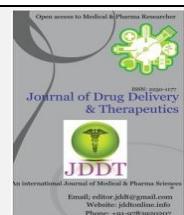


Available online on 15.11.2018 at <http://jddtonline.info>

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

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Review Article

Current trends in drugs avoided in pregnancy

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ABSTRACT

During pregnancy several drugs are having contraindication, hence their use is less and dangerous to mother along with fetus. Drugs play an important role in improving the health and promoting well-being. However to produce desired effect, they have to be safe, efficacious and have to be used rationally. During pregnancy medication is less preferred but in some times cannot be escaped to treat the ailments in mother. Avoiding medications may be desirable, it is often not possible and may be dangerous because some women enter pregnancy medical conditions that require continuous and episodic treatment (e.g. asthma, hypertension, epilepsy). So here we discussed the medication that can be used safely during pregnancy along with unsafe and highly contraindicated for both mother and fetus. Certain drugs given during pregnancy may prove harmful to unborn child is one of the classical problem in the medical treatment. The main purpose of this review is to prepare a list of safe medications which can be taken during pregnancy with unsafe and highly contraindicated drugs. And also a quick reference for health care professionals.

Keywords: Current, Pregnancy, Drugs, Fetus



Article Info: Received 01 Oct, 2018; Review Completed 02 Nov 2018; Accepted 03 Nov 2018; Available online 15 Nov 2018

Cite this article as:

Anitha B, Malavika S, Kumar B, Ramesh Y, Current trends in drugs avoided in pregnancy, Journal of Drug Delivery and Therapeutics. 2018; 8(6):342-350 DOI: <http://dx.doi.org/10.22270/jddt.v8i6.2035>

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INTRODUCTION

Pregnancy occurs when sperm meets an egg. Pregnancy is a period in which a fetus is developed into a women's womb it contains one or more than one fetus¹. It is known as gestation period in the blood (or) urine pregnancy is confirmed symptoms of early pregnancy are-nausea, vomiting, mood swing, missed period, tender breast^[1]. It contains three trimesters, first trimester from 1-12 weeks, in this stage conceiving takes place and also miscarriage. Second trimester from 13-28 weeks, in this stage fetus movement can be felt. Third trimester from 29-40 weeks, in this stage parental care is very essential². It has been reported that 8% of pregnant women need drug due to various chronic diseases and pregnancy related problems³. About 59% of pregnant women are needed a medication other than a vitamin or mineral supplements⁴. About 13% of pregnant women's are taking dietary herbal supplements. More than 90% of pregnant women take prescription or nonprescription drugs or use social drugs such as tobacco or alcohol or illicit drugs at sometime during pregnancy^[4]. Pregnant women are normally excluded from clinical trials and results from animal studies need not apply to human population⁵. Hence providing treatment to pregnant women is a problem. Fear of causing fetal harm and death by a given drug in pregnancy has raised many challenges to clinical research

about the safety use of drugs in pregnancy⁵. Medication safety information in pregnancy is usually obtained from case reports, epidemiological studies and animal studies; all of which have some limitations that make determining risks of a drug use during pregnancy difficult⁶. The use medications in pregnancy should be evaluated by the benefits and risks to the mother and fetus⁷. Upon evaluation, some medications may be used sparingly during some trimesters contraindicated in others. All efforts should be made to optimize the risk-benefit ratio. It's very important for the pregnant mothers to follow up of do's and don'ts during the gestation period⁷. The most important thing is the medication containing the mixture of chemicals, when interact together may cause the teratogenic effect to the baby⁸. So it is very important for the health care professionals and pregnant woman to know which drugs can be take and which should not take during this period^[8].

Principles of therapy in pregnancy:⁹

Prescribe drugs only when clearly indicated, through weighing benefits to mother against the risks to the fetus, based on the stage of pregnancy and drug information the drug should be selected, give the drug with low effective doses and for the shortest effective time, an older and safe drug is preferred over a newer drug during first trimester,

provide counseling to pregnant women about the use of immunizations during pregnancy, should be avoided. Live vaccines-possible harmful effects to fetus. (measles, mumps, polio, rubella). Toxoids (diphtheria, tetanus) and inactive virus vaccines (influenza, rabies, hepatitis B) are considered safe for use. Who are attacked by hepatitis B, rabies, tetanus, or varicella, hyper immune globulins (IGIVs) can be given to pregnant women, IV administration of hyper immune globulins reduce the risk of infection.^[19]

Principles of therapy in lactation: ^{10, 11}

Give drugs only when needed, avoid taking the contraindicated drugs or stop breast feeding, drugs taken by the systemic route can reach the infant in breast milk, lowest effective doses and for the shortest effective time should be prescribed, Stopping the breast feeding during maternal drug therapy is not recommended unless necessary. Women with HIV infection should not breast feed. Transmitted to the nursing infant, in some cases, mother may discard milk while receiving therapeutic drugs, to maintain lactation.

