lines for the arrhythmic condition, the mechanisms of action of the drug (or class of drug), the record of safe use of the drug during pregnancy, and the potential overall risk of the treatment. The use of antiarrhythmic drugs in pregnancy requires attention to potential changes in pharmacokinetics due to the changes in maternal physiology, such as metabolism and an increase in intravascular volume.[59,60] For example, intravascular volume changes peak in the third trimester of pregnancy and pregnant patients often require a medication increase to achieve the same intended clinical effect. Therefore, it is important to monitor drug levels or, alternatively, to monitor the physiological effect of drugs (eg, ECG monitoring for QT prolongation).[59]

Maternal therapy with beta-blockers during pregnancy has been associated with intrauterine fetal growth restriction. Most of the studies on maternal beta-blocker therapy are based on pregnant patients with hypertensive disorders of pregnancy, where fetal growth could be affected by the underlying condition, in this case hypertension, and not necessarily the drug itself.[61] However, a study of beta-blockers prescribed for maternal cardiac conditions, with a separate analysis of pregnant patients with isolated tachyarrhythmias as the indication, demonstrated a significant effect of beta-blockers on fetal growth after adjusting for other potential confounders.[62] Although concern regarding fetal growth restriction has been highlighted for atenolol and labetalol particularly, it is important to recognize that the maternal indication for medications differed among the different beta-blockers, and the overrepresentation of maternal hypertensive disorders in these subgroups may have affected the results significantly.[63] In a review of cardiovascular medications in pregnancy, atenolol had a former United States Food and Drug Administration (FDA) risk category D rating for its use during pregnancy.[64] In a more recent study, Grewal et al[65] reported the birth weight reduction associated with beta-blockers to be less than 200 grams, and therefore not of great clinical consequence in most instances. Thus, in the setting of potentially life-threatening scenarios (eg, some inherited arrhythmia syndromes [IAS]) a maternal indication for prescription of a beta-blocker takes priority over potential fetal growth-restriction concerns, and beta-blocker therapy should be continued during pregnancy and the postpartum period (Figure 2). Dosages and risks for common antiarrhythmic drugs are outlined in Table 5. Additional resources for drug safety during pregnancy include MotherToBaby (https://mothertobaby.org), Reprotox (https://reprotox.org/member), and Teris (https://deohs.washington.edu/teris/).

During lactation, special consideration should be given to medications that may adversely affect the newborn. While some medications are safe in pregnancy, their metabolism and concentration in breast milk can be of concern during lactation. One example of this is the beta-blocker nadolol, which has a high concentration in breast milk.[66] The excretion of beta-blockers into breast milk is largely determined by the degree of protein binding; medications with low binding are more heavily excreted into breast milk.[67] For example, based on protein binding and renal excretion, nadolol presents a high risk for accumulation in infants. If clinically acceptable for the maternal cardiac indication, propranolol or metoprolol might be preferred over nadolol in breastfeeding. Yet the discussion of medications during breastfeeding should include consideration of the underlying conditions of the pregnant patient, the optimal treatment for their arrhythmia, and whether there is a reasonable alternative that has similar efficacy but is safer for breastfeeding (Figure 2). If there are no medication alternatives that are efficacious for the patient and safe with lactation, lactation may need to be avoided or monitored closely for potential side effects (eg, excess bradycardia in the case of nadolol). This decision should be based on a shared decision-making discussion with the patient and family that considers the negative impact of deferring the recommended pharmacological therapy on maternal health in the postpartum period balanced against the importance of breastfeeding to the postpartum patient and baby. Risks of antiarrhythmic drugs during lactation are outlined in Table 5. More information on drug safety during lactation can be found in the Drugs and Lactation Database (LactMed) (https://www.ncbi.nlm.nih.gov/books/NBK501922).

Prior to 2015, the FDA used a 5-tier set of alphabet categories (A, B, C, D, and X), introduced in 1979, to designate the safety of a drug for use during pregnancy (Figure 3).[64] The system was simple to understand for category A drugs, which were generally safe to use, and category X drugs, which were contraindicated. However, because the category system did not accurately or consistently communicate differences in degrees of fetal risk, its implementation led to misinterpretation and avoidance of drug categories B, C, and D, which generally had limited or ambiguous data Thus, on June 30, 2015, the FDA introduced the new Pregnancy and Lactation Labeling Rule to replace the prior risk categories and to help physicians better communicate the potential drug risks to patients during pregnancy and lactation (Figure 3).[70,71] Under the Pregnancy and Lactation Labeling Rule, package

| | Propranolol | Metoprolol | Nadolol | Atenolol | Mexiletine | Quinidine | Sotalol |
|---|---|---|---|---|---|---|---|
| Use during pregnancy | Safe | Safe | Safe | Risk | Caution | Safe | Safe |
| Use when breastfeeding | Safe | Safe | Caution | Risk | Caution | Safe | Safe |

**Figure 2** Antiarrhythmic drug safety for commonly used drugs in pregnancy.[68,69]