Management of Atrial Fibrillation in Pregnancy

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Abstract

Pregnancy is accompanied by a variety of cardiovascular changes in normal women; all of these changes are thought to promote arrhythmogenesis. Atrial fibrillation is unusual during pregnancy and it can represent a benign, self-limited lone atrial fibrillation or can be hemodynamically significant in parturient with or without structural heart disease. Management of atrial fibrillation should be the same as in non-pregnant women, but requires faster intervention, even in patients with a normal heart function, and cautious use of medication to avoid harm to the fetus. We might remember that synchronized electrical cardioversion has been performed safely during all stages of pregnancy.

Introduction

Pregnancy is accompanied by a variety of cardiovascular changes in normal women. At first, the levels of estrogens increase and cause augmented adrenergic receptors sensitivity; also the blood volume and the cardiac output increase; this results in myocardial stretch and an increase in cardiac end diastolic volumes. Moreover the augmented sinus heart rate may cause altered myocardial refractoriness, potentially setting up or stabilizing re-entry. All of these changes in pregnant women are thought to promote arrhythmogenesis.\(^1\)

Most pregnant women complain of palpitation, dizziness, and even syncope, but these symptoms are rarely associated with significant cardiac arrhythmias. Shotan et al. demonstrate a high incidence of ectopic activity in normal healthy patients presenting with symptoms, mostly palpitations, during gestation, but usually they are not predictive of cardiac arrhythmia.\(^2\) Whereas atrial fibrillation (AF) is the most common arrhythmia in adults, affecting \(\sim 0.5\%\) to \(1\%\) of the total population and \(> 8\%\) of patients older than 80 years, it is unusual during pregnancy.\(^3\) Szekely et al. in a study on pregnant women with rheumatic heart disease, found that atrial fibrillation was present at the onset of pregnancy in \(8\%\) of women but a new onset atrial fibrillation occurred during pregnancy only in \(2.5\%\) of women.\(^4\) Moreover Khairy et al. in a study of 90 pregnancies of 53 women with congenital heart disease, did not show any AF.\(^5\)

When a healthy woman develops AF during pregnancy, she should be evaluated for congenital heart disease, rheumatic valvular disease, alcohol abuse, electrolyte imbalance and hyperthyroidism.\(^6,7\) It is advisable to consider that in some cases AF may be also a potential adverse effect of terbutaline therapy, a beta-2-sympathomimetic medication used since the 1970s to treat preterm labor. In 1998 the Food and Drug Administration alerted physicians and other health professionals to concerns about subcutaneous administration of terbutaline sulfate via infusion pump for off-label use as treatment and prevention of preterm labor (tocolytic therapy).\(^8,9\)

The AF in pregnancy state can represent a benign,
self-limited lone AF or can be hemodynamically significant in parturient with or without structural heart disease; the reduction in blood pressure occasionally can result in fetal bradycardia and in the need for immediate treatment with antiarrhythmic drugs, electrical cardioversion, or urgent caesarean section; in these cases the cardiologist should manage the patient working with an obstetric specialist.

If there isn’t acute heart failure, the initial management is the ventricular rate control with digoxin, a β-blocker, or a nondihydropyridine calcium channel antagonist to extend diastolic filling time; however, intravenous administration of digitalis glycosides or nondihydropyridine calcium channel antagonists to patients with AF and a preexcitation syndrome may paradoxically accelerate the ventricular response and it is not recommended. About β-blockers the data suggest that cardioselective agents such as metoprolol and atenolol are the preferred agents because they might interfere less with β2-mediated peripheral vasodilation or uterine relaxation and because the incidence of fetal hypoglycemia associated with them is very low. Digoxin has a long history of safe and effective use in pregnant women; it crosses the placenta freely but it is not teratogenic and does not cause adverse effects in the fetus if appropriately dosed; only digitalis toxicity has been associated with miscarriage and fetal death; however we might remind that during the third trimester, serum digoxin levels may appear falsely elevated due to the presence of digoxin-like substances interfering with radioimmunoassay.

Verapamil and diltiazem are indicate only in selected cases and when β-blockers and digoxin are unsuccessful because the use of verapamil during pregnancy has been reported in some cases as the cause of maternal and/or fetal bradycardia, heart block and depression of contractility and there is also a retrospective analysis of 27 newborns exposed during the first trimester to diltiazem that suggests a possible association with congenital malformations at birth. When the patients, after control rate, are hemodynamically stable it could be better to wait 24 h because quite frequently the patients will spontaneously convert to sinus rhythm.

All commonly used antiarrhythmic drugs cross the placenta. The risks of congenital malformations at birth are higher if the exposure to drugs is during the first trimester but even after this period undesirable effects may still occur including depression of uterine blood flow, interference with fetal growth and with labor.