Physiological changes: ¹²

Weight increases and changes body shape (due to increases in breast tissue, blood volume in the extra vascular and extra cellular fluid), the average weight gain in pregnancy is 12.5 Kg. During normal pregnancy 1 Kg weight due to protein,^[13] The rate of albumin production increased but, plasma albumin levels are decreased (due to increased plasma volume), fibrinogen levels are increased and total body fat also increased. The ratio of LDL and HDL increases in pregnancy.^[14] Renal blood flow increased and glomerular filtration rate secondary to increased to cardiac output.

Pharmacokinetic changes: ^{15, 16}

The drug effect can be changed by the changes pharmacokinetic in pregnancy, hydrophilic drugs are more diluted and distributed in non pregnant women than pregnant women. Increased dose may require. Hydrophobic are more soluble in pregnant women, The free drug have therapeutic or adverse effects on the mother and for placental transfer to the fetus, excretion of drugs increased by kidneys, mainly which are excreted primarily unchanged in the urine (digoxin, lithium). In the pregnancy, the increased size of uterus decreased renal blood flow in supine position, This results in decreased excretion and prolonged effects of renally excreted drugs.

Drug effects on the fetus: ^{17, 18, 19, 20}

The rate transfer drug depends on the chemical properties of drug such as protein binding, pH difference, lipid solubility and molecular weight of drug, only free unbound drug crosses the placenta, during pregnancy maternal albumin level are decreases while fetal albumin increases. As a result concentration of free drug increases which cross the placenta to reach the fetus, Fetal pH is slightly more acidic than maternal pH and so weak bases are more likely crossed the placenta, Lipid soluble drugs can easily diffuse across the placenta, Drug with low molecular weight (<500 g/mol) diffuse freely across the placenta, Drugs with low molecular weight (500-1000 g/mol) cross the placenta less easily, Drugs with high molecular weight (>1000 g/mol) do not cross the placenta, Trans placental transfer drugs

increase in the third trimester due to increased maternal and placental blood flow, decreased thickness and increased surface of placenta, During first trimester, drug teratogenicity most likely occurs, when fetal organs are formed, During the second and third trimesters, drug adverse effects are: growth retardation, respiratory problems, infection, or bleeding.

Drug categories in pregnancy:

Drugs are teratogenic only at specific times during embryogenesis. Teratogenicity is a condition when any drug of chemical substance which produce deviations or abnormalities in the development of embryo. Therefore to avoid such problems it is very important to know which drugs should be prescribed during pregnancy^[21]. Food and drug administration (1979) of America enforce the rule for the categorization of the drug that is contraindicated during pregnancy so a classification has been carried out as following.

The FDA has categorized the potential teratogenic risk of medications by an A, B, C, D, X system^[22, 23, and 24].

Category A: Controlled studies in women have failed to demonstrate a risk to the fetus in the first trimester and there is no evidence of risk in later trimesters. The possibility of fetal harm appears remote. Medications in this class are considered safe to use in pregnancy. Examples of medications in this class are vitamins and levothyroxine.

Category B: Either animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal studies have demonstrated risk to the fetus that was not confirmed in controlled studies in pregnant women in the first trimester and there is no evidence of a risk in later trimesters.

Medications in this class are generally considered safe. Examples of medications in this class are acetaminophen and amoxicillin.

Category C: Studies in animals have revealed adverse effects on the fetus and there are no controlled studies in women, or studies in women and animals are not available. Drugs from this class can be given to pregnant women if the benefit to the mother outweighs the risk to the fetus. Examples of medications in this class are diltiazem and spironolactone.

