Neonatal Abstinence Syndrome: An Update

by

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Faculty Disclosure

- I am the developer of the inter-observer reliability program for the Finnegan Scoring Tool.

Objectives

1) Describe the incidence & cost of NAS
2) Discuss non-pharmacologic and pharmacologic strategies to treat NAS
3) Identify factors that can influence the appearance of signs of NAS
4) Discuss one new assessment strategy for treating NAS
5) Identify the misconceptions about the use of the FNAST

What is NAS?

- Causes alterations in functioning:
  - CNS disturbances
  - Metabolic, vasomotor, Respiratory Disturbances
  - Gastro-Intestinal Disturbances

Finnegan, et al, 1975

Drugs Associated with NAS

- Opioids:
- Heroin
- Methadone
- Fentanyl
- Morphine
- Demerol
- OxyCodone
- Buprenorphine

- Nonopioid CNS Depressants
- May present with some or mimic symptoms of NAS
- Benzodiazepines
- SSRI's
- Barbiturates
- Anticonvulsants
- Antipsychotics
- Alcohol
- Gabapentin (Neurontin)

What is Addiction?

- A chronic, relapsing, disease involving drug-seeking and abuse by long-lasting chemical changes in the brain
- Uncontrollable craving, seeking, and use of a substance such as a drug or alcohol

Fenton, et al., 2013; American Society of Addiction Medicine, 2011

NO?? ??? NO?? YES??
YES?? YES?? NO?? YES??
NO?? ARE INFANTS BORN ADDICTED TO DRUGS? YES??
???
YES?? NO?? NO??
??? YES?? ??? YES??

Magnitude of Problem

- 2009-2012 – incidence ↑ from 3.4 to 5.8 /1,000 births (71% ↑)
- KY, TN, Mississippi, Alabama highest incidence (16.2/1000 life births) compared to OK, TX, AK, LA with the lowest (2.6/1000 live births)
- WV 51 cases/1000 live births in 2017 (Dept of Health & Human Services, 2018)

Department of Health & Human Services, WV, 2018 report (https://dhhr.wv.gov/News/2018/Pages/DHHR-Releases-Neonatal-Abstinence-Syndrome-Data-for-2017-.aspx); Patrick, et al., 2015b

Magnitude of Problem

- Population-Based Studies
- 2004-2013 – 7% of NICU admissions from NAS
- 2003-2013 – NAS admissions ↑ from 7/1000 admissions; 27 cases/1000 in 2013
  - LOS ↑ from 13 days to 19 days
- One baby born in US every 25 minutes with NAS

Toila, et al., 2015

Arkansas

- 2013
  - 118 opioid prescriptions written for every 1,000 people (3.5 million prescriptions) compared to 79 written/1000 people in US
  - 5% decline between 2013 & 2015 – 111 opioid prescriptions written/1000 persons
- NAS - ↑from 0.4 per 1000 births in 2004 to 6.2% in in 2013 (7 fold increase)

(NIH, 2018 https://www.drugabuse.gov/drugs-abuse/opioids/opioid-summaries-by-state/arkansas-opioid-summary)

New Information

- Increase in NAS is attributed to misuse of prescription opioids (77% ↑)
- Hospital Readmission 2X as likely
- Male infants (n=484) were more likely to be diagnosed and treated for NAS than female infants (n=443) (9% ↑)

Charles, et al., 2017; Patrick, et al., 2015b

Neonatal Cost of Care

- 4 fold increase from 2003-2012
- 2013 - Cost rose from $61 million with 68,000 hospital days to $316 million with 291,000 hospital days

Carr & Hollenbeak, 2017

Frequency of NAS

- 50-80% of heroin exposed infants develop NAS
- 60-90% of methadone and buprenorphine exposed infants develop NAS
- 60-80% of infants with NAS will require pharmacologic management

Hamdan, et al., 2017; Farid, et al, 2008; Sarkar & Dunn, 2006

Severity of Signs

- Exposure to methadone – more severe signs
- Exposure to buprenorphine – mild signs
- Marijuana – no withdrawal reported, ↑ signs when taken with buprenorphine
- SSRI's
  - Don't exhibit signs of NAS
  - Drug affects
  - Neonatal Adaptation Syndrome

Tolia, et al., 2018; O'Conner, et al, 2017; Hamdan, et al., 2017

Onset of Signs

- Depends upon:
  - Type of drug
  - Additional Substances
  - Timing of maternal dose
  - Infant metabolism
  - Gestational age and birth weight
  - Genetics????

