

Interpretation of Lactation References

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Lactation and Medications

Factors increasing drugs transfer into breastmilk:

- Lipophilicity of the drug
- Low protein binding
- Long half-life
- Absorption in the gut

Verstegen R, et al. British J Clin Pharm, 2020; 88(10):4311-4327. <https://doi.org/10.1111/bcp.14538>



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References available

LactMed

- Maintained by NIH
- Available as online database or mobile app

Briggs Meds in Pregnancy in Lactation

- Print or online book (linked online to UpToDate - Lexidrug)

InfantRisk

- Hotline, website, mobile app for lactating mothers
- Run by a pharmacy team at Texas Tech University

E-Lactancia

- Online Spanish-English resource
- Run by MD and pharmacist team



Reading LactMed: Digoxin

Summary of Use during Lactation

Because of the low levels of digoxin in breastmilk, amounts ingested by the infant are small and would not be expected to cause any adverse effects in breastfed infants. If the mother is to receive digoxin intravenously, avoidance of breastfeeding for 2 hours after the dose will lessen the dose the infant receives.



Reading LactMed : Digoxin

Drug Levels

Maternal Levels. In 11 women taking digoxin 0.25 mg daily orally, milk digoxin levels obtained on days 3 to 7 postpartum were relatively constant at 0.644 mcg/L.[1] The amounts in milk represent an infant dosage of about 2.3% of the maternal weight-adjusted dosage or 0.097 mcg/kg daily, which is about 1% of the neonatal maintenance dosage.

Milk digoxin levels were 0.41 and 0.78 mcg/L in two mothers taking oral digoxin 0.25 mg daily.[2]

Milk digoxin levels ranged from undetectable (<0.5 mcg/L) to 1 mcg/L in 5 women treated with unspecified doses of digoxin. Milk and serum levels were similar.[3]

A milk digoxin level of 1.9 mcg/L was measured in a mother taking 0.75 mg daily of digoxin during pregnancy and postpartum.[4]

After an intravenous bolus dose of digoxin 0.5 mg in 11 women, digoxin serum and milk levels rapidly equilibrated, with high levels occurring rapidly, dropping to low levels by about 2 hours after the dose. A pharmacokinetic simulation using data from these mothers indicate that a fully breastfed infant would obtain a serum level of only about 3% of a therapeutic level with maternal intake of 0.5 mg daily of digoxin.[5]

Infant Levels. In two breastfed infants whose mothers were taking oral digoxin 0.25 mg daily, digoxin was undetectable (< 0.1 mcg/L) in their serum after 10 days of maternal therapy.[2]

A mother took 0.75 mg daily of digoxin during pregnancy and postpartum. Her infant had a serum level of 0.2 mcg/L after nursing for 7 days, having decreased from a level of 0.6 mcg/L at birth.[4]



Reading Briggs: Digoxin

Breast-feeding Summary

Digoxin is excreted into breast milk. Data for other cardiac glycosides have not been located. Digoxin milk:plasma ratios have varied from 0.6 to 0.9 ^(Ref). Although these amounts seem high, they represent very small amounts of digoxin due to significant maternal protein binding. No adverse effects in the nursing infant have been reported. In 2001, the American Academy of Pediatrics classified digoxin as compatible with breastfeeding ^(Ref).



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Fun Math: Digoxin

Mom (70kg) is taking Digoxin 0.25 mg daily. Last serum level was 1.5 ng/ml

- Breast milk (BM) : plasma ratio = 0.6 – 0.9
 - BM Concentration = 0.9 – 1.35 ng/ml
 - plasma concentration x BM:Plasma ratio = estimated BM conc.



