A review of arrhythmias in pregnancy

Introduction

Arrhythmias are common in pregnancy occurring both in women with structurally normal and abnormal hearts, with and without pre-existing arrhythmias and those with congenital heart disease[1, 2, 3]. Women with congenital heart disease, structural heart disease and pre-existing arrhythmias are at highest risk[1-3]. They may however present for the first time in pregnancy[2].

Physiology in pregnancy

Heart rate increases by 30 to 50% due to increased adrenergic activity. Preload increases as a result of increased circulating volume[4.] Afterload decreases due to decreased systemic vascular resistance[4]. These factors increase cardiac output. Hormonal changes include increased oestrogen, B-Human chorionic gonadotrophin and adrenergic activity. Autonomic activity mostly sympathetic activity increases.

Arrhythmogenesis

The exact aetiology of arrhythmias in pregnancy is unclear but hormonal, haemodynamic and autonomic changes are postulated to play a part[4]. Increased intravascular volume increases preload stretching cardiac chambers thereby activating stretch activated channels resulting in membrane depolarisation, shortened refractory period, slowed conduction and a mismatch of depolarisation and refractoriness[5]. Increased adrenergic activity and autonomic stimuli are proarrhythmic.

Clinical presentation and evaluation

Women suspected of arrhythmias present most often with palpitations, dizziness, syncope and less often breathlessness or chest pain. Others are detected during evaluation of a murmur. Sudden cardiac death is rare. The investigation of a possible arrhythmia is the same as in the non-pregnant woman. A thorough history and clinical examination is essential. Laboratory investigations including full blood count, coagulation, electrolytes, glucose, thyroid function tests; an electrocardiograph and an echocardiograph (ECG) to detect underlying structural heart disease should be performed. Holter monitoring may be beneficial but has a low yield, whilst stress testing runs the risk of foetal bradycardia.

Electrocardiographic changes

Anatomical and physiological changes in the heart and chest wall produce electrocardiographic changes. The resting heart rate is increased with decreased PR, QRS and QT intervals. The heart is displaced upwards and to the left producing left axis deviation. Stretch of the chambers particularly the left atrium produces cardiac conduction abnormalities. Supraventricular tachycardias and ventricular extrasystoles are common. T wave inversion and Q waves may occur inferiorly[6].

Management

Supraventricular tachycardias

Paroxysmal supraventricular tachycardias (PSVT) are the most common arrhythmias occurring during pregnancy causing 24/100000 hospital admissions[7]. There is conflicting data whether pregnancy increases the risk of first onset of PSVT[2, 8]. Tawan et al's study of 38 women showed 13 (34%) had first onset in pregnancy (RR 5.1; 95%:CI 2.8-9.2). Lee et al study of 207 women showed only 8

(3.8%) of women had initial onset in pregnancy without increased risk.[2,8]. In those with pre-existing PSVT episodes increased in frequency and intensity[2].

Management of the *acute episode* as in the non-pregnant state focuses initially on vagal manouvers with progression to adenosine if unsuccessful. Adenosine has been shown to be safe during the second and third trimesters but unfortunately there is not enough data to evaluate safety during the first trimester.[9] It is recommended that foetal heart monitoring is performed when adenosine is given as although the half life is only 10 seconds this can have significant effects on the foetus. If unsuccessful intravenous beta-blockers can be tried[10]. Beta blockers (especially atenolol) run the risk of intra uterine growth retardation. Verapamil should be avoided due to its long half life and risk of maternal hypotension[10]. If the above are unsuccessful or the patient is unstable then electrical cardioversion is the treatment of choice[10]. It is usually well tolerated by the foetus but it is important to avoid haemodynamic instability.

Chronic prophylatic therapy should be avoided unless necessary to control recurrent and sustained symptomatic arrhythmias. Digoxin is felt to be safe in pregnancy although its efficacy is questionable and of course it should only be considered in those without an anterograde conducting accessory pathway[10]. There is limited data regarding flecainide use[11]. However it has been successfully used to treat foetal SVTs[12]. Developmental toxicity has been seen in animal studies. Sotalol appears to be safe although foetal bradycardia has been noted[11]. Amiodarone causes intrauterine growth retardation, premature birth and thyroid abnormalities and should not be used except in emergencies[13].

Radiofrequency ablation is the treatment of choice for recurrent symptomatic episodes resistant to drug therapy[10]. This should be performed in the second or third trimester if possible. Fluoroscopy exposure to the foetus should be minimised. This can be done conventionally by abdominal shielding or pulsed fluoroscopy. More recently magnetic navigation systems have become available and their use is advocated if available to minimise and occasionally eliminate screening[14]. In view of the risks during pregnancy women with frequent episodes of symptomatic SVT who are planning a family should be advised to be ablated 1st[10].

