Hormones, birth, breastfeeding, and their impact on perinatal mood disorders

Alison Stuebe, MD, MSc
astuebe@med.unc.edu

Case
CC/ID: 29 yo G2P1011 at 4 weeks postpartum presents for lactation consultation for sore nipples

HPI: Presented to LC for evaluation of sore nipples, and infant found to be at birth weight, with 4 oz gain in last 2 weeks. The LC asks her to complete an EPDS.

The EPDS

In the past 7 days:
1. I have been able to laugh and see the funny side of things.
2. I wake up at night and can’t get back to sleep.
3. I have found new things I like.
4. I have been irritable or angry for no good reason.
5. I have been sad or feeling down.
6. I have been eating a lot.
7. I have felt that everything I do is an effort.
8. I have been feeling wistful or envious.

On further discussion, she reports that immediately after the baby’s birth, the patient remembers feeling euphoric and being unable to sleep. Now, she reports worsening sleeplessness, tearfulness, anxiety and depression, waking frequently to check on the baby.

She denies any personal history of anxiety or depression, but her mother has frequent paranoid thoughts and episodes of manic behavior, to the extent that she no longer has contact with her mother. Her maternal grandmother had similar psychiatric symptoms, and the patient says, “I don’t want to be that kind of mother for my baby.”

Today’s objectives

• Understand the relationship between breastfeeding and postpartum depression
• Discuss mechanisms linking these two disorders
• Apply strategies for integrated management of mood disorders and breastfeeding problems
Conventional Wisdom: Breastfeeding prevents postpartum depression

“The many health benefits of breastfeeding include less risk of postpartum depression for you.”
- The Joint Commission

Does not breastfeeding cause depression?

“At the level of a mother’s basic biology, the decision to bottlefeed unwittingly mimics conditions associated with the death of an infant. Child loss is a well documented trigger for depression particularly in mothers, and growing evidence shows that bottle feeding is a risk factor for postpartum depression.”

Or does bad breastfeeding cause depression?

Prospective data from 2586 women who initiated breastfeeding in the Infant Feeding Practices Survey II.

Higher state anxiety during the postpartum stay was associated with shorter breastfeeding duration in a prospective cohort study.


The Relationship Between Infant-Feeding Outcomes and Postpartum Depression: A Qualitative Systematic Review


**Discuss mechanisms linking these two disorders**

Breastfeeding is a two-person organ system

Breastfeeding is a two-person organ system

Breastfeeding Success

Let Down

Latch

Moving Milk

Breastfeeding Success

Let Down

Latch

INCORRECT

CORRECT

Stress and Milk Volume

Distraction and Milk Volume (g)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Ice water</th>
<th>Math + shock</th>
<th>Toe Pull</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>167</td>
<td>69</td>
<td>163</td>
<td>114</td>
</tr>
<tr>
<td>Oxytocin</td>
<td>139</td>
<td>114</td>
<td>114</td>
<td></td>
</tr>
</tbody>
</table>

Newton & Newton, J. Pediatr 1948; 33:658-764
Demand drives supply
Emptying lobules drives ongoing milk production.

Breastfeeding Success
Let Down
Moving Milk
Latch

Moving Milk
Breastfeeding Success
Let Down
Latch

Depression and infant behavior
- Exposure to depression in utero associated with differences in infant
  - Neonatal neuromuscular maturity
  - Early suckling behavior
  - Infant temperament
- Does exposure to depression in utero affect latch, feeding cues, and temperament, thereby latch and milk removal?


Maternal mood affects behavior


What’s the underlying physiology?

Neurosteroids and perinatal depression

**Peripartum neuroendocrinology**

Mean plasma concentrations of estrone (E1), estradiol (E2), estriol (E3), and progesterone (P) during pregnancy. Fetal and maternal neuroendocrine changes around partuition.

'About two days after delivery some women become excited, sleepless, and incoherent; they have a flushed face, a rather full pulse and slight elevation of temperature; this is called 'milk fever,' and coincides with the beginning of the flow of milk.'

- George Savage, 1875

GABA receptors are downregulated during pregnancy, and must return to normal levels after partuition to maintain steady level of inhibition.

In a knockout mouse model, loss of the GABA(R)delta gene prevents postpartum recruitment of GABA(R), and results in aberrant mothering behavior and decreased pup survival.


What’s the underlying physiology?

Oxytocin and the autonomic nervous system

- What happens to lactation when you interfere with oxytocin-vagal pathways?
  - The cPAG is a brain region implicated in maternal response to nursing in rats
  - Researchers studied the effect of lesion in cPAG region on maternal behavior
  - Damaging this region of the brain interfered with feeding behavior

Effect on weight gain

Effect on attack behavior
Increased vagal tone, maternal behavior
Reduced stress reactivity, decreased depression and anxiety

Stressor
Central oxytocin pathways
Hypothalamus
Pituitary
CRH
ACTH
Adrenal
Modulation of cortisol

Maternal oxytocin response to feeding at 8 weeks among women with depression/anxiety symptoms (dashed line) or without mood symptoms (solid line).


Oxytocin AUC during feeding and maternal mood.

Source: Grewen & Meltzer-Brody, In press

Does the relationship between oxytocin and cortisol vary among individuals?

Oxytocin AUC during feeding and cortisol during TSST among women with and without mood symptoms at 8 weeks postpartum.

Do postpartum mood symptoms modify the association between oxytocin and cortisol?

