neurobehavioral signs, unique to each infant, in the domains of sleep-awake control, motor and/or muscle tone, autonomic functioning, and sensory processing and/or modulation.[3] Conventional NAS care incorporates nonpharmacologic treatment (ie, the assessment of the variable dysregulation in specific domains of infant functioning particular to each infant, assessment of maternal capacities to understand and address them, and alterations to the environment and handling to minimize dysregulation with maternal support and education)[3] as the principal, first-line therapy for any substance-exposed infant.[4] Pharmacotherapy is indicated for infants displaying persistently impaired functioning despite maximal, individualized nonpharmacologic treatment. NAS scoring tools, such as the Finnegan tool[5] and variants traditionally used to guide the introduction and weaning of pharmacotherapy, have weaknesses such as subjective scoring and scoring of items that can be attributed to typical newborn behaviors or other conditions, potentially leading to overtreatment and lengthy hospitalizations.

A new approach, the Eat, Sleep, Console (ESC) assessment tool, combined simultaneously with other interventions, including the "nonpharmacologic care bundle(s)," attention to maternal needs, and alterations in pharmacotherapy, is being recently promoted. The ESC approach forgoes the identification and/or description of NAS-associated signs and symptoms that are variable and specific to each infant and their impact on dyadic functioning and development. Instead, ESC focuses on evaluating infants in 3 functional capacities: the ability to eat (infant able to eat $\geq$1 oz per feed or breastfeed well), sleep (sleeps undisturbed for $\geq$1 hour), and be consoled from crying within 10 minutes.[6] Medication for NAS is reserved for infants not meeting these criteria (ie, those unable to eat, sleep, or stop crying despite the significant presence of any other sign or symptom of neurobehavioral dysregulation due to NAS).

Promoters of ESC define as effective outcomes reduced medication, shorter length of hospital stay, and lower cost[6,7] as opposed to outcomes based on defining how the approach achieves optimal care for the infant affected by NAS. Just as there may be harm in supplying more medication than is necessary for NAS treatment, there is likely to exist short- and long-term harm from undertreatment of neonatal neuroregulatory dysfunction. We cannot assume that

www.hospitalpediatrics.org
DOI:https://doi.org/10.1542/hpeds.2019-0119

Address correspondence to Lauren M. Jansson, MD, The Center for Addiction and Pregnancy, Johns Hopkins Bayview Medical Center, 4940 Eastern Ave, D4E, Baltimore, MD 21224. E-mail: ljansson@jhmi.edu

HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Funding support from NIH/NIDA R01 DA041367.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

Dr Jansson drafted the initial manuscript and revised and reviewed the manuscript; Dr Velez revised and reviewed the manuscript; and both authors approved the final manuscript as submitted.

Department of Pediatrics School of Medicine, Johns Hopkins University, Baltimore, Maryland

less medication, 1 of the primary described outcomes of ESC intervention, is better. The goal of any provider should not be to pharmacologically treat as few infants as possible but to identify and treat with medication those infants who exhibit persistent neurobiological dysregulation that impacts the neonatal well-being and/or development despite maximal nonpharmacologic intervention tailored to their NAS expression. Similarly, reduced infant hospitalization days, and hence cost (other described benefits of ESC), may reduce familial disruption and benefit payers and those families that are supportive and able to access comprehensive care and treatment services for the mother and the infant. However, families affected by addiction will have varying levels of resources, distress, and capacity for coping; many families are poorly equipped to manage an infant with NAS, or the mother has not been engaged in OUD treatment. For those families, minimal time to ensure that the infant is thriving or to educate women regarding the care of their infants and/or fewer opportunities to explore and intervene for other issues related to maternal OUD may result in higher and largely immeasurable overall costs for the dyad and society in the long run. For example, longer hospital stay and discharge to a biological parent have been associated with higher enrollment into early intervention services for infants diagnosed with NAS in 1 study.[8]

The minimized appreciation of NAS as the infant's ability to function in only 3 areas is problematic and represents a narrow view of the essential neurobehavioral functioning of a newborn. An unstated premise of ESC is that the signs and/or symptoms of NAS that are displayed by the infant are benign and/or inconsequential, so much so that they need not be described, assessed, measured, or included as important to the short- or long-term treatment of the infant with NAS. In truth, the signs and/or symptoms displayed by a newborn undergoing NAS are central to both understanding the functioning (typical or atypical) of and optimal treatment of the infant by the provider and the mother as well as to the pediatric care of the infant postdischarge.[4] The neurodevelopmental domains of motor and tone control, sleep-awake state organization, autonomic regulation, and sensory processing should be assessed periodically and supported during the neonatal period and beyond to promote healthy development.[9–12] Failure to assess and intervene for concerns in the variable domains affected by NAS can alter neurostructural, neurophysiological, and neuropsychological development in the infant precisely at a critical time of brain development. Protocols permitting a wide range of neurobiologic dysfunction at this critical time of brain plasticity may adversely affect the trajectory of infant development[13] and the dyad's interaction.

