Use of drugs during pregnancy

No drug is safe beyond all doubt in early pregnancy. Use of medications in pregnancy has to be instituted with utmost caution. Although it is true that the first trimester of pregnancy (2 to 8 weeks, 4-10 weeks from last menstrual period) is the most vulnerable period for drug induced malformations, it is not safe to assume that medications cannot affect malformations later in pregnancy. The benefit-to-risk ratio for the mother as well as the baby needs to be carefully evaluated before deciding on the appropriate drug regimen.

Categorization of drugs

Category of drugs using during pregnancy: Depending on its effect on fetus

Category –A:

Taken by large number of pregnant women and no proven direct or indirect harmful effects observed. Drugs includes methyldopa, paracetamol.

Category –B:

Drugs taken by limited number of pregnant women and women of child bearing age and no direct and indirect harmful effects been observed. Example of category-B drugs are amoxicillin, cephradine etc.

Category C:

Drugs which, owing to their pharmacological effects, have caused or may be suspected to cause harmful effects to fetus. Example- rifampicin, propylthiouracil.

Category D:

Drugs which have caused, are suspected to have caused, or may be expected to cause, an increase incidence of human fetal malformations or irreversible damage. Example- phenytoin, carbamezapine, danazol.

Category –X:

Drugs that have such a high risk of causing permanent damage to the fetus that they should not be used in pregnancy or when there is a possibility of pregnancy. Example- thalidomide, finasteride.

General considerations when prescribing in pregnancy

1. Assess or reassess the need for medication in any woman planning a pregnancy, or who becomes pregnant.

2. Consider whether it is appropriate to try non-drug measures.

3. Review medical history.

4. Consider obstetric history and family history of malformations.

5. Balance the risks of medication against benefit of treatment on mother and fetus.

6. Consider safety of medication (stage of pregnancy, route of administration, dose)

7. Use the lowest effective dose for the shortest possible time.

8. Monitor efficacy of medication throughout exposure.

9. Always assess risks and benefits on an individual patient basis.

10. Ensure the most up-to-date information is being used. Robust pregnancy outcome data regarding drug exposure is lacking, especially for newer drugs and those that are rarely used in women of childbearing age.

11. Patient counseling regarding drug exposure during pregnancy.

Antibiotic their sensitivity and pregnancy status

Spectrum/group			Antibiotic	Sensitivity	
	Penicillin	Narrow spectrum penicillin	Benzyl penicillin (penicillin G), procaine penicillin and phenoxymethylpenicillin (penicillin V)	Streptococci, Staphylococci, Clostridium, and Listeria genera	Safe, category-B
		Moderate spectrum	Ampicillin and amoxycillin.	Narrow spectrum + gram negative	Safe, category-B

		penicillin		coverage without Pseudomonas coverage	
		Broad spectrum penicillin	Piperacillin, carbenicillin and ticarcillin	Above plus activity against *Pseudomonas aeruginosa*	Safe, category-B
Betalactam antibiotic	Cephalosporin	1st generation	Cephalexin, Cephradine	1st Generations cephalosporin = Broad spec. penicillins, Excellent activity against Gram positive and some activity against Gram negative	Safe, category-B
		2nd generation	Cefuroxime, cefprozil	As for 1st generation Plus Haemophilus (including beta-lactamase producers), retain Gram positive activity and extended Gram negative	Safe, category-B

				activity	
		3rd generation	Cefixime, cefotaxime, ceftriaxone and ceftazidime	Have further anti Gram negative activity and retain Gram positive activity, ceftazidime also has activity against *Pseudomonas aeruginosa*	Safe, category-B
		4th generation	Cefepime	3rd generation plus pseudomonas, staph. aureus and streptococci	Safe, category-B
		Next generation Cephalosporin	Ceftaroline, Ceftobiprole (IV)	4th generation plus MRSA	
	Other Beta lactams	Monobactum	Aztreonam	Gram negative coverage only	Safe, category-B
		Carbapenem	Imipenem, Meropenem	Betalactam activity and anaerobes	Imipenem unsafe category-C, Meropenem safe,

