Arrhythmias in Pregnancy

Alejandra A Miyazawa

Introduction

The pregnant patient is often met with a degree of trepidation by doctors due to the need to consider the safety of not only the patient, but the foetus, and the substantial physiological changes the woman's body undergoes. Cardiac disease is the most common cause of indirect maternal death and accounts for 12% of all maternal deaths in the UK (1). This can be explained by women becoming pregnant at older ages and patients with congenital heart disease are surviving longer. Arrhythmias are common in pregnancy, even in the absence of structural heart disease, and may be a first presentation or an exacerbation of a pre-existing cardiac condition (2,3). Often patients are symptomatic with palpitations due to benign arrhythmia (ectopic beats, sinus tachycardia) and may only require reassurance. However, even arrhythmia generally considered to be benign, may cause concern for the pregnant woman and their foetus (3-5). Moreover most anti-arrhythmic drugs cross the placenta and some may be harmful to the foetus, therefore careful consideration should be taken in the management of arrhythmia in the pregnant patient (6).

> **Take Home Messages**
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> - Palpitations are common in pregnancy and should always be investigated.
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> - Management of arrhythmia in the pregnant patient requires careful consideration for the safety of the foetus and the mother.
>
> - Electrical cardioversion is preferred over chemical cardioversion

Mechanisms of Arrhythmogenesis in Pregnancy

During pregnancy, increased metabolic demands of the mother and the foetus lead to changes in cardiovascular physiology. Plasma volume increases by up to 40% at 24 weeks gestation, leading to an increase in pre-load and cardiac output. Systemic vascular resistance is reduced due to active vasodilatation (3,7,8,12). The increased circulating volume leads to atrial stretching which in turn activates ion channels and induces membrane depolarisation, shortening the refractory period and slowing conduction (5,8). Heart rate increases by 30% due to increased adrenergic and autonomic activity, further compounding the pro-arrhythmic milieu (3,7,8,12).

The Resting ECG

The resting ECG of the pregnant patient often reveals a (sinus) tachycardia, which leads to shortening of the PR, QRS and QT intervals. As the uterus enlarges and elevates the diaphragm, the electrical axis shifts towards the left. Small Q waves and T wave inversion are often seen in the inferior leads. Premature atrial and ventricular complexes are common (3,5,9).

Clinical Presentation and Diagnosis

Pregnant patients presenting with palpitations, pre-syncope or syncope always require further investigation. This should include a detailed history and examination, and a 12 lead ECG, routine bloods, holter monitor and a trans-thoracic echocardiogram. It is necessary to exclude any systemic conditions that may present with arrhythmias such as thyroid

dysfunction, anaemia, and infection. As pregnancy is often a woman's first healthcare review, structural heart conditions should be excluded with a baseline transthoracic echocardiogram. It is important to diagnose the arrhythmia leading to symptoms and identify any exacerbating or causal factors to ensure the most appropriate management (3,9).

SUPRAVENTRICULAR ARRHYTHMIAS

Paroxysmal supraventricular tachycardias are common in pregnancy and can occur in 20-44% of cases (7,10).

AVNRT/AVRT

If persistent, initial management is with vagal manoeuvres. If successful, the patient should be counselled on how to self-terminate should these recur. Second line management should be adenosine boluses (18-24mg) due to its short half-life. Although not harmful to the foetus, adenosine can encourage conduction down an accessory pathway and therefore should be administered in a monitored environment with access to resuscitation equipment. In pregnancy, adenosine deaminase, which breaks down adenosine, is often reduced by approximately 25%; however, due to the increase of intravascular volume, the volume of distribution remains unchanged (3,11). Not enough studies have been performed in pregnant patients receiving adenosine in the first trimester and therefore caution should be exercised. It is deemed safe in the second and third trimester (8,11). On a recently published review of cardiac medications used in pregnancy, adenosine was deemed to be safe for use in the USA, particularly due to its short half-life, although foetal bradycardia has been described.(12)

In patients with Wolff-Parkinson-White (WPW) syndrome, beta-blockers are the treatment of choice as calcium channel blockers and digoxin can exacerbate conduction via the accessory pathway and cause pre-excited atrial fibrillation leading to ventricular fibrillation. Atenolol is generally avoided due to concerns with intra-uterine growth retardation (IUGR). Other associated side effects of beta-blockers with low incidence include foetal bradycardia, apnoea, and hypoglycaemia. In patients without WPW, verapamil is often a safe second-line treatment to be given in pregnancy and in the breast-feeding patient (3,11,12).

Table 1 summarises the safety profile of anti-arrhythmic drugs in pregnancy and breastfeeding.