Atrial tachycardias

Atrial tachycardia is rare during pregnancy. It is normally not associated with structural heart disease, is usually well tolerated by mother and foetus, refractory to treatment and usually reverts following delivery. Unless unstable treatment should be aimed at rate control using digoxin, beta-blockers and calcium channel blockers[10].

Atrial fibrillation/flutter

These conditions are rare in pregnancy and their occurrence should prompt a search for structural heart disease. The incidence is about 2 in 100, 000[2]. Electrical cardioversion is preferred to chemical to minimise foetal risks[10]. Whilst there is a theoretical risk of foetal arrhythmia it is extremely low due to the minimal electrical energy delivered to the foetus and high foetal fibrillation thresholds. Nevertheless foetal monitoring should be performed during cardioversion. Electrical cardioversion should be performed if unstable or within the first 48 hours to avoid the need for anticoagulation. Outside of the above indications rate control should be employed if possible using digoxin, a beta-blocker or calcium channel blocker used in combination if necessary[10].

Warfarin should be avoided in the first trimester due to its teratogenicity and in late pregnancy due to delivery related bleeding risk. Heparin is preferred during these periods and in the United Kingdom low molecular weight heparin is routinely used[15]. Anticoagulant requirement should be assessed as in non-pregnant individuals using the CHA_2DS_2VASc criteria[10, 15]. There is not enough data on newer oral anticoagulants dabigatran, rivaroxaban and apixaban in pregnancy.

Ventricular Arrhythmias

Premature beats become more common during pregnancy. Ventricular tachycardia (VT) and ventricular fibrillation (VF) however is rare[16]. Monomorphic VT is usually associated with a normal heart and then, usually of right ventricular outflow tract morphology marked by an ECG pattern of left bundle branch block with an inferior axis. It runs a benign course, almost never accelerates to an unstable rhythm and is best managed with beta-blockers. Normal heart left ventricular tachycardia is much rarer, remains benign and responds well to beta-blockers[16].It remains important to rule out structural heart disease and long QT syndrome as the presence of these significantly changes the management and prognosis. As a minimum, patients presenting with VT during pregnancy should have an echocardiograph and ECG.

Ventricular tachycardia may be related to longstanding structural heart disease either known or newly diagnosed or may be the first presentation of a peripartum cardiomyopathy or myocardial infarction. When myocardial infarction occurs in pregnancy it is usually caused by either coronary spasm or dissection[17].Management should be of the specific causative condition as in the non-pregnant woman. Most anti-arrhythmics can be used if required although because of its toxic effects on the foetus amiodarone should be avoided if possible[18]. If an implantable defibrillator becomes necessary it should be implanted using an abdominal shield and/or ultrasound guidance to minimise radiation exposure to the foetus[18]. Pregnancy can be safely continued with an ICD in-situ although it should be switched off during caesarean delivery due to the risk of electrocautery associated discharge.

Specific conditions

Long QT syndrome

In patients with long QT syndrome the typical arrhythmia is polymorphic VT. Events are less common during pregnancy due to the relatively increased heart rate. However they cluster in the post-partum period and patients should remain on their prophylatic beta-blockers throughout pregnancy and especially post-partum[19]. Management of polymorphic VT is with correction of electrolyte abnormalities, withdrawal of offending drugs and cardioversion if necessary.

Hypertrophic Cardiomyopathy

Most women with this condition tolerate pregnancy reasonably well and mortality is low. Episodes of non-sustained VT may increase. Nevertheless although there are reports of fatal VTs most women can be steered through the pregnancy without the use of anti-arrhythmics[20].

Brady-arrhythmias

These occur rarely during pregnancy and are usually well tolerated. Pacing indications are the same as in the non-pregnant. If a pacemaker is required radiation shield and/or echocardiographic guidance should be used to minimise foetal radiation.

Anti-arrhythmic drugs during pregnancy

No anti-arrhythmic drug has undergone controlled trials for safety in pregnant women and data is based mainly on small case report series. The potential risk must therefore be taken into account when treating arrhythmia. However it is important to avoid situations leading to hemodynamic instability and posing a significant risk to mother and foetus. Risk from anti-arrhythmics is likely to be greatest in the first trimester. A pragmatic approach should be taken noting that most reports indicate safety and only a few anti-arrhythmics have been shown to be harmful during pregnancy.

The FDA classifies drug risk during pregnancy based on available data (Table 1). No anti- arrhythmic is classified A due to the lack of available trials on the other hand none is absolutely contraindicated. Most are class as C, lignocaine and sotalol are classified as B and only amiodarone and atenolol are classified as D.

