

Management of depression and anxiety in the perinatal period

Dr. Lisa Gagnon
Women's Mental Health Clinic
FMC
Lisa.gagnon@albertahealthservices.ca

Faculty / Presenter Disclosure

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Objectives

- Discuss mental health generally during pregnancy and postpartum.
- Review unique features of some illnesses during this reproductive event.
- Discuss the risks of untreated illness.
- Present an overview of the safety of psychotropic medications in pregnancy and lactation.

Perinatal Mental Health - General Considerations

- Up to **20%** of women
- Risk of developing major mental illness:
 - Not elevated in pregnancy
 - *Greatly* elevated postpartum
- No specific DSM-5 diagnoses
 - With peripartum onset
 - Illness considered same as other periods
- Most screening instruments not validated

Oates & Cantwell (2011); Gibson & Gray, in Martin (Ed:2012)

Epidemiology of Suicide

- Risk of suicide much lower in pregnant:
 - *Except* in teenage population
- *Leading cause of maternal death in pregnancy*
- Under-detected
- Labelled inappropriately if substance use

Appleby (1991); Confidential Inquires into Maternal and Child Health (2007); Oates & Cantwell (2011); Gibson & Gray, in Martin (Ed, 2012)

Epidemiology of Suicide

- Postpartum risk *similar* to other times of life:
 - Elevated risk with history of mental health problems (66%)
 - In UK, more than half were Caucasian, married, employed, >30 and in comfortable situations
 - Young, single and unemployed women were more likely profile with substance use

Oates (2003); Oates & Cantwell (2011)

Epidemiology of Suicide

- 59% affective psychosis or severe depression
- 31% substance
- One third were referred to social services.
- Majority with a previous history were well in pregnancy
- Associated with higher risk of infanticide

Fisher et al. in WHO & UK (2009); Oates (2003); Oates & Cantwell (2011)

Intimate Partner Violence

- 1-6% of women in pregnancy and postpartum
- Increased risk of suicide in perinatal time
- Associated with
 - Depression (3x the risk)
 - Anxiety
 - Post-traumatic stress disorder
 - Multiple disorders

Cerulli et al. (2011); Gazmarain et al. (1996); Gold et al. (2012); Howard et al. (2013); Jasinski

Depression and Anxiety

- *Highly co-morbid*
- Major depression (10-13%)
 - Elevated in high risk pregnancies
 - Postpartum depression most studied
- Anxiety less studied:
 - BUT likely **more** common than depression
 - In pregnancy, effects neurodevelopment *and* obstetrical outcomes
 - In some more than one anxiety disorder

Brandt Karsnitz (2011); Lee et al. (2007); McGrandles & Duffy in Martin (Ed. 2012); Wenzel et al. (2003); Wenzel (2011)

Generalized Anxiety Disorder

- The 6 months criteria is limiting in this population.
 - Studies suggest similar prevalence to general population.
 - Highest rates in first trimester when studied in a clinical population.
- Look at functioning and impairment



Brandt Karsnitz (2011); Bulist et al. (2011)

Obsessive-Compulsive Disorder

- Pregnancy *similar* to other times
 - Eg., contamination thoughts, cleaning...
- Postpartum develops rapidly
 - More harm thoughts (intentional or not)
 - ➡ Ego-dystonic
 - Less likely to have obsessions

McGuinness et al. (2011); Misri & Kendrick (2007); Russell et al. (2012); Wenzel (2011)

Obsessive-Compulsive Disorder

- Interferes with mother-infant relationship
 - Under or overinvolved parenting
- Compulsions can be very time consuming
- 1.5-2 times more prevalent in pregnancy and postpartum
- High degree of sub-threshold OCD

Russell et al. (2012); Wenzel (2011)

Depression in Pregnancy

Mothers *and* families suffer

Risks of associated with antenatal depression:

- ▣ Non-compliance with prenatal care
- ▣ Self-medication
- ▣ Poor weight gain
- ▣ Suicide
- ▣ Premature delivery
- ▣ *Greatest risk factor for postpartum depression*

Grigoriadis et al. (2013) Lusskin et al. (2007); Misri & Kendrick (2007); Viguera et al. (2011)

Depression and Anxiety in Pregnancy

- ▣ Highly reactive infants
- ▣ More sleep, activity and feeding problems
- ▣ Hyperactivity and externalizing problems
- ▣ Self-reported anxiety
- ▣ Decreased breastfeeding initiation
- ▣ Recent studies suggest maternal anxiety effect on infants is moderated by genes

Grigoriadis et al. (2013); Lusskin et al. (2007); Misri & Kendrick (2007); Tiemeier et al. (2012)

Edinburgh Postnatal Depression Scale (EPDS)

- ▣ 10 question
- ▣ Screening tool for depression and anxiety
- ▣ Validated for both pregnancy and postpartum
- ▣ Self-rated scale
- ▣ Possible depression >10

Cox et al. (1987); O'Hara & McCabe (2012)

Pharmacotherapy in Pregnancy

- ▣ Monotherapy favored
- ▣ Selection:
 - ▣ History of efficacy
 - ▣ Prior exposure in pregnancy
 - ▣ Available reproductive safety
- ▣ May need higher doses in last trimester.
- ▣ All psychotropic medication off label.

