Newborn Critical Care Center (NCCC) Clinical Guidelines

Management of Neonatal Opioid Withdrawal Syndrome
Eat, Sleep and Console (ESC)

BACKGROUND

The use of illegal substances during pregnancy closely mirrors that of the non-pregnant population, with alcohol and tobacco being the most common, followed by cannabis. However, a study of infants born 1999-2014 demonstrated a 333% increase in infants exposed to opioids during pregnancy. Additionally, current trends locally reflect frequent polysubstance use with stimulants such as cocaine or methamphetamine mixed (knowingly or unknowingly) with Fentanyl. Additional exposure comes from medications for opioid use disorder (MOUD); in 2019 "6.6% of surveyed pregnant women reported the use of prescribed opioids during pregnancy, with 1 in 5 reporting misuse of opioids" (D'Angelo, et al, 2019). Prenatal exposure to these substances may cause withdrawal symptoms and a prolonged hospitalization course, therefore it is more critical than ever to evaluate our assessment and treatment of infants with prenatal exposure to opioids and illicit substances.

Neonatal Opioid Withdrawal Syndrome (NOWS, previously described as Neonatal Abstinence Syndrome (NAS)) typically refers to a constellation of symptoms resulting from an opioid withdrawal characterized by behavioral dysregulation that occurs within 2-3 days of birth for infants chronically exposed to opioids in-utero. This includes prescribed drugs such as methadone, buprenorphine (Subutex, suboxone), oxycodone and illicit substances such as heroin, fentanyl, and others. Signs and symptoms of NOWS include altered sleep, hypertonia, tremors, irritability, poor feeding, vomiting/diarrhea, sweating, fever, tachypnea and other autonomic nervous system disturbances.

The Newborn Critical Care Center (NCCC) had previously used the Finnegan scoring system to assess symptoms of NOWS and to determine the necessity of pharmacologic treatment. However, the Finnegan scoring system has never been validated, and cutoffs for treatment have never been tested (Grossman, et al., 2018). Studies have subsequently demonstrated that use of the ESC guidelines is both family-centered and cost-effective. The use of ESC vs Finnegan has led to a substantial decrease in pharmacologically treated infants from 82% to 40%, a decrease in length of stay from 18 days to 10 days, and an average cost savings of $11,000 per treated infant without any increase in readmission or adverse events (Grossman, et al, 2018). As such, many centers have recently shifted to use of Eat, Sleep, Console tool, including UNC.

Eat, Sleep, Console (ESC) is a tool that was initially introduced in 2014 as a collaborative faculty effort amongst Boston Medical Center, Yale, and The Children's Hospital at Dartmouth Hitchcock Medical Center in response to the sharp increase in NOWS cases. The study was created to analyze a more functional scoring approach based on three premises in infants $\geq$ 35 weeks: Can the baby eat >1 oz per feed or breastfeed well? Can the baby sleep undisturbed for $\geq$1 hr? Can the baby be consoled if crying within 10 mins? These three abilities were deemed to be the essential functions of a newborn. This approach also emphasizes that "mom is medicine," with skin-to-skin and breastfeeding viewed both as ways to understand symptoms and to provide treatment.

Assessments with the ESC tool are initiated shortly after birth and continue every 3 to 4 hours after feedings. If the infant is unable to eat, sleep, or be consoled due to withdrawal symptoms, the nurse will have a huddle with the infant's family/caregiver to discuss current non-pharmacologic care being provided. If appropriate, current non-pharmacologic care is reinforced or increased. If, at the next care interval, the infant's withdrawal symptoms continue to interfere with his or her eating, sleeping, or ability to be consoled, the medical team is alerted for another huddle with the nurse and family/caregiver. If at this time non-pharmacologic interventions no longer provide the desired result, as-needed medication may be ordered. If this does not relieve the infant's withdrawal symptoms, scheduled medication may be initiated.

THE TEAM HUDDLE

A team huddle is indicated if the infant has a "Yes" response to any ESC Assessment items or requires much support to soothe, the huddle should include the provider, bedside nurse, and if possible, the infant's parent/caregiver. The team huddle should include any possible ways to optimize non-pharmacologic care, a discussion of the infant's response to consoling interventions, and ways to improve feeding or the environment. All efforts should be made to encourage a parent or support person to be present at all times in order to optimize comfort measures. If all non-pharmacologic interventions have been optimized and the infant continues to have poor feeding, sleeping, or difficulty consoling due to NOWS, then pharmacologic treatments should be considered.

