Peripartum Agitation

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Peripartum Agitation: Overview of Basic Principles

What is Agitation?

- Definitions:
  - Combative and aggressive behavior, physical restlessness, or extreme irritability (1).
  - Increased verbal or physical activity accompanied by increased arousal and decreased functionality.
- Agitation in pregnancy should be considered an obstetric emergency due to risk of harm to mother and/or baby/fetus.
- Risks of untreated agitation are generally considered greater than one-time medication intervention.
  - Agitation associated with complications such as preterm delivery, placental abnormalities, low birth weight, postnatal death, spontaneous abortion (4).
  - Leaving alcohol withdrawal untreated leads to increased risk for preterm birth and low birth weight (1).
  - One-time dose of anti-psychotic and/or benzo generally considered to be low risk.

What is Causing the Agitation? -- Determine Likely Underlying Etiology

- Rule out Underlying Medical Condition
  - Delirium due to medical condition, amniotic or venous thromboembolism, pre-eclampsia/eclampsia, hyperthyroidism, trauma, infection, among others.
- Psychiatric Illness
  - New onset vs exacerbation/decompensation of existing condition.
  - Abrupt discontinuation of psychotropic medications due to concern over fetal risk (1).
  - Post-partum psychosis
  - "Personality" characteristics
- Drug Intoxication or Withdrawal
- Pain
- Traumatic Brain Injury (TBI)

Step 1: Verbal De-escalation and Behavioral Re-direction

- Safety First
- Respect Personal Space
- Speak Slowly in Calm, Low Voice
- Be Concise
- Be Present and Genuine
- Establish Trust
- Listen
- Validate
- Provide Accurate Reflections
- Normalize Reactions
- Identify Wants/Feelings
- Offer Choices/Options
- 'Agree' or 'Agree to Disagree'
- Do Not be Provocative

Examples of Verbal Strategies

- What helps you at times like this?
- I think you would benefit from medication, or I think you need a medication.
- I know you *feel* like _____ and that must be tough. Others in this predicament have also *felt* this way. In my experience, I have *found* that _____.
- Offer warm blanket, food, etc.

Ensure safety of yourself, staff & scene (1)

- Ensure patient and the room are free of safety hazards/weapons.
- Remain at a safe distance from patient with clear exit from room.
- Alert appropriate security personnel and/or have mechanism for alerting additional staff/security.

Step 2: General Principles of Pharmacological Interventions

- Goal: Address safety and allow for complete assessment/treatment of underlying cause.
- Choice of medication should ideally be suited to underlying etiology of agitation.
- When treating pharmacologically:
    - Offer PO first to honor autonomy.
    - Use IM/IV only if refusal of PO, Danger to Self (DTS) and/or Danger to Others (DTOs).
    - If does not have decisional capacity (ex. floridly delusional), okay to start with IV option.
- General approach:
    - Start with PRN option.
    - Recommend scheduling medications if persistent, regularly occurring agitation.
    - Taper/Discontinue once agitation has resolved for a few days.
- Consider onset of action
    - IV works the fastest: approximately 5-20 minutes.
    - PO generally takes at least 30 mins-1 hour.
- Put in a not to exceed (NTE) in order.
- Never feel like you have to order a medication immediately. If unsure, go lay eyes on the patient.
- **Pregnancy specifics:**
    - Limit medications as able (ex. choose already prescribed medication).
    - Potential options: diphenhydramine, haloperidol, olanzapine, lorazepam.
    - One-time doses of benzodiazepines and anti-psychotics are generally considered low risk and not associated with an increased risk in congenital malformations.
    - Contra-indicated: valproic acid

Step 3: Restraints: Last resort intervention only during pregnancy

- Use only if imminent risk to 1.) mother 2.) fetus/newborn 3.) staff or others AND failure of prior interventions/least restrictive options.

- DO: Use least restrictive options possible (fewer restraints the better). Continue frequent monitoring of patient/vital signs/fetal heart tones while in restraints. Ensure adequate comfort, hydration, nutrition, and medical stability throughout process. Limit/end restraints as much as possible.