					category-B
Non-betalactam antibiotic		Aminoglycosides	Amikacin, gentamicin, streptomycin, tobramycin and kanamycin	Excellent activity against Gram negative bacilli	Unsafe category-D
		Tetracyclines	Tetracycline, doxycycline	Have both Gram positive and Gram negative organisms coverage, it also covers particular pathogens that few other antibiotics can, such as *Chlamydia* and *Legionella*.	Unsafe category-D
		Macrolides	Azithromycin, erythromycin and clarithromycin.	Gram positive organisms (*S. pyogenes* and *S. aureus*), CAP pathogens (*S. pneumoniae* and *H. influenzae*) and C*hlamydia* and *Legionella*	Safe, category-B, clarithromycin category-C
				Have both Gram	Unsafe

		Quinolones	Levofloxacin, ofloxacin, norfloxacin and ciprofloxacin	positive and Gram negative organisms coverage, ONLY oral antibiotics with significant activity against *Pseudomonas aeruginosa*	category-C
		Glycopeptides	Vancomycin	Active against Gram positive organisms. The major use in methicillin resistant Staphylococcus aureus (MRSA) infection	Unsafe category-C
			Metronidazole	Active against anerobic organism	Safe, category -B
			Nitrofurantoin	Active against Gram negative bacteria	Safe, category -B

Summary of antibiotic use during pregnancy

Following groups of antibiotic can be used during pregnancy (category-B)

1. All betalactams antibiotic (penicillin, cephalosporin)
2. Among carbapenems –meropenem.

3. Betalactamase inhibitor e.g. clavulanic acid, tazobactam. So amoxicillin-clavulanic acid combination is safe.
4. Macrolids e.g. azithromycin, erythomycin
5. Metronidazole
6. Nitrofurantoin

Choice of antibiotic according to site of infection during pregnancy	
Site of infection	Antibiotic
To cover Gram positive bacteria	Azithromycin, phenoxymethylpenicillin, amoxicillin, erythromycin, cephradine, cefuroxime etc.
To cover Gram negative bacteria	Cefuroxime, nitrofurantoin, cefixime, ceftriaxone, meropenem etc.
To cover both Gram positive and Gram negative bacteria	Cefuroxime, amoxicillin, cefixime
Respiratory tract infection	Azithromycin, phenoxymethylpenicillin, amoxicillin, erythromycin, cephradine, cefuroxime etc.
Urinary tract infection	Cefuroxime, nitrofurantoin, cefixime, ceftriaxone, meropenem etc.
Typhoid fever	Azithromycin, ceftriaxone, cefixime
To cover anaerobic bacteria	Metronidazole

Antimalarial drugs

Quinine sulphate, chloroquine is safe to use during pregnancy.

Antihelminth

Routine dewarming is not recommended during pregnancy. Antihelminth (albendazole and mebendazole) can be used in documented helminthiasis during pregnancy or where prevalence of anemia is high during pregnancy. But should avoid in first trimester. Albendazole and

mebendazole can be used in 2nd and 3rd trimester. Albendazole 400 mg single dose. Mebendazole 100 mg total 5 doses.

Antifungal

Systemic antifungal

1.Amphotericin B remains the drug of choice for systemic, invasive mycotic infections-whether life-threatening or less severe.

2.Terbinafine is also safe. (category-B).

Topical drugs

Topical azoles include bifonazole, clotrimazole, fenticonazole, isoconazole, ketoconazole, omoconazole, oxiconazole, sertaconazole, tioconazole, miconazole and econazole. They are indicated (safe) for superficial fungal infections involving the skin (Candida sp. Malassezia furfur, dermatophytes) and oral and vulvo-vaginal candidiasis.

