

## **DRUG CHOICES IN PREGNACY AND BREASTFEEDING**

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### **Abstract**

More than 50% of pregnant women use medications during their pregnancy. On the other hand, women who are breastfeeding even when they are sick, ask doctors weather it is safe to take medication during breastfeeding. In both cases using medications is possible if it is necessary and approved by doctors. If a woman is planning her pregnancy, and she uses medications, she must consult her doctors weather it is safe to take her therapy. If the drugs that they are using are harmful for fetus or babies, women should take contraception until therapy is substitute with safe medications. Smoking and drinking must be stopped during pregnancy and breastfeeding. Nevertheless, there are more and more women who are using medications during pregnancy.

**Key Words:** *breastfeeding, medications, pregnancy, toxicity.*

The incidence of congenital malformation that are connected to taking medication during pregnancy is 2-3%. Medications are reaching fetus through placenta.

Drags are affecting fetus by several mechanisms:

1. They can directly damage fetus or cause abnormal development of some organs, and that can lead to congenital malformations;
2. They can change placental functioning by narrowing of some blood vessels, and that can lead to decreased blood flow in placenta. Decreased blood flow leads to impairment in fetal growth and development, and very often these babies are with smaller weight;

3. Some drugs can cause contraction of uterus and this condition leads to decreased nutrition of the fetus. Contraction of some parts of the uterus can lead to generalized contractions and preterm delivery.

**Table 1.** Influence of medications on fetal development in different phases.

<b>Time frame</b>	<b>Possible effect of the medication</b>	<b>Fetal condition</b>
20 days after fertilization	Death or no effect	Fetus resistant on congenital malformations
3-8 weeks after fertilization	No effect, Spontaneous miscarriage, Congenital malformations, Permanent damage that is not very significant, but in time it becomes more visible.	Organ development, Congenital malformations.
Second and third trimester	Changes in development and function of organs and tissues that are already developed.	Finished organ development.

**Table 2.** FDA Pregnancy Categories.

<b>Pregnancy category</b>	<b>Category descriptions</b>
A	Adequate, well-controlled studies in pregnant women had not shown an increased risk of fetal abnormalities in any trimester of the pregnancy, Animal NA.
B	Human No adequate, well-controlled studies in pregnant women AND Animal No evidence of harm to the fetus OR Human Adequate, well-controlled studies in pregnant women had not shown an increased risk of fetal abnormalities in any trimester of

	pregnancy, Animal Studies have shown adverse effects.
C	Human No adequate, well-controlled studies in pregnant women AND Animal studies have shown no adverse effects, Humans No adequate well-controlled studies in pregnant women, Animals no study have been conducted.
D	Adequate well-controlled or observational studies have demonstrated a risk for fetus. However, the benefits of therapy may outweigh a potential risk. For example, a drug may be acceptable in life-threatening situation or serious diseases for which safer drugs cannot be used or are ineffective.
X	Adequate well-controlled or observational studies in pregnant women has demonstrated positive evidence of fetal abnormalities or risk. The use of the product is contraindicated in women who are or may become pregnant.

There are drugs that are extremely toxic for the fetus and they should never be given to a pregnant woman, and they can cause terrible malformations. Such is a case with Thalidomide. On the other hand, there are medications that cause malformation in animals but have no effects on humans.

Meclizine - a drug used as antiemetic is such a drug. Also, there are medicaments that can be replaced with more secure ones, such is a case with Heparin which is more secure drug than Warfarin. There are drugs who have teratogenic effect of the fetus even after stopping of their consumption. Isotretinoin is a retinol derivate drug, that is used for acne problems, and can be stored in the fat tissue and it takes 2 weeks to be completely excreted from body. Women that use this drug are supposed to take contraception for 4 weeks after the last consummation of this drug. After these 4 weeks, they can start planning their pregnancy.

Anxiolytics - Diazepam if taken in late pregnancy, can cause irritability and increased reflexes in newborns.

Antibiotics –Fluoroquinolones can cause abnormalities of bones and junctions of the fetus. Nitrofurantoin- in women with G6PD can cause rupture of the erythrocytes. Streptomycin can cause damage of baby's ear and hearing. Sulfonamides –when given in late pregnancy, can cause jaundice and fetal malformations. Tetracyclines– can lead to slower development of the bones and can cause brain,medulla spinalis damage and can lead to development of spina bifida.