Category D: Evidence of human fetal risk has been documented, but the benefits to the mother may be acceptable despite the risk to the fetus. Drugs in this class may be used in pregnancy if the benefits to the mother outweigh the risk to the fetus (i.e. a life threatening situation or a serious disease for which safer medication cannot be used or are not efficacious). Examples of medications in this class are phenytoin and valproic acid.

Category X:

Studies in animals or humans have demonstrated teratogenic effects. The risk to the fetus clearly outweighs any potential benefit to the mother. Drugs in this category are contraindicated in pregnancy. Examples of medications in this class are thalidomide and warfarin.

Common problems in pregnancy: ^{25, 26} Anemia, Constipation, Gastro esophageal reflux, Gestational diabetes, Nausea and vomiting, Hypertension.

Table 1: List of Antibiotics used in pregnancy:^{27, 28, 29}

Generic (brand)	Pregnancy Category	Crosses placenta	Reported adverse effects to mom or baby use in pregnancy	Place in therapy
Nitrofurantoin	B	Yes	Fetus: Hemolytic anemia	----
Sulfamethoxazole / trimethoprim	C	SMX: Unknown TMP: Yes	Fetus: SMX: jaundice, hemolytic anemia, and possibly kernicterus TMP: neural tube defects (NTD), oral clefts, cardiac defects, and urinary tract defects	Not recommended in pregnancy
Meronidazole (Flagyl) Topical:- (metro gel)	B	Yes	Fetus: Low birth weight babies, spontaneous abortions, and carcinogenic possibilities. Not mutagenic or teratogenic	Safe for use only in 2 nd and 3 rd trimester Contraindicated in 1 st trimester
Tetracycline's	D	Yes	Fetus: Hypo spadia (1 st trimester only), inguinal hernia, limb hypoplasia, teeth discoloration (2 nd , 3 rd) Cataracts, cleft palates, spine bifida, polydactyl, Maternal: liver toxicity, irreversible shock	No recommended in pregnancy
Fluoroquinolones	C	Yes	Erosion of weight bearing cartilage in rats and dogs, but no human reports	Not recommended in pregnancy
Macrolides	Azithro, Erythro: B Clarithro: C	Yes	Fetus: Cardiovascular abnormalities and cleft palate with clarithromycin	
Clindamycin	B	Yes	Fetus: Increase in neonatal infection and low birth weight seen with vaginal preparation	For BV as oral alternative, but not the topical Group B strep. disease in patients with penicillin allergy
Cephalosporin's	B	Yes	None reported	Generally considered safe in pregnancy unless penicillin allergic
Penicillin's +/ -Beta-lactamase inhibitor	B	Yes	None reported	Safest class of abx in pregnancy if not allergic for syphilis
Amino glycosides (Amikacin, Gentamycin and Tobramycin)	D	Yes	Fetus: ototoxicity/ deafness Neuromuscular weakness, respiratory depression with concomitant gentamicin and Magnesium sulfate	Do not use in pregnancy not unless the benefit out weight the risk to the fetus.

Carbapenems: ³⁰ Category B/C/B in pregnancy, likely cross the placenta, Very little human data

Lactation: Excreted into breast milk in low amount, Unknown effects but likely low clinical significance

Linezolid: Pregnancy Category C, No human data available

Lactation: Unknown, myelo suppression in animals

Chloramphenicol: Risk during pregnancy It is an antibiotic which is useful in serious infections such as typhoid fever. Not have any adverse effect but can cause 'grey baby syndrome' and reversible bone marrow when it is given just before the delivery.

Anti tubercular Agent: ³¹

Streptomycin: Anti tubercular drug. It causes a minor effect to the fetus after crossing the placenta. It is mainly given to whom are resistant to rifampicin.

Miscellaneous: Tetanus injection: Injectable preparation is administered during second and third trimester of pregnancy to prevent tetanus ³¹.

Probenecid: It is administered along with the penicillin and it is safe to be used during pregnancy.

Calcium and Vitamin-D: These can be safely given in the deficiency states and in accurate doses.