Key points for topical antifungal drugs

Topical antifungals all display limited systemic absorption, and they may be used in pregnancy, except for potassium iodide, which was shown to be associated with fetal goiter.

Analgesic

1. Paracetamol can be used thought the pregnancy.

2. Opioids (codeine, oxycodone, hydromorphone, hydrocodone and morphine, as well as drugs such as pethidine and tramadol) can be used throughout the pregnancy but should avoid prolong use due to risk of dependency and addiction.

3. NSAIDs should be used with caution in first trimester and must be avoided in last trimester because of their potential to cause premature closure of the fetal ductus arteriosus and persistent pulmonary hypertension. High doses of NSAIDs in the third trimester may also reduce perfusion of the fetal kidneys and decrease fetal urine output.

4. Topical NSAIDs are safe to use as systemic absorption is less but should avoid use in large surface area.

TCA

Tricyclic antidepressants may help to control persistent pain and reduce opioid exposure. Tricyclic antidepressants have not been associated with an increased rate of birth defects or long-term neurodevelopmental effects.

Muscle relaxants during pregnancy

Safe muscle relaxant is cyclobenzaprine (category-B).

PPI

Pantoprazole is safe (category-B).

H2 blocker

Ranitidine, cimetidine and famotidine is safe (category-B).

Antacids

Magnesium hydroxide is category-A drug. However, it may be best to avoid magnesium during the last trimester of pregnancy. Magnesium could interfere with contractions during labor.

Antiemetic

Meclizine hydrochloride, metoclopramide, cyclizine, ondansetron, palonosetron is safe to use during pregnancy.

Antivertigo

Meclizine hydrochloride is safe.

Antidiabetic

Oral- metformin, glibenclamide (Glibenclamide should be used rather than other sulphonylureas because it does not cross the placenta).

Injectable-insulin is safe.

Antihypertensive

Following antihypertensive drugs are safe during pregnancy

1. Methyldopa up to 2000 mg/day

2. Labetalol initially 100 mg BD can increase to 2.4 gm/day

3. Nifedipine 10-20 mg BD maximum 90 mg/day

4. Amlodipine 5-10 mg/day

5. Doxazosin not use commonly and not available in our country.

Antiasthmatic

All antiasthmatic drugs (salbutamol, steroid, theophylline, montelukast) are safe during pregnancy.

Antihistamine

Oral antihistamines like cetirizine, levocetrizine, chlorpheniramine, diphenhydramine, fexofenadine and loratadine is safe during pregnancy.

Antitubercular drugs

Category-1 drugs are safe.

Antirheumatic drugs

Hydroxychloroquine, sulfasalazine, azathioprine, steroid, ciclosporin, tacrollmus, anti TNF are safe.

Sedatives

1. Non-benzodiazepines drugs like zolpidem and diphenhydramine (category-B) can be used along with non-pharmacological management.

2. Sedating tricyclic antidepressants such as amitriptyline or nortriptyline in those who has depression, may be a better choice for women with sleep disturbance and have not been associated with an increase in risk of congenital malformation.

3. Benzodiazepines should not be used.

Antidepressants

Citalopram, fluoxetine, sertraline, TCAs (amitriptyline, nortriptyline) can be used.

Antiepileptic drugs

1. Carbamazepine and lamotrigine have the lowest incidence of major fetal malformations.

2. Levetiracetam is also safe.

3. The risk of major fetal malformations is higher with sodium valproate.

Antidiarrhoeal drugs

Loperamide can be used (category-B).

Laxative

Lactulose can be use (category-B).

Management of migraine during pregnancy

1. Migraine often improves during pregnancy but if attacks occur they should be managed with simple analgesia and antiemetics.

2. If necessary, prophylaxis can be given with aspirin, β-blockers or tricyclic antidepressants.

3. Safety data on use of triptans during pregnancy are limited but reassuring. Triptans can therefore be used for the treatment of migraine if other therapies are ineffective.