Review Article

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Drugs Used in Pregnancy

Abdolsamadi, HR.* Jazaeri, M. Torkzaban, P.*****

*Associate Professor, Department of Oral Medicine, Faculty of Dentistry, Hamadan University of Medical Sciences, Hamadan, Iran.

**Assistant Professor, Department of Oral Medicine, Faculty of Dentistry, Hamadan University of Medical Sciences, Hamadan, Iran.

***Assistant Professor, Department of Periodontics, Faculty of Dentistry, Hamadan University of Medical Sciences, Hamadan, Iran.

INTRODUCTION

Administration of drugs to a pregnant patient is of significant concern. Two main concerns must be addressed when considering whether to give a drug to pregnant women or not. The first is that the drug may be teratogenic and the second is that the drug can affect near-term fetus. One must always be aware of the teratogenic, toxic or other harmful effects of the drug on the developing fetus. The physiologic changes during pregnancy and the consequent alteration in the pharmacokinetics lead to changes in drug absorption, distribution, metabolism and excretion. As a general rule, it is best not to give any drug during pregnancy, especially during the first trimester as it is period of organogenesis.[1,2] Fortunately, most of the drugs commonly used in dentistry are not contraindicated during pregnancy. Tetracycline and streptomycin are notable exceptions.[3] The fetus may metabolize a particular drug via a different pathway from that of the mother or its metabolic product may bind more avidly in the fetus, leading to accumulation of the drug or its metabolites in the fetus. In addition, since body systems of the fetus are not fully developed, the fetus cannot process medicines like the mother's system; therefore, the same drug can harm the fetus.[4,5]

Corresponding Author: P. Torkzaban Address: Member of Dental Research Center and Assisstant Professor, Dept. of Priodontology of Faculty of Dentistry of Hamadan University of Medical Sciences, Fahmideh Blv, Hamadan, Iran. Tel: +98 8118354018 Email:Torkzaban@umsah.ac.ir

PREGNANCY TRIMESTERS

Pregnancy involves three trimesters, each lasting 3 months.

First trimester: During this trimester, different body organs in the fetus are forming. It is the most critical time for teratogenicity. Dental prophylaxis with detailed instructions and a visual examination of the oral cavity without x-rays should be performed if the patient is pregnant. Elective dental treatments should be avoided in the

morning as women may have nausea in the morning.

Second trimester: It is an excellent time for the patient to undergo dental prophylaxis if needed. The patient's periodontal status should be carefully evaluated during this period.

Third trimester: Women begin to feel uncomfortable and it is difficult for her to lie in the prone position for long periods. Drugs that may affect the newborn should not be given during this trimester. Positioning of the patient in the dental chair might exert pressure on the inferior vena cava, resulting in syncope. Stress can precipitate premature labor. Due to hormonal changes, gingival tissue exhibits exaggerated response to local irritants.[6–8]

PHARMACOKINETICS IN PREGNANCY

Drug absorption: High circulating levels of progesterone slow the gastric emptying as well as gut motility, resulting in slower drug absorption. Parenteral drug administration is preferred in order to obtain a quick response. Drug compliance may be poor because of nausea and concerns about adverse effects.

Drug metabolism: The hepatic and the renal plasma flow increases during pregnancy probably by high concentrations of circulating progesterone. This can lead to more rapid metabolic degradation, especially of highly lipid soluble drugs. However, this is of little clinical consequence.

Drug excretion: During pregnancy the renal plasma flow increases by 100% and glomerular filtration rate by 70%. Hence, drugs which depend for their elimination mainly on the kidney are eliminated more rapidly than in non-pregnant stages; notable examples include ampicillin, gentamicin and cephalosporin.

Recommended drugs to be used in pregnancy				
Type	Drugs	1st trimester	2nd and 3rd trimester	Comment
Local anesthetics	Lidocaine	Yes	Yes	First choice anesthetics, fetal bradycardia near term
	Mepivacaine	Yes	Yes	Fetal bradycardia near term
	Bupivacaine	No	No	Embryocidal in rabbits and high lipid solubility
	Benzocaine	Yes	Yes	Fetal bradycardia near term
Vasoconstrictors	Epinephrine	Yes	Yes	It can produce hypoxia (use cardiac dose)
Analgesics	Paracetamol	Yes	Yes	Teratogenic at over dose level
	Codeine	Limited dose	Limited dose	Respiratory distress near tern high dose contraindicated
	Aspirin	No	No	Bleeding, prolonged parturition, premature closure of paten ductus arteriosus
	Ibuprofen	Yes (cautiously)	No	Same as aspirin
Antibiotics	Penicillin	Yes	Yes	Safe
	Erythromycin	Yes	Yes	Safe except exfoliate from
	Tetracycline	No	No	Stains teeth, affects bone
	Clindamycin	No	No	Only if alternative does not exist
	Cephalosporin	Yes	Yes	Safe only if used as indicated
	Metronidazole	No	No	Carcinogenic and mutagenic in animals
Antifungal	Clotrimazole	No	Yes with caution	Poorly absorbed following topical or intravaginal application, abnormal liver function test in adults can occur.
	Ketoconazole	No	No	Embryotoxic in rats
	Nystatin	Yes	Yes	safe
Sedative	Benzodiazepines	No	No	Cleft lip, neural tube defect
	N_2O with 50% O_2	No	Possible with adequate O_2	Ensure adequate oxygen intake, female operators avoid chronic exposure