Hudak & Tan, 2012; Ashraf et al, 2014

Onset of Signs

- Alcohol – 3-12 hours
- Barbiturates - 1-14 days
- Buprenorphine – 48 hours (24 – 168 hours)
- Caffeine – At birth
- SSRI – Hours to days
- Heroin (opioids with short t1/2) – 12-24/peak 72 hours
- Methadone – 48 hours to as long as 7-14 days

Hamdan et, al, 2017; Sanz, et al, 2005; Pierog, et al, 1977; Tierney, 2013

Onset of Signs

- Cocaine/Methamphetamine
  - Signs appear 2-3 days after birth
  - Metabolites in during first 7 of life
  - First week: signs are drug effect
    - Irritability
    - Hyperactive Moro
    - Increased sucking

Hamdan, et al., 2017

Clinical Observation

- Infants exposed to drugs with a short half-life, such as morphine, should be observed for minimum of 3 days
- Infants exposed to drugs with a long half-life, such as methadone, should be observed in the hospital for a minimum of 5-7 days

Sanlorenzo, et al., 2018

Premature Infant

- Lower risk of having signs of NAS
  - < 35 weeks more immature CNS
  - Less fat stores
  - Differences in total drug exposure

Hamdan, et al., 2017

Genetics (2013)

- Genes in adults (SNPs)
  - PNOC (Prepronociceptin) – protein nocistatin
    - Mu-opioid receptor (OPRL1)
  - Catechol-0-methyltransferase (COMT)
- Study in Infants
  - 5 hospitals in Mass & Maine
  - DNA samples were genotyped for SNPs, and then NAS outcomes were correlated with genotype.

Wachman, et al, 2013

Genetics (2013)

- 86 mother/infant dyads
- 36wks or greater; exposed to methadone or buprenorphine
- Collected cord blood, maternal peripheral blood, or a saliva sample
- Outcome
  - Variants in the PNOC and COMT genes were associated with a shorter length of hospital stay and less need for treatment

Wachman, et al, 2013

Genetics (2017)

- 113 mother/infant dyads from 2 sites
- Full-term
- Exposed to methadone or buprenorphine
- Other significant drugs of exposure
  - Marijuana
  - Cigarette smoking
  - Other un-prescribed opioids

Wachman, et al, 2017

Genetics (2017)

- Collected cord blood, maternal blood or saliva from all mother/infant pairs
- SNP (Single Nucleotide Polymorphisms)
  - PNOC (Prepronociceptin) alleles
  - COMT (Catechol-O-Methyltransferase) alleles
- Associated with NAS outcomes

Wachman, et al, 2017

Genetics (2017)

- **PNOC**
  - **Mother with PNOC rs4732636 A allele had ↓ need for treatment with medications (p=0.004)***
  - **Mother with PNOC rs351776 A allele had infants treated more often with 2 medications (p=0.04)*and required longer hospitalizations (3.3 days) (p=0.01)***
  - **Mother with PNOC rs2614095 A allele had infant with improved outcomes**

* clinical significance; not statistical

Wachman, et al, 2017

Genetics (2017)

- **COMPT**
  - **Mother with COMPT rs4680 G allele had infants with ↓ risk for treatment with 2 medications (p=0.04)***
  - **Mother with rs740603 A allele had infants who were treated less with any medication (p=0.02)***

* clinical significance; not statistical

Wachman, et al, 2017

Detection & Screening

Testing for drug exposure:

– **Urine**
  - **Obtain as soon as possible after birth**
  - **High false-negative (up to 60%) rate because only reports recent drug exposure**
  - **Tests for recent use of cocaine and its metabolites, amphetamines, marijuana, barbiturates, and opiates**

– **Meconium**
- **Reliable for detecting opioid and cocaine exposure after the first trimester**
- **Can be used to detect a range of other illicit and prescribed medications.**
- **Meconium sample is stored at room temperature, it decreases cocaine and cannabinoid levels by 25% per day.**

Hamdan, et al., 2017

Differences between Meconium and Umbilical Cord

- **Barbiturates: 100% match**
- **Amphetamines: 97% match**
- **Cocaine: 96% (prevalence in meconium)**
- **Opioids: 85% (prevalence in meconium)**
- **Benzodiazepines: 91% (prevalence in cord**
- **Marijuana: 76% (prevalence in meconium)**

Colby, 2017

Detection & Screening

- **Hair Analysis**
  - **Hair begins to form at approximately 6 months' gestation**
  - **Positive result indicates use during the last trimester.**
  - **Hair testing is advantageous because the specimen can be collected at any point during the first 3 months of life, after which time infant hair replaces neonatal hair.**

Hamdan, et al., 2017

Differential Diagnosis

- **Hypoglycemia**
- **Hyperthyroidism**
- **Hypocalcemia**
- **Sepsis**
- **Subarachnoid hemorrhage (seizures)**

Hamdan, et al., 2017

Assessment of NAS

- Many tools used to assess NAS
- FNAST recommended by APA and is the most common tool used to assess for signs of NAS
- Contains 21 of most common withdrawal signs
- Documented as an easy & reliable tool once staff have been adequately trained

Hamdan, et al., 2017

Assessment of NAS

- NNNS (NICU Network Neurobehavioral Scale) (Tronic & Lester, 2013)
  - 2004
  - Neurological integrity & behavioral functioning
  - Requires certification
  - Used in studies
- ESC (Eat, Sleep & Console) (Grossman, et al., 2018)
  - New

Eat, Sleep, Console (ESC)

- Study January, 2018
- Compared ESC with use of FNAST scores in same babies to determine if:
  - Earlier discharge
  - Decreased need for pharmacologic therapy
  - All babies, from what I can see, received non-pharmacologic care

  Note in one diagram, parental presence

Grossman, et al, 2018

ESC

- Study January, 2018
  - Approach
    - Eat $\geq$ 1 oz per feeding or breastfeed well
    - Sleep undisturbed for $\geq$ 1 hour
    - Consoled, if crying, within 10 minutes
    - If not meeting these outcomes, increased nonpharmacologic care or start morphine (0.05mg/kg/3 hours)

Grossman., et al, 2018

ESC

- Eating & Sleeping determined to be essential newborn functions
- If withdrawal signs did not interfere with eating and sleeping, withdrawal was managed
- Did not use FNAST
- Focus: Non intrusive functional approach

Grossman., et al, 2018

ESC

- Goals
  - proportion of patients started on morphine using the ESC approach compared with the predicted number of patients who would have been started on morphine by using the FNASS approach
  - proportion of days each approach recommended pharmacologic management

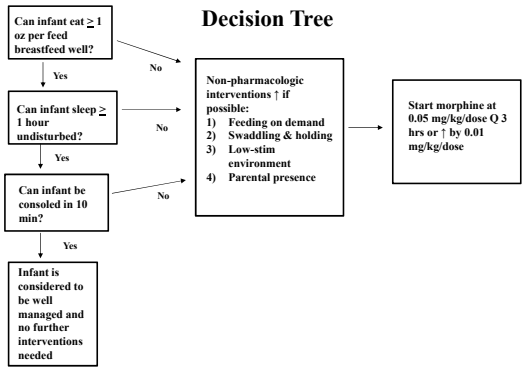
Grossman., et al, 2018

ESC

- Design
  - Retrospective (17 months)
  - Same babies
    - FNAST completed Q 4 hours (experienced nurses but not reliable)
    - ESC administered (not sure when, no protocol)
  - FNAST scores not used for treatment
  - ESC only used for treatment
  - Predicted treatment decisions based on FNAST scores; used average daily score