Antihypertensive drugs (angiotensin -converting -enzyme) when taken in late pregnancy, can lead to kidney malformations, can cause decrease in amniotic fluid, and can give malformation of the face,legs, arms and lungs of the fetus. Beta blockers decrease heart rate of the fetus, can cause hypoglycemia and decreased development of the fetus. They cause hypotension in pregnant women. Calcium channels blockers can cause decelerated growth of the fetus. Thiazides are diuretics and they lead to decreased level of – Na, K,O<sub>2</sub> in the cells and tissues of the fetus, and can cause decreased plates cells and can cause fetal decelerated growth.

Analgesics NASID - Naproxen, Ibuprofen, Aspirin, taken in large doses in the first trimester can lead to spontaneous miscarriage and later on they can cause early closure of ductus arteriosus, can cause jaundice and necrotizing enterocolitis and brain damage.In pregnant women they can cause bleeding during labor.

Vaccines -of live virus (rubeola and varicella) should be avoided in pregnant women. Other vaccines, such as against cholera, hepatitis, diphtheria, rabies, mumps, are given in pregnant women only if there is real danger of infection. Pregnant women should be protected and vaccinated against flu.

Psychoactive substances: Antidepressive dugs serotonin reap take inhibitors -(SSRI s) - paroxetine are often given during pregnancy because there is incidence of 7% to23 % of development of depression.The benefit is overcoming the damage of the drug. If pregnant women use Paroxetine, evaluating echotomography of the heart of the baby should be done regularly. Antidepressants can cause addiction in newborns. To prevent that, doses of these drugs should be decreasedin the last trimester. If the symptoms of depression are significantly worsened, antidepressants should be taken in normal doses. Not treated depression can lead to postpartum severe depression.

Cigarettes - 20% of pregnant women smoke during pregnancy although they know that nicotine is bad for babies and can cause decrease in weight. Congenital malformations of the heart, brain and face are more frequent in pregnant women who smoke. SIDS (sudden infant death syndrome) is syndrome that is more frequent in babies whose mothers are smokers. Placenta previa, abruptio placentae, early delivery infection of uterus, spontaneous miscarriages and premature born babies are more common in babies of mothers who smoke. Usually, these babies have weaker physical and psychological development and have episodes

of strange behavior. These changes result of increased Carbon monoxide and nicotine levels. Carbon monoxides decrease oxygen delivery to organs and tissues. Nicotine on the other hand can cause spasms of blood vessels, and that can lead to decreased blood delivery of oxygen.

Alcohol -Women who regularly drink have twice more incidence for abortion and, they have babies with decreased weight. Fetal-alcohol syndrome is the most severe complication, and it occurs even in women who drink couple of glass of alcohol every day. This syndrome is manifested in congenital malformations of the face, impairment of brain development, behavioral and intellectual disorders of the child.

Caffeine- Consuming one cup of coffee daily does not interfere with the development of the baby. Caffeine is present not only in coffee but also in soda drinks, chocolate even in some dugs. The caffeine transfers the placenta easily, stimulates the heart in fetus and decreases iron absorption. Drinking 7 cups of coffee daily can decrease birth weight, can cause spontaneous miscarriages, and increases the percentages of stillborn babies.

Consuming the forbidden –illegal substances opioids, marihuana, cocaine, amphetamine, leads to higher incidence of infectious diseases including HIV, behavioral disturbances, the baby’s addiction of opioids in newborn babies. These women have higher incidence of stillborn and spontaneous miscarriages.

Drugs during breastfeeding -Mothers who must take some medication during lactation period usually ask weather that drug is safe for her child and weather they can continue to breastfeed their babies. The answer depends on whether the drug enters the milk, whether is absorbed by the baby, how that drug has influence on that baby, how much of the milk baby is consuming, how that drug influences the baby. How much milk the baby is consuming, depends on how old is the baby and weather the baby has additional food intake.

Some medications like epinephrine, heparin, insulin, do not pass blood/milk barrier and it is suggested that these drugs are safe to be consumed by the mother. Some drugs enter the milk, but in very small quantities and so they can not cause damages in babies. But some medications like gentamicin, kanamycin, streptomycin, tetracycline, enter the mother milk, but the baby is absorbing them very little.

