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Review Article

Cardiovascular diseases in pregnancy

Dimitrios Godosis, Spyridon Komaitis, Konstantinos Tziomalos, Maria Baltatzi, Georgios Ntaios, Christos G Savopoulos, Apostolos I Hatzitolios

1st Medical Propedeutic Department, Medical School, Aristotles University of Thessaloniki, AHEPA Hospital, Thessaloniki, Greece

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Abstract: Gestation is a period of significant physiological changes that can severely affect the function of many systems, including the cardiovascular. The deviation from the standard that occurs during pregnancy may cause the deterioration of pre-existent cardiovascular diseases or the appearance of new ones. In this review we will present the most common congenital and acquired cardiovascular diseases, their clinical expression and therapeutic procedures according to the latest international guidelines.

Keywords: Gestation, pregnancy, cardiovascular, heart disease, hypertension, stroke, arrhythmias

Introduction

The cardiovascular system is the most severely affected by the physiological changes of gestation. These changes may be the underlying cause of serious cardiovascular events and consequently women with pre-existent history of cardiovascular disease or women appearing new symptoms during pregnancy must be thoroughly screened and treated. The most common cardiovascular diseases faced by the internist during gestation include hypertensive disorders, acquired and congenital heart diseases, arrhythmias and stroke.

Acquired heart diseases

Aortic stenosis during pregnancy is usually of rheumatic etiology and frequently coexists with mitral stenosis [1]. Maternal mortality can be as high as 40% in these patients [1]. The method of delivery and the type of anesthesia is individualized according to the severity of symptoms.

Aortic regurgitation is also of rheumatic origin in most cases and is often well tolerated during pregnancy. Bed rest and sodium restriction is recommended but some patients might require diuretics, inotropic agents or even aortic valve replacement [2, 3].

Mitral stenosis is symptomatic in most pregnant women and symptoms include tachycardia, tachypnea and dyspnea which might manifest as paroxysmal nocturnal dyspnea or even as orthopnea [1]. Asymptomatic patients may continue their normal lifestyle and no medical intervention is required. Symptomatic patients, particularly those with dyspnea, have to reduce their activities and bed rest is sometimes recommended. Beta blockers are the first-line pharmacologic agents for severe maternal tachycardia.

Mitral regurgitation develops in 7% of patients with a history of rheumatic cardiac disease. Pregnancy is well tolerated in these patients and mitral regurgitation may improve due to the reduction in systemic vascular resistance that occurs during pregnancy.

Coronary heart disease (CHD) is rare in pregnant women. However, pregnancy is an independent risk factor for myocardial infarction (MI). Moreover, the prevalence of CHD in pregnancy is also increasing due to the more frequent presence of CHD risk factors in women (e.g. obesity and smoking) and because older women can nowadays become pregnant. The prompt diagnosis and management of MI can reduce maternal and fetal morbidity and mortality. However, MI symptoms, such as angina, are

frequently attributed to the hemodynamic changes of pregnancy. Therefore, a high index of suspicion is required. Myocardial enzymes should be measured and an electrocardiogram should be performed in all pregnant women with symptoms suggestive of MI. Percutaneous coronary intervention (PCI) before delivery is the most effective way of management of MI. If PCI is not available, thrombolysis should be considered as a second-line choice.

Cyanotic congenital heart diseases

Tetralogy of Fallot (ToF) is the commonest cyanotic congenital heart disease. Most patients undergo surgical treatment during infancy or childhood. In a study in 40 pregnancies in 27 patients with surgically corrected ToF, there were no maternal deaths, one woman required thiazide diuretics for shortness of breath and one infant was born with pulmonary atresia [4]. Moreover, women with ToF will produce pulmonary regurgitation and can become symptomatic during pregnancy thus needing either diuretic treatment or admission for bed rest [5]. They are also at risk of producing arrhythmias, endocarditis or right ventricular failure. In terms of the last one, therapists should consider preterm delivery, while antibiotic prophylaxis in case of endocarditis is totally necessary [6].