Grossman., et al, 2018

Decision Tree



Grossman., et al, 2018

ESC

- Results (n=50; 296 days)
  - ESC approach: 6 babies required treatment with morphine compared to 31 infants who would have received treatment using the FNAST approach
  - ESC approach: morphine was initiated or ↑ over total of 8 days (3%) compared to a total of 76 days with the FNAST approach (26%)
  - My assumption: 13 babies did not have issues

Grossman., et al, 2018

Conclusion

- Infants with ESC were treated less with morphine
- ESC is an effective treatment approach for the management of infants with NAS

Grossman., et al, 2018

Sounds Good: More information

- How were the babies consoled? Protocol? Were parents required to hold babies 24/7?
- How consistent was the non-pharmacologic management?
- How often did the babies awaken to eat (on demand feedings)? FNAST completed Q 4 hrs
- Was there an ESC scoring tool or protocol?
- How to determine reliability with this method?

Sounds Good: More Information

- When were comparisons made looking at ESC approach and FNAST approach?
  - FNAST scores completed Q 4 hrs
  - No mention of when comparisons were made.
  - How often was the ESC approach used?
- Were babies awakened for vital signs? (advantage of ESC is don't need to awaken baby to assess for withdrawal)

Sounds Good: More Information

- **How many times did it take for the baby to not meet ESC expectations before treatment was given?**
- **Mentioned that infants were not re-admitted into the hospital within 30 days of discharge. What is the chance that mothers will not bring the baby back to the same hospital?**

Sounds Good: More Information

- **Should the drug the baby was exposed to be considered in terms of LOS?**
- **AAP recommends that for short acting opioids babies should be observed for 3 days and for long acting opioids (methadone) observe in hospital for 7 days** (Hamdan, et al., 2017).
- **40/50 babies exposed to methadone**
- **Average LOS in this study was 5.9 days**
  - **Likely to be re-admitted within 30 days after discharge** (Patrick, et al., 2015a)
- **Should results of retrospective study determine a change in practice?**

QI Project

- **3 phases**
  - **Standardized non-pharmacologic care bundle**
    - **Parental presence (mothers were primary treatment)**
    - **Skin-to-Skin**
    - **Holding**
    - **Calm low stimulation environment**

    Note: Finnegan scores for priority items (poor feeding, diarrhea, vomiting, unable to console, poor sleep)

Wachman, et al., 2018

QI Project

- **Phase 2**
  - **Education of providers**
  - **Non-pharmacologic, parent-led, rooming-in care, sign prioritization, and function-based ESC care**
  - **Pharmacologic plan: withheld first 24 hrs if infants were exposed to nicotine and anti-depressants rather than opioid**
  - **Treatment with methadone rather than morphine**
  - **Treatment begun for scores $\geq$ 8**

Wachman, et al., 2018

QI Project

- **Phase 3**
  - **Finnegan scoring replaced by ESC**
  - **Methadone vs morphine for treatment**
  - **ESC documented Q 3-4 hrs after feeding**
  - **Cuddler program (150 volunteers: 8am to midnight)**

Wachman, et al., 2018

Result

- **Compared Phase 1 with Phase 3**
  - **Phase 1 – mother primary caregiver, limiting Finnegan score items, Methadone**
  - **Phase 3 – implementation of ESC**
- **Findings**
  - **54% ↓ need for pharmacologic treatment (87 to 40%)**
  - **21% ↓ LOS (17 to 11%)**
  - **19% ↓ treatment days (16 to 13 days)**
  - **36% ↑ parental presence at bedside (56% to 76%)**

Wachman, et al., 2018

Important Points

- **No significant changes in outcome switching from the Finnegan sign prioritization and formal ESC approach.**
- **Benefits related to the Finnegan prioritization and non-pharmacologic care bundle rather than the ESC**