ACOG Practice Bulletin (2008); Yatham et al. (2005)

Pharmacotherapy in Pregnancy

- ▣ Risks with medications:
 - ▣ Organ malformations (1st trimester)
 - ▣ Spontaneous abortions (1st)
 - ▣ Obstetrical complications (all)
 - ▣ Neonatal withdrawal / toxicity (3rd)
 - ▣ Long term neuro-developmental outcomes (all)

Pearson et al. (2007)

Depression and Anxiety in Pregnancy - Treatment

- ▣ **Selective Serotonin Reuptake Inhibitors (SSRI):**
 - ▣ No increased risk *overall* of major malformations
 - ▣ ? Slight increased risk of cardiovascular malformations (paroxetine especially)
 - ➡ Clinical significance?
 - ➡ Illness factors?

Grigoriadis et al. (2013); Ornoy & Koren (2013)

Depression and Anxiety in Pregnancy - Treatment

□ SSRIs:

- Increase risk of spontaneous abortion.
- *Inconsistent* results with lower birth weight
- *Inconsistent* results with decreased gestational age
- Relation to illness?
- *Slight* increased risk of postpartum hemorrhage

Broy & Berard (2010); Davies et al. (2007); Einarson et al. (2009); Malm et al. (2006); Palmsten et al. (2013); Rahimi et al. (2006); Hemels et al. (2005); Lennesta¹ & Ka¹lleⁿ (2007); Ornoy & Koren (2013); Ross et al. (2013); Simon et al. (2007); Wu Wen et

Depression and Anxiety in Pregnancy - Treatment

□ SSRI use in third trimester:

- *Inconsistently* associated with Persistent Pulmonary Hypertension of the Newborn (PPHN).
- PPHN if a risk is quite rare (<1%).
- Other stronger risk factors.

Byatt et al. (2013); Jong et al. (2012)

Depression and Anxiety in Pregnancy - Treatment

□ SSRIs and neonatal adaptation:

- Poor neonatal adaptation (15-30%).
- Higher prevalence in premature.
- Transient and self-limited.

Davies et al. (2007); Grigoriadis et al. (2013); Kallen (2004); Lennesta¹ & Ka¹lleⁿ (2007); Malm et al. (2006); Sanz et al. (2005)

Depression and Anxiety in Pregnancy - Treatment

□ SSRI in long term neurodevelopment:

- ***Most studies demonstrate *no* impairment.
- Subtle effects on motor development.
- ??? Association with autism
- More research needed.

Croen et al. (2011); Gentle & Galbally (2011); Hviid et al. (2013); Misri et al. (2006); Ornoy & Koren (2013); Rai et al. (2013); Sanford Zeskind & Stephens (2004); Sorensen et al. (2013);

Depression and Anxiety in Pregnancy - Treatment

□ Bupropion

- Less efficacious for anxiety.
- *Limited evidence for all areas.*
- ? Increased risk of cardiac defects.
- No increased risk of all malformations.
- Higher rates of spontaneous abortion.
- ? Associated with ADHD.

Awan et al. (2010); Byatt et al. (2013); Chun-Fei-Chan (2005); Cole et al. (2007); GSK (2007); OTIS (2012); Williams (2005)

Depression and Anxiety in Pregnancy - Treatment

□ SNRIs (Mirtazepine and Venlafaxine):

- Limited research all areas (esp. long term outcomes).
- No increased risk of major malformations.
- Increase rate of spontaneous abortion.
- Neonatal withdrawal.

