GUIDE TO CARDIOVASCULAR DISEASE MEDICATIONS FOR PREGNANT AND BREASTFEEDING WOMEN

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INTRODUCTION

As with any medication in pregnancy, a careful assessment of fetal risk to maternal benefit should be undertaken in regard to cardiovascular medications. Table 6 contains a short review of the hemodynamic physiology and its effects on drug concentration, kinetics and dosage of cardiovascular medications in pregnancy.[1] Tables 7 and 8 are summaries of cardiovascular drugs that may cause adverse events or are contraindicated in pregnant or breastfeeding women [2-6]

Table 6: Factors Affecting Drug Metabolism in Pregnancy

Maternal physiologic change	Effect on drug concentration and kinetics	Effect on drug dosage
Progressive increase in plasma volume by 50%	Hemodilution	Higher loading doses needed Steady state concentrations do not change
Decrease in plasma protein levels	Decreased protein-bound drug and total drug concentration over non-pregnant state, higher free unbound drug concentration	Potentially increased toxicity at beginning of dosing interval due to fluctuation in unbound drug concentration May need more frequent dosing without change in total daily dose
Increased renal blood flow and clearance, possible activation of cytochrome P450 system	Increased drug clearance, sub-therapeutic concentrations	May need increased dosages

Table 7: Cardiovascular Drugs and Adverse Effects in Pregnancy

Drug	Use	Risk Category*	Side Effects	Breastfeeding
Adenosine	Maternal and fetal arrhythmias	C	No reported side effects, limited first trimester data	Limited data, Unlikely passage into milk due to short half life and acute use
Amiodarone	Maternal arrhythmias	D	IUGR, congenital goiter, hypo-or hyper-thyroidism, prolonged QT in the newborn	Not Recommended
Beta blockers	Maternal hypertension, maternal arrhythmias, mitral stenosis, cardiomyopathy, hyperthyroidism, Marfan syndrome	Labetalol: C Metoprolol: C Propranolol: C Carvedilol: C Atenolol: D	IUGR, low placental weight, fetal bradycardia	Compatible, consider monitoring newborn heart rate (esp. atenolol)
Digoxin	Maternal and fetal arrhythmias, heart failure	C	No fetal side effects	Compatible
Diuretics (Furosemide, hydro-chlorothiazide)	Hypertension, congestive heart failure	C	Growth restriction, hyponatremia and hypokalemia, thiazides can inhibit labor and suppress lactation	Compatible
Flecanide	Maternal and fetal arrhythmias	C	Limited data, case reports of fetal SVT	Limited data, probably Compatible
Hydralazine	Hypertension	C	None reported	Limited data, probably Compatible
Nifedipine	Hypertension, tocolysis	C	Hypotension	Compatible
Nitrates	Myocardial infarction, ischemia, hypertension, pulmonary edema, tocolysis	C	Limited data, fetal distress	Limited data, Unlikely passage into milk due to acute use
Procainamide	Maternal and Fetal arrhythmia	C	Limited data, no reported fetal effects	Compatible

Table 7 continued: Cardiovascular Drugs and Adverse Effects in Pregnancy

Drug	Use	Risk Category*	Side Effects	Breastfeeding
Quinidine	Maternal and Fetal arrhythmia	C	Preterm labor, miscarriage, transient fetal thrombocytopenia and damage to eight nerve	Compatible
Sodium nitroprusside	Hypertension, aortic dissection	C	Limited data, possible thiocynate fetal toxicity	No data, possible toxicity
Sotalol	Maternal arrhythmias, hypertension, fetal tachycardia	B	Limited data, reported cases of fetal death, neurologic morbidity, newborn bradycardia	Compatible
Verapamil	Maternal and fetal arrhythmias, hypertension, tocolysis	C	Limited data, no adverse fetal or newborn effects reported	Compatible

*Risk category from: U.S. Food and Drug Administration Pharmaceutical Pregnancy Categories.

Table 7 adapted and used with permission from: Blanchard DG, Daniels LB. Cardiac Diseases CH 52. In: Creasy R, Resnick R, Iams J, Lockwood C, Moore T, eds. *Creasy and Resnik's maternal-fetal medicine: Principles and practice, 7th ed.* Philadelphia: Saunders; 2013:855-6.

*FDA Pharmaceutical Pregnancy Risk Categories	
Category A	Adequate and well controlled human studies demonstrate no risk.
Category B	Animal studies demonstrate no risk, but no human studies have been performed. OR Animal studies demonstrate a risk, but human studies have demonstrated no risk.
Category C	Animal studies demonstrate a risk, but no human studies have been performed. Potential benefits may outweigh the risks.
Category D	Human studies demonstrate a risk. Potential benefits may outweigh the risks.
Category X	Animal or human studies demonstrate a risk. The risks outweigh the potential benefits.

Reference: U.S. Food and Drug Administration classification of drug risk. From: Office on Women's Health in the U.S. Department of Health and Human Services, Pregnancy and medicines fact sheet: http://womenshealth.gov/publications/our-publications/fact-sheet/pregnancy-medicines.html, accessed May 1, 2015.

Table 8: Drugs Usually Contraindicated in Pregnancy

Drug	Use	Risk Category*	Side Effects	Breastfeeding
ACE inhibitors and Angiotensin Receptor blockers	Maternal hypertension	X	Oligohydramnios, IUGR, prematurity, neonatal hypotension, renal failure, anemia, death, skull ossification defect, limb contractures, patent ductus arteriosus	Compatible
Warfarin (Coumadin)	Anticoagulation	X	Crosses placental barrier, fetal hemorrhage in utero, embryopathy, CNS abnormalities May be used if benefits outweigh risks (for example, history of prosthetic valves)	Compatible
HMG-CoA reductase inhibitors (statins)	Antilipemic agent	X	Possible increase in congenital central nervous system and limb abnormalities if used in the first trimester	Limited data Breastfeeding is discouraged

*Risk category from: U.S. Food and Drug Administration classification of drug risk. From: http://womenshealth.gov/publications/our-publications/fact-sheet/pregnancy-medicines.html, accessed May 1, 2015.

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