Wachman, et al., 2018

Things to Consider

- **Parental presence and use of cuddlers***
  - **Is it realistic to assume that mothers or family members will be present 24/7 with the baby?**
  - **Worry about feelings of guilt**
  - **Can units start a cuddler program?**
  - **Rooming-in is important**
    - **1978 knew important for mothers and infants to be together to promote bonding** (Spinner, 1978)

Wachman, et al., 2018

Things to Consider

- **Non-pharmacologic care bundle (not new)**
  - **First described in 1978 that 50% of infants with NAS can be managed by simple nursing techniques such as swaddling** (Madden, 1978)
  - **AAP, 1998 encouraged the use of supportive techniques (swaddling, dim lighting) to decrease signs of NAS**
  - **Have we not maximized the use of non-pharmacologic care?**

Things to Consider

- **Current standard of general care for infants with NAS**
  - **↓ light & noise**
  - **Cluster care**
  - **Swaddling/Holding**
  - **Non-nutritive sucking**
  - **Adequate nutrition**
    - **Demand feedings (caution)**
    - **Breastfeeding**

McQueen, et al., 2016

Non-Pharmacologic Management

- **Breastfeeding (↓ signs, ↓ LOS)**
- **Prone position (↓ scores, ↓ agitation)**
- **Rooming-in (↓ signs; ↓ LOS)**
- **Acupuncture/acupressure (↓ meds, ↑ sleep)**
  - **In particular laser acupressure** (Raith, 2015)
- **Non-oscillating water beds (↓ signs, ↓ meds)**

Edwards & Brown, 2016

Things to Consider

- **Monthly in person and on-line education about the new approach**
  - **Can this be implemented in our units today?**
- **Could we start treatment with using 2 FNAST scores $\geq$ 8 or 1 score $\geq$12 rather than the 3 and 2 if no differences were found when comparing the two approaches?**
- **Deletion of FNAST items without testing – decrease reliability of the tool especially if using score $\geq$ 8 to treat.**

Misconceptions About the FNAST

- Not designed to predict outcomes
  - Developed to assess the severity of NAS
- Does not look at infant functioning
  - Incorporates feeding, sleeping and consoling along with other important signs
- Takes to long to complete
  - Takes a few minutes when know what to look for
- Too long
  - Contains the most common 21 signs of NAS. If signs not present they won't be scored

Misconceptions About the FNAST

- Does not incorporate non-pharmacologic management
  - Non-pharmacologic management is care related. FNAST is designed to assess the severity of NAS
  - Part of general care that should be implemented no matter what scoring tool is used
  - Reliability program includes the importance of non-pharmacologic strategies

Misconceptions About the FNAST

- Need to wake up the baby and put them in a crib to score
  - Scoring should be done with routine care which is Q 3-4 hours
  - Parents are encouraged to hold their baby as much as possible
  - Rooming in is encouraged if possible
  - Neurologic items are scored when the baby has awakened; not so with other items

Review of FNAST


Finnegan Neonatal Abstinence Scoring Tool (FNAST)

Patient ID: Name: Today's Weight: DOB: Date:

Signs & Symptoms	Time												Comments
Central Nervous System Disturbances													
Crying Excessive High Pitched	2												
Crying Cont. High Pitched	3												
Sleeps < 1 Hr After Feeding	3												
Sleeps < 2 Hr After Feeding	2												
Sleeps < 3 Hr After Feeding	1												
Hyperactive Moro Reflex	2												
Markedly Hyperactive Moro Reflex	3												
Mild Tremors: Disturbed	2												
Mod-Severe Tremors: Disturbed	3												
Mild Tremors: Undisturbed	1												
Mod-Severe Tremors Undisturbed	2												
Increased Muscle Tone	2												
Excoriation (Specific Area)	1												
Myoclonic Jerk	1												
Generalized Convulsions	5												
Metabolic, Vasomotor And Respiratory Disturbance													
Sweating	1												
Fever > 101 (37.3-38.5C)	2												
Fever > 101 (38.4c)	3												
Frequent Yawning (> 3)	1												
Mottling	1												
Nasal Stuffiness	1												
Sneezing (>3)	2												
Nasal Flaring	2												
Respiratory Rate (>60/Min)	3												
Respiratory Rate (>60/Min With Retraction	5												
Gastrointestinal Disturbances													
Excessive Sucking	1												
Poor Feeding	2												
Regurgitation	2												
Projectile Vomiting	3												
Loose Stools	2												
Watery Stools	3												
Score													
Total Score													
Average Daily Score													
Inter-Observer Reliability %													
Initials Of Scorer 1													
Initials Of Scorer 2													

