

MEDICINES DURING PREGNANCYMandeep Kaur^{1*}, R.K. Patil² and H.C. Patil³¹Assistant Professor, Department of Pharmacy Practice, AIPBS, Bathinda, Punjab.²Professor, Department of Pharmacy Practice, AIPBS, Bathinda, Punjab.³Principal, AIPBS, Bathinda, Punjab.***Corresponding Author: Dr. Mandeep Kaur**

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ABSTRACT

Pregnancy is a very enthusiastic and eager feel but it is also having a great responsibility to the baby because most of the medicines are harmful for the infant. There are some teratogens like radiations which cause birth defects like abnormal growth as well as these effects child's heart, kidney and brain also. Thalidomide tragedy is a most common example for teratogens. Cocaine, opioids, cannabis are the common drugs which can harm the fetus. On the other side, there are drugs that are having adverse effects as well as beneficial effects also and that are also used in pregnancy for their quality of being good. Cocaine, opioids, cannabis are the common drugs which can harm the fetus. But there are some drugs that helpful to treat some common symptoms like rantac improves heartburn, acetaminophen treats headache and fever, some laxatives and stool softeners like duphalac treats constipation and diarrhea. In first trimester drugs like vitamin B6 are very helpful and in second trimester some alcohol free lozenges are helpful to treat sore throat while in third trimester avoid NSAIDs as well as at breastfeeding morphine containing drugs should avoid. FDA makes some categories having pregnancy categories that controls the side effects and harmful effects and provide a better improvement to the mother and new born baby, that welcomes very happily to a new coming generation and provide them a secured life.

KEYWORDS: Pregnancy, Breastfeeding, Thalidomide Tragedy, Teratogens.**INTRODUCTION**

Pregnancy is an exciting time. However, it can also be a scary time if you are not sure how your medicines will affect your baby. Not all medicines are safe to take when you are pregnant. Even aspirin or ibuprofen could cause problems if you take it during the last 3 months of your pregnancy.^[1] There is no systematic and ongoing approach to the development of such guidance for most maternal conditions, and therefore a need for both development of guidance and dissemination to appropriate providers. Safer medication use during pregnancy also means taking steps to avoid unnecessary exposure to known teratogens in pregnancy.^[2] Each year, millions of pregnant women are confronted with serious medical illness: hypertension, diabetes, autoimmune diseases such as arthritis and lupus, influenza, significant psychiatric illness, even cancers.^[3]

Teratology

A teratogen is anything in the environment – a chemical or substance like radiation that can cause a birth defect. These are agents that act to irreversibly alter growth, structure, or function of the developing embryo or fetus. Recognized teratogens include viruses (eg, rubella, cytomegalovirus, congenital lymphocytic choriomeningitis virus), environmental factors (eg,

hyperthermia, irradiation), chemicals (eg, mercury, alcohol), and therapeutic drugs (eg, inhibitors of the renin-angiotensin system, thalidomide, isotretinoin, warfarin, valproic acid, carbamazepine)^[4] The thalidomide tragedy is perhaps the example that comes first to mind when considering medication use during pregnancy. One in twenty five (1:25) babies born in this country has a birth defect.^[5] Prescribing a drug to a pregnant woman is like taking a journey through uncharted territory; navigation is made no easier by the darkness cast by "thalidomide's long shadow."^[6] Thalidomide was a widely used drug in the late 1950s and early 1960s for the treatment of nausea in pregnant women. It became apparent in the 1960s that thalidomide treatment resulted in severe birth defects in thousands of children. Though the use of thalidomide was banned in most countries at that time, thalidomide proved to be a useful treatment for leprosy and later, multiple myeloma. In rural areas of the world that lack extensive medical surveillance initiatives, thalidomide treatment of pregnant women with leprosy has continued to cause malformations. It causes sealed limbs in children.^[7]

To define research priorities, we need to understand patterns and factors associated with actual use of the wide range of specific medications that are taken during

pregnancy, and particularly during the first trimester, which includes the period of organogenesis, when concerns about teratogenic effects are greatest. It is also critical to identify the prevalence of exposure to both prescription and OTC medications and how use of medications changes over time.^[8]

Obstetrical outcome of drug use in women

When non-medically prescribed drug use or abuse occurs in pregnant women, considerable morbidity can be expected for both the mother and her offspring. In particular, illicit drug use during pregnancy places the mother at increased risk of a variety of obstetrical complications, which are listed below according to time in the pregnancy: Early pregnancy loss;

- Abruptio placentae (premature detachment of the placenta from the wall of uterus);
- Amnionitis (inflammation of the amnion, the thin membrane surrounding the fetus that contains the amniotic fluid);
- Intrauterine growth restriction;
- Placental insufficiency;
- Septic thrombophlebitis (a condition characterized by a venous clot, inflammation and infection); Pre-eclampsia (a sudden rise in blood pressure, excessive weight gain, generalized edema, proteinuria, severe headache and visual disturbances);
- Eclampsia (convulsions or coma occurring with pregnancy-associated high blood pressure)
- Late intrauterine death;
- Premature labour;
- Premature rupture of membranes; and
- Postpartum hemorrhage.