- DO NOT USE: abdominal restraints, restraints that increase risk of falling forward (wrist restraints behind the back), four-point restraints, restraints during labor & delivery, use out of convenience or punishment (6).

- 20 weeks+: Place pregnant patient partway to the left with support under the right hip – right hip should be 10-12 cm off the bed with supporting pillows/blankets.
    - Do not restrain in supine position or on right side due to risk of inferior vena cava compression syndrome (hypotension, tachycardia, fetal distress due to compression vena cava, blocking flow of venous blood to the heart; 5,6).

Be mindful of implicit bias and thoughtful about escalation of interventions

Pharmacological Interventions: Specific Medications*

- Choose medication based on most likely underlying cause of agitation when possible (ex. lorazepam for alcohol withdrawal). Limit medications as able (ex. choose already prescribed medication).
- Mild: **PO meds**
  - Diphenhydramine 25 – 50 mg PO, IM (can worsen delirium)
- Moderate: **Consider IV/IM**
  - Haloperidol 0.5 mg – 2 mg PO, IV, IM
  - Olanzapine 2.5 mg – 5 mg Rapidly dissolving, PO, IM (do not co-administer IM olanzapine and benzodiazepine; following IM olanzapine, wait at least one hour and monitor for respiratory depression prior to use of benzo)
  - Lorazepam 0.5 – 2 mg PO, IV, IM
- Severe: **IV/IM**
  - Haloperidol +/- lorazepam +/- diphenhydramine

Pharmacological Interventions: Pregnancy Considerations

- Limit number of medications.
  - Give patients known medications first to limit exposures to fetus (ex. patient already receiving olanzapine).
  - Match IM/PO/IV medications.

- Anti-psychotics
  - Most data on haloperidol, olanzapine, and quetiapine during pregnancy. One-time doses are generally low risk and not associated with an increased risk in congenital malformations compared to general population (risk 2-3%) (1, 7).
  - 1st generation (haloperidol): less likely to have sedative or hypotensive effect compared to low potency anti-psychotic (4).
  - Less clear data on risperidone; recommend to generally avoid given other options available (unless patient already scheduled on this medication). Risperidone has higher relative infant dose and some studies show small increased risk of cardiac malformations (7).
  - If frequent administration of anti-psychotics in 3rd trimester, newborns should be monitored for theoretical risk of neonatal EPS. FDA warning (2011) about risk of exposure in 3rd trimester including neonatal EPS, sedation, breathing and feeding difficulties, increased/decreased muscle tone, agitation, tremor. These complications may resolve on their own or require additional hospitalization.

- Benzodiazepines
  - One-time doses may not have adverse effects; no study has assessed risk of outcomes after one time exposure, though data on long term treatment is reassuring (1).
  - Regular use early in pregnancy may be associated with spontaneous abortion.
  - One study showed possible association of benzodiazepines with congenital malformations with co-administration of SRRI; however, this study has not been replicated (13).
  - If frequent administration during third trimester, monitor newborns for floppy baby or neonatal withdrawal syndrome. Symptoms may include sedation, hypotonia, feeding difficulties.

- Contra-indicated: valproic acid (not generally used for acute agitation)

- Dosing: Medications metabolized by CYP P450 enzymes more rapidly metabolized during pregnancy and may require higher doses.
  - Examples: CYP3A4 – clonazepam/quetiapine; CYP2D6 – risperidone; Glucuronidation – lorazepam)