Important Points

- FNAST is only designed for use during the neonatal period
- Cannot be used for infants older than 1 month of age
- Can't change or delete items and have an accurate score
- Give half feeding before scoring; rest after scoring

Reality

- Know what your looking for it takes minutes to make an assessment
- Assessments are coordinated with feedings or when vital signs are due
- If signs of withdrawal are well controlled your FNAST score will be low
- FNAST scores will be low if someone is there to hold the baby (mother or cuddler)

Accuracy in Scoring

- **Know item definitions**
  - **Eliminates inconsistency with scoring**
- **Institute inter-observer reliability when scoring at least once a shift after initial reliability**

Inter-observer Reliability

- **The two nurses compare their scores**
- **Determine their percent agreement**
- **Goal: Achieve 90% agreement or greater**

D'Apolito & Finnegan, 2019

Total Number of Items of Agreement	Total Number of Items of Disagreement	Percentage Score
21	0	100%
20	1	95%
19	2	90%
18	3	85%
17	4	80%

Easy To Score Items

- **Nasal stuffiness** (score 1)/Nasal flaring (score 2)
- **Temperature** (37.2-38.3 score 1; 38.4 or > score 2)
- **Sweating** (present score 1)
- **Sneezing** (> 3 times score 1)
- **Yawning** (> 3 times score 1)
- **Respiratory rate** (>60 no retractions score 1; > 60 with retractions score 2)
- **Mottling** (score 1)
- **Seizures** (score 5)

Crying

- **Score 2 if excessive high pitched and unable to *self console in 15 sec or continuous up to 5 minutes despite intervention*.**
- **Score 3 if unable to *self console in 15 sec or continuous >5 min despite intervention*.**

D'Apolito & Finnegan, 2010

Sleep

- **Based on longest period of sleep light or deep after feeding.**
- **Score 3 if <1 hour**
- **Score 2 if <2 hours**
- **Score 1 if <3 hours**

D'Apolito & Finnegan, 2010

Moro Reflex

- ***Hyperactive:*** **elicit from quiet infant.**
- **Score 2 for hyperactive-jitteriness that is rhythmic, symmetrical, and involuntary.**
- **Markedly Hyperactive:**
- **Score 3 for jitteriness as above with clonus of hands/arms. May test at hands or feet if unclear (more than 8 to 10 beats).**

D'Apolito & Finnegan, 2010

Tremors Disturbed

- *Tremors are* involuntary, rhythmical muscle contraction and release involving to and from movements
  - Disturbed:
- Score 1 for mild/disturbed- of hands or feet while being handled.
- Score 2 for moderate/severe disturbed - of arms or legs while being handled.

D'Apolito & Finnegan, 2010

Tremors Undisturbed

- NOT touching baby after the infant has been handled (wait 15-30 seconds)
- Score 3 for mild undisturbed - Tremors of hands or feet when not handled.
- Score 4 for moderate/severe undisturbed - Tremors of arms and/ or legs or both when not handled.

D'Apolito & Finnegan, 2010

Increased Muscle Tone

- *To test:* perform pull to sit maneuver.
- Score 2- no head lag with total body rigidity. Do not test while asleep or crying. Other maneuvers may be used.

D'Apolito & Finnegan, 2010

Excoriation

- Score 1 if present on heels of feet, cheeks, or elbows
- Do not score for diaper area. This is related to loose or watery frequent stools.

D'Apolito & Finnegan, 2010

Myoclonic Jerks

- Involuntary twitching of muscle.
- Score 3 for twitching at face/ extremities or jerking at extremities (more pronounced than jitteriness of tremors).