ELIGIBILITY CRITERIA FOR MANAGEMENT WITH ESC APPROACH:

A. Infants ≥ 35 weeks with a history of maternal opioid exposure

ESC ASSESSMENT

A. Does the infant have poor feeding due to NOWS?
    i. **NO**: defined as breastfeeding 8-12 times per day with an effective latch and milk transfer OR feeding an expected volume for age (10-15 mL for first 24 hours, ≥30mL after 24 hours) with an alternative feeding method.
    ii. **YES**: unable to coordinate feeding within 10 minutes of showing hunger OR sustain feeding for at least 10 minutes at breast or take appropriate volume for age (see above) and is demonstrating significant withdrawal symptoms (e.g. fussiness, tremors, uncoordinated suck, excessive rooting).
    iii. ***Special Note***: Do not answer YES if poor eating is clearly due to non-opioid related factors (e.g. prematurity, transitional sleepiness or spittiness in first 24 hours of life, inability to latch due to infant/ maternal anatomical factors).

B. Does the infant sleep less than 1 hour after feeding due to NOWS?
    i. **NO**: Normal sleep patterns for gestational and postnatal age should be taken into account. Sleep < 1 hour may be normal in the first few days after birth, particularly in breastfed infants who are cluster feeding.
    ii. **YES**: Baby unable to sleep for at least one hour after feeding due to opioid withdrawal symptoms (e.g., fussiness, restlessness, increased startle, tremors).
    iii. ***Special Note*:** Do not indicate YES if sleep disturbance is clearly due to non-opioid related factors (e.g., symptoms in first day likely due to nicotine or SSRI

withdrawal, physiologic cluster feeding in first few days of life, interruptions in sleep for routine newborn testing).

C. Can the baby be consoled?
    i. **YES**
    ii. **NO**: baby unable to console within 10 minutes (due to opioid withdrawal symptoms) despite infant caregiver/provider effectively providing any/all of the Consoling Support Interventions below.
    iii. ***Special Note:*** Do not indicate NO if infant's inconsolability is clearly due to non-opioid related difficulties (e.g., caregiver not responsive to infant hunger cues, circumcision pain).

If the infant is <35 weeks, or the answer to any of the above criteria is YES (after accounting for non-opioid related factors), the team should perform a team huddle and discuss the optimization of non-pharmacologic care (see list of non-pharmacologic intervention/methods below). ESC is not a standard practice for the care of preterm infants experiencing withdrawal symptoms, but the sleep and consoling items of ESC Care Tool can be employed. Given the feeding immaturity of premature infants, the eating portion of the tool may need to be excluded. If the infant's feeding ability and tolerance is worse than expected based on the infant's gestational age, then the bedside RN can indicate "Yes" for "Poor eating due to NOWS."

NON-PHARMACOLOGIC METHODS

ESC places emphasis on non-pharmacologic methods of care. Such strategies include partnering with parents at the bedside in infant care, rooming in, skin-to-skin contact with the parent, breastfeeding for eligible infants, and a low-stimulation environment (See ESC Parent Handout (include hyperlink).

Maximizing non-pharmacologic methods include the following concepts:

A. Educating families on the value of maximal presence at the bedside to support the baby during times when consoling is needed
    i. Infant should be cared for in 6 NCCC if at all possible, to allow for parental rooming-in
B. Encouraging the practice of skin-to-skin contact in care
C. Infants should be fed on demand
    i. Breastfeeding can help decrease the incidence of NOWS, the need for pharmacologic treatment, and the length of hospital stay. Breastfeeding is encouraged if mother is active in a treatment program for 3 months prior to delivery with continued participation, with an otherwise negative urine toxicology screen on admission, and no other contraindications to breastfeeding, (see Breastfeeding Medications and Contraindications, Academy of Breastfeeding Medicine Protocols: Substance Use and Breastfeeding for reference). *A lactation consult should be obtained*.
        i. Mothers who have had a positive urine toxicology screen on admission or less than 4 weeks before delivery, but who are in a treatment program and have received adequate prenatal care, should not give breast milk at

time of delivery. However, if mother wishes to establish milk supply and be reconsidered, this can be discussed in conjunction with the treatment program and lactation consult.

1. Horizons contact information: Elisabeth Johnson via epic chat, at 919-966-9803 or at elisabeth_johnson@med.unc.edu
2. www.unchorizons.org

ii. For infants receiving breast milk, additional powder of Similac Sensitive can be added to provide 22 kcal/oz if the infant demonstrates excessive weight loss or inadequate weight gain. If the infant is not breastfeeding, the use of Similac Total Comfort or Similac Sensitive 22 kcal/oz should be the formula of choice unless contraindicated. Discontinue fortification when weight gain is firmly established. Discharge on the higher calorie formula will generally not be necessary.

