# Treatment Approaches to Insomnia in Perinatal Patients

Joshna Singh, MBBS

Assistant Professor of Psychiatry

Jacobs School of Medicine and Biomedical Sciences

Buffalo, NY

# Speaker:

## Joshna Singh, MBBS

Assistant Professor of Psychiatry
Jacobs School of Medicine and Biomedical Sciences ,Buffalo NY

Contact
716-835-1246, jsingh1@buffalo.edu

# Disclosures

"Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose."

# Question 1

How often do you screen for sleep disturbances in perinatal patients ?

A. Routinely
B. Only when the patient brings it up
C. Rarely
D. Not at all

# Question 2

Which of the following best describes your comfort level in managing perinatal insomnia ?

A. Very comfortable – I manage it regularly
B. Somewhat comfortable – I manage mild cases
C. Not comfortable – I refer to someone else
D. I haven't considered it a clinical priority before

# Insomnia Disorder

Despite adequate opportunity and circumstances for sleep

- *Difficulty falling asleep*
- *Difficulty staying asleep and/or*
- *Difficulty with waking too early*

Accompanied by daytime consequences or impairment

- *Fatigue*
- *Difficulty with concentration*
- *Mood changes*
- *Daytime sleepiness*
- *Worry about sleep*

Experienced for at least 3 nights per week

*Ref: International Classification of Sleep Disorders*

# Epidemiology

- Comorbidity in 50-80% patients with psychiatric diagnosis
- Insomnia is more common in women than men
- Reproductive hormonal transitions make women vulnerable to insomnia
- 15% to 80% of women report sleep problems during the first trimester
- 66% to 97% of women experience sleep problems in the third trimester
- 50% of postpartum women are at risk of chronic insomnia (up to 2 years)

*Ref: Smith et al 2002, Hillary et al 2009,baker et al 2009 Gao M, et al BMC Pregnancy Childbirth. 2019 , Siversten et al 2015*

# Causes of Insomnia in Perinatal Period

## Predisposing Factors

### A. Physical adaptations of pregnancy

- *Pain*
- *Difficulty finding comfortable position to sleep, frequent urination*
- *Nausea and vomiting*

### B. Hormonal adaptations (cognitive hyperarousal)

- *Ruminations, vivid dreams*
- *Worry about baby, pregnancy and labor*

### C. Female sex

***Ref : Swanson et al 2022, Mindell et al 2015***

# Causes of Insomnia in Perinatal Period

## Precipitating Factors

- Health /physical changes (sleep disordered breathing, RLS and obstructive sleep apnea )
- Stressors
- Psychiatric conditions

## Perpetuating Factors

- Spending long time in bed
- Sleeping later
- Day time napping
- Little exposure to daytime bright light, exposure to bioactive light at night

*Ref : Swanson et al 2022, Mindell et al 2015*

# Question 3

Insomnia in pregnancy can negatively impact:

A. Maternal mental health
B. Maternal physical health
C. Infant health
D. All of the above

# Risk from Untreated Insomnia in Pregnancy

- Mother
  - Inflammation
  - Pre-eclampsia
  - Gestational Diabetes
  - Gestational HTN
- Baby
  - Pre-term birth
  - Low birth weight
  - SGA, LGA
  - Increased risk of C-section
  - Still birth

***Ref: Kendle et al 2022, Lu et al 2021,Choudhary et al 2018***

# Risk from Untreated Insomnia in Pregnancy

- Increased risk of  depression during pregnancy
- Increased risk of postpartum depression
- Increased severity of postpartum depression
- Increased risk of perinatal anxiety and OCD
- Increased risk of postpartum psychosis
- Increased risk for suicidal ideation(with or without perinatal depression)
- Increases the odds of suicidal risk by threefold
- Increased the risk of postpartum suicide attempts within 1 year of childbirth

***Ref: Swanson et al 2011, Wilson et al 2019, Osnes et al 2020, Sharma et al 2003 , Palagini et al 2024***

# Assessment

- Detailed history from patient and (if possible) her bed partner
- Details of sleep onset, duration, quality of sleep, frequency and number of awakenings, daytime alertness, snoring, apnea, and limb movements
- Screen for mood and anxiety symptoms
- Assess prescription and nonprescription medication use, general medical conditions, substance use, and pre-existing psychiatric disorders
- Sleep dairies can be very helpful
- Pittsburg Sleep Quality Index as objective sleep measure

