

## Medicines During Pregnancy

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There was a case from Germany in 1960 where a pregnant women named 'Sigi' took the drug - thalidomide - which was advertised as effective, safe, and non-addictive hypnotic for treatment of her insomnia. She delivered a monster which had no limbs (phocomelia). Her cherished dream of many years shattered to pieces!

This and many other cases of foetal malformations shook the conscience of the doctors and awakened the medical profession to the grim reality of drug-induced teratogenicity, i.e. the production of structural, biochemical and behavioral abnormalities in the offspring when the drug is given to the mother during pregnancy.

Since the thalidomide disaster, regulatory agencies in different countries have become very strict in respect of introducing new drugs until and unless teratogenic potential has been properly evaluated. This is easier said than done because there are wide species differences and the relevance of animal testing for predicting teratogenic effect in man is highly questionable.

Most physicians are now aware of the concept of "critical period" of developmental sensitivity to drugs. It is between 21 and 35 days of intrauterine life. During this period, the main organ systems, including CNS, heart and gut, differentiate and are most vulnerable to the deleterious effects of drugs. However, it is to be clearly understood that it is in the later stages of pregnancy that histological, biochemical and functional developments are their most active stages and drugs may interfere with these. Thus all stages of pregnancy must be regarded as potentially hazardous for the foetus, and not just the first semester.

Fortunately, only a few drugs are definitely known to cause congenital birth defects. But unfortunately, relatively few drugs are known to be completely safe during pregnancy.

It is again unfortunate that for most of the currently used drugs definite evidence is not available regarding their safety or otherwise. That is why it is ideal if no drug is given to a pregnant woman.

This is impracticable. So if a drug has to be given, it should be in the smallest effective dose for the shortest duration. Another dictum in medical practice should be to avoid newly introduced drugs since their full teratogenic potential has not been assessed.

### **Antibiotics, Chemotherapeutic Agents In Pregnancy**

**Anti-Malarials:** Malaria in a pregnant woman should be promptly and effectively treated. It is recommended that the total dose of chloroquine be calculated on weight basis, i.e. 25 mg/kg body weight, and given over a period of 3 days. Quinine should be reserved for resistant cases. In an attempt to counteract any stimulant action of quinine on the uterus, some obstetricians recommend the concurrent use of a tocolytic agent. Pyrimethamine + sulphadoxine combination is to be avoided if possible.

**Anti-amoebic Agents:** Metronidazole is safe in recommended doses. No foetal malformations have been reported. Diloxanide (for trophozoites in the gut) should be avoided since its safety status is unclear.

**Anti-Tubercular Drugs:** Isoniazid, ethambutol and pyrazinamide can be safely used. No serious teratogenicity has been reported with the use of rifampicin. However, there are a few reports of bleeding in neonates due to hypoprothrombinemia. It may, therefore, be advisable to give Vitamin K to the mother near term.

**Anti-Helminthics:** Mebendazole, albendazole, pyrantel pamoate etc. are considered safe for use during pregnancy.

**Penicillins:** Benzyle penicillin, ampicillin, amoxycillin, cloxacillin are not teratogenic but sensitivity reactions should be watched in the mother which may have deleterious effect on the foetus.

**Cephalosporins:** No foetal toxicity has been reported and they are widely used during pregnancy.

**Sulphanamides:** They can aggravate neonatal jaundice by displacing bilirubin from serum albumin. They should not be used when labor is imminent.

**Cotrimoxazole:** It interferes with folic acid absorption and metabolism. Although it has been used in pregnancy without any apparent harm to the foetus, it is advisable to give folic acid supplements (5 to 10 mg per day) to the mother.

Aminoglycosides: Gentamycin, streptomycin, neomycin and kanamycin (amikacin) are ototoxic (eighth nerve damage) and nephrotoxic for the foetus and are contraindicated in pregnancy.