Quinidine has the longest record of safety in pregnant women; even if rarely it may cause mild uterine contractions, premature labor, neonatal thrombocytopenia, and, at toxic doses, damage to the fetal eighth cranial nerve, but it remains the agent of choice, for pharmacological cardioversion in hemodynamically stable patients who develop AF during pregnancy. Also procainamide is safe; however the prolongation of the QT interval to longer than 500 msec during drug therapy with quinidine or procainamide should prompt a critical reevaluation of the risks and benefits of that therapy and consideration of therapeutic alternatives, in concert with a search for underlying predisposing factors such as hypokalemia or drug interactions. Flecainide and propafenone are also used for treatment of atrial fibrillation; no teratogenic effects were reported and none of the case reports of maternal flecainide and propafenone use had shown adverse effects in the fetus, but despite this facts insufficient experience with these drugs is available to assess their safety. Sotalol is generally regarded as safe, but it is known that it prolongs QT duration and also for this drug, there are not yet sufficient clinical experiences and reports regarding its use in pregnancy.

On the other hand amiodarone, when used in pregnancy, is associated with serious adverse effects such as fetal hypothyroidism (9% of newborns of mothers on chronic amiodarone therapy) hyperthyroidism and goitre; given amiodarone’s potential side effects, its use should be avoided during pregnancy unless absolutely needed.
and ajmaline have few case reports and their teratogenic potential in humans is unknown.\textsuperscript{23-24}

When the pregnant woman’s AF cannot be chemically converted, if the patient becomes hemodynamically unstable, but even in stable patients in order to avoid the use of drugs, electrical cardioversion could be performed as it seems to be safe at all stages of pregnancy. In some case reports the cardioversion has been also repeated more times in pregnant women with good results, for the mother and the fetus. However during and immediately after maternal cardioversion, fetal monitoring is recommended because transient fetal dysrhythmia has been reported. Nevertheless significant effects on the fetus would not be expected because the mammalian fetus has been shown to have a high fibrillation threshold and the current density reaching the uterus is usually very small. Electrical cardioversion can be performed under sedation with propofol, which is chosen for its rapid onset, short duration and safety in pregnancy. Cardioversion might even be performed initially without the use of antiarrhythmic drugs, thereby avoiding potential side effects. Anti-arrhythmic therapy is reserved for patients with recurrent, hemodynamically significant episodes of atrial fibrillation.\textsuperscript{25-26}

Also in pregnancy protection against thromboembolism is recommended for all patients with AF except those with lone AF and/or low thromboembolic risk (young individuals without clinical or echocardiographic evidence of cardiopulmonary disease, including hypertension); in these cases, the risks of anticoagulation outweigh its benefits. Therapy with anticoagulant or aspirin should be chosen according to the stage of pregnancy.

The safety of aspirin ingestion during the first trimester remains uncertain; data from human studies are contradictory. On the contrary, available evidence suggests that low-dose aspirin during the second and third trimester is safe for the fetus.\textsuperscript{27-28}

The role of anticoagulation to prevent systemic arterial embolism has not been systematically studied in pregnant women with AF and recommendations for their use are based on case series and the opinion of experts; moreover their use is based predominantly on experience in patients with prosthetic heart valves or venous thromboembolism.

Warfarin, the preferred agent for long-term anticoagulation outside pregnancy, is teratogenic and is associated with a 15% to 56% reported risk of miscarriage and, depending on the case series, has up to a 30% risk of congenital anomalies; moreover it should be contraindicated during the first trimester of pregnancy;\textsuperscript{29} less commonly, it causes central nervous system abnormalities and fetal bleeding with exposure after the first trimester. However in CARPREG study 6 pregnancies in which the mother received warfarin during all or part of pregnancy embryoopathy was not observed.\textsuperscript{30}

The preferred agents for anticoagulation in pregnancy are heparin compounds. Neither unfractionated heparin (UFH) nor low-molecular-weight heparin (LMWH) crosses the placenta and both are considered safe in pregnancy. Furthermore, LMWH has a better safety profile, with fewer side effects such as thrombocytopenia, bleeding and osteoporosis.

In pregnancy, a higher dose of anticoagulant and more frequent administration of UFH or LMWH are required to maintain therapeutic level because of the increase in plasma volume, glomerular filtration rate and placenta degradation heparinase; additionally, there is an increase in protein binding of heparin. For full-dose anticoagulation, LMWH should be given subcutaneously in a dose of 100 anti-Xa U/kg twice daily and the dose adjusted to maintain the anti-Xa level between 0.5 and 1.0 U/mL 4 to 6 hours after injection, UFH is adjusted to target midinterval aPTT in therapeutic range (1.5–2.5), and the dose of warfarin is adjusted to therapeutic INR of 2–3. UFH or LMWH should be discontinued 12 hours before planned induction of labor. Heparin or LMWH should be started postpartum and overlapped with warfarin for 4 to 5 days.\textsuperscript{31-36} To minimize bleeding complications, resumption of anticoagulation should be postponed until 12 hours after vaginal delivery, 2 to 12 hours after epidural removal, or 24 hours after cesarean delivery.

In conclusion, AF is a rare occurrence during pregnancy. In women with permanent AF and heart disease consultations regarding the potential risk should be available prior to pregnancy.
Management of AF should be the same as in non-pregnant women, but requires faster intervention, even in patients with a normal heart function, and cautious use of medication to avoid harm to the fetus. Because no drug is absolutely safe, pharmacologic therapy is best avoided during pregnancy or used only when necessary. We might remember that synchronized electrical cardioversion has been performed safely during all stages of pregnancy for tachyarrhythmias unresponsive to drug therapy and associated with hemodynamic decompensation but it could be the first treatment for AF and it could avoid the drugs use.

References