D'Apolito & Finnegan, 2010

Optimal Scoring

- Important to know the item definitions
- Important to establish an inter-observer reliability strategy to assure accurate scoring
- Scoring is dynamic and not static

Important Points

- No matter what assessment tool is used:
  - All infants should receive non-pharmacologic care to manage signs of NAS
  - Rooming-in is the best if it can be done
  - Cuddler program is a great idea if hospitals can support it
  - All assessments of NAS should be reliable
  - Scoring does not require infant to be in bassinette

Point to Remember

- All infants with suspected/determined NAS should have non-pharmacologic care
- If no withdrawal is present, no signs of withdrawal will be scored
- Important to remember that not every baby will exhibit signs initially
- No one way is better than the other
- Do what is best for the baby

What Treatment is Best?

- Still don't know for sure
- What do we do?
  - Turn to the literature
  - Turn to our colleagues
  - Take a guess

Goals of Treatment

- Give adequate amounts of medication to control signs of withdrawal and prevent complications such as seizures, dehydration, weight loss (Hudak & Tan, 2012)
- Restore normal infant behaviors (Siu & Robinson, 2014)
- Facilitate mother-infant interaction (Valez & Jansson, 2008)

Most Common

- Opioids
  - Neonatal Oral Morphine
  - Methadone
- Barbiturates
  - Phenobarbital
- Clonidine
- On the horizon: Buprenorphine?

Hudak & Tan, 2012

Neonatal Oral Morphine

- Drug of choice (Sanlorenzo., et al., 2018)
- Increases and decreases of the drug is common
- Safer as treatment – short t½ (about 9 hours)
  - Can be increased rapidly for higher scores
- Concentrations: 0.2 or 0.4mg/ml
- Steady state reached 24 to 48 hours after initial dose
- Dose: 0.03 – 0.1mg/kg/dose Q 3-4 hours
  - Maximum dose – 0.2 mg/kg/dose

AAP, 1998; Neofax Essentials, 2017

Comparison of Methadone and Morphine

- Retrospective review
  - 26 infants
  - Length of stay (LOS); length of treatment (LOT)
- Findings
  - Findings:
    - Significant differences
    - Oral morphine:
      - Shorter LOS & LOT
      - Decreased cost

Young, et al., 2015

Methadone

- 116 infants
- Randomized to receive morphine/placebo or methadone/placebo
- Results
  - 14% ↓ LOS (16 days vs 19 days)
  - 16% ↓ LOT (12 days vs 15 days)

Methadone: alcohol free powder reconstituted by pharmacy. Not methadone used today.

Davis, et al., 2018

Buprenorphine

- Partial μ-opioid receptor agonist
- Has a ceiling effect for respiratory depression
- Lowers potential for misuse
- Decreases effects of physical dependency
- In adults - t½ is 24-60 hours

SAMHSA, 2016

Buprenorphine vs Morphine

- 24 infants
- Randomly assigned to buprenorphine or morphine
- Dose: buprenorphine 15.9 mcg/kg/day
- Results
  - Buprenorphine
    - Shorten LOT (9 vs 14 days)
    - Shorter LOS (16 vs 21 days)
    - No differences in need for adjunct therapy

Krafft, et al., 2011

Phenobarbital

- Does not reduce gastrointestinal signs of withdrawal (diarrhea)
- Large doses can depress the CNS (feeding problems, delayed bonding)
- t½ - 40-200 hours in neonate
- Serum concentrations of 20-30 mcg/ml provide adequate control of signs

Finnegan, et al, 1979; Neofax Essentials Online, 2017

Clonidine

- Sympatholytic
- Decreases amount of norepinephrine released into the synapse lowering firing rate of adrenergic neurons
- Initial dose 0.5 – 1mcg/kg
- Maintenance dose – 3-5 mcg/kg/day divided Q 4-6 hrs
- t½ in neonate – 44-72 hrs
- No alcohol