Mostly, the drugs that does not need prescriptions are considered to be safe to be taken during breastfeeding. Exceptions are antihistaminic. Aspirin and salicylates, if they are taken for long period of time, are considered as not safe to be taken by women who are breastfeeding. Acetaminophen and ibuprofen, are considered safe if they are taken in regular doses.

Antihypertensive drugs are considered safe to be taken during breastfeeding. Beta blockers can be taken during breastfeeding, but the baby needs to have regular and frequent controls so that we can have a prompt reaction if bradycardia and hypotension occur.

Warfarin can be taken by women who are breastfeeding. Exception is if the baby is born premature. Caffeine and theophylline can be consumed by mothers who are breastfeeding, but checkups should be done regularly if irritation or tachypnea occurs. Anxiolytics, antidepressants, which are given as regular therapy, demand that the baby should be under control. These drugs remain in body for a long period of time, so babies in the first months of their lives could be affected, especially their nervous system. Benzodiazepines can lead to lethargy, somnolence and weight loss. Babies eliminate phenobarbital very slowly so this drug can cause somnolence. Therefore, dose should be diminished. Drugs that should not be used in breastfeeding period are amphetamines, chemotherapy drugs, chloramphenicol, ergotamine, lithium, radioactive substances, and some illegal ones.

### **Anesthesia for non-obstetric procedures in pregnant women.**

In 1-2% of the pregnant women sometimes operation must be performed. The most frequent causes for the operations are appendicitis, torsion of the ovaries and trauma. Regional anesthesia is the first choice when that is possible. Gynecologists and neonate-pediatricists should be consulted. NSAID should be avoided because of the risk of premature closure of ductus arteriosus. It is recommended the low doses of aspirin to be given. From 15<sup>th</sup> to 56<sup>th</sup> day of development of human embryo, is the most sensitive of teratogenic substances. Although studies are incomplete, sedatives, hypnotics and opioids don't have damaging effects on embryo as it was considered before. Benzodiazepines are not teratogenic if they are used once during pregnancy, but there is higher incidence palatoschisis after more frequent use of these drugs. Midazolam, opioids and propofol are drugs of choice for small gynecological interventions.

### **Breastfeeding and Anesthesia**

Solubility of the drugs in lipids of the milk, and quantity of the milk that baby is consuming during one breastfeeding, are defining the complete dose of the drug that is in the milk. The most of anesthetics are liposoluble. In the blood lipids are in 0,37%, in the milk 4.75 and in the brain 10-12%. That means that the most quantities of the anesthetics are found in the brain of the mother. Lip solubility index is lower in the milk compared to those of the brain. That is why concentrations of the drugs is smaller in the milk than in the brain. Howie 2006, and Lang 2003, said that women who are breastfeeding, who after the operation are awake, are capable of breastfeeding their babies without any doubts. Women who are breastfeeding their babies after the operations usually are prescribed to take antibiotics analgetic. The quantity of the drug in the milk depends on the milk/plasma index. If that index is smaller, it means that drug has a shorter period of time in the milk and is excreting faster.

**Table 3.** Milk/plasma.

Drug	Milk/plasma index	References
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Lidocaine	0.17-0.35	Giuliani 2001
Aspirin	0.033-0.05	Findlay 1981
Paracetamol	1.0	Notarianni 1987
Naproxen	0.01	Spigset 2000
Ibuprofen	0.008-0.06	Spigset 2000
Indomethacin	0.01-1.48	Spigset 2000
Codeine	2.16-2.46	Spigset 2000
Morphine	2.45	Spigset 2000
Pethidine	0.68-1.59	Spigset 2000
Fentanyl	2.10	Spigset 2000
Halothane	1.0	Cote 1976
Thiopentone	1.0	Anderson1987
Propofol	1.0	Schmitt 1987
Midazolam	0.15	Matheson 1990
Nitrazepam	0.27	Matheson 1990

## Conclusion

With good communication between the doctor and mother, the security of the pregnant woman and mother of a newborn child is increased. Teamwork of the gynecologist, neonatologist and anesthesiologist, as well as good education are imperative for treating these patients.

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