The neurodevelopment of the infant with NAS is influenced by the experiences during and after hospitalization. Evidence supports the central importance of the caregiver (maternal and others, including the clinicians) accurately interpreting and appropriately responding to the child's expressions of his or her bodily cues. An environment and handling of a newborn that are not responsive to the impaired functioning of a dysregulated central and/or autonomic nervous system can become a source of early life stress, which can impact the functioning and programming of the hypothalamic-pituitary-adrenal axis[14] and/or cause dysmaturation of the autonomic nervous system,[15] both associated with later neuropsychiatric and medical problems. Parents may develop less ability to respond effectively to their newborn if they do not adequately understand the NAS display beyond the infant's ability to eat, sleep, or stop crying and how to alter handling and the environment to respond effectively to the infant's early signs of stress or dysregulation.

Evidence reported involving ESC interventions has other limitations.[13,16,17] The ESC results are not based on randomized controlled studies of new protocols versus traditional care. Each publication describes different procedures and modifications initiated at different points, and protocols vary in medication management, rooming-in versus NICU care, and nonindividualized nonpharmacologic bundle interventions. These concurrent, varied interventions make it difficult, if not impossible, to assess proponents' claims.[6,7] Baseline rates of pharmacologic treatment were higher in those centers implementing ESC (87%–98%)[6,7] versus others using nonpharmacologic care and standard assessments (~50%–60%).[18,19] Reported results of method implementation are not substantially different from those reported by centers evaluating different methods of care improvement for the infant and/or mother (Table 1). Finally, ESC provides differential treatment to opioid-exposed infants on the basis of a maternal diagnosis of OUD (versus infants with

TABLE 1 Reduction in Pharmacotherapy Rates for NAS by Described Alterations in Treatment

Author, Year	Method Applied	Premethod Incidence, %[a]	Postmethod Incidence, %
Grossman et al,[6] 2017	ESC plus other interventions	98	14
Wachman et al,[7] 2018	ESC plus other interventions	87	40
Welle-Strand et al,[20] 2013	Breastfeeding	80	54
McKnight et al,[21] 2016	Rooming-in	83	15
McCarthy et al,[22] 2015	Maternal methadone split dosing	(60–80; undefined)	29
Wiegand et al,[23] 2015	Maternal medication (methadone versus buprenorphine-naloxone)	52	25
Kelty and Hulse,[24] 2017	Maternal medication (methadone versus naltrexone)	42	8

[a] Of infants prenatally exposed to opioids requiring pharmacotherapy for NAS.

iatrogenic NAS due to treatment with opioids for pain), which is ethically problematic.

There is every reason to support innovation in clinical care that reduces costs, and new treatment paradigms may offer advantages over traditional care. However, new protocols should be studied rigorously and before implementation with ethical safeguards and should contain comprehensive evaluations of the following: (1) short-term infant functioning (including unique neonatal dysfunction and perhaps pain) and neurobehaviors, (2) long-term child functioning (including neurocognitive, social-emotional, and behavioral development), (3) maternal functioning (including treatment adherence, violence exposure, psychosocial characteristics, and psychological and neurocognitive functioning), and (4) dyadic communication (including the infant capacity for yielding interpretable cues and the maternal perception of these cues and of infant development), dyadic interaction (including attachment), and the environment.

The clinician's judgment is paramount, and an instrument cannot replace it. NAS is a complex and poorly understood disorder. Although the Finnegan has limitations, data that have been published by using ESC is insufficient for generalized use, yet this is occurring.[16] The providers adopting ESC are using an unproven instrument that has not been shown to optimize outcomes that may have more problems than the Finnegan. Neonatologists and pediatricians should resist the premise that vulnerable infants should be discharged to vulnerable mothers as soon as possible. Rather, the right starting point for addressing NAS is optimal, nonstigmatized treatment of the pregnant and parenting woman with OUD; universally applied, individualized nonpharmacologic care for infant, defined after thoroughly understanding the unique NAS expression and including the mother; and careful pediatric follow-up with attention to the individual NAS expression of each child and its effect on development. There is a need to assess current NAS treatment and care strategies in the context of the maternal and familial functioning and the environment and to examine models of care for the infant affected by NAS in tandem with the mother affected by OUD that go beyond hospitalization days and pharmacotherapeutic treatment rates to those that promote optimal short- and long-term outcomes for the dyad. To do otherwise may be more harmful than beneficial.