Ebstein's anomaly represents 1% of all congenital heart diseases and is characterized by the displacement of the tricuspid valve, enlarged right atrium, regurgitant tricuspid valve and small right ventricle. In pregnancies combined with Ebstein's anomaly, no maternal deaths were reported and the live birth rate was 79% [7, 8].

Eisenmenger's syndrome refers to elevated pulmonary vascular resistance and pulmonary artery pressure resulting from a congenital left-to-right intracardiac shunt. Eventually, the intracardiac shunt becomes right-to-left or bidirectional. Many aspects of the intrapartum care of patients with Eisenmenger's syndrome remain controversial. Regional anaesthesia [9, 10] and invasive hemodynamic monitoring [11-13] are recommended. In some case reports, aggressive therapy with inhaled nitric oxide, epoprostenol, sildenafil, and L-arginine were successful [14-17]. In general, patients with Eisenmenger's syndrome should be advised against becoming pregnant because of the high mortality risk [18]. In addition, contraception should be recommended to all patients of child-bearing potential. If pregnancy occurs, therapeutic termination should also be offered.

Primary pulmonary hypertension is rare and the maternal mortality ranges from 30 to 56% [19, 20]. Neonatal morbidity and mortality are also high [19]. Accordingly, patients with primary pulmonary hypertension should be advised against becoming pregnant. If pregnancy occurs, it should be managed as in patients with Eisenmenger's syndrome.

Acyanotic congenital heart diseases [1, 21]

Patent ductus arteriosus (PDA) is corrected in most patients during infancy or childhood. However, some patients with uncorrected PDA may become pregnant. In general, patients with corrected PDA tolerate a pregnancy well. In some unoperated patients with a large left-to-right shunt, secondary pulmonary hypertension may develop and is associated with high morbidity and mortality rates.

Atrial septal defect is generally well-tolerated in pregnant women and does not require any treatment. However, some patients may develop secondary pulmonary hypertension, which results in reverse flow in the shunt, cyanosis and, if pregnancy occurs, increased morbidity and mortality.

Many ventricular septal defects (VSD) close spontaneously and those that don't are usually operated on before adulthood. In patients with large VSD, congestive heart failure, pulmonary hypertension or arrhythmias may develop. Most women with corrected VSD tolerate pregnancy well.

Coarctation of the aorta (CoA) is usually diagnosed early and is corrected surgically. Pregnancy is well tolerated in patients with corrected CoA. However, patients with extracardiac (e.g. aortic, intervertebral and circle of Willis aneurysms) or cardiac manifestations (e.g. septal defects or a bicuspid aortic valve) are at increased risk for complications during pregnancy. In pregnant women with uncorrected CoA, aortic dissection or rupture can occur and are associated with high morbidity and mortality rates [22, 23].

Because cardiac output increases during pregnancy, patients with severe aortic stenosis (AS)

may develop symptoms such as angina, syncope, or even MI and sudden death. Therefore, limitation of activity is recommended. In patients with mild or moderate AS, pregnancy is well-tolerated. However, these patients are at high risk of presenting hypovolemia during delivery. Caesarean section is recommended only when obstetrical indications are present.

Mild to moderate pulmonic stenosis (PS) (i.e. transvalvular gradient < 80 mmHg) is well tolerated during pregnancy. Percutaneous or surgical correction before pregnancy is recommended in patients with severe PS.

The aortic dilatation in patients with Marfan syndrome may worsen near term or postnatally and increases the risk for aortic dissection or rupture. Aortic or mitral regurgitation is also commonly present in these patients, further complicating pregnancy. Therefore, pregnancy is contraindicated in patients with Marfan syndrome. These women should be informed about the form of inheritance of the syndrome (autosomal dominant) and their offspring should be evaluated for the presence of Marfan syndrome.

In conclusion, most pregnant women with congenital heart disease can be reassured that pregnancy is safe. In complex heart diseases, close monitoring by both obstetricians and cardiologists is required.