Atrial Fibrillation and/or Atrial Flutter

Atrial fibrillation and/or flutter are relatively uncommon in pregnancy. If present, they are usually due to an underlying structural heart disease, electrolyte disturbance or thyrotoxicosis. It is important to treat the underlying condition in the first instance as reversion to normal sinus rhythm is common. Although these arrhythmias are well-tolerated, one should aim to revert to normal sinus rhythm to reduce the need for anticoagulation, particularly as pregnancy itself is a pro-thrombotic state. Rhythm control should be attempted in the first instance with a beta-blocker. In the haemodynamically unstable patient or if the mother and/or foetus is at risk, electrical cardioversion is deemed safe and preferred over chemical cardioversion as it minimises foetal risk; however, despite an extremely low incidence, foetal monitoring must be performed during the procedure to identify foetal arrhythmias early (3,7,8). Amiodarone is avoided in pregnancy as it may lead to foetal hypothyroidism and IUGR. In certain cases, it cannot be avoided if the arrhythmia is life-threatening and unresponsive to other medical therapy (7,8).

For patients where the aim is rate control, beta-blockers (outside of the first trimester), verapamil and digoxin, have all deemed to be relatively safe in pregnancy. We do not have enough experience with diltiazem in pregnancy to ensure its safety, and it has also been associated with skeletal abnormalities and IUGR (3). Patients on digoxin must be monitored for toxicity as it has been associated with miscarriages and foetal death. Due to an increased volume of distribution, digoxin levels are often reduced and patients require increased doses of the drug to maintain levels within the therapeutic margin. This potentially increases the risk of digoxin toxicity (7,12).

Patients with a CHA_2DS_2VASC score of at least 2 should be considered for anticoagulation due to the increased thrombo-embolic risk. Warfarin is teratogenic in the first trimester; however, it can be given from the second trimester up to 1 month before the expected delivery date. Subcutaneous injections of low molecular weight heparin are safe to be given in the first trimester and during the last month of pregnancy. Dabigatran has been shown to be unsafe and foeto-toxic and should not be used in high doses. Not enough research has been done with the other newer oral anticoagulants to assess their safety in pregnancy and therefore they should all be avoided (7,9,13,14).

VENTRICULAR ARRHYTHMIAS
Although ventricular premature beats are common in pregnancy, ventricular tachycardias (VT) and fibrillation are rare. In a structurally normal heart, monomorphic VT originating from the right ventricular outflow tract is the most common. This is characterised by the presence of a LBBB pattern and inferior axis on the 12 lead ECG. They very rarely progress to unstable rhythms and respond well to beta-blockers (3,7,8).

Patients with VT and known structural heart disease are at risk of sudden cardiac death and should be treated promptly with electrical cardioversion. Intravenous lignocaine or amiodarone may be considered. It is important to restore sinus rhythm, even in the haemodynamically stable patients, as soon as possible to prevent myocardial ischaemia leading to degenerating cardiac rhythm (7).

Implantable cardioverter defibrillators are safe to be used in pregnancy and should be implanted in all patients with high risk of sudden cardiac death. If implanted during pregnancy, precautions should be taken to limit fluoroscopy exposure to the foetus with the use of abdominal shields (7).

Radiofrequency Catheter Ablation
Radiofrequency catheter ablation with abdominal shielding can be considered in drug-resistant and very symptomatic patients. It is important to minimise fluoroscopy exposure to the foetus. If necessary, during pregnancy, this should be performed in the second or third trimester. In female patients of child-bearing age who are involved in family planning, in the presence of frequent episodes of symptomatic supraventricular tachycardias, ablation should be considered prior to pregnancy (7,8).

Bradyarrhythmias
Bradyarrhythmias are rare in pregnancy given the normal physiological response to pregnancy results in higher heart rates. During delivery, a Valsalva manoeuvre will often trigger a sinus bradycardia. In rare cases, a supine hypotensive syndrome of pregnancy has been described, where the uterus can compress the venous return via the inferior vena cava

and result in a paradoxical sinus slowing. This responds well to a left lateral decubitus position (3,7,15).

Congenital complete heart block in the mother is rare and often well tolerated with a narrow QRS complex. Permanent pacemaker implantations can be performed safely during pregnancy with reduced fluoroscopy exposure to the foetus (3,7,8).

Conclusion

Arrhythmias are common in pregnancy and can often be managed conservatively. Management of these patients is similar to the non-pregnant patient. Generally, pregnant patients can be managed safely with medication with little risk to the mother and foetus. For the treatment of SVT, vagal manoeuvres should be attempted in the first instance. If unsuccessful, adenosine should be used with caution in the first trimester and may be helpful to reveal the underlying rhythm and/or terminate the arrhythmia. In atrial fibrillation and atrial flutter beta-blockers are often first line in the haemodynamically stable patient. Calcium channel blockers and digoxin are relatively safe alternatives if beta-blockers are contra-indicated. Restoration of a normal sinus rhythm is paramount and if not self-terminating with conservative manoeuvres, it is usually safe to proceed with electrical cardioversion at any stage of pregnancy.