More fun math (still Digoxin)

- Babies consume ~ 150 ml/kg/day BM
 - 5 kg baby drinks ~ 750 ml BM/day
- Digoxin consumed per day for this 5 kg baby:
 - Low end: $750 \text{ ml BM} \times 0.9 \text{ ng/ml} = 675 \text{ ng digoxin}$
 - High end: $750 \text{ ml BM} \times 1.35 \text{ ng/ml} = 1012.5 \text{ ng digoxin}$
- Digoxin enteral bioavailability:
 - Elixer: 70-85%
 - Tablet: 60-80%



Yes, MORE fun math with Digoxin

- BM dose digoxin for 5 kg baby = 0.675 – 1.0125 mcg/day
 - 0.135 – 0.2025 mcg/kg/day (minus the fraction not absorbed)
- Usual infant therapeutic dose: 12.5 mcg/kg/day

At this dose, digoxin is safe for Mom to take →
baby will not achieve therapeutic levels.



Relative Infant Dose (RID)

$$\text{RID} = \frac{\text{Infant daily dose per kg via milk}}{\text{Maternal daily dose per kg}} \times 100$$

- RID of 100%: infant dose via milk = Mom's dose per weight
- RID of 5 – 10% is generally considered safe for baby
 - In our Digoxin exercise: RID ~4.9%

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Case 1: Resistant Hypertension

FIT Presenter: Aardra Rajendran, MD

Cardiovascular Medicine Fellow, University of Pennsylvania



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Case

39 YO F G2P1001 with history of chronic hypertension (dx mid-20s) with superimposed preeclampsia, palpitations with infrequent PVCs, obesity (BMI 39.7 kg/m²), OSA (not wearing CPAP regularly) presents to Obstetrics clinic at 10w.

1st Pregnancy

3 years prior: First pregnancy

- Switched from labetalol to nifedipine 30 mg due to missing nighttime labetalol doses

Delivery: 38w C-section for fetal malpresentation

- Developed chronic HTN w/ superimposed preeclampsia w/ severe features (BP 188/104)
- Received IV magnesium, IV labetalol x1, IV hydralazine x1, and PO furosemide 20 mg x 5d

Discharged: BP 157/81

- Nifedipine 90 mg, labetalol 100 mg BID
- Breastfeeding? Yes

Outpatient: baseline BP 130-140 / 80-90

- Labetalol 300 mg BID, amlodipine 10 mg, and HCTZ 25 mg

2nd Pregnancy

10w: Ob intake visit- BP 137/86

- Presented on amlodipine 10 mg, labetalol 300 mg BID, HCTZ 25 mg -> **stopped HCTZ 25 mg**
- Seen by Cardiology and followed by Ob over the next several weeks:
 - Recommended continued monitoring BP at home

17w: Specialist visit– BP 130-140 / 80-90

- Cardiology: **Stopped amlodipine 10 mg** -> **started nifedipine 90 mg daily.** Continuing labetalol 300 mg BID
 - Labetalol- concern for missed doses
 - Nifedipine- ?frequent headaches, no vision changes; however, had a hx of sinus headaches
- Renal: Prescribed **methyldopa 250 mg BID** which she had challenges obtaining from her local pharmacy.

2nd Pregnancy

Delivery: BP 144-155 / 85-105

- HELLP labs negative, urine protein 13 mg/dL, urine protein:Cr ratio 0.17
- 38w C-section for fetal malpresentation

Discharge: BP 139/87

- Nifedipine 90 mg, labetalol 300 mg BID, PO Lasix 20 mg x 5d
- Breastfeeding? Yes

DISCUSSION

Postpartum

Followed by Cardiology, Nephrology: Secondary HTN workup 8m postpartum

- **EKG - mild LVH**
- Renal Doppler negative
- **TTE – LVEF 56%, mild LVH (IVS 1.1 cm), grade I diastolic dysfunction**
- Cr 0.72, eGFR by Cystatin C – 78, UA protein negative, Urine protein 7, UPCR 0.06, UACR 14
- Plasma metanephrines negative
- Thyroid studies normal
- **Plasma aldosterone 10.6 ng/dL; Plasma renin activity (PRA) < 0.1 ng/mL/hr**
 - **Aldosterone to renin ratio (ARR)-106 (> 30)**
- **CT-AP ordered to evaluate for adenoma but has not been completed**