Table 2: List of Anti epileptic drugs ^{32, 33, 34, 35}

Generic (brand)	Pregnancy Category	Crosses placenta	Reported adverse effects to mom or baby use in pregnancy	Place in therapy
Carbamazepine (Tegretol)	D	Yes: levels 50-80% of maternal, highest in fetal liver and kidneys	Fetus: dysmorphic facial feature, cranial defects, cardiac defects, spina bifida, fingernail hypoplasia, developmental delay, mild mental retardation, neural tube defect	Compatible – Maternal Benefit >> Embryo/Fetal Risk If drug is required during pregnancy it should not be withheld because the benefits of preventing seizures outweigh potential fetal harm.
Ethosuximide (Zarontin)	C	Unknown	Fetus: spontaneous hemorrhage, patent ductus arteriosus, cleft lip/palate, mongoloid facies, short neck, altered palmar crease and accessory nipple, hydrocephalus	Limited human data. Probably compatible. Succinamide anticonvulsants: DOC for tx of petit mal epilepsy in 1st Trimester.
Felbamate (Felbatol)	C	Unknown	Fetus: mental retardation. Maternal: aplastic anemia, acute liver failure	Limited Human Data – Animal Data Suggest Moderate Risk. Drug crosses placenta in animals, not yet described in humans. But should occur because of LMW
Phenytoin (Dilatin)	D Dose related teratogenic effect	Unknown	Fetus: congenital abnormalities, hemorrhage at birth, neurodevelopment abnormalities Maternal: folic acid deficiency	Compatible – Maternal Benefit >> Embryo/Fetal Risk Significant Risks: major/minor congenital abnormalities, hemorrhage at birth, neurodevelopment Maintain lowest level required to prevent seizures in order to lessen risk of fetal anomalies
Fosphenytoin (Cerebyx)	D	Unknown	Fetus: congenital malformations, orofacial clefts, cardiac defects, minor anomalies, mental deficiency Maternal: An increase in seizure frequency may occur during pregnancy because of altered phenytoin pharmacokinetics	Benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective)
Gabapentin (Neurontin)	C	Unknown	Limited human data does not allow an assessment as to the safety of gabapentin	Limited Evidence: If required, benefits appear > fetal risk
Lamotrigine (Lamictal)	C	Yes	Fetus: frequency of major defects among 1 st trimester monotherapy exposure was 2.9% (12 of 414)	Human data Suggest Low Risk; Adjust dose maintain clinical response
Levetiracetam (Keppra)	C	Unknown	Risk to human fetus/embryo unknown	Risk to human embryo/fetus is unknown
Oxcarbamazepine (Trileptal)	C	Yes	Fetus: no major congenital malformations reported, mild facial defects observed in one case	No epoxide metabolites: lower risk of teratogenicity compared to other agents, Supplement with folic acid
Phenobarbital (Luminal sodium)	D	Yes	Fetus: congenital defects, hemorrhage at birth, addiction, AE of neurobehavioral development Maternal: Benefit > Risk	Benefits > Risk during at lowest effective level
Pregabalin (Lyrica)	C	Unknown	Fetus: congenital defects, hemorrhage at birth, addiction, AE of neurobehavioral development Maternal: Benefit > Risk	Use only if maternal benefit > fetal risk
Tiagabine (Gabitril)	C	Unknown	Fetus: one incidence with unspecified malformations, otherwise unknown	Safest course: Avoid in 1 st trimester; later trimesters unknown
Primidone (Mysoline)	D	Unknown	Newborn: neurologic manifestations	If benefits > risks (e.g., drug needed in life-

			(overactivity /tumor); mechanism for hemorrhagic effects is due to suppression of VitK-dependent clotting factors, recommend administration of VitK to infant immediately after birth	threatening situation or serious disease with no safer drug)
Topiramate (Topamax)	C	Yes	Hypospadias in males (relationship not established); Data too limited to assess embryo/fetus risk	Avoid if possible in 1st trimester
Valproic acid(Depakene)	D	Yes	Fetus: neural tube defects, minor facial defects, defects of the head, face, digits, urogenital tract, mental and physical growth.	Benefits > Risks (e.g., drug needed in life- threatening situation or serious disease with no safer drug)
Zonisamide (Zonegran)	C	Unknown	Congenital anomalies possible	Avoid if possible in 1st trimester
Trimethadione	D	Unknown	Fetus: mental retardation, craniofacial defects, genitourinary defects, malformed hands, clubfoot	Contraindicated in 1st trimester
Clonazepam (klonopin)	D	Unknown	Human data suggest low risk; fetal and neonatal toxicity has been reported	Safest course is to avoid during the 1st trimester; however, if indicated, it should not be withheld because of pregnancy
Lorazepam (Ativan)	D	Yes	Fetus: high IV doses may cause "floppy infant" syndrome, higher incidence of respiratory distress	Benefits > Risks (e.g., drug needed in life- threatening situation or serious disease with no safer drug)
Carbamazepine(Tegretol)	D	Yes	Fetus:minor craniofacial defects, fingernail hypoplasia, developmental delay, mild mental retardation	If required, Benefits > risks