DRUG	FDA Category*	LISTED COMPLICATIONS	BREASTFEEDING
Adenosine	C	Pregnant women may respond to lower doses due to a reduction in adenosine deaminase. Use with caution in first trimester. Relatively safe in 2nd and 3rd trimester.	Safe due to short half-life
Amiodarone	D	Might be used in special circumstances: when other therapies fail and tachyarrhythmia is present with haemodynamic instability. Use at lowest effective dose. Risk of hypothyroidism, goitre, bradycardia, foetal growth restriction, and preterm birth.	Avoid due to prolonged half-life
Atropine	C	Insufficient data.	Unknown
Beta-blockers	C (Atenolol D)	IUGR, bradycardia, apneoa, hypoglycaemia, hyperbilirubinaemia. *Avoid atenolol in 1st trimester due to risk of IUGR.	Labetalol (safe) Metoprolol (acceptable) Carvedilol (unknown)
Digoxin	C	Miscarriage and foetal death in toxicity.	Safe
Diltiazem	C	Skeletal abnormalities, IUGR, and foetal death.	Unknown
Disopyramide	C	Limited data. Unable to recommend regular use in pregnancy. Premature uterine contractions.	Unknown
Flecainide	C	Insufficient data; no reported significant complications.	Unknown
Lignocaine	B	Foetal distress may occur in foetal toxicity.	Safe
Mexiletine	C	Limited data.	Unknown
Procainamide	C	Chronic use may be associated with lupus-like syndrome, gastrointestinal disturbance, hypotension and agranulocytosis. Foetal distress may occur in foetal toxicity.	Avoid
Propafenone	C	Insufficient Data.	Unknown
Sotalol	B	Transient foetal bradycardia.	Avoid
Verapamil	C	Rapid injection may cause maternal hypotension and foetal distress.	Safe

Table 1.   Anti-arrhythmic drug safety in pregnancy and breastfeeding (3,7,8,11,12).
*FDA Food and Drug Administration. Categories: A) No demonstrated risk to foetus based on well-controlled human studies; B) No demonstrated risk to the foetus based on animal studies; C) Adverse effects demonstrated on animal studies, no well-controlled human studies, but potential benefits may warrant use of the drug in pregnant women despite potential risks; D) Demonstrated fetal risk, potential benefits may warrant use of the drug; X) Contraindicated in pregnancy - demonstrated high risk for human foetal abnormalities outweighing potential benefit

REFERENCES

1. Knight M, Bunch K, Tuffnell D, et al (Eds.) on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2014-16. Oxford: National Perinatal Epidemiology Unit, University of Oxford 2018.
2. Gómez Flores JR and Márquez MF. Arritmias en el embarazo ¿Cómo y cuándo tratar? Arch Cardiol Mex 2007; 77 (S2): 24-31.
3. Adamson DL and Nelson-Piercy C. Managing Palpitations and arrhythmias during pregnancy. Heart. 2007 Dec; 93(12): 1630–1636. doi: [10.1136/hrt.2006.098822]
4. McAnulty JH. Arrhythmias in pregnancy. Cardiol Clin. 2012 Aug;30(3):425-34. DOI: 10.1016/j.ccl.2012.04.002.
5. Knotts RJ and Garan H. Cardiac arrhythmias in pregnancy. Semin Perinatol. 2014 Aug;38(5):285-8. DOI: 10.1053/j.semperi.2014.04.017.
6. Trappe H-J. Cardiac arrhythmias in the pregnant woman and the foetus. European Cardiology.2008:4(2):67-71. DOI: http://dx.doi.org/10.15420/ecr.2008.4.2.67
7. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al. 2018 ESC Guidelines on the management of cardiovascular diseases during pregnancy. European Heart Journal. 2018;39: 3165–3241. DOI: 10.1093/eurheartj/ehy340
8. Hayes C. A Review of Arrhythmias in Pregnancy. BHRS Editorials. September 2013 [Cited: 2018 Dec 9]. Available from: http://www.bhrs.com/files/files/Editorials/130924-Final-Editorial%2C%20C%20Hayes.pdf
9. Gowda RM, Khan IA, Mehta NJ et al. Cardiac arrhythmias in pregnancy: clinical and therapeutic considerations. Int J Cardiol. 2003; 88(2-3):129-33.
10. Silversides CK, Harris L, Haberer K, et al. Recurrence rates of arrhythmias during pregnancy in women with previous tachyarrhythmia and impact on fetal and neonatal outcomes. Am J Cardiol. 2006;97(8):1206–1212.
11. Joglar JA and Page RL. Treatment of cardiac arrhythmias during pregnancy: safety considerations. Drug Saf. 1999;20(1):85-94.
12. Halpern DG, Weingberg CR, Pinnelas R, et al. Use of Medication for Cardiovascular Disease During Pregnancy: JACC State-of-the-Art Review. J Am Coll Cardiol 2019;73:457-476.
13. Ferrero S, Colombo BM and Ragni N. Maternal arrhythmias during pregnancy. Arch Gynecol Obstet. 2004;269(4):244-53.
14. Soma-Pillay P, Nene Z, Mathivha TM, et al. The effect of warfarin dosage on maternal and fetal outcomes in pregnant women with prosthetic heart valves. Obstet Med. 2011 Mar;4(1):24-7.
15. Solanki G. A review on supine hypotension syndrome. Int J Pharm Res. 2012;2(2):81-82.