Started tirzepatide with PCP to help with weight loss

Encouraged to use CPAP regularly

Postpartum

Diagnosed with primary hyperaldosteronism

- **Started spironolactone 50 mg** -> weaning down nifedipine 90 mg, labetalol 300 mg BID
- BP 110 – 120s / 80s
- Placed on **Baxdrostat** list (small-molecule aldosterone synthase inhibitor) pending FDA approval:
 - At 12 weeks: 2mg Baxdrostat –15.7 mmHg (95% CI, –17.6 to –13.7) vs Placebo –5.8 mmHg (95% CI, –7.9 to –3.8). Hyperkalemia in 3% with 2mg Baxdrostat.
 - Trial excluded pregnant and breastfeeding individual; reproductive-age women were on reliable contraception during the study. **Safety profile in pregnancy and lactation has not been established.**

Efficacy and Safety of Baxdrostat in Uncontrolled and Resistant Hypertension

Authors: John M. Flack, M.D., Michel Azizi, M.D., Jenifer M. Brown, M.D., Jamie P. Dwyer, M.D., Jakub Fronczek, M.D., Erika S.W. Jones, M.D., Daniel S. Olsson, M.D., [+6](#), for the BaxHTN Investigators* [Author Info & Affiliations](#)

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DISCUSSION

Antiarrhythmic Use in Pregnancy & Lactation

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Initial History & Presentation

- 37F G1P0 - currently 24 weeks gestation
- PMHx: Obesity (pre-pregnancy BMI 34 kg/m²)
- ED visit 2 weeks ago with palpitations, fatigue, mild dyspnea for 12 hours
 - new onset AFib RVR
 - TTE with structurally normal heart
 - Considered DCCV though patient declined due to safety concerns
- Successfully converts with IV metoprolol and is discharged on PO metoprolol 25mg BID & prophylactic LMWH



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History & Presentation Continued

- Over the past 2 weeks, has had breakthrough episodes of Afib despite titration of metoprolol to 50mg BID
- Returns to our outpatient clinic today with ongoing palpitations and fatigue
- She asks if there is anything else that she can take that may suppress these episodes and is safe to take while pregnant



Vitals & Physical Exam

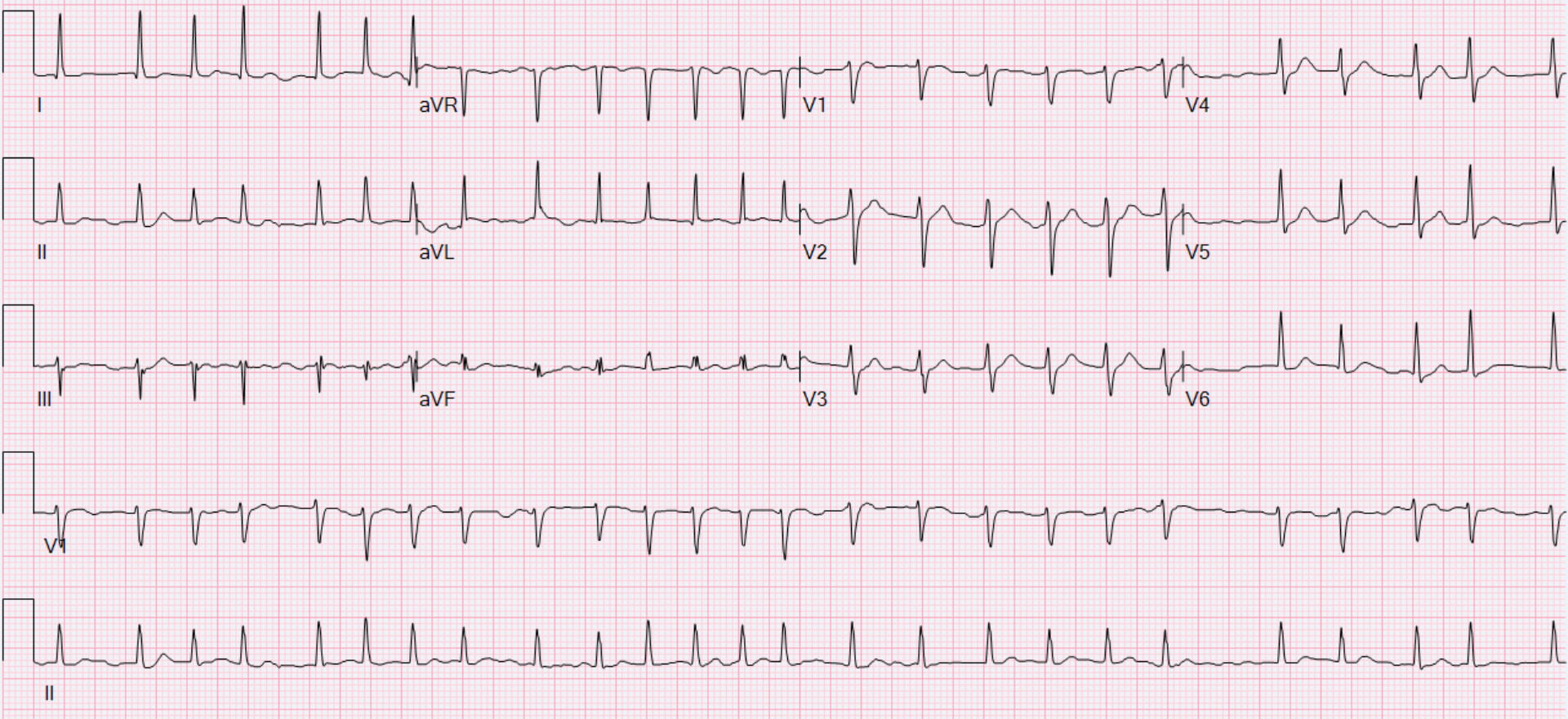
- HR 150 bpm (as high as 160 bpm), BP 110/70 mmHg, SpO2 97% (room air)
- General: awake, no acute distress
- Pulmonary: clear to auscultation bilaterally
- Cardiac: irregularly irregular, no M/R/G
- Abdomen: soft, non-tender
- Extremities: no lower extremity edema