Oxytocin receptor polymorphisms, social support and stress response

Oxytocin receptor polymorphisms and postpartum mood

Carriage of the A allele was associated with an increased risk of depression symptoms among 260 participants in the Pregnancy, Infection and Nutrition Postpartum Study (*p* < 0.01).

<table>
<thead>
<tr>
<th>rs53576</th>
<th>EPDS: 13 at 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>GG</td>
<td>0.9%</td>
</tr>
<tr>
<td>AG/AA</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

Mood, mother and infant: The psychobiology of impaired dyadic development

Specific Aim 1: Use lactation as a physiologic challenge to quantify the extent to which PPD reduces oxytocin, dysregulates stress reactivity, and diminishes maternal sensitivity.

Specific Aim 2: Use standardized mother-infant interactions to determine if a period of chronic PPD is related to maternal sensitivity in the development of infant emotional regulation and secure attachment.

Specific Aim 3: Determine the extent to which diminished maternal oxytocin and reduced sensitivity mediate associations between PPD, impaired infant emotional regulation, and insecure attachment.

Discuss treatment plans for characteristic mood disorders associated with the perinatal period

Case

- CC/ID: 35 yo G2P2 at 5.5 months postpartum seen in consultation for breastfeeding associated pain.
- She describes the pain as "consistent burning with deeper pain on and off throughout the day. Sometimes, it feels that I cannot completely "empty" my breast. Pain radiates to my arm / armpit.”
- EPDS: 15

Clinical Pearl: Screen early and often for postpartum depression/anxiety

- PPD affects up to 15% of mother-infant dyads
- Edinburgh Postnatal Depression Survey is a validated screening tool that takes <5 minutes to complete
- Like all screening tools, interpret the EPDS in the context of the clinical situation
  - Score: 13 sensitivity 75%, specificity 84% for MDD
  - Review responses, not just the total score
- Key questions:
  - Are you sleeping?
  - Are you eating?
  - Are you engaged in life outside your home?
- Offer or refer for psychotherapy

Clinical Pearl: Start with non-medical therapy

- Are you sleeping?
  - Must balance importance of on-demand feeding with maternal medical need for sleep
- Are you eating?
  - Protein, regular meals
- Are you engaged in life outside your home?
Clinical Pearl: Sleep & breastfeeding are not mutually exclusive

- Optimizing sleep
  - The goal for sleep is 6 hours of continuous sleep
  - Use sleep aids as needed
  - Enlist help of partner to bring baby to mom just for feeding during her 6 hours of sleep

- Optimizing feeding
  - Limit feedings to 30-40 minutes total time per feeding
  - Intense feeding plans generally only can be sustained for 3-4 days by anyone
  - Focus on what is most productive & find other ways to accomplish the rest
  - Milk making hormones are highest level between 2-5 AM
    - Consider longer sleep interval from evening till middle of this range, rather than across this range
    - Maximize breast emptying following this time frame
  - Mother must have time to enjoy her baby, not just feed

Clinical Pearl: Include sleep aid when starting medication

- Trazodone
  - Start at 25mg and increase up to 200mg if needed for sleep (50mg is usual dose)
  - Addressing sleep can vastly improve mood symptoms
- Benzodiazepines
  - Klonopin 0.5mg at bedtime and tab BID as needed until SSRI “kicks” in
    - Used because of its longer half life, can use smaller amounts less often
- Sertraline
  - Best safety profile of currently available SSRIs
  - Start at 25mg QAM x 6 days, then increase to 50 mg
    - Onset of effects 2-3 weeks
  - Collaborate with pediatric provider

Clinical Pearl: Depression affects both mood and maternal sensitivity

- When seeing a mom with a history of depression / anxiety, evaluate maternal symptoms and mother-infant interaction
  - This mother was unaware of infant’s response to overactive let-down, including coughing, writhing, and clamping to control flow
  - Depression / anxiety associated with impaired maternal sensitivity and intrusive behaviors
- Treatment requires both addressing mood symptoms and helping mom respond to infant cues while addressing presenting symptoms
  - Review cues, work with mother to understand baby’s needs and desires

Case 3

- Presenting concern
  - Pain with breastfeeding during let-down, thus pumping and bottle-feeding
- History of postpartum depression
  - 1st and 3rd children, hospitalization for major depressive episode in 5 years ago
  - EPDS today 4, seen by psychiatrist this morning
- Observed feeding
  - Infant established good latch, but pulled away and clicked tongue during let down at time of increased maternal pain.
  - On/off latch after the let down, milk frequently spilling from sides of mouth. Choking with second let down.

Maternal sertraline and infant serotonin

To learn more
Academy of Breastfeeding Medicine Protocols
http://www.bfmed.org/
UNC Breastfeeding Management Algorithms
http://mombaby.org/breastfeeding
Postpartum Support International
http://www.postpartum.net/
UNC Center for Women’s Mood Disorders
http://www.med.unc.edu/psychmed/mood-disorders/perinatal

Today’s agenda
• Understand the relationship between breastfeeding and postpartum depression
  ▪ There is considerable overlap between breastfeeding difficulties and depressive symptoms – we need to screen for and treat both
  ▪ The evidence suggests that breastfeeding does not prevent PPD
• Discuss mechanisms linking these two disorders
  ▪ Shared mechanisms affect lactation and maternal mood, suggesting that breastfeeding problems and depression may be biologically linked
• Apply strategies for integrated management of mood disorders and breastfeeding problems
  ▪ Screen early and often, start with non-medical therapy, address both sleep and feeding, and teach mothers to recognize and respond to baby’s cues