Use of dental drugs by a nursing mother

Types	Drugs	Acceptable	Watch infant for symptoms of
Local anesthetics	Amides	Yes	Central nervous system changes
Vasoconstrictors	Epinephrine	Yes	Hyperactivity or irritability
Analgesics	Aspirin	Yes with caution	Avoid feeding for 1 hour after dose, occasional low doses pose no hazard, chronic high dose may pose problems
	NSAID	Yes with caution	Use ibuprofen (concentration in milk is low) avoid long-acting NSAIDs
	Acetaminophen	Yes	Present in small amounts (peak 1-2 hours)
	Opioids	Yes	Small doses no problems and in larger doses sedation, poor feeding and constipation
Antibiotics	Penicillin	Yes	Allergic symptoms, diarrhea
	Erythromycin	Yes	Present in milk, diarrhea
	Cephalosporin	Yes	Allergic symptoms, diarrhea
	Tetracycline	No	Tooth staining
	Clindamycin	Yes/no	Diarrhea, pseudomembranous colitis
	Metronidazole	No	Carcinogenic in animals
Antifungal	Nystatin	Yes	Not absorbed into systemic circulation from mouth or gastrointestinal tract
	Clotrimazole	Yes	Excreted in milk, use nystatin first
	Ketoconazole	No	Carcinogenic in animals
Antiviral	Acyclovir	Yes	Concentrated in milk
Anxiolytics	Nitrous oxide	Yes	Excreted through mother's lung
	Benzodiazepines	No	Sedation, infants metabolize oxidized agent more slowly

Increased total blood volume: There is an increased total blood volume because of increased fluid retention, leading to changes in cardiac output, blood pressure and glomerular filtration rate. This results in changes in the volume of distribution of drug, metabolism, absorption, excretion of drugs, protein binding of drugs and passage of drug through placenta.

Teratogenicity: It refers to the capacity of a drug to cause fetal abnormalities when administered to a pregnant mother. Drugs can affect a fetus at three stages, i.e. stage of fertilization and implantation, stage of organogenesis and stage of growth and development.[9–11]

Drugs	Abnormalities
Thalidomide	Phocomelia
Anticancer drug	Multiple defect, fetal death
Tetracycline	Discolored and deformed tooth, retarded bone growth.
Phenytoin	Craniofacial and limb defect, cleft lip, cleft palate
Phenobarbitone	Various malformations
Carbamazepine	CNS defect
Retinoids	Various abnormalities
Alcohol	Fetal alcohol embryopathy

DENTAL MANAGEMENT OF PREGNANT PATIENTS

Elective treatment: It can be postponed easily for the pregnant patient after parturition. However, emergency care should be taken into consideration. The best method of treatment is to eliminate source of pain. Therefore, for the removal of caries or an infected pulp, the surgical procedure should be carried out under small doses of local anesthetics to minimize the use of systemic drugs. Dental procedures are best performed in the 2nd trimester for the benefit of the fetus and optimal comfort of the pregnant woman.

First trimester: It is roughly 12-13 weeks. During this first 12 days from conception to implantation, known as 'pre-implantation period', exposure to harmful drugs can kill the embryo. From the 13th day, there is period of organogenesis; therefore, the fetus is susceptible to insults and injuries resulting in malformation.

Second and third trimesters: After completion of organogenesis, there is considerable growth and development of existing structures like teeth, bones, CNS, endocrine

glands, genitals and the immune system. Malformation is less in the 2nd and 3rd trimesters but drugs like streptomycin can still be harmful causing retardation of physical and mental growth, premature labor or neonatal toxicity. The adverse effect of drugs on the fetus is dependent on the drug and the phase of pregnancy in which the drug is administrated.

Preventive dental prophylaxis: preventive dental prophylaxis should be undertaken at the beginning of the 2nd or 3rd trimesters.

Radiographs: radiographs are contraindicated in all but emergency situations; when taken, lead shielding is mandatory.

Reduce chair time: prolonged chair time must be avoided to prevent supine hypotension.

Position: sitting position is best for the patient since low head position may exert pressure on vena cava and aorta during the 2nd trimester.

Fainting: in case of fainting, place the patient on the left side with legs and head elevated. Oxygen and lime juice with glucose could be given and vital sign monitored.

Serious complications: more serious complications such as seizures and active vaginal bleeding of severe cramping require emergency care in hospital.[12–14]

GUIDELINES FOR PRESCRIBED DRUGS IN PREGNANCY

Don't use drug unless it is absolute necessary; use drugs in pregnant patients only when it is absolutely necessary.

Ruling out the possibility of pregnancy; rule out the possibility of pregnancy in every female patient in the reproductive age group and restrict drug use.

Risk and benefit ratio; prioritize drug use in the situation and avoid drugs if appropriate, i.e. risk-benefit ratio should be calculated.

Lower doses; use lower than usual doses of the drug if necessary for short term.[15–17]

CONSIDERATIONS DURING LACTATION

Almost all the drugs are excreted into the breast milk to some extent. An infant normally ingests approximately 1% of the total material dose of a drug. Dental practitioners must remember that drugs should be selected which have short half-life, sustained-release formulations should be avoided, and drugs should be taken immediately after nursing.[18]

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