Table 3: List of Diabetes mellitus ³⁶

generic (brand)	class	pregnancy category	crosses placenta	reported adverse effects to mom or baby from use in pregnancy	place in therapy
Glyburide (Giabeta, Micronase, Glynase)	Sulfonylurea	C	Yes	Possible ear defects in 1 st trimester, fetal hypoglycemia	Insulin is recommended first line by the ADA; ACOG recommends use of this agent in D2 or GDM
Glipizide (Glucorol)	Sulfonylurea	C	Yes	Possible ear defects in 1 st trimester, no teratogenicity in animal studies	Not recommended; limited human data
Glimipiride (Amaryl)	Sulfonylurea	C	Unknown	Skeletal malformation in high doses	Not recommended; No human data
Metformin (Glucophage, Fortamet,Glumeza)	Biguanide	B	Unknown	Neural tube defects in animals at high doses. Few abnormalities in humans at normal doses and likely due to poor BG control	Insulin is recommended first line by the ADA; ACOG recommends use of this agent in D2 or GDM
Sitagliptin (Januvia)	Dipeptidyl peptidase IV inhibitor	B	Unknown	No good studies in humans; animal studies show no defects/complication at high dose	Possible; No human data
Pioglitazone (Actos)	TZD	C	Unknown	Developmental delay, decreased fetal weight in animals	Not recommended
Rosiglitazone (Avandia)	TZD	C	Yes	Fetal death/retardation was seen in animal studies	Not recommended
Exenatide (Byetta)	Incretin mimetic	C	Unknown	Decreased fetal growth, skeletal malformations in animal studies	Not recommended
Pramlintide (Symlin)	Amylino mimetic	C	Unknown	Animals: neural tube defects, cleft palate at high doses	Not recommended
Regular insulin	Short acting	B	NO	None reported	Drug of choice

(HumulinR,Novolin R)	insulin				
Lispro insulin (Humalog)	Rapid acting insulin	B	NO	Case reports: sudden neonatal death, growth retardation; controlled studies: as efficacious as regular insulin	Recommended
Glulisine insulin (Apidra)	Rapid acting insulin	C	Unknown	No available studies	Not recommended unless benefits > risks
NPH insulin (Humulin N, Novolin N)	Intermediae acting	B	NO	None reported	Recommended
Glargine insulin (Lantus)	Long acting	C	Unknown	No available studies	Not recommended unless benefits > risks
Detemir insulin (Levemir)	Intermediae long acting	C	Unknown	Visceral abnormalities were seen in animals	Not recommended