Broy & Berard (2010); Byatt et al. (2013); Einarson et al. (2007); Lennesta¹ & Ka¹lleⁿ (2007); Ornoy & Koren (2013); OTIS (2013)

Anxiety in Pregnancy – Benzodiazepine Treatment

- *Slight increase risk* of cleft lip and palate
- No overall increased risk of malformations
- High doses at delivery associated with floppy baby
- ? Preterm birth and low birth rate
- May be associated with neonatal withdrawal

ACOG Bulletin (2008); Enato et al. (2011); Misri (2007); OTIS (2010)

Anxiety in Pregnancy – Benzodiazepine Treatment

- Possible fatal interaction with diphenhydramine
- Long term effects disputed
- Slow taper
- Use those without active metabolite and shorter half life (e.g. lorazepam)

ACOG Bulletin (2009); Kargas et al. (1985); OTIS (2010)

Alternative Therapies for Depression &/or Anxiety

- Some evidence for:
 - Omega-3 fatty acids
 - Folate
 - Exercise
 - Bright light therapy

- Less evidence for acupuncture and massage

Deligianndis et al. (2013)

Depression and Anxiety in Pregnancy - Treatment

- Limited research on efficacy of other treatment options:
 - Psychotherapy
 - Nutrition

Postpartum Blues

- 50-85% of women.
- Begin 2-3 days postpartum.
 - Depressed mood
 - Crying spells
 - Mood lability
 - Irritability
 - Anxiety

Stern & Herman (2004)

Postpartum Depression

- 60% symptom onset in 6 weeks, but clinically up to one year.
- DSM-5 specifier is 4 weeks postpartum.
- Prevalence ranges from 13-19%.

O'Hara & McCabe (2013); Viguera et al. (2011)

Postpartum Depression

- Modest risk factors:
 - Low socioeconomic status
 - Single
 - Unwanted pregnancy
 - Obstetrical stress
 - Difficult infant temperament

O'Hara & McCabe (2013)

Postpartum Depression

- Moderate to strong risk factors:
 - Depression & anxiety in pregnancy
 - Stressful life events
 - Neuroticism
 - Postpartum blues
 - Low social support (*partner support)
 - Psychiatric history especially of depression
 - Low self-esteem

O'Hara & McCabe (2013)

Postpartum Depression

- Depression associated with infant:
 - Attachment insecurity
 - Cognitive developmental delays (boys>girls)
 - Social difficulties
 - Expressive language impairment
 - Long-term behavioral problems
 - Health related consequences
- Chronicity of depression important

Henshaw in Martin (Ed, 2012); Hodnett (2009); O'Hara & McCabe (2013); Vliegen et al. (2014)

Depression in NICU

- Prospective study 39%
- 32% had suicidal ideation
- Significantly associated with:
 - Acute Stress Disorder
 - Posttraumatic Stress Disorder

Lefkowitz et al. (2010)

Chronic Depression

- 30% of community samples
- 50% clinical samples
- ➔ more than 1 year postpartum
- Risk factors:
 - Lack of partner support
 - Previous depression
 - Sexual abuse
 - Situational stress
 - Personality related

Vliegen et al. (2014)

PSTD in Postpartum

- Caused by childbirth: 1.5-6% (higher in stillbirth and prematurity)
- Associated factors:
 - Extreme pain
 - fear for mother's life or for infant's life
 - perception of lack of obstetrical care
 - feelings of powerlessness
 - high level of medical intervention
- 0-5% in fathers

Alcorn et al. (2010)

Depression and Anxiety in Postpartum - Treatment

- SSRI in lactation:
 - Medication exposure lower than in pregnancy
 - All *moderately safe or safer*
 - Sertraline and paroxetine best safety profile
 - Fluoxetine has long half life and active metabolite.

ACOG Practice Bulletin (2008); O'Hara & McCabe (2012)

Depression and Anxiety in Postpartum - Treatment

- Venlafaxine in lactation *moderately safe*:
 - Higher level in breast milk than SSRI
 - Parent drug little transfer to infant
 - Metabolite has greater amount of transfer

ACOG Practice Bulletin (2008); Freeman (2008); Misri (2007);
Misri & Kendrick (2007); Sanz et al. (2007); Weissman et al.
(2004)

Depression and Anxiety in Postpartum - Treatment

- Bupropion in lactation *moderately safe*:
 - Higher levels than SSRI in breast milk.
 - One seizure noted.

ACOG Practice Bulletin (2008); Freeman (2008); Misri (2007);
Misri & Kendrick (2007); Sanz et al. (2007); Weissman et al.
(2004)

Anxiety in Postpartum - Treatment

- Benzodiazepines in lactation:
 - All considered *moderately safe* with exception of diazepam in long term use
 - Main side effect is sedation

ACOG Bulletin (2008); Kelly et al. (2012)

Depression and Anxiety in Postpartum - Treatment

- Psychotherapy:
 - Studies focused on depression.
 - Four approaches:
 - General counseling
 - Interpersonal psychotherapy (IPT)
 - Cognitive behavioral therapy (CBT)
 - Psychodynamic therapy
 - Response to various therapies.
 - Little research showing effect on infant.

O'Hara & McCabe (2012)

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