REFERENCES

1. Winkelman TNA, Villapiano N, Kozhimannil KB, Davis MM, Patrick SW. Incidence and costs of neonatal abstinence syndrome among infants with Medicaid: 2004-2014. *Pediatrics*. 2018;141(4):e20173520
2. Kocherlakota P. Neonatal abstinence syndrome. *Pediatrics*. 2014;134(2). Available at: www.pediatrics.org/cgi/content/full/134/2/e547
3. Velez M, Jansson LM. The opioid dependent mother and newborn dyad: non-pharmacologic care. *J Addict Med*. 2008;2(3):113–120
4. Jansson LM, Velez M. Neonatal abstinence syndrome. *Curr Opin Pediatr*. 2012;24(2):252–258
5. Finnegan LP, Connaughton JF Jr, Kron RE, Emich JP. Neonatal abstinence syndrome: assessment and management. *Addict Dis*. 1975;2(1–2):141–158
6. Grossman MR, Berkwitt AK, Osborn RR, et al. An initiative to improve the quality of care of infants with neonatal abstinence syndrome. *Pediatrics*. 2017;139(6):e20163360
7. Wachman EM, Grossman M, Schiff DM, et al. Quality improvement initiative to improve inpatient outcomes for neonatal abstinence syndrome. *J Perinatol*. 2018;38(8):1114–1122
8. Peacock-Chambers E, Leyenaar JK, Foss S, et al. Early intervention referral and enrollment among infants with neonatal abstinence syndrome [published online ahead of print May 16, 2019]. *J Dev Behav Pediatr*. doi:10.1097/DBP.0000000000000679
9. Brazelton TB. Assessment of the infant at risk. *Clin Obstet Gynecol*. 1973;16(1):361–375
10. Lester BM, Tronick EZ. History and description of the Neonatal Intensive Care Unit Network Neurobehavioral Scale. *Pediatrics*. 2004;113(3, pt 2):634–640
11. Als H. Toward a synactive theory of development: promise for the assessment and support of infant individuality. *Infant Ment Health J*. 1982;3(4):229–243
12. Ayres AJ. *Sensory Integration and Learning Disorders*. Los Angeles, CA: Western Psychological Services; 1972
13. Gomez-Pomar E, Finnegan LP. The epidemic of neonatal abstinence syndrome, historical references of its' origins, assessment, and management. *Front Pediatr*. 2018;6(33):33
14. Conradt E, Sheinkopf SJ, Lester BM, et al; Maternal Lifestyle Study. Prenatal substance exposure: neurobiologic organization at 1 month. *J Pediatr*. 2013;163(4):989–94.e1
15. Mulkey SB, du Plessis AJ. Autonomic nervous system development and its impact on neuropsychiatric outcome. *Pediatr Res*. 2019;85(2):120–126
16. Schiff DM, Grossman MR. Beyond the Finnegan scoring system: novel assessment and diagnostic techniques for the opioid-exposed infant. *Semin Fetal Neonatal Med*. 2019;24(2):115–120
17. Jones HE, Kraft WK. Analgesia, opioids, and other drug use during pregnancy and neonatal abstinence syndrome. *Clin Perinatol*. 2019;46(2):349–366
18. Jansson LM, Dipietro J, Elko A. Fetal response to maternal methadone administration. *Am J Obstet Gynecol*. 2005;193(3, pt 1):611–617
19. Jansson LM, Velez ML, McConnell K, et al. Maternal buprenorphine treatment and infant outcome. *Drug Alcohol Depend*. 2017;180:56–61
20. Welle-Strand GK, Skurtveit S, Jansson LM, Bakstad B, Bjarkø L, Ravndal E. Breastfeeding reduces the need for

withdrawal treatment in opioid-exposed infants. *Acta Paediatr*. 2013;102(11): 1060–1066

21. McKnight S, Coo H, Davies G, et al. Rooming-in for infants at risk of neonatal abstinence syndrome. *Am J Perinatol*. 2016;33(5): 495–501
22. McCarthy JJ, Leamon MH, Willits NH, Salo R. The effect of methadone dose regimen on neonatal abstinence syndrome. *J Addict Med*. 2015;9(2): 105–110
23. Wiegand SL, Stringer EM, Stuebe AM, Jones H, Seashore C, Thorp J. Buprenorphine and naloxone compared with methadone treatment in pregnancy. *Obstet Gynecol*. 2015;125(2):363–368
24. Kelty E, Hulse G. A retrospective cohort study of birth outcomes in neonates exposed to naltrexone in utero: a comparison with methadone-, buprenorphine- and non-opioid-exposed neonates. *Drugs*. 2017;77(11):1211–1219