SSRIs in Pregnancy & Lactation

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Outline

- Epidemiology & Prevalence of Psychiatric Disorders during Pregnancy & Postpartum
- Symptoms & Diagnosis during Pregnancy & Postpartum
- Effects of Stress during Pregnancy & Postpartum
- Challenges of Treatment during Pregnancy & Postpartum

Epidemiology and Prevalence

Epidemiology & Prevalence

- Pregnancy is not a protective factor against psychiatric illness
  - No difference between trimesters 3-5% depression
  - Perhaps a slight increase in:
    - Generalized anxiety disorder (5-10% increase)
    - Obsessive-compulsive disorder (<=0.5% increase)
    - Postpartum worsening in anxiety disorders much more frequent (>20-30%)
- Postpartum blues:
  - 50-85% of postpartum women
- Postpartum depression:
  - 10-20% of postpartum women
  - 50% of women who are depressed during pregnancy end up suffering from postpartum depression
- Postpartum psychosis:
  - <1% of postpartum women
  - 30% of those with bipolar disorder

Symptoms & Diagnosis

Onset

- Postpartum Blues:
  - Within 2 weeks
- Postpartum Depression:
  - Within 3 months (up to 1 year)
- Postpartum Psychosis:
  - Within 3 days (up to 2 weeks)

Symptoms

- Postpartum Blues:
  - Affect depressed and labile
  - Emotional hyper-responsiveness
  - 20% develop PPD
- Postpartum Depression:
  - Fits criteria for MDD (SIG E CAPS), in particular:
    - Suicidal ideations, lack of attachment to the infant, excessive guilt, anhedonia
- Postpartum Psychosis:
  - Delirium/manic/psychotic symptoms
    - Disorientation, cognitive deficits, confusion, hallucinations

Effects of Stress: Pregnancy & Postpartum

Psychological challenges

- Pregnancy as a developmental stage and life transition
- Conflicts over increased dependency needs
- Burdening maternal ideal
- Reestablishing narcissistic balance
- Identification struggle with the mother's mother
- Separation from mother and rivalry
- How to involve expectant fathers and transition to paternity

St-Andre, M. Psychotherapy during pregnancy: opportunities and challenges. AM J Psychother. 1993

Effects of stress during pregnancy

- Psychological:
  - Substance use during pregnancy
  - Abortion
  - Lack of medical follow-up
  - Inability to work
  - Inability to attach and care for child
  - Later, in the child: internalizing and externalizing problems during childhood and teenage years

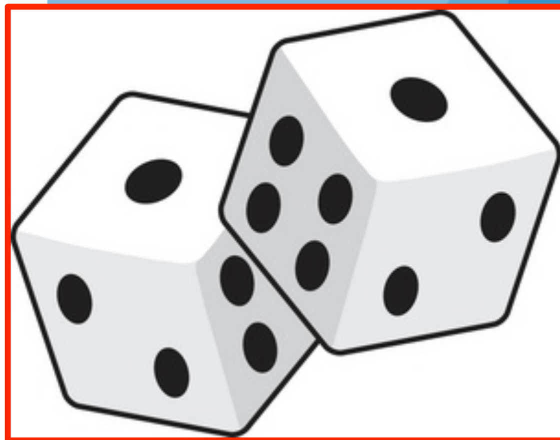
- Biological:
  - Preterm labor
  - Low birth weight
  - Preeclampsia/eclampsia
  - Later, in the child: Chronic health problems during adulthood (HTN, cardiac, diabetes)

COHEN, L. & al. (2010). « Treatment of mood disorders during pregnancy and postpartum », Psychiatric Clinics of North America, 33(2), p. 243-293.