***Ref:Selvaria et al 2010***

# Question 4

What is the biggest barrier you face in managing perinatal insomnia ?
Maternal mental health

A. Limited referral option for CBT-I
B. Concerns about medication safety
C. Time constraints in visit
D. Lack of training in sleep interventions
E. Patients don’t bring it up

# CASE

- 32 y/o, married Caucasian female, lives with her husband and 2 y/o daughter. Currently 28 weeks pregnant. She is a stay-at-home mother. Referred to me for c/o of insomnia as OBGYN no longer felt comfortable managing ongoing symptoms.
- Long standing h/o of anxiety starting middle school, first received treatment when she was 15 years old. She had multiple failed trials of  medications including Zoloft, Prozac, Cymbalta and Wellbutrin. She has been most stable on Celexa.
- During her first pregnancy, she stopped medication before conceiving. First two trimesters went well. She developed insomnia in her third trimester but did not seek any help. After the birth of her daughter, she could not sleep for 10 days. She was" tremulous and wired". She developed significant ritualistic behaviors around sleep and would constantly obsess about it. She was initially started on Celexa 20 mg and then was eventually started on trazodone by PCP but advised to stop breast feeding .

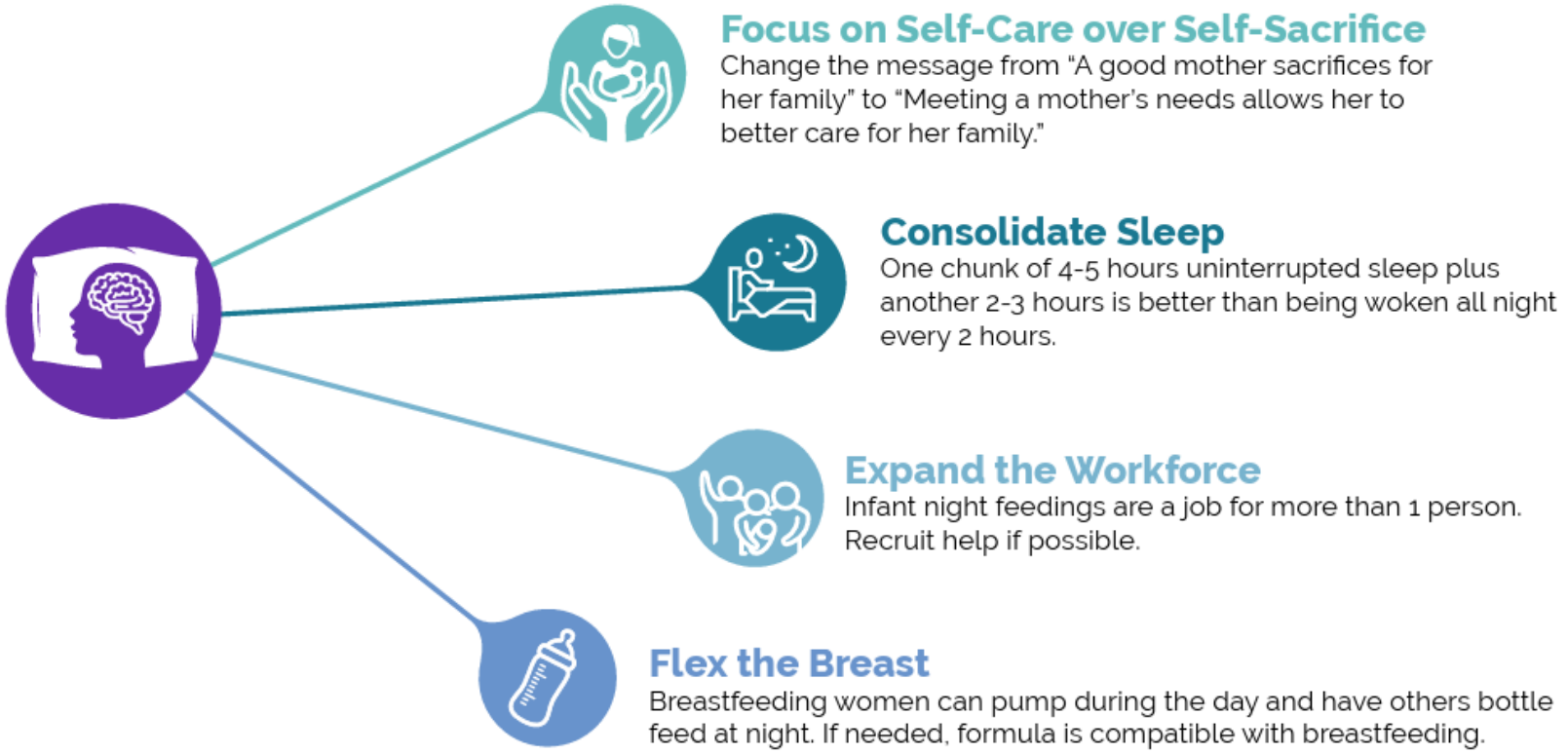
# CASE

- She stopped her trazodone after 6 month but was drinking two drinks of bourbon before bed to sleep. She stopped alcohol as she started planning for second pregnancy. She stopped her Celexa as soon as she found out she was pregnant the second time. She became increasingly anxious within weeks, requiring visit to local psychiatric emergency room, admission to OBS unit and then PHP. She was discharged on Celexa 40 mg, melatonin 2.5 mg and trazodone 100mg. She failed Benadryl, hydroxyzine during this period.
- Past H/o: No hospital admissions, no suicide attempts
- F/H: H/o of alcohol abuse in father and anxiety in mother

# Non- Pharmacological: Sleep Hygiene

- Most common exacerbating factor: hypervigilant effort around sleep
- Education about normal sleep wake cycles and how to maintain it
- Role of exercise