D. Swaddling and holding can be effective soothing techniques.
E. Diaper dermatitis is common due to diarrheal symptoms and should be diligently attended to for comfort.
F. The environment should be low stimulation (i.e. low lights, soft voices, minimal interruptions to sleep)
G. Consider the utility of the following multidisciplinary consult services:
   i. Occupational Therapy
   ii. Physical Therapy
   iii. Speech Therapy
   iv. Social work

When mother or other family is not available for holding and kangaroo care, consider the use of a vibrating mattress or the SNOO.

TIMING, LOCATION, AND DOCUMENTATION OF ESC ASSESSMENTS

A. ESC care assessments will be documented in the flowsheet section of Epic (see ESC Epic Documentation) (include hyperlink)
B. Assessments will be initiated within 4-6 hours of birth, and should be performed every 3-4 hours at the same time as other routine care such as feedings and vital signs.
C. Add problem for intrauterine drug exposure or neonatal opioid withdrawal syndrome into daily progress note. Document scores using the dot phrase .ESC which will pull in the last 5 ESC scores.
D. Assessments will continue for a minimum of 72 hours for infants exposed to opioids.
E. If the infant requires pharmacologic treatment, ESC assessments will continue for 48 hrs after the discontinuation of opioid replacement therapy.

PHARMACOLOGIC TREATMENT

Pharmacologic treatment should only be considered after proper assessment, huddling, and employment of non-pharmacologic methods has failed to provide appropriate management of symptoms. In centers who employ the ESC methodology effectively and successfully, only 10-40% of infants with prenatal opioid exposure require pharmacologic treatment, with most pharmacologic therapy initiated between day 3-5 of life for methadone and buprenorphine-exposed infants.

If the answer to any of the ESC assessment questions following optimization of non-pharmacologic care continues to be yes, the team should consider a single PRN morphine dose (**0.03 mg/kg/dose PO**).

If the answer to any of the above questions continues to be yes following a PRN dose of morphine x2, scheduled dosing may be considered. Scheduled Morphine dosing should be initiated at **0.03 mg/kg/dose PO q 3 hr** (recommended to accommodate administration with enteral feeding schedule) and **may be titrated up by 0.02 mg/kg/dose PO. Morphine dosing should not exceed 0.12 mg/kg/dose PO.** Of note**, IV and PO dosing are not equivalent**, and PO doses and ranges listed must be converted to IV if infant is NPO. Pharmacy involvement is recommended. However, if unable to contact pharmacy, ***can consider IV dosing to be approximately 1/3 of PO dosing, eg:***

0.03 mg/kg/dose PO = 0.01 mg/kg/dose IV

Considerations for Adjunctive Therapy: Phenobarbital is the drug of choice for infants with a history of polysubstance abuse and/or as an adjunct to morphine therapy. Consider using phenobarbital if polysubstance use is suspected/confirmed (including benzodiazepines, barbiturates, antipsychotics, antidepressants, other sedatives/hypnotics, tobacco). If Morphine dose exceeds 0.12 mg/kg/dose PO, or if unable to wean for 7 consecutive days, a loading dose of phenobarbital (20 mg/kg/dose) should be administered once. A maintenance dose of phenobarbital (5 mg/kg/dose PO) should be administered following the loading dose. Do not weight adjust. Of note, the doses of Phenobarbital used for withdrawal are not high enough to prevent seizures.

WEANING OF PHARMACOLOGIC TREATMENT

A. Once the infant is able to meet ESC criteria for at least 48 hrs may start weaning scheduled dose by 10% of maximum dose every 24 hrs as tolerated.
B. Consider increasing the frequency of weans to two times per day if the infant is doing well.
C. Dose should continue to be weaned until minimum dose of 0.02 mg/kg/dose or unmeasurable.
D. Generally, the dose and not the interval should be weaned. If the infant is unable to successfully wean off of the medication, may consider spacing interval at lowest dose until infant tolerates weaning off.
E. If adjunctive therapy required with phenobarbital, discontinue phenobarbital on second to last step of morphine wean to assess for tolerance of discontinuation. Given the long half-life of phenobarbital, this will wear off gradually over 4 days.

See ESC Algorithm for a summary and quick-reference algorithm for ESC guidelines.

DISCHARGE CRITERIA

All babies with opioid exposure at any point during pregnancy who are deemed at risk for NOWS should be monitored in the hospital for at least 96 hours. Additional criteria to consider:

A. Newborn should be observed off medications (opioids) for a minimum of 48 hours
B. If the length of stay is greater than one week because of withdrawal symptoms, weight gain should be established for a minimum of 48 hours prior to discharge with adequate oral nutrition intake
C. Social Work should have been consulted, a plan of safe care offered, and a referral to a treatment program (if not otherwise already established) should be offered to the mother
D. Concerns regarding child protection and guardianship have been addressed
E. Assess how the home environment will support the mother and baby
F. A warm handoff to the provider who will follow the infant as an outpatient should be performed

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