Challenges of Treatment: Pregnancy and Pospartum

KEYPOINT:

EXPOSURE



NON-EXPOSURE DOES NOT EXIST IN REPRODUCTIVE PSYCHIATRY:

- THE FETUS IS EITHER EXPOSED TO THE MENTAL CONDITION

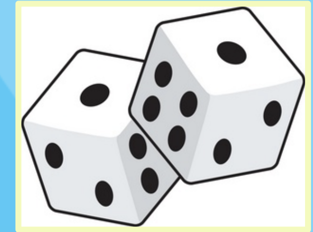
OR

- TO THE TREATMENT FOR MENTAL ILLNESS

Challenges of psychotherapy

- Accessibility
- Speed of response
- Treatment-resistance
- Adherence
- Inappropriate treatment for psychosis
- Insufficient treatment as a stand-alone for bipolar disorder

Balancing the risks during pregnancy



RISKS OF UNTREATED DEPRESSION

- Miscarriage (1.1x)
- Stillbirth (2x)
- Major congenital anomaly (1.5x)
- LBW or SGA (1.5-1.6x)
- Preterm birth (2.4x)
- Poor neonatal adaptation (2.1x)
- Admission to NICU (1.8x)
- Neonatal developmental delay (1.2x)

RISKS OF ANTIDEPRESSANT TREATMENT

- NO INCREASED RISK: cardiac defects, birth weight, IQ, behavior, reactivity, mood, activity in offspring
- 1st trimester:
  - Miscarriage: small increase (1.6X), maybe higher with SNRI (2X)
- 3rd trimester:
  - Preterm birth: small increase (mean: -0.9 weeks)
  - Neonatal adaptation syndrome (10-30% of neonates, last 2-5 days)
  - Preeclampsia and eclampsia (1.5-1.6X for SNRI and TCA, NOT SSRIs)
  - Persistent pulmonary hypertension: 1.4-2.5x risk (1/1000 in general population)

SSRIs and Autism

- **Q: Does SSRI increase up to 87% the chance of having a child with autism if she took antidepressants during pregnancy, as mentioned in the media?**
- A: The risk went from 1% to 1.87% in the main analysis.
- No association between prenatal antidepressant exposure and autism spectrum disorders when the sample was restricted to children formally diagnosed by a psychiatrist or a neurologist.

SEE CENTRE IMAGE: https://www.chusj.org/fr/soins-services/P/Pharmacie/Centre-IMAGe/Actualites?FAQ1506

SSRIs and Autism

- Four other large, well-designed studies (average sample size of 430 000 children):
  - Did NOT find an association between prenatal exposure to antidepressant medication and autism spectrum disorders

- In the 5 studies showing positive associations (smaller average sample size of 45 000 children):
  - Controlling for maternal history of depression almost nullified the association between antidepressants and autism spectrum disorders

- *SEE CENTRE IMAGE: https://www.chusj.org/fr/soins-services/P/Pharmacie/Centre-IMAGe/Actualites?FAQ1506*

SSRI and Speech Disorders

- Prospective birth cohort 1996-2010
- n=845 345 pregnant women and singleton offpsring
- Speech, scholastic or motor disorders
- Birth to 7 years of age
- No difference between SSRI-exposed and untreated maternal depression in any psychiatric outcomes
- In a subgroup analysis, mothers who filled 2 SSRI prescriptions had a 37% increase in speech disorders in their children at 4 years old
- But risk for speech disorders was higher in both SSRI-exposed and untreated maternal depression, compared to unexposed group

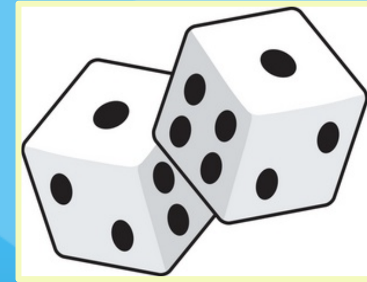
Brown AS et al. Association of selective serotonin reuptake inhibitor exposure during pregnancy with speech, scholastic, and motor disorders in offspring, JAMA Psychiatry 2016 Oct 12

SSRI and Speech Disorders

- Consistent with other previous studies:
  - Untreated maternal depression:
    - Short-term: Sleep, orientation, motor changes
    - Long-term: Externalizing and internalizing symptoms, decreased language discrimination
  - Antidepressant exposure during pregnancy:
    - Short-term: Sleep, habituation, autonomic and motor activity
    - Long-term: Subtle motor and language changes in some studies, particularly in those babies with neonatal adaptation syndrome; no effects in the majority of studies however

Suri, R et al. Acute and long-term behavioral outcome of infants and children exposed in utero to either maternal depression or antidepressants: a review of the literature, J Clin Psychiatry 75:10 October 2014

