Selective Serotonin Reuptake Inhibitors in Neonatal Abstinence Syndrome

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Via Christi Family Medicine Residency
KAFP Spring Symposium, 2014

Objectives

The learner will be able to

- Discuss screening, diagnosis and management of antidepressant withdrawal in the newborn patient
- Describe the pathophysiology of neonatal abstinence syndrome
- Identify community resources to support mothers with depression during pregnancy and the postpartum period
Case: History of Present Illness

- A three day old female born to a 31 year old G4P3 GBS negative mother at 41 weeks gestation presents with 2 day history of tachypnea after being discharged from the hospital at 24 hours of age.

Case

- Review of Systems:
  - GENERAL: No fevers or decreased activity
  - HEENT: No sneezing, rhinorrhea or eye discharge
  - Cardiopulmonary: + tachypnea. No cyanosis
  - GI: + soft stools 3-4 times daily
  - FEN: Bottle feeding 3oz q 3hours
  - GU: Several wet diapers daily
  - NEURO: No tremors or rigidity
Case

- Physical Exam
  - Weight 2948g (Birth wt 2960g)
  - Temp 97.6 F
  - PR 156 (range 100-180)
  - RR 56 (range 30-60)
  - HEENT: Anterior Fontanel soft, flat PERRL, Bilateral red reflex
  - Cardio: S1 S2 no murmurs, femoral pulses strong bilaterally, capillary refill less than 2 seconds
  - Pulm: tachypneic, shallow breathing observed. Breath sounds clear bilaterally
  - ABD: + bowel sounds, no masses
  - Ext: no hip clicks or clunks
  - Skin: Mild jaundice

Case

- Working Diagnosis:
  - Tachypnea in newborn
  - Rule out sepsis
  - Maternal history of Sertraline use during pregnancy

- Plan:
  - Admit to NICU for work-up and observation
Case

• NICU management:
  – Continuous pulse oximetry and telemetry
  – Labs:
    • CBC
    • CMP
    • CRP
    • Blood cultures
    • Respiratory virus panel
  – CXR showed no abnormality
  – No empiric antibiotics were initiated
  – Patient remained tachypneic throughout admission
  – Discharged after 72 hours in stable condition

Case

• Final Diagnosis:
  – Tachypnea secondary to maternal Sertraline use in pregnancy
Neonatal Abstinence Syndrome

- The collection of behavioral and physiologic findings associated with withdrawal in the newborn
- Caused by in-utero exposure to opiates, stimulants, antidepressants and psychotropic medications
- Symptoms involving the autonomic, neurologic, gastrointestinal, respiratory and endocrine symptoms can be seen

Incidence

- Studies postulate an incidence of 20 to 77.6% of NAS in fetuses exposed to SSRIs during antepartum.
- One meta-analysis calculated that SSRI exposure late in pregnancy caused an odds ratio of 4.08 (p = 0.07) of neonatal symptoms
Pathophysiology

• Inhibition of pre-junctional reuptake of serotonin
• Neonatal symptoms thought to be due to
  – Decreasing serum levels of serotonin
  – Direct effects of serotonin
• There is considerable variability in timing, onset and severity of symptoms
• Literature does not support a relationship between the risk of NAS and dosage of SSRI

Clinical Manifestations

• Can be categorized into four systems
  – Gastrointestinal
    • Diarrhea, vomiting, poor sucking, regurgitation
  – Central nervous system
    • Early depression followed by excitation
  – Autonomic
    • Temperature instability, nasal congestions, fever, sweating
  – Respiratory
    • Tachypnea/dyspnea
Antidepressant Half-Life

