ECHO Idaho: Perinatal Substance Use Disorder

Medications and Substances in Pregnancy: Exposure and Risk
May 13, 2020
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The speaker has no relevant financial relationship(s) to disclose.

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Learning Objectives

• Review how “substances” and medications can affect mom and baby during different phases of pregnancy and postpartum.

• Review the concepts of harm reduction and how to evaluate the risk/benefit ratio for women and their babies.

• Discuss some common medications and substances that providers will encounter in pregnancy.
Wilson’s 6 rules of teratology

1) Genetic makeup influences susceptibility
2) Stage of exposure influences susceptibility
3) Agents act in specific ways (pathogenesis)
4) Stage of exposure determines manifestation
5) Maternal metabolism and placental passage
6) Dose-response effect is present but complex
Effects vary on stage of exposure

- **Teratogenic effects** (structural defects)
- **Organ growth and brain development** “
  (growth restriction and CNS effects)
- **Newborn effects**
  (immune function, withdrawal, behavior)
Harm Reduction

• Accepts, for better and or worse, that licit and illicit drug use is part of our world and chooses to work to minimize its harmful effects rather than simply ignore or condemn them.
• Understands drug use as a complex, multi-faceted phenomenon that encompasses a continuum of behaviors from severe abuse to total abstinence, and acknowledges that some ways of using drugs are clearly safer than others.
• Establishes quality of individual and community life and well-being—not necessarily cessation of all drug use—as the criteria for successful interventions and policies.
• Calls for the non-judgmental, non-coercive provision of services and resources to people who use drugs and the communities in which they live in order to assist them in reducing attendant harm.
• Ensures that drug users and those with a history of drug use routinely have a real voice in the creation of programs and policies designed to serve them.
• Affirms drug users themselves as the primary agents of reducing the harms of their drug use, and seeks to empower users to share information and support each other in strategies which meet their actual conditions of use.
• Recognizes that the realities of poverty, class, racism, social isolation, past trauma, sex-based discrimination and other social inequalities affect both people’s vulnerability to and capacity for effectively dealing with drug-related harm.
• Does not attempt to minimize or ignore the real and tragic harm and danger associated with licit and illicit drug use.
Opioids/Opiates

- Opioid receptor agonists/antagonists
- Oxycodone/hydrocodone/heroin/codeine
- Methadone
- Buprenorphine
- Naloxone (and combinations)
- Kratom
Natural History of Opioid Use Disorder

- Euphoria
- Normal
- Withdrawal

Tolerance & Physical Dependence

Acute use
Chronic use
Other substances

• Amphetamines
• Methamphetamine
• Cocaine
• Alcohol
• Tobacco
• Marijuana
Risk vs Benefits

https://study.com/academy/lesson/risk-benefit-analysis-definition-example.html
FDA Categories

A. Adequate and well-controlled (AWC) studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of a risk in later trimesters).

B. Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no AWC studies in pregnant women, OR animal studies demonstrate a risk and AWC studies in pregnant women have not during the first trimester (and there is no evidence of risk in later trimesters).

C. Animal reproduction studies have shown an adverse effect on the fetus, there are no AWC studies in humans, AND the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks. OR animal studies have not been conducted and there are no AWC studies in humans.

D. There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, BUT the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks (for example, if the drug is needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective).

X. Studies in animals or humans have demonstrated fetal abnormalities OR there is positive evidence of fetal risk based on adverse reaction reports from investigational or marketing experience, or both, AND the risk of the use of the drug in a pregnant woman clearly outweighs any possible benefit (for example, safer drugs or other forms of therapy are available).
## FDA Categories

<table>
<thead>
<tr>
<th>Animal Studies</th>
<th>Human Studies</th>
<th>Benefits &gt;&gt; Risk</th>
<th>Benefit +/- Risk</th>
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<tbody>
<tr>
<td>A. No risk demonstrated</td>
<td>No risk* demonstrated</td>
<td></td>
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<tr>
<td>B. No risk demonstrated</td>
<td>No human studies</td>
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<tr>
<td>C. Animal risk noted</td>
<td>No risk* demonstrated</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>D. No animal studies</td>
<td>No human studies</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>X. Human risk noted</td>
<td></td>
<td>YES</td>
<td>Inadequate alternatives</td>
</tr>
</tbody>
</table>

* Adequately Controlled Studies
Pregnancy and Lactation Labeling Rule

• Pregnancy
  – Pregnancy Exposure Registry
  – Risk Summary
  – Clinical Considerations
  – Data

• Lactation
  – Risk Summary
  – Clinical Considerations
  – Data

• Females and Males of Reproductive Potential
  – Pregnancy Testing
  – Contraception
  – Infertility
Category X......alternatives?

- Warfarin
- “Statin” drugs (e.g., rosuvastatin, atorvastatin)
- Isotretinoin
- Fluorouracil (topical)
- Silver sulfadiazine (topical; late pregnancy)
- Testosterone and derivatives
- Leuprolide
- Ribavirin
- Dantrolene
- Methotrexate
- Raloxifene
- Dutasteride (avoid handling capsules in pregnancy)
- Finasteride (avoid handling capsules in pregnancy)
- Hydroxyzine (early pregnancy)
- Aspirin (third trimester)
- Flurazepam
- Triazolam
- Temazepam
- Misoprostol
- NSAIDs (e.g., naproxen, piroxicam, meloxicam) (third trimester)
- Celecoxib (third trimester)
Prescription Medications

- Psychiatric Meds
- SSRI’s
  - Paroxetine – CV?
- Quetiapine
- Trazadone
- Methylphenidate

- Antiepileptics
  - Valproic acid – NTD’s
- Carbamazepine
- Levetiracetam
- Oxcarbazepine
- Lamotrigine
- Topiramate

- Avoid Polypharmacy
- Optimize medications first
Key Points

• Birth defect risk is primarily first trimester
• Risks and benefits of medications should be discussed at length with patients before changes are made
• Don’t hesitate to confer with the team!
• Harm Reduction and absolute risks
• Pregnancy is an opportunity to impact maternal and family health
References and Resources

- IBM Micromedex: 6200 South Syracuse Way, Suite 300, Greenwood Village, CO 80111-4740; 800-525-9083 (in US and Canada); http://www.micromedex.com
- REPROTOX (Reproductive Toxicology Center): 7831 Woodmont Avenue, Suite 375, Bethesda, MD 20814; 301-514-3081; http://www.reprotox.org
- Mother to Baby: 200 W. Arbor Drive, #8446, San Diego, CA 92103-9981; 886-626-6847; http://mothertobaby.org
- U.S. Food and Drug Administration: Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling
THE END