Table 4: List of Analgesics Drugs ^{37, 38, 39, 40}

Generic (brand)	Class	Pregnancy category	Crosses placenta	Reported adverse effects to mom or baby from use in pregnancy	Place in Therapy
Aspirin (Bufferin, Ecotrin)	NSAID	C	Yes	Fetal: increased perinatal mortality, teratogenic effects, pulmonary HTN, bleeding risk, premature ductus arteriosus closure Maternal: anemia, ante/post partum hemorrhage, prolonged labour	Should not be used in pregnancy, consider acetaminophen
Ibuprofen (Advil, Midol)	NSAID	B D In 3 rd trimester	UNKNOWN	Fetal: ductus arteriosus constriction, Pulmonary HTN in 3rd trimester, Maternal: prolonged labor, spontaneous abortion	Should be avoided when possible and completely avoided during the 3rd trimester. Consider acetaminophen
Naproxen (Aleve, Anaprox, Midol, Naprosyn, Pamprin)	NSAID	B; D In 3 rd trimester	Yes	Fetal: ductus arteriosus constriction, intracranial hemorrhage, primary pulmonary HTN	Should be avoided when possible and completely avoided during the 3rd trimester. Consider acetaminophen.
Acetaminophen	Analgesic antipyretic	B	Yes	Fetal: overdose can lead to liver toxicity Maternal: overdose can lead to liver toxicity	Drug of choice for analgesia and fever during pregnancy
Butorphanol (Stadol)	Narcotic analgesic	C D if prolonged use	Yes	Fetal: sinusoidal fetal heart rate pattern, addiction, respiratory depression Maternal - addiction	Used for analgesia during labor
Morphine (Duramorph, Kadian)	Narcotic analgesic	C; D if prolonged use	Yes	Fetal: addiction, possible relation to inguinal hernia and respiratory depression Maternal: addiction	Should only be used when analgesia or anesthetic is clearly indicated
Fentanyl (Actiq, Duragesic)	Narcotic analgesic	C; D if prolonged use	Yes	Fetal: respiratory depression, dependence and loss of fetal heart rate variability without hypoxia	Only use when benefits > risks
Hdromorphone (Dilaudid)	Narcotic analgesic	C D if prolonged use	Yes	Fetal: respiratory depression	Only use when benefits > risks Manufacturer recommended CI in pregnancy
Tramadol (ultram)	Narcotic analgesic	C	Yes	Fetal: dose related fetal toxicity in animals, respiratory depression and addiction	Should be avoided until further evidence concerning the dose related fetal toxicity is available
Ergotamine[Er gomar]	Sympathomimetic	X	Yes	Fetal: increase uterine tone leading to fetal hypoxia, teratogenic and fetal toxicity	Do not use in pregnancy

Table 5: Cough and cold medications in pregnancy and lactation ^{41, 42, 43}

Drug or Drug Class	Pregnancy	Lactation
Decongestants	Pseudoephedrine, in the lowest dose and shortest duration possible is considered the decongestant of choice. However it may be prudent to avoid its use in the first trimester of pregnancy. Oxymetazoline and xylometazoline can be considered when used at appropriate doses for short durations.	Systemic decongestants are best avoided if breast milk production is poor or marginal. Oxymetazoline and xylometazoline are considered drugs of choice
Antihistamines	The first generation antihistamines, especially chlorpheniramine, are preferred. If not tolerated or effective, second generation agents such as loratadine can be recommended.	Due to possible adverse effects on the infant from first generation antihistamines, second generation agents are preferred in lactating mothers.
Antitussives-Codeine	Codeine is best avoided during pregnancy.	Avoid or limit codeine use in lactation due to risk of infant toxicity.
Antitussives-Dextromethorphan	Dextromethorphan is the preferred antitussive in both pregnancy and lactation. Consider lack of evidence of efficacy.	Dextromethorphan is the preferred antitussive in both pregnancy and lactation. Consider lack of evidence of efficacy.
Expectorant	Guaifenesin is considered safe in pregnancy and lactation. Consider lack of evidence of efficacy.	Guaifenesin is considered safe in pregnancy and lactation. Consider lack of evidence of efficacy.
Analgesics-Acetaminophen	Acetaminophen is considered the analgesic/antipyretic of choice in both pregnancy and breastfeeding.	Acetaminophen is considered the analgesic/antipyretic of choice in both pregnancy and breastfeeding.
Analgesics-ASA and NSAIDS (naproxen and ibuprofen)	ASA and NSAIDs are considered compatible with pregnancy in the first and second trimester, but should be avoided in the third trimester. Low-dose ASA is considered to pose lower risk during pregnancy and breastfeeding.	Non-aspirin NSAIDs are generally considered compatible during breastfeeding and ibuprofen is the NSAID of choice due to greatest safety data. Low-dose ASA is considered to pose lower risk during pregnancy and breastfeeding.
Lozenges	Medicated throat lozenges are considered safe in pregnancy and breastfeeding.	Medicated throat lozenges are considered safe in pregnancy and breastfeeding.
Herbs for Cough and Cold	Echinacea and ginseng (all forms) should be avoided during pregnancy and breastfeeding.	Echinacea and ginseng (all forms) should be avoided during pregnancy and breastfeeding.