Most commonly problems during pregnancy are GI complications which causes due to anatomic and Physiologic changes. These involves^[9]

- Constipation
- Hemorrhoids
- Appendicitis
- Diverticulitis
- Inflammatory bowel disease
- Colorectal cancer

Drugs that harm the fetus

Cannabis and Opium are main drugs which are used in pregnancy for motion sickness. Opium contains 25 different alkaloids narcotine, morphine, papaverine and methylmorphine are commonly used from them.^[10] A substitute of morphine and codeine that is called heroin (diacetylmorphine)^[11] Amphetamine is also currently part of a series of pills used in medicine. Although amphetamine itself is an addictive drug with euphoric effects, more commonly abused drug is its derivate methamphetamine (MA).^[12]

Opioids

Heroin and morphine: Morphine was isolated in 19th century while heroin was discovered in 1875 from opium. Opium produced from *Papaver somniferum* and it contains dried uses of unripe poppy plant.^[13] Female rats that were given morphine during pregnancy showed a reduced care for their offspring compared with control females, who were injected with saline Morphine mothers were less often present in the nest, less in contact with pups and less licking and grooming their pups than controls.^[10] Prenatal application of morphine to pregnant rats also affects the susceptibility to seizures^[10]

Cocaine

Because cocaine stimulates uterine contractility, there is also an increased risk of premature rupture of membranes and preterm labour or delivery, conditions that affect 17–29% of pregnancies of cocaine-abusing women. Clinicians should observe pregnant cocaine users for hypertension, hyperthermia (greatly increased body temperature), abdominal pain and increased heart rate—and in the case of heavy cocaine use, arrhythmias, myocardial infarction, respiratory failure, stroke and seizures.^[14]

Amphetamines

Amphetamines belong to a group of drugs called 'psychostimulants'. Amphetamines stimulate the central nervous system, which speeds up the messages going to and from the brain to the body. Using amphetamines during pregnancy can affect the baby's development before birth and has been linked with early labour and miscarriage.^[15]

Amphetamine use in pregnancy may increase the risk of:

- Reduced blood flow and oxygen to the baby from the narrowing of the blood vessels
- Miscarriage
- Prematurity
- Bleeding from the site of the placenta (afterbirth)
- Reduced growth of your baby in pregnancy
- Stillbirth

Amphetamine use in pregnancy has been linked to increased risk of the following abnormalities to the foetus:

- Smaller head size
- Eye problems
- Cleft lip and palate
- Delayed motor development
- Limb Defects Changes to the brain which may cause bleeding
- Heart abnormalities

Methamphetamines

A central nervous system stimulant, methamphetamine causes the brain to be flooded with dopamine, a chemical that stimulates pleasure.^[16] Methamphetamine,

commonly known as “meth,” “crystal,” “crank,” “ice” and “speed” – is an illegal and dangerous drug that can be snorted, swallowed, smoked, injected or inhaled.^[17] Methamphetamine use during pregnancy affects development of a baby's:

- Brain
- Spinal cord
- Heart
- Kidneys

Cannabis

Marijuana is the most commonly used illicit drug among women of reproductive age or by women who are pregnant. Any form of smoking can disrupt the supply of oxygen and nutrients to the fetus, which can result in restrictions in the growth of the fetus including overall length, foot length, head size and body weight.^[18]

Alcohol

Medical problems associated with alcohol use progress more swiftly in women. Female alcoholics have 50–100% higher rates of premature death than male alcoholics, with more female alcoholics dying from circulatory disorders and cirrhosis of the liver than their male counterparts.^[19]

Factors which effect the fetal growth

- Gestational age,
- Route of administration,
- Absorption of the drug,
- The dose of the drug medication,
- Maternal serum levels, and
- The maternal and placental clearance system.

