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Information for Provider on Antipsychotics during Pregnancy and Breastfeeding – February 2023

This chart is produced by the University of Illinois at Chicago (UIC) by Illinois DocAssist as a summary of research on antipsychotics in human pregnancy and breastfeeding

ANTIPSYCHOTIC RISKS IN PREGNANCY

Safety Data: No randomized control trials. Safety data derived largely from cohort studies, registry data, and prescription monitoring registries. Older studies suggested more adverse outcomes as they did not control for confounders such as presence and severity of maternal mental illness which is associated with adverse outcomes. Newer and better designed studies demonstrate less risks than previously believed. Because of antipsychotics' small molecular size, typically cross placenta at higher rates.[13]

Safety Ratings: Transition from Pregnancy Category (A, B, C, D, X) to PLLR (Pregnancy, Lactation, and Reproductive Labeling) as categories are confusing and did not accurately or consistently communicate differences in fetal risk. PLLR provides a risk summary based on available data in animal and human studies as well as clinical considerations for prescribers.

Obstetric Risks

- Both maternal illness and antipsychotics are associated with dose-dependent increased risk of preterm birth.[9, 14, 21]
- Second generation antipsychotics are associated with higher risk of gestational DM, but more recent registry data found no increased risk of diabetes or gestational weight gain. Women taking antipsychotics were more likely to begin pregnancy with a higher BMI. [6, 8. 9, 22]

Infant Risks

- **Congenital malformations**
  - New and well-designed studies show no associated increased risk for congenital malformations. [7, 9, 19, 21]
- **Infant weight**
  - Some concern for increased infant weight related to metabolic risks of SGA, but registry data show mean birthweight of infants is within range of expected weight. [5, 14, 21]
- **Adaptation**
  - Some evidence of a withdrawal/adjustment phenomenon with self-limited altered tone, difficulty breathing, or difficulty feeding [9, 21]
  - Increased risk of neonatal EPS which may last up to 1 year (most resolve in 10 days[1]), worse with higher D2-potency agents (haloperidol, chlorpromazine, risperidone.) [19]
- **Neurodevelopmental**
  - Neuromuscular delays at 6 months which resolve by 12 months. [14, 21]
  - No difference in behavior, development, nor IQ at 5 years old. [1]

If you have questions or need a consultation, contact Illinois DocAssist at 866-986-2778 to speak with a psychiatric consultant.

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ANTIPSYCHOTIC RISKS IN BREASTFEEDING

Safety data: Includes limited studies examining relative infant dose, medication concentration in breastmilk, and infant plasma concentration as well as reports of adverse events.

Risks:

- Poor feeding, lethargy, irritability, not waking to feed, jitteriness, poor weight gain.
- Infants are exposed to much higher doses in-utero, therefore women should not be counseled to discontinue medications or not breastfeed due to low comparative exposure from breast milk.
- Theoretical risk to milk production based on prolactin disturbance by antipsychotics, but inconsistent data and not a reason to avoid breast feeding [6]

Safety rating:

Dr. Hale's Lactation Risk Categories L1-L5

L1 SAFEST – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk.

L2 SAFER – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.

L3 MODERATELY SAFE – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.

L4 POSSIBLY HAZARDOUS – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.

L5 CONTRAINDICATED – Studies have shown significant risk to nursing infants. The drug should NOT be used during breastfeeding.

Clinical Considerations

- No medication is risk free.
- The risks of psychotropic use in pregnancy and lactation must be weighed with the risks of untreated or undertreated psychiatric illness to the mother and child.
- In psychotropic naive women, quetiapine is the drug of choice in pregnancy and breastfeeding.
- If a patient is pregnant and stable on a non-first line medication, the risk of changing medications (relapse of symptoms, multiple drug exposures in pregnancy) may outweigh the benefits for the mother-infant dyad.
- Untreated or undertreated psychosis is associated with preterm labor, decreased obstetric and medication adherence, increased rates of substance use (especially tobacco), suicide, impaired bonding and attachment with infant, postpartum mood or psychotic episodes, and risk of mental disorders in infant.
- Treatment target is remission of symptoms.
- Drug metabolism in pregnancy may change due to alterations in enzymatic activity such as CYP 2D6 and 3A4 and increased creatinine clearance. May consider supra-therapeutic doses in the context.

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	Medication	Advantages	Disadvantages	Relative Infant Dose	Lactation Rating*	Potential adverse effects of breastfeeding
First Generation Antipsychotic	Haloperidol	• Long-acting injectable • More data compared to SGA	• Risk of infant EPS • Concomitant use of anticholinergics to manage side effects have increased risk of teratogenicity[19]	0.2-12%	L3	• Sedation
	Chlorpromazine	• Data supporting treatment of pregnancy-induced nausea/vomiting[18] • More data compared to SGA	• Risk of infant EPS • Concomitant use of anticholinergics to manage side effects have increased risk of teratogenicity[19] • Increased metabolic side effects	0.3%	L3	• Sedation
Second Generation Antipsychotic	Quetiapine	• Lower placental passage and breastmilk compared to other antipsychotics [20]	• No IM formulation • Increased metabolic side effects	0.02-0.1%	L2	• Drowsiness, weight gain, delayed milestones[21]
	Risperidone	• Long-acting injectable	• Increased metabolic side effects • Risk of infant EPS • Possible statistically significant RR of 1.26 for any major malformation[6]	2.8-9.1%	L2	• Sedation
	Olanzapine		• Highest rate of placental transfer[19] • Greatest increased risk of metabolic side effects[19]	0.28-2.24%	L2	• Sedation
	Paliperidone	• Long-acting injectable	• Increased metabolic side effects • Less data than other agents	ND	L3	
	Aripiprazole	• Long-acting injectable • Less risk of metabolic side effects[2]		0.7-6.44%	L3	
	Ziprasidone	• Less risk of metabolic side effects	• Less data than other agents	0.07-1.2%	L2	
	Lurasidone	• Less risk of metabolic side effects	• Less data than other agents	ND	L3	
	Clozapine	• Best in treatment refractory women	• Frequent lab monitoring • Increased metabolic side effects	1.33-1.4%	L3	• High secretion into breast milk • Theoretical risk for neonatal agranulocytosis or seizure (though no reported cases)[19]

L1 SAFEST – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk.
L2 SAFER – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
L3 MODERATELY SAFE – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.
L4 POSSIBLY HAZARDOUS – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.
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