Table 1: FDA Class description

FDA Class	**Description**
Class A	controlled studies show no risk
Class B	Animal reproduction studies have failed to demonstrate a risk to the foetus and there are no adequate and well-controlled studies in pregnant women.
Class C	studies in pregnant women are lacking, and animal studies are positive for fetal risk, or lacking
Class D	positive evidence of risk can be used if potential benefit outweighs risk
Class X	contraindicated do not use, regardless of potential benefit

Adenosine – First line therapy and commonly used without reports of serious side effects. There has only ever been 1 report of foetal bradycardia following maternal administration.

Digoxin – Crosses the placenta and there are reports of low birth weight and premature labour. Some reports however indicate safety.

Class I a - There have been reports of 8th nerve toxicity and thrombocytopenia with quinidine however it has a long record of use in pregnancy. Disopyimide has been reported to cause uterine contractions and has been less commonly used to due to fears of premature birth. Procainamide has no reported side effects but has not been commonly used.

Class I b – Lignocaine has been widely used and has a favourable safety profile, CNS depression occurs at toxic levels but does not appear to be exacerbated in the fetus. Mexilitine has much more limited data, neonatal hypoglycaemia and low birth rates have been reported.

Class Ic – Flecainide and Propafanone both cross the placenta. Flecainide administration to the mother has been used to treat foetal SVT but use of both these agents has been limited due to fears of inducing foetal arrhythmias. However no adverse effects have been reported.

Class II – Beta-blockers have been widely used and should be continued in long QT syndrome to avoid the risk of ventricular arrhythmias. Reports of intrauterine growth retardation appear confined to atenolol and propanolol which should not be used.

Class III- Amiodarone can cause congenital defects, growth retardation and hypothyroidism and should be avoided. Sotalol has no known side effects.

Class IV - Verapamil and diltiazem can both cause hypotension. Heart block has been recorded but there is sparse data.

Table 2: Anti-arrhythmic drugs

Vaughn William Cl	Drug	FDA class	Benefit	Risk	Breast Feeding
	Adenosine	C	Used as first line to treat SVTs Short half life	No evidence of increased risk of teratogenesis or adverse foetal effects	No data Safe due to short half life
	Digoxin	C	Extensive use, good safety profile	In toxic dosages may cause preterm labour and foetal death	Safe
1A	Quinidine	C	Good safety profile in pregnancy; however, not used because of concern over safety profile in non-pregnant women	Mild uterine contractions, preterm labour, neonatal thrombocytopenia, foetal 8th nerve damage	Safe
1A	Procainamide	C	No data available	lupus-like syndrome, gastrointestinal disturbance, hypotension, agranulocytosis	Safe
1A	Disopyramide	C	Too little data to recommend regular use	Premature uterine contractions	Unknown
1B	Lidocaine	B	Animal studies no adverse effects	In toxic doses CNS depression and, foetal distress	Safe
1B	Mexilitene	C	No data	Limited data available	
1C	Flecanide	C	Limited literature for treatment of maternal arrhythmias; however, maternal ingestion used to treat fetal SVT	Insufficient data but no reported significant complications. Concerns over its pro-arrhythmic potential in fetus have limited its use in past	Unknown
1C	Propafenone	C	Unknown	Insufficient data	Unknown
II	Atenolol	D	No reason to use over other beta blockers	Preterm labour, IUGR, foetal brady cardia	Avoid
II	Metoprolol	C	Animal studies show adverse effects	IUGR possibly	Caution
II	Propanolol	C	Animal studies show adverse effects	IUGR	Caution
III	Sotalol	B	Safe	Transient fetal bradycardia	Safe
III	Amiodarone	D	Only for short term use in emergencies	foetal hypothyroidism, hyperthyroidism, goitre, IUGR, prematurity	Avoid
III	Ibutilide	C	No data	Embryocidal and teratogenic in rats	Contraindicated
IV	Verapamil	C	Safe	Skeletal abnormalities, IUGR, foetal death	Safe
IV	Diltiazem	C	Safe	Limited data available	Unknown

Conclusion

Arrhythmias are common in pregnancy and most often benign. Pregnancy through hormonal, haemodynamic and autonomic changes increases arrhythmogenesis. Heart rate increases and ectopics are common. Patients may present most often with palpitations, pre-syncope, syncope, dizziness and less often chest pain or breathlessness. Sudden cardiac death is almost unheard of. Paroxysmal supraventricular tachycardias are the most common. Treatment of the acute episode involves AV nodal blocking manoeuvres. Adenosine can be safely used. Digoxin and beta-blockers may be used if needed. If the patient is unstable direct current cardioversion is necessary. Atrial fibrillation/flutter is less encountered and usually associated with structural heart disease. Rhythm control is preferable to rate control. The threshold for anticoagulation is lower due to the prothrombotic state of pregnancy. Low molecular weight heparin may be used. Warfarin is best avoided in the first trimester and before labour. Women with pre-existing arrhythmias should be considered for ablation.

In women with ventricular arrhythmias an underlying structural cause should be sought. ICD is safe in pregnancy and ablation can be performed.

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