Table 6: List of Drugs during Immunizations ⁴⁴

generic (brand)	Class	pregnancy category	crosses placenta	reported adverse effects to mom or baby from use in pregnancy	place in therapy
Human papillomavirus (Gardasil)	Inactivated vaccine	B	Unknown	Currently under study	Do not use during pregnancy
Hepatitis B (Engerix-B, Recombivax HB)	B	Inactivated vaccine	C	Unknown	No risk to the mom or baby have been reported The vaccine should be given pre or post exposure in women at risk for infection.
Influenza (injection)(Afluria, Fluarix, Flilaval,Fluvirin, Fluzone)	Inactivated vaccine	C	Unknown	Studies of immunization of over 2000 women showed no fetal adverse effects associated with vaccination	ACOG recommends the vaccine be given to pregnant women in the 2nd and 3 rd trimesters during flu season. All at risk for pulmonary complications should be vaccinated, regardless of trimester
MMR (M-M-R II)	Live vaccine	C	Unknown	Fetal infection with live attenuated virus may occur	Do not use during pregnancy, Avoid pregnancy for 12

					weeks after injection
Pneumococcal Vaccine (Pneumovax)	Inactivated vaccine	C	Maternal Ab yes	Risk to the fetus in the 1st trimester is unknown.	Use if indicated in high risk patients
Td (Decavac)	Toxoid	C	Unknown	No evidence of teratogenicity	Use if indicated
TdP (Adacel, Boostrix)	Toxoid	C	Maternal Ab yes	Antibodies may also interfere with the infant's immune response to infant doses of DTaP, so infant may not be protected.	Use if at high risk for pertussis
Varicella Vaccine	Live vaccine	C	Unknown	Fetal infection may occur	Do not use during pregnancy

Social drugs: In addition to counsel the pregnant women regarding use of various prescribed and non-prescribed medications during pregnancy. They should be informed about risk of using following substances during pregnancy ⁴⁵.

Cigarette smoking: Maternal smoking is one of the few known preventable causes' prenatal morbidity and mortality ⁴⁶. The most consistent effect of smoking on the fetus during pregnancy is reduction in birth weight. Birth defects of heart, brain and face are also more common among babies of smokers. Risk of sudden infant death syndrome (SIDS), Mis-located placenta (placenta previa), premature detachment of placenta, premature rupture of the membranes, preterm labor, uterine infections, miscarriages, stillbirths, premature births are increased⁴⁷. Changes in uterine and placental oxygenation may be the causes of infant death, pre-maturity or spontaneous abortions. Therefore all women's should be informed of the risk of smoking on the fetus and encouraged to quit smoking during pregnancy ⁴⁸.

Alcohol: Fetal alcohol syndrome is one of the most serious consequences of drinking during pregnancy ⁴⁹. Risk of miscarriage almost doubles for women who drink alcohol in any form during pregnancy and birth weight of babies is substantially below normal ⁵⁰. This syndrome includes inadequate growth before or after birth, facial defects, a small head, mental retardation and abnormal behavioral development.

Caffeine: Caffeine is found in various quantities in many beverages, analgesics, diet aids and stimulants; hence it is the most commonly ingested drug during pregnancy.

Evidence suggests that consuming caffeine during pregnancy possess little or no risk to the fetus. Caffeine contained in coffee, tea, and some sodas and some drugs is a stimulant that readily crosses the placenta to the fetus ⁵¹. If taken in high dose it may stimulate the fetus increasing heart and breathing rate. Caffeine also may decrease blood flow across placenta and decreases the absorption of iron, increasing risk of anemia.

CONCLUSION

The safe and unsafe medications during pregnancy is a very important prospective of life as it carries the two lives conjoined for the certain period of time. During that time period both the mother and fetus should be safe, sound and grow healthily. This review summarizes the safe and unsafe list of drugs during pregnancy it is the responsibility of all clinicians including pharmacists to counsel patients with complete, accurate and current information on the risks and benefits of using medications during pregnancy. The first safe methods to refrain from such interaction during pregnancy are always consulting the medical practitioners and prescribe the drugs even of OTC category especially during the pregnancy as there are so many complications in it. It is the important that the benefits and risk of stopping treatment to be explained and informed properly. Drug may also be less effective during pregnancy because of pharmacokinetic changes such as increased metabolism. Doses of these drugs may need to be adjusting during pregnancy. Also when selecting drugs to be used in pregnancy effectively, drugs that have been in use for a long time are often preferable because fetal safety has been established even through newer alternatives may be available.

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