- Amount exposure to light at different time during the day
- Stimulus control (bed restriction to sleep only)
- Decreasing caffeine and fluid restriction late in evening
- Role of alcohol and nicotine in sleep
- Maximizing hours of consolidated sleep in postpartum period

# Prescribing Sleep (*Ref: Leistikow et al 2022*)



**Focus on Self-Care over Self-Sacrifice**
Change the message from "A good mother sacrifices for her family" to "Meeting a mother's needs allows her to better care for her family."

**Consolidate Sleep**
One chunk of 4-5 hours uninterrupted sleep plus another 2-3 hours is better than being woken all night every 2 hours.

**Expand the Workforce**
Infant night feedings are a job for more than 1 person. Recruit help if possible.

**Flex the Breast**
Breastfeeding women can pump during the day and have others bottle feed at night. If needed, formula is compatible with breastfeeding.

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  Recruit help if possible

- ***Flex the Breast***

  Extra pumping during day and have other bottle feed at night

  If needed, formula is compatible with breast feeding

# Cognitive Behavior Therapy-Insomnia

- CBT-I used as adjunct or alternative to medication
- Greater reduction in insomnia severity
- Higher remission rates
- Faster remission
- 40-60% patient maintain benefit over long term follow up
- Improvement in self reported sleep time over and above objective assessment
- Effective for patients with co-morbid psychiatric illness

***Ref: Bei et al 2010,Manber et al 2019 R, Anderson et al 2018, Taylor et al 20114, NIH 2005***

# Cognitive Behavior Therapy-Insomnia

- Individual or small group therapy
- 4-8 sessions averaging 6 hours of total therapy
- Face to face intervention has shown to be more effective
- Digital CBT-I is progressively showing improved effectiveness
- Digital CBT-I with coach shows better results (CBT-I coach )
- Insomnia coach can be used independently
- 2 small RCT with Sleepio in pregnant women
- Other resources: Sleeprest(SHUT-i) and Sleepstation(NHS,UK)

# Question 5

If non-pharmacological options for treatment of insomnia are exhausted, clinician can consider using which of the following medications:

A. Benzodiazepines
B. Benzodiazepine receptor agonists
C. Antihistamines
D. Antidepressants
E. Any of the above

# Pharmacological

- Melatonin
- Antihistamine ( Doxylamine, Diphenylhydramine, Hydroxyzine)
- Benzodiazepines (Lorazepam, Alprazolam, Clonazepam)
- Benzodiazepine Receptor Agonist( Zolpidem, Zopiclone, Zaleplon)
- Antidepressant ( Trazodone, Mirtazapine, Doxepin,Elavil )
- Atypical antipsychotics (Olanzapine, Quetiapine)

# Melatonin

- 1% women use melatonin during pregnancy
- No monitoring by FDA
- Limited data and mostly from animal studies
- Available data conflicting
- Supplemented doses are much higher than physiologic doses
- Exogenous supplementation can alter endogenous secretion and affect fetal circadian rhythm

***Ref: Freeman et al 2016,Prazinko et al 2000,Choudhry et al 2018***

# Antihistamine

- Data primarily from studies when used as anti-emetics
- Available data is limited but does not show association with congenital malformation or poor neonatal outcomes
- Theoretical risk of decrease in milk supply
- **Doxylamine(25-50 mg)** is the preferred and often the first line medication for insomnia
- **Diphenhydramine**: Very limited data

  Studies have not shown any consistent association with any specific congenital malformation. No adverse effects in BF, occasional use ok
- **Hydroxyzine**: Huma data limited

  No consistent pattern of malformation. No specific data available related to BF

***Ref : Li et al 2013,Andreak et al 2012,smedt et al 2014.Choudhary et al 2018***

# Benzodiazepines

- Prenatal use not associated with increased risk of congenital malformation
- Prenatal use not associated with cardiac malformation
- Antenatal SSRI and benzo use in combination was associated with increased risk of congenital malformation
- Frequent and daily dosing in late pregnancy associated with risk of neonatal intoxication or neonatal withdrawal syndrome
- Increased risk of small head circumference and neonatal ICU care
- Data for breast feeding with short acting BZD is reassuring
- Data on longer term neurodevelopmental outcomes is relatively reassuring

***Ref: Grigoriadis et al 2019, Oberlander Et al 2008, Iqbal 2002, Grigoriadis 2020, Kelly 2012,Lupatelli 2019***

# Benzodiazepines

- BZD with short half life and preferably with no active metabolites (lorazepam ) are preferred over clonazepam or diazepam
- Alprazolam: RID (8.5%) very short acting, high risk of dependency
- Lorazepam: Short acting, RID low (2.5 %),***drug of choice***
- Clonazepam: RID 2.8 and more commonly seen in practice
- Diazepam: RID 4.7%
- Relative Infant Dose: parameter to indicate drug migration to infants through breast milk. If this value is less than 10%, it is considered unlikely to have a clinical effect on the infant

# Benzodiazepine Receptor Agonist

- Zolpidem(5 mg), Zopiclone, Zaleplon
- Limited data
- Recent large prospective study did not find association with congenital formation but found statistically significant risk for intestinal atresia (based on 4 cases,3 had concomitant medication use)
- Several small studies have shown risk for poor neonatal outcome like C/S, SGA, PTB, respiratory depression (not adequately controlled for depression, anxiety and insomnia )
- Abuse potential
- Supra-therapeutic doses have risk for congenital malformation
- Data during breast feeding is reassuring

***Ref: Wikner et al 2011, Wang 2010, Pons 1989***

# Antidepressant

- Trazodone

  New emerging data but still limited

  No consistent pattern of major congenital malformation

  Distributed in milk in small amounts

- Mirtazapine: (RID 0.5-3%)

  Limited human data

  No known teratogenicity

  Few sexual S/E and anti-emetic

  Risk of metabolic syndrome

- Amitriptyline: (RID1-2%) considered safe during pregnancy and breast-feeding
- Doxepin: Can consider in pregnancy, but avoid in breastfeeding( hypotonia, respiratory depression)

# Atypical Antipsychotics

- Not FDA indicated
- Sedating atypical antipsychotics like quetiapine and olanzapine have reassuring safety data in pregnancy and breastfeeding
- Low dose, short term use can be beneficial
- Both medications have increased risk for macrosomia and gestational diabetes
- Infants should be monitored for sedation

***Ref: Huybrechts et al 2016,Parker et al 2016***

# CASE

- What was done right ?
- What would you have done differently ?
- What more you would have liked to do ?

# Thank You !