Labs

- WBC 10.4, Hgb 12.9, Plt 351
- Na 133, K 4.0, Cr 0.60, Mag 2.07
- LFTS and TFTs within normal range
- Respiratory pathogen panel negative
- Echocardiogram previously performed - normal LV ejection fraction, no structural abnormalities





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What is the next best step for medical management?

A. Increase metoprolol

B. Flecainide

C. Digoxin

D. Amiodarone



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Clinical Course

- Started on PO flecanide with improvement of symptoms and suppression of Afib burden; continued on prophylactic LMWH through remainder of pregnancy
- She delivers at 39 weeks via uncomplicated vaginal delivery and is now exclusively breastfeeding
- 10 days post-partum → returns to ED with recurrent palpitations, found to be in atrial fibrillation 140 bpm



How would your management change now that she is breastfeeding instead of pregnant?



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Thank You!



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When “GDMT” Meets Gestation: Redesigning Heart Failure Therapy for Pregnancy and Lactation

Case Presentation by Rachana Raghupathy, MD

FIT Member, ACC Reproductive Health and Cardio-Obstetrics Workgroup

32 year-old G3P0 female with a history of HF with moderately reduced EF secondary to prior cocaine and methamphetamine use (now in remission) presenting for severe dyspnea on exertion and lower extremity edema. She is currently 20 weeks pregnant.



First, A Little Backstory..

- 3 years ago, presented with HF, found to have LVEF 45%
- Started on GDMT:
 - metoprolol succinate 50mg
 - losartan 50mg
 - spironolactone 25mg
 - dapagliflozin 10mg
 - furosemide 20mg as needed
- Stopped using illicit drugs
- **Inconsistent follow up**

Back To Today...

- Found out 3.5 months ago that she was **pregnant**. With **2 prior miscarriages**, was worried about whether she can safely carry this pregnancy to term.
- **Asked ChatGPT**, who told her that her current cardiac medications are not safe in pregnancy. **She subsequently discontinued all medications abruptly.**
- **Has not been on any heart failure medications for months**
 - Currently **only taking semaglutide** (for weight management and has helped her avoid illicit substances), which she is getting from a friend and administering “just a tiny bit” weekly
- About 4 weeks ago, developed **dyspnea on exertion and orthopnea**, worsened up until presentation today

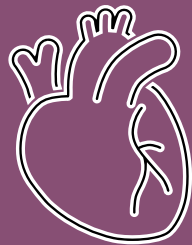
Back To Today...