FDA Pregnancy Categories

The FDA has established five categories to indicate the potential of a drug to cause birth defects if used during pregnancy. The categories are determined by the reliability of documentation and the risk to benefit ratio. They do not take into account any risks from pharmaceutical agents or their metabolites in breast milk. The pregnancy categories are:

Category A

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

Example drugs or substances: levothyroxine, folic acid, magnesium sulfate, liothyronine

Category B

Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

Example

drugs: metformin, hydrochlorothiazide, cyclobenzaprine, amoxicillin, pantoprazole

Category C

Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Example

drugs: tramadol, gabapentin, amlodipine, trazodone, prednisone

Category D

There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Example

drugs: lisinopril, alprazolam, losartan, clonazepam, lorazepam

Category X

Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

Example

drugs: atorvastatin, simvastatin, warfarin, methotrexate, finasteride

Category N

FDA has not classified the drug.

Example

drugs: aspirin, oxycodone, hydroxyzine, acetaminophen, diazepam

Need for safer medicines in pregnancy

Most of the drugs in pregnancy can cause harm to the fetus so the drugs having less side effects in pregnancy are used for pregnant ladies. Drugs like paracetamol, cephalosporins and antacids are having no harmful effect to the patient. The treatment of morning sickness has been difficult since Debendox (doxylamine, dicyclomine, and pyridoxine), known as Bendectin in the United States, was taken off the market in the early 1980s.^[10]

This chart lists over-the-counter (OTC) medicines considered low risk for pregnant women when taken for the occasional mild illness. It also mentions a few that are not safe. We've listed a few brand names as examples, but there are many more on the market. Of course, nothing is 100 percent safe for all women, so it's a good idea to check with your doctor or midwife before taking any kind of medicine during pregnancy – even an over-the-counter product. Don't take more than the recommended dose and, if possible, avoid taking anything during your first trimester, when your developing baby is most vulnerable.

Table 1: drugs which are safe for pregnancy^[1]

Common sign and symptoms seen in pregnancy	Treatment
Heartburn, gas and bloating, upset stomach	Antacids for heartburn (Rantac, Aciloc,); Simethicone for gas pains (capcid SYR, Gasnil).
Cough or cold	Guaifenesin, an expectorant (Ambrax, Ascoril); Dextromethorphan, a cough suppressant (Alex DPS, Anacof DM, Ascoril D); Not safe to take: Cold remedies that contain alcohol, e.g: The decongestants pseudoephedrine and phenylephrine, which can affect blood flow to the placenta.
Pain relief, headache, and fever	Acetaminophen (A- 125, Cafepar, Calpol).
Allergy relief	Chlorpheniramine, an antihistamine (C Cal, C Mox); Loratadine, an antihistamine (Claidin, D- Loratin); Diphenhydramine, an antihistamine (Becodryl, Caladryl Lotion).
Constipation, hemorrhoids, and diarrhea	Psyllium (Multivite Women, 2 DEP); Polycarbophil (Caldikind Plus, Multivite Women); Methylcellulose (Citrucel, Unifiber); Other laxatives and stool softeners (Dulcolax, Duphalac); Hemorrhoid creams (Anusol, Preparation H, Tucks); Loperamide, anti-diarrhea medication (Lopamide, Starlop);
Yeast infections and other fungal infections such as athlete's foot	Clotrimazole (Candid V, Mycocid V); Miconazole (Fungitop, Candistat); Terbinafine (Teraderm, Terbo);
Insomnia	Diphenhydramine (Benadryl, Becoryl); Doxylamine succinate (Unisom Nighttime Sleep-Aid)
Cuts and scrapes	Polysporin

Drugs used in first trimester

Women who are between four and 12 weeks pregnant may safely take the following over-the-counter medications. In morning sickness, vitamin B6: take 50 mg/day to start; if not helpful increase by 50 mg 2 to 4 times/day until you reach a total of 200 mg/day but not to take more than 200 mg each day. If mild headaches, pains occurs than try comfort measures and take acetaminophen.^[20]

Drugs used in second trimester

Women who are between four and 12 weeks pregnant may safely take the following over-the-counter medications. In nasal congestion due to cold than use a simple nasal spray and if cough persists than non alcoholic cough syrup is used. For sore throat, alcohol free lozenges are used. If constipation persists than milk of magnesia given to the patient. As well as for insomnia 50 mg vitamin B6, warm milk is used.^[21]

Drugs for third trimester

Women should avoid using NSAIDs after 32 weeks gestation, owing to the possibility of antiplatelet or prolonged bleeding effects.^[22] Several forms of fentanyl, including the patch, have been on the market for many years without reports of serious adverse effects, and it is considered effective for all types of chronic pain, including cancer and noncancer pain.^[23] In one, a high-dose fentanyl patch (ie, 125 µg/h) was used throughout pregnancy, and the newborn infant manifested mild withdrawal symptoms at 24 to 72 hours after birth.^[24]