Neofax Essentials Online, 2017

Clonidine vs Morphine

- 31 infants ≥ 35 weeks GA
- Randomized; 15 received morphine; 16 received clonidine
- Dose: Morphine 0.4mg/kg/day ; Clonidine 5mcg/kg/day Q3hrs
- Dose escalation (25%) daily: max morphine dose – 1mg/kg/day; max clonidine dose – 12 mcg/kg/day
- Dose ↓ 10% Q other day once signs controlled
- Finnegan scores - ≥ 8 Q 3 hrs for 2 consecutive scores or 2 consecutive scores 12 or greater

Bada, et al, 2015

Clonidine vs Morphine

- Results:
  - No difference in birth weight or age at treatment
  - Less treatment days with clonidine vs morphine (median 28 days vs 39 days) (p=.02)
  - Summary NNNS scores – over time infants treated with clonidine had less arousal (p=.04) and less excitability (p= .02) and less lethargy (p=.04) than infants receiving morphine
  - No differences on the Bayley or Preschool Language Scale

Bada, et al, 2015

Oral Sucrose

- Should not be used to treat neonatal abstinence
- Infants have poorly functioning endogenous opioid system
- Sucrose is ineffective in calming opioid exposed infants suffering from withdrawal signs

Blass & Ciaramitaro, 1994

How Oral Sucrose Works

- Sucrose → stimulates neurons of peripheral nerves secrete endogenous endorphins (epinephrine/nor-epinephrine) → travel to opioid receptors in brain (mu receptors) → reduces pain
- Short-term pain; Lasts 5-8 min

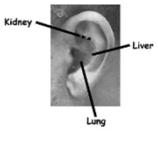
Laser Acupuncture and Drug Therapy

- Study
  - 28 newborns; 14 each group (acupuncture and drug therapy and control group just drug therapy
- Drugs
  - Tincture of opium (0.4mg/ml)
  - Phenobarbital (Loading dose 10mg/ml then maintenance

Raith et al., 2015

Laser Acupuncture and Drug Therapy

- Acupuncture
  - Every day until opioid was discontinued
  - 5 laser acupuncture points on ears for various body organs (CNS, lung, liver, kidney, shen men)



Raith et al., 2015

Laser Acupuncture and Drug Therapy

- Laser: Labpen MED 10 emitted 677 nm wavelength output power of 10 mW
- Safety: acupuncturist wore safety glasses; infants eyes covered with bili mask
- Implemented one hour after feeding

Raith et al., 2015

Laser Acupuncture and Drug Therapy

- Results
  - ✓ No differences between the groups for baseline data with exception of birth weight (laser group 3190 vs 2617 in just pharmacologic treatment group (p= 0.029)
  - ✓ Phenobarbital levels were within normal range on day 4 for both groups (36.7 vs 36.5)
  - ✓ Significantly shorter pharmacologic treatment with opioid in laser group vs just pharmacologic treatment group (28 days vs 39 days; p= 0.013)
  - ✓ Significantly shorter length of stay in laser group (35 days vs 50 days; p= 0.048)
  - ✓ Average Finnegan scores were similar between the two groups (7.1 vs 7.2; p=0.99)

Raith et al., 2015

Summary

- Infants are not born addicted to drugs
- The incidence & cost of NAS continues to rise nationwide
- The onset & severity of NAS is influenced by the type of drug, poly-substance exposure, timing of last maternal dose, infant's metabolism and genetics

Summary

- Premature infants have a lower risk for NAS d/t lower GA, less fat & ↓ drug exposure
- ESC is a new method described in literature to manage NAS; however, specificity of implementation is lacking
- Many misconceptions about the FNAST that are published but not true
- FNAST is most used tool to assess signs of NAS

Summary

- No matter what NAS assessment tool is used all infants should receive non-pharmacologic strategies and encourage rooming in if possible
- Can't delete items from the FNAST without rigorous study to scientifically determine the best indicators of NAS

Summary

- FNAST is designed to assess the severity of NAS, not to determine outcomes or assess non-pharmacologic treatment strategies
- Various pharmacologic strategies are used to treat NAS. No best strategy has been identified

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