Role of Family Physician in Guiding Drug Use during Pregnancy

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To

The Memory Of

My Father

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ABSTRACT

Health care providers face a dilemma when a pregnant woman develops a condition that usually is treated with a pharmacologic agent. It is well known that pregnancy can induce changes in the plasma concentrations of some drugs. Understanding of these pharmacokinetic changes, basic teratology associated with drugs as well as the pregnancy drug risk categorization can assist professionals in recognizing which pharmaceuticals should be used or avoided in treating a pregnant woman. The role of family physician in guiding drug use during preconception as well as antenatal care was elucidated. Some ethical issues regarding maternal-fetal medicine were discussed, and the impact of alcohol and illicit drugs on the mother and the fetus was reviewed.

Keywords:

Pregnancy - Pharmacokinetics - Placenta - Fetus - Drug - Family Medicine - Alcohol - Teratology

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LIST OF ABBREVIATIONS

ABC ATP Binding Cassette

ACAAI The American College of Allergy, Asthma, and Immunology

ACE Angiotensin Converting Enzyme

ACOG The American College of Obstetricians and Gynecologists

ADA American Diabetes Association

AEDs AntiEpileptic Drugs

AIDS Aquired Immunodeficiency Syndrome

ASHP American Society of Health-System Pharmacists

ATP Adenosine TriPhosphate

BCRP Breast Cancer Resistance Protein

C.G.D.U.P. the Collaborative Group on Drug Use in Pregnancy

CAs Congenital Anomalies

CDC Center for Disease Control and Prevention

Cmax Peak plasma concentration

CYP Cytochrome P

Da Dalton

DVT Deep Venous Thrombosis

ECF ExtraCellular Fluids

FDA Food and Drug Administration (USA)

G6PD Glucose-6-Phosphate Dehydrogenase

GDM Gestational Diabetes Mellitus

GFR Glomerular Filtration Rate

GPs General Practitioners

GST Glutathione S-Transferase

HG Hyperemesis Gravidarum

HIV Human Immunodeficiency Virus

IBD Inflammatory Bowel Disease

LT4 Levothyroxine

MDR MultiDrug Resistence gene

MRP Multidrug Resistance-associated Protein

MW Molecular Weight

NADP Nicotinamide-Adenine Dinucleotide Phosphate

NAS Neonatal Abstinence Syndrome

NTD Neural Tube Defect

OC Oral Contraceptives

OTC Over-The-Counter

OTIS The Organization of Teratology Information Specialists

PCOS Polycystic Ovarian Syndrome

PEPT Peptide Transporters

P-gP P-glycoprotein

PK Pharmacokinetics

RCTs Randomized Controlled Trials

RDS Respiratory Distress Syndrome

TERIS Teratogen Information System

TIS Teratogen Information Service

Tmax Time of peak plasma concentration

TSH Thyroid Stimulating Hormone

UGT uridine diphosphate glucuronosyltransferase

USPSTF US Preventive Services Task Force

UTI Urinary Tract Infection

INTRODUCTION

Since the thalidomide disaster over 40 years ago, we have known that medication use in early pregnancy poses a potential risk to the fetus. Yet, drugs typically enter the marketplace and are used in pregnancy without our being able to reliably predict whether they carry teratogenic risk. Premarketing pharmacologic, animal, and clinical studies often fail to accurately identify drugs of concern. In the postmarketing setting, case series and small cohorts of exposed pregnant women, like the ongoing pregnancy registries for newly marketed drugs, can only detect major human teratogens such as thalidomide or isotretinoin. While major teratogens fortunately appear to be few, less dramatic teratogens may be more numerous and more widely used and could therefore lead to a greater excess number of birth defects than major teratogens (Hernandez-Diaz 2006).

Pharmacotherapy during pregnancy is often necessary mainly because of the need to treat the mother either for chronic diseases (e.g. epilepsy, diabetes, asthma, or hypertension) or for acute illnesses (e.g. infections, seizures and gastrointestinal disorders) or even for severe complications such as tumors. On the other hand, there is an increasing demand to treat the fetus via maternal drug administration, e.g. for fetal tachycardia or to prevent materno-fetal transmission of HIV infection (Ceckova-Novotna et al. 2006).

Pregnant women are worried about medication use during pregnancy and need good advice. Women usually overestimate the teratogenic risk of medication exposures during pregnancy and therefore, may avoid prescriptions or exhibit non-compliance with recommended therapy. A study noted that women exposed to non-teratogenic medications in early pregnancy estimated the risk of a major fetal abnormality at about 25%. Pregnant women may avoid necessary medications out of fear or poor advice (Gibson