**For more details about specific medications and effects during pregnancy, see table below.*

Peripartum Agitation Medications

Medication	Potential Indications	Maternal Acute Side Effects	Effects on Fetus/Birth in:		Starting Dose Ranges	Onset of Action	Notes
			Early Pregnancy	Late Pregnancy			
Haloperidol (1st line if etiology of agitation unknown)	Mod/Severe Agitation Delirium/ Organic etiology Primary Psych (ex. psychosis)	EPS (higher risk) Dystonia Sedation NMS Anti-cholinergic Effects QTc prolongation (worse with IV)	No evidence of increased congenital anomalies (evidence from retrospective study > 100 pregnancy, prospective study > 180 pregnancies, meta-analysis >130,000 pregnancies)	Risk of neonatal EPS for ongoing use; no data of increased risk from one time use. FDA warning (updated 2011) for EPS, sedation, breathing/ feeding difficulties, agitation, tremor, change in muscle tone; may resolve spontaneously or require additional hospital care.	PO: 0.5-1 mg TID PRN IV: 0.5 - 2 mg TID PRN IM: 5 mg once time Can increase to 4-20 mg/day NTE: 20 mg/day	PO: 45 – 60 mins IV > IM: 15 – 30 mins	Get EKG baseline to evaluate QTc. Continue to monitor with increased doses. IV preferred over IM if IV available (IM higher risk of EPS) IM: recommend giving with diphenhydramine 25 – 50 mg to prevent EPS Consideration: Less likely to have sedative or hypotensive effects than low-potency anti-psychotics
Olanzapine (alternative choice)	Mod/Severe Agitation Primary Psych (ex. mood stabilization, psychosis)	Sedation Orthostatic hypotension EPS Metabolic syndrome	No evidence of increased risk of congenital anomalies. Multiple studies/reviews showed rates of ectopic, premature or post-term birth, spontaneous abortion does not appear higher. Canadian study of 166 pregnancies showed no increased risk for gestational DM/HTN, preterm birth.	Risk of neonatal EPS for ongoing use; no data of increased risk from one time use. FDA warning (updated 2011) for EPS, sedation, breathing/ feeding difficulties, agitation, tremor, change in muscle tone; may resolve spontaneously or require additional hospital care.	PO: 2.5 – 5 mg PO or IM BID PRN Can increase to 10-20 mg/day NTE: 20 – 30 mg/day	PO: 30 mins – 1 hour IM: 15 – 30 minutes	Get EKG baseline to evaluate QTc. Continue to monitor with increased doses. Do not administer IM medication with benzodiazepine (risk of respiratory distress) Highest placental transfer (72.1%)

Quetiapine (alternative choice)	Primary psych (mood stabilization) Delirium Anxiety	Sedation Weight gain Metabolic syndrome Possible risk of increased gestational diabetes	Not expected to increase risk of malformations (>5000 exposures, multiple case reports) based on limited data.	Risk of neonatal EPS for ongoing use; no data of increased risk from one time use FDA warning (updated 2011) for EPS, sedation, breathing/ feeding difficulties, agitation, tremor, change in muscle tone; may resolve spontaneously or require additional hospital care.	25 – 100 mg PO NTE: 300 mg daily for agitation		Lowest possible placental transfer (3.7%)
Lorazepam (preferred benzo in pregnancy)	Alcohol or Benzo withdrawal Stimulant intoxication AMS 2/2 NMS, serotonin syndrome, catatonia Personality	Sedation Respiratory distress Memory Impairment Risk of falls/ Incoordination Tolerance Dependence Withdrawal	In general, does not appear to be associated with increased congenital anomalies. Data on congenital malformation association in one study with SSRI and benzos but has not been replicated. Increased risk of spontaneous abortions.	Exposure associated with "floppy baby" syndrome and neonatal withdrawal (requiring ICU admission); more likely from long term use	0.5 – 2 mg PO, IV, IM up to 2-3 times daily Increase as needed to 2-6 mg daily divided in doses NTE: 10 mg/day in divided doses	PO: 15 – 30 mins IM, IV: rapid	Black box warning: avoid use with opioids; abuse/misuse potential
Diphen-hydramine	Mild agitation Anxiety	Sedation Anti-cholinergic effects GI distress Impaired coordination	Limited published data in pregnancy. Generally, not expected to increase risk of congenital abnormalities. There are some reports of associations with cardiac malformations (d-transposition great arteries) and cleft palate, though data is not consistent	One case report of neonatal withdrawal symptoms (irritability, sedation, tremulous, diarrhea).	25 – 50 mg PO, IV, or IM Q1-4 hours NTE: 300 mg/day	PO: 15 – 20 mins IM, IV: rapid	Dose dependent anti-cholinergic effect can make delirium worse

Peripartum Agitation References

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