<table>
<thead>
<tr>
<th>Drug</th>
<th>Amine Effects</th>
<th>Molecular weight</th>
<th>Protein Binding</th>
<th>Half-life</th>
<th>Metabolite half-life</th>
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<tbody>
<tr>
<td>Fluoxetine</td>
<td>5-HT</td>
<td>309</td>
<td>94.5%</td>
<td>48-72 hours</td>
<td>15 days norfluoxetine</td>
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<td>Paroxetine</td>
<td>5-HT</td>
<td>329</td>
<td>95%</td>
<td>21 hours</td>
<td>non-active metabolites</td>
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<td>Sertraline</td>
<td>5-HT</td>
<td>306</td>
<td>98%</td>
<td>26-65 hours</td>
<td>62–104 hrs (desmethyl sertraline)</td>
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<tr>
<td>Fluvoxamine</td>
<td>5-HT</td>
<td>318</td>
<td>80%</td>
<td>15.6 hours</td>
<td>non-active metabolites</td>
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<tr>
<td>Citalopram</td>
<td>5-HT</td>
<td>405</td>
<td>80%</td>
<td>36 hours</td>
<td>59 hrs desmethyl citalopram</td>
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<td>Escitalopram</td>
<td>5-HT</td>
<td>414</td>
<td>56%</td>
<td>27-32 hours</td>
<td>59 hrs (s+) desmethyl citalopram</td>
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Differential Diagnosis and Evaluation

**Conditions**
- Seizures
- Hypocalcemia
- Hypoglycemia
- Hypoxic-ischemic encephalopathy (HIE)
- Sepsis
- Hyperthyroidism
- Poor feeding

**Work-up**
- CBC with manual diff
- CRP
- UDS
- Blood sugar
- Metabolic panel
- Blood culture
- Other testing*
Management

- Work-up to rule out other causes as symptoms dictate
- Finnegan scoring, with three consecutive scores >8 necessitating NICU admission
- Because most newborns (70%) will have no symptoms, if initial score is <3, infant can be observed in non-acute hospital setting
- Discharge after minimum 48-72 hours and normal Finnegan score
- Close contact with parents encouraged
- Breastfeeding permitted and is thought to decrease duration of symptoms, but no randomized control trials (RCT) have been performed
# Selective Serotonin Reuptake Inhibitors in Neonatal Abstinence Syndrome

Zita Magloire, MD

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<thead>
<tr>
<th>SYSTEMS</th>
<th>SIGNS AND SYMPTOMS</th>
<th>SCORE</th>
<th>AM</th>
<th>4</th>
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<td>Fever &lt; 101°F (33.3°C)</td>
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<td>Respiratory Rate &gt; 60/min</td>
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<td>Respiration Rate &gt; 60/min with Retractions</td>
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<td>Projectile Vomiting</td>
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**SUMMARY**

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<thead>
<tr>
<th>TOTAL SCORE</th>
<th>SCORER'S INITIALS</th>
<th>STATUS OF THERAPY</th>
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Future Research

• Does breastfeeding newborns with in-utero exposure to SSRIs reduce symptoms of NAS?
• How effective is tapering of SSRI use in third trimester to prevent NAS?
• Does choice of SSRI affect incidence, duration or severity of NAS?
• What are effective treatments for NAS associated with SSRI use in pregnancy?

Maternal Depression

• Use all available recourses
  – Wichita Healthy Babies
  – Social work
  – Community Resources (family, church, etc)
  – Weekly or biweekly follow-up visits (physician, counselor and other support persons/groups)
• Review risks/benefits of tapering SSRIs in third trimester
Action Items

- Identify at risk infants
- Provide close observation for the first 48-72 hours of life
- Use objective measures such as Finnegan scoring
- Provide interventions as necessary
- Provide maternal/family support
References

• Jannson, L M. Neonatal abstinence syndrome. UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2014.
• Hale TW. Medications and mother’s milk. 11th ed. 2004, Pharmasoft Publishing, Amarillo, Texas, USA.
• Kieviet N, Dolman KM, Honig A. The use of psychotropic medication during pregnancy: how about the newborn? August 2013 Volume 2013:9 Pages 1257 - 1266