- Vitals: 99F, HR 90bpm, BP 133/78, SpO2 100% on RA
- Relevant physical exam: heart RRR on auscultation, **systolic murmur appreciated at LUSB, JVP 10cm** above sternal notch, **1+ bilateral pitting edema**. Lungs CTAB. Gravid abdomen
- Workup reveals:
 - **CMP**: electrolytes and liver markers normal, but evidence of **acute kidney injury**
 - **NT-proBNP**: **4500** (ref range <125 pg/mL)
 - **HS-Troponin I**: **116→120** (ref range 15-34 ng/L)
 - **Urine drug screen**: negative
 - **EKG**: **normal sinus rhythm** with ventricular rate of 88bpm
 - **TTE**: **globally reduced LVEF of 34%**, normal diastolic function, **mild eccentric MR** with annular dilatation, likely functional. **LVEF has worsened from prior study 3 years ago**
 - **Fetal sonogram**: fetal heartbeat appreciated, estimated gestational age 19 weeks, normal amniotic fluid index. **Normal test**

This Admission

- Admitted to the floor, where she is optimized on **IV diuretics.**
- Mild AKI improves
- 6 days later, she is stabilized for discharge

She says to you, “I really can’t lose this baby – I’ve lost 2 already. Do I need to be taking meds at home for my heart to avoid this from happening again?”



Discussion

Which heart failure medications are safe to use during pregnancy?

This Admission

- She is started on the following medications:
 - **Metoprolol succinate** 25mg (plan to go back to prior dosing if able)
 - **Hydralazine 25mg/isosorbide dinitrate** 20mg TID
 - **Furosemide** 20mg as needed for shortness of breath or swelling
- **Discontinue:** dapagliflozin or semaglutide
- **STRONGLY** encouraged she follow up closely as an outpatient for monitoring and medication adjustments

A Few Months Later...

- She arrives back at the hospital for **scheduled induction at 36 weeks' gestation**
- **She has been following closely with her OBGYN, MFM, and HF**
- Has a **vaginal delivery** with OB anesthesia and CCU on standby
- She gives birth to a baby boy. Placenta is safely delivered. Expected bleeding is controlled

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- Has a **vaginal delivery** with OB anesthesia and CCU on standby
- She gives birth to a baby boy. Placenta is safely delivered. Expected bleeding is controlled
- Immediately after delivery, she becomes **severely short of breath and hypoxic. BP drops to 88/50 (MAP 63)**. STAT TTE reveals LVEF of 20%
 - She is started on BiPAP and sent to the CCU
- She is started on **IV dobutamine** and continued on **BiPAP** for the day. While on inotrope support, she is able to **wean off BiPAP to nasal canula**
- **Within 72 hours**, she is **weaned off IV dobutamine** and stabilized for transfer to the floor

“So when can I start breastfeeding? Will my meds be safe for my baby?”



Discussion

Which heart failure medications are safe to use during breastfeeding/lactation?

Discharge Medication Reconciliation

- On the floor, she is started on the following:
 - **Continue metoprolol succinate** 50mg
 - **Start enalapril** 5mg daily
 - **Start spironolactone** 12.5mg daily
 - **Furosemide** 20mg as needed for shortness of breath, leg swelling, weight gain > 3lbs
 - Discussed that use of **diuretics may reduce breastmilk supply**
- **DO NOT TAKE:** dapagliflozin or semaglutide (was taking prior to pregnancy)

The background is a solid purple color. It features several decorative elements: a cluster of white dots in the top-left corner, a larger, irregularly shaped area of white dots in the top-center, a solid purple abstract shape on the right side, a solid purple abstract shape on the left side, and another cluster of white dots in the bottom-left corner.

Thank you for joining us!