Chloramphenicol: Gray-baby syndrome can occur in neonates and it is a dangerous complication. Avoid this antibiotic at term. Cleft lip or palate has also been suspected due to chloramphenicol.

Tetracyclines: Tooth discolouration and dysplasia as well as inhibition of bone growth may occur. Contraindicated in pregnancy.

Erythromycins, Lincomycins, Vancomycin: They can be safely used.

Quinolones (Ciprofloxacin, norfloxacin): Since there is insufficient information available regarding their teratogenic potential, they are best avoided in pregnancy.

Anti-Fungals: Nystatin, miconazole and amphotericin are considered to be safe. There is some evidence of teratogenicity in animals with the use of ketoconazole and griseofulvin but the significance of this in humans is uncertain.

It must be stressed that severe maternal disorders such as hyperemesis, toxaeemias or epileptic fits may be more dangerous than the potentially teratogenic drugs used in their treatment.

### **Drugs Taken by the Father**

It is also relevant to mention here that teratogenic effect on the foetus may occur if some drugs are taken by the father as well. Finasteride, a drug used to treat prostatic hypertrophy, is excreted in the semen and may do damage to the foetus. Men taking the drug are advised to use condom lest their partner becomes pregnant with a malformed foetus. Griseofulvin may damage sperm cells and, therefore, men are advised not to father children during, or for 6 months after, treatment.

### **For further information, please write to:**

Rajasthan Voluntary Health Association 147 Milap Nagar, Tonk Road, Jaipur - 302 018 Tel. 512021, 510178).

RVHA has recently set up an Obstetric Drug Information Cell, with a computerized data-base on- the safety status of drugs in pregnancy and

lactation.. This Cell provides relevant information to doctors as well as the patients.

Drugs Contraindicated or Used with Caution in Pregnancy

## **DRUG**

Opioid analgesics: morphine pethidine, dextropropoxyphene

NSAIS"s: aspirin, Ibuprofen, indomethacin, diclo-fenac etc.

Anti-epileptics: phenytoin, phenobarb, ethusucimide, sodium carbamazepine

Anti-anxiety drugs: diazepam and analogues

Anti-depressants: imipramine and analogues, amitriptyline etc.

Lithium

Anti-neoplastic drugs

Corticosteroids: systemic use

Local use

Oral Hypoglycaemics

Androgens

Oestrogens

Progestagens

Anti-thyroid drugs

ACE inhibitors: enalapril, captopril, lisinopril etc.

Beta Blockers: Propranolol, atenolol, timolol etc.

Diuretics: thiazides, frusemide

Retinoids: e.g. tretinoin for acne Local anaesthetics

Anticoagulants

Fibrinolytics : streptokinase etc.

Antihypertensive agents: clofibrate, probucol

### **POSSIBLE ADVERSE EFFECTS**

- Withdrawal syndrome if mother is chronic user, respiratory depression in new-born if given 2-3 hours before delivery
- Neonatal clotting defects, premature closure of ductus arteriosus; given at term may delay labor
- Craniofacial defects, oral clefts, spina bifida, cardiac abnormalities, mental and growth deficiencies
- Neonatal hypotonia, withdrawal symptoms in newborn
- Neonatal tachycardia, tremors, convulsions
- CVS malformations, foetal growth retardation Multiple foetal malformations
- Growth retardation and adrenal cortex suppression
- No possible harm

- Neonatal hypoglycemia, (use insulin which is safe)
- Virilization of female foetus
- Feminization of male foetus, adenocarcinoma of vagina, cervix in later life.
- Virilization of male foetus, various congenital abnormalities.
- Foetal and neonatal hypothyroidism
- Foetal hypotension, oligohydramnios and neonatal renal failure
- May cause bradycardia in newborn
- Electrolyte disturbance in foetus, neonatal thrombocytopenia
- Serious foetal malformations
- Foetal bradycardia, hypotonia
- Neonatal bleeding
- Premature separation of placenta
- Retardation of growth