2024 Virtual Conference

Advances and Concerns in Neonatal Abstinence Syndrome

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Clinical Trials to Improve Neonatal Abstinence Syndrome Outcomes

- **Clinical trials for pregnant women**
  - CTN 0080
  - STORC
- **Clinical trials specifically for the infants**
  - Lofexidine
- **Currently only treatment for infants**
  - Morphine
  - Methadone
  - Adjunctive medications
    - Clonidine
    - Ativan
    - Phenobarbital
  - Non-Pharmacological Measures

Lofexidine

- **Randomized trial with morphine as a comparator**
- **Phase II:**
  - Dose cohort design
  - Pharmacokinetic Sampling
  - ECGs for safety monitoring

- **Cohort 1 is complete**
  - Lofexidine seemed effective but it worked very differently than expected
  - Two new clinical measures were developed
    - Modified Global Clinical Impression-Severity
    - NOWS Clinical Status Assessment

- **Actively enrolling in Cohort 2**
  - 35 weeks gestation
  - Confirmed opioid exposure

Advances in Treatment Options - Why it Matters!

- Clinical trials not only involve treatment methods
  - Engage mothers in the care of the infant
  - Help establish healthcare and/or treatment for mothers in some cases
  - Help eliminate gaps and barriers to health care
  - Development of improved outcome measures

- Exposure and combinations of exposure are ever changing
- New Symptoms are emerging as exposure changes
- Scoring methods are outdated or not feasible
  - Finnegan
  - Eat Sleep Console
- Long term effects of exposure and current treatment methods are not well understood
- Little to no current literature to help guide our treatment decisions
  - Recent Case Study involving Xylazine Exposure

	Gestation (wks)	Birth Weight (kg)	Birth Length (cm)	Head Circumference (cm)	APGAR
Baby A	39	3.96	52	34	9,9
Baby B	39	2.61	48.26	32	9,9
Baby C	37	1.878	45.75	30	8,9
Baby D	33	2.25	45	not measured	5,8
Baby E	40	2.762	46.99	32.5	7,9
Baby F	35	3.508	50.8	34	8,9

Baby A	Maternal UDS: Amphetamine, Opioids, Fentanyl Umbilical Toxicology: Amphetamine, Cocaine, Fentanyl, **Xylazine**
Baby B	Maternal UDS: Buprenorphine, EDDP, Fentanyl, Methadone, Mirtazapine, **Xylazine** Umbilical Toxicology: Fentanyl, Methadone, **Xylazine**
Baby C	Maternal UDS: 6-MAM, Benzoylecgonine, Codeine, Fentanyl, Morphine, **Xylazine** Umbilical Toxicology: Cocaine, Fentanyl, **Xylazine**
Baby D	Maternal UDS: Amphetamine, Fentanyl, Methamphetamine, Morphine, **Xylazine** Umbilical Toxicology: Amphetamines, Methamphetamine, Cocaine, Fentanyl, Methadone
Baby E	Maternal UDS: Benzoylecogonine, Fentanyl Umbilical Toxicology: Cocaine, Fentanyl, **Xylazine**
Baby F	Maternal UDS: 6-MAM, Amphetamine, Benzoylecogonine, Codeine, Fentanyl, Methamphetamines, Morphine, THC-COOH Umbilical Toxicology: Amphetamines, Methamphetamine, Cocaine, Fentanyl, **Xylazine**, Opiate, Cannabinoids

Unique Symptoms Identified with Prenatal Xylazine Exposure

Feeding Difficulties

- All neonates required nasogastric (NG) tube placed soon after birth
- Extended NG tube supplementation
- Consistent weight loss
- Struggled to maintain glucose levels with oral feeding
- Uncoordinated suck-swallow reflex /w frequent choking or gagging
- Possible early satiation during feeding
- Low rates of excessive suck

Weight (kg)	Birth Weight (kg)	DOL 14 Weight (kg)	Discharge Weight (kg)	Number of days with NG tube	Length of stay
Baby A	3.96	3.605	4.585	33	47
Baby B	2.61	2.678	3.5	20	48
Baby C	1.878	2.265	2.45	4	18
Baby D	2.25	2.115	3.008	10	36
Baby E	2.762	2.9	4.256	3	56
Baby F	3.508	3.17	4.086	11	38

Unique Symptoms Identified with Prenatal Xylazine Exposure

- Sudden onset of severe symptoms (presentation minutes after delivery in some)
- Facial expressions indicating discomfort (scowling) even during rest periods
- Severe myoclonic jerks
- Overall sedation characterized by a lack of restful sleep
- Excessive cry
- Abrupt state changes
- Extreme irritability and/or poor response to some palliative care measures such as holding, cuddling, and rocking by caregivers.

Unique Symptoms Identified with Prenatal Xylazine Exposure

- Increased heart rate and blood pressure

Cardiovascular	Heart Rate	Heart Rate	Systolic	Diastolic
Baby A	Median	144	87	45
	Peak	178	122	72
	Trough	98	37	32
Baby B	Median	148	89.5	47.5
	Peak	198	130	70
	Trough	103	65	33
Baby C	Median	156	90	51
	Peak	188	103	70
	Trough	121	75	35
Baby D	Median	158	85	44
	Peak	196	99	72
	Trough	127	61	30
Baby E	Median	153	91	47
	Peak	194	127	74
	Trough	118	69	33
Baby F	Median	141	90	49
	Peak	178	113	69
	Trough	110	74	35

Treatment for Prenatal Xylazine Exposure

Pharmacological treatment:

• Morphine	moderate success
• Clonidine or other alpha-2 agonist	moderate success
• Phenobarbital	increased symptoms
• Lorazepam	improved rest

Treatment for Prenatal Xylazine Exposure

Feeding Issues

- Multiple bottle nipples were attempted
- Neonates would not take a nonnutritive sucker (pacifier)
- Neonates' uncontrolled tongue movements would push the nipple out of the mouth.
- Normal feed took an extended period and seemed to exhaust the neonate.
- Once exhausted, the neonate would sleep unable to finish the oral feed and thus NG supplementation was required.
- Speech therapy was consulted, we are trying numerous techniques now: on-demand feeding, syringe feeding, etc.

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Healthy Connections