Drugs and breast feeding

Frequency and duration of breastfeeding was lowered in the morphine mothers compared with controls. Amphetamines concentrate in breast milk and may cause poor sleep patterns and irritability in the infant. High doses may also reduce milk production.^[15] Women who used various amounts of alcohol or marijuana and moderate amounts of cocaine during their pregnancy were not deterred from breastfeeding their infant. Nicotine is secreted into human milk and has been associated with decreased milk production, decreased weight gain of the infant, and exposure of the infant to environmental tobacco smoke.^[18]

CONCLUSION

Medications used in therapeutic doses for acute and chronic pain appear to be relatively safe in pregnancy. To minimize fetal risk, initiate drug interventions at the lowest effective dose, especially in late pregnancy, and select analgesics only after careful review of a woman's medical or medication history. Clinical studies have failed to reach a consensus regarding congenital anomalies, and there is no evidence of a withdrawal syndrome in the newborn infant. Recent studies document a negative effect of prenatal exposure on infant neurobehavior as well as on long-term behavior, cognition, language, and achievement.

REFERENCES

1. www.fda.gov/pregnancy, medicine and pregnancy, 2012; 1-2.

2. Margaret A Honein, Suzanne M Gilboa & Cheryl S Broussard, The need for safer medication use in pregnancy, *Expert Review of Clinical Pharmacology* 2013; 6(5): 453–455.
3. Margaret Olivia Little, Anne Drapkin Lyerly and Ruth R. Faden, Pregnant women & medical research: a moral imperative, *Bioethics Forum*, 2009; 2(2): 60-66.
4. Catalin S. Buhimschi, MD, and Carl P. Weiner, Medications in Pregnancy and Lactation, *OBSTETRICS & GYNECOLOGY*, 2009; 113(1): 166-188.
5. Rajesh Kumari, Tejaswarup Kethni, clinical pharmacy in a south Indian government maternity hospital, *JPPR*, 2003; 33(2): 131-132.
6. Prescribing Medicines in Pregnancy, Australian Drug Evaluation Committee; 1999, 1-90
7. James H. Kim and Anthony R. Scialli, Thalidomide: The Tragedy of Birth Defects and the Effective Treatment of Disease, *toxicological sciences*, 2011; 122(1): 1-6.
8. Peter Rubin, Drug treatment during pregnancy, *BMJ*, 1998; 317: 1503–6.
9. Allen A. Mitchell, Suzanne M. Gilboa, Martha M. Werler, Katherine E. Kelley, Carol Louik, Sonia Hernandez-Díaz, Medication Use During Pregnancy, With Particular Focus On Prescription Drugs: 1976-2008, *Am J Obstet Gynecol.*, 2011; 205(1): 1-17.
10. Sherri A Longo, Robert C. Moore, Bernard J. Canzoneri, Alfred Robichaux, Gastrointestinal conditions during pregnancy, *Clinics in colon and rectal surgery*, 2010; 23(2): 80-89.
11. R. Slamberova, Drugs in Pregnancy: the Effects on Mother and Her Progeny, *physiological research*, 2012; 61(1): 123-135.
12. Opiate chemistry and metabolism, XII- Biotech- C- Opiate Chemistry, 1-5.
13. Euphrosyne Gouzoulis-Mayfrank, Joerg Daumann, Neurotoxicity of drugs of abuse—the case of methylenedioxymphetamines (MDMA,ecstasy), and amphetamines, *Dialogues Clin Neurosci*, 2009; 11: 305-317.
14. NIDA InfoFacts: Heroin, 1-4.
15. Collado F, Torres LM. Association of transdermal fentanyl and oral transmucosal fentanyl citrate in the treatment of opioid naive patients with severe chronic noncancer pain. *J Opioid Manag*, 2008; 4(2): 111-5.
16. Loretta Finnegan, Franco Vaccarino, Colleen Dell, A textbook on “Licit and Illicit Drug Useduring Pregnancy:” 2013; 14-30.
17. Malaika Babb, Gideon Koren, Adrienne Einarson, Treating pain during pregnancy, *Canadian Family Physician*, 2010; 56: 1-25.
18. Amphetamines used during pregnancy, Department of Health, www.ndmch.com, 2002; 1-2.
19. Committee opinion, Methamphetamine abuse in woman of reproductive age, 2011; 1-5.
20. Marijuana, Reproduction, and Pregnancy, science based information, ADAI, 1-3.
21. Louise Alliston, Drinking alcohol during pregnancy, Health promotion agency, 2014; 15-25.
22. Medicine and Pregnancy, FDA, www.fda.gov/pregnancy
22. Regan J, Chambers F, Gorman W, MacSullivan R. Neonatal absti
23. Nence syndrome due to prolonged administration of fentanyl in pregnancy. *BJOG*, 2000; 107(4): 570-2.
24. Amphetamines, 1-3.