Balancing the Risks Postpartum



- RISKS OF UNTREATED DEPRESSION
- Neonatal developmental delay (2-3x)

- RISKS OF ANTIDEPRESSANTS
- Little evidence for severe side effects
- Irritability, hypoglycemia, restlessness, motor abnormalities, rarely, seizures
- All antidepressants have % excretion into the breast milk that is lower than 10%

Antidepressant % Excretion

Table 1. Relative infant doses of commonly used antidepressants

ANTIDEPRESSANT	RELATIVE INFANT DOSE, %
Bupropion[8]	2
Citalopram[8]	3-10
Desvenlafaxine[9,10]	5.5-8.1
Duloxetine[8]	<1
Escitalopram[8]	3-6
Fluoxetine[8]	<12
Fluvoxamine[8]	<2
Mirtazapine[8]	0.5-3
Paroxetine[8]	0.5-3
Sertraline[8]	0.5-3
Venlafaxine[8]	6-9

RESOURCES

- MothertoBaby
- MotherRisk
- LactMed
- IMAGE
- American Academy of Pediatrics
- WHO Working Group on Human Lactation

KEYPOINT:

WHOLE PERSON CARE

RESPECT FOR THE AUTONOMY OF THE PATIENT:

- DISCUSS ALTERNATIVE TREATMENTS
- INFORMED CONSENT
- DECISION WITH THE PATIENT AND NOT FOR THE PATIENT

Alternatives to Pharmacotherapy

LIGHT THERAPY

- White light on awakening
  - Dose: 20-30 min per day at 10,000 lux
  - Duration: 4-6 weeks or +
  - Remission rate: 75% for SAD, 50% for non-seasonal depression
  - Adverse effects: In general, well tolerated

Rarely: Eyestrain, headache, nausea, irritability, agitation,
Mania; caution if: Light sensitivity (systemic lupus erythematosus,
certain antibiotics, anti-inflammatories or St. John's Wort),
eye condition, a history of skin cancer

Alternatives to Pharmacotherapy

- Omega-3s
  - Remission rate: 38% vs. 18% placebo in RCT
  - Dose: EPA > DPA, at least 1g EPA 1-2x/day, duration: 8 weeks
  - More evidence as an add-on rather then for monotherapy
  - Safe during pregnancy
- SAMe
  - Remission rate: 34% remission rate vs. 6% placebo in non-RCT
  - Longer trials needed
  - Dose: 800 mg per day, duration: 6-12 weeks
  - Demonstrated safe in the third trimester
- St-John's Wort
  - Remission rate: 15% remission rate vs. 5% in RCT
  - Dose: 900-1800 mg per day, duration: 8 weeks
  - Less data vs. antidepressants in terms of safety during pregnancy

Alternatives to Pharmacotherapy

- L-methylfolate
  - for MTHFR mutations only?
  - Remission rate: 32% vs. 15% placebo in RCT
  - Dose: 15 mg per day, duration: 8-12 weeks
  - Safe during pregnancy
- Exercise
  - Remission rate: 60% vs. 68% meds vs 65% combination in non-RCT
  - Dose: 20-30 min 3x per week, duration: 10-16 weeks
  - Safe during pregnancy
- Individual psychotherapy, self-help books, support groups
  - Remission rate: 30-85% in RCTs
  - Dose: 1x per week, duration: 8-12 sessions
  - Safe during pregnancy

KEYPOINT:

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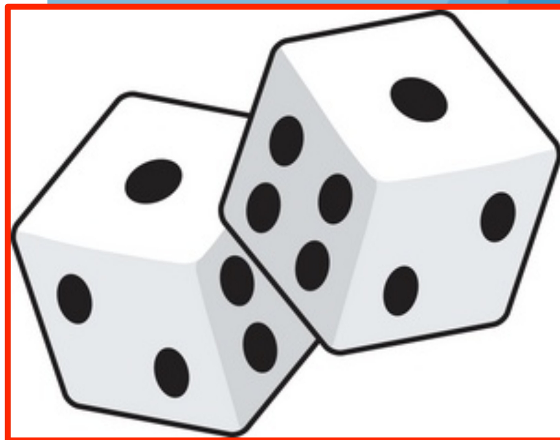

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Thank you

Any questions?

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*Need referral from MD