Arrhythmias in pregnancy

More than half of women experience different kinds of arrhythmias during pregnancy, such as ectopy and supraventricular tachycardias [21]. The hormonal and hemodynamic changes as well as the increased activity of the sympathetic nervous system during pregnancy increase the risk for arrhythmias. Pregnant women with palpitations should be thoroughly examined, a 24h-recording of Electrocardiograph (ECG) should be obtained and the presence of underlying systemic disorders should be excluded. Drug treatment should be administered only to patients with severe symptoms. Of the class IA agents, quinidine is generally well tolerated. Procainamide should be a first line option for acute treatment of undiagnosed wide complex tachycardia. All IA agents should be administered in the hospital under cardiac monitoring due to the potential risk of ventricular arrhythmias. Lidocaine, an IB agent, has local anaesthetic role but is also generally well tolerated as an antiarrhythmic agent. Phenytoin has a high risk of congenital malformations. In terms of IC agents, flecainide is effective in treating fetal supraventricular tachycardia complicated by hydrops. Beta-Blockers can be used with relative safety in pregnancy. However, recent data suggest that they may cause intrauterine growth retardation if administered during the first trimester. From the class II agents, amiodarone causes congenital abnormalities; it should used only to treat life-threatening arrhythmias that fail to respond to other therapies. Adenosine is generally safe to use in pregnancy, and is of first choice for treating maternal supraventricular tachycardia. Digoxin is one of the safest antiarrhythmics to use during pregnancy [24]. When necessary, electrical cardioversion can be safely performed during pregnancy [25].

Hypertensive disorders in pregnancy

Hypertension in pregnancy is classified into chronic, gestational, pre-existing hypertension plus superimposed gestational hypertension with proteinuria, antenatally unclassified hypertension and preeclampsia [26, 27].

According to current guidelines pregnant women with systolic blood pressure (SBP) 140-149 mmHg or diastolic blood pressure (DBP) 90-95 mmHg should be offered non-pharmacological management, including close supervision and restriction of activities. In women with gestational hypertension (with or without proteinuria), drug therapy is indicated when BP is ≥ 140/90 mmHg. In pregnant women with preexisting hypertension without organ damage, the threshold for drug therapy may be 150/95 mmHg. SBP ≥ 160-170 mmHg or DBP ≥ 110mmHg in pregnant women are considered an emergency and require hospitalization [28-31].

The choice of the antihypertensive agent depends on the severity of hypertension. A-methyldopa is the agent of choice in patients with non-severe hypertension; side-effects include drowsiness, dry mouth and depression [30, 32, 33]. Selective beta blockers (e.g. atenolol or metoprolol) and calcium channels blockers (e.g. nifedipine sustained release or nitrendipine) are second-line agents [34]. Beta blockers should be used only during the third

trimester in order to avoid fetal growth restriction, except in patients where BP is not well controlled with a-methyldopa or hydralazine monotherapy. Hydralazine is administered per os in chronic hypertension and i.v. in acute hypertensive crisis [35]. However, it may cause several side effects including palpitations, headache and dizziness. In these cases, co-administration of a-methyldopa or beta blockers is recommended [36]. Sodium nitroprusside is useful in hypertensive crisis. However, prolonged administration should be avoided because it may result in fetal cyanide poisoning. Magnesium sulfate is the agent of choice for the treatment of preeclampsia and prevention of eclamptic convulsions. It also exerts neuroprotective properties to the fetus, although toxic fetal effects have been reported when it is given in high doses. Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers are strictly prohibited during pregnancy because they have been associated with serious fetal side effects. During the peripartum period, a-methyldopa, metoprolol, labetalol and ACE-inhibitors are safe, although the latter may impair the renal function of the newborn.

In terms of use of aspirin during pregnancy, it is suggested that low-dose aspirin can reduce the risk of recurrent pre-eclampsia by about 15% [37]. On the other hand, according to a meta-analysis by Ruano et al, it is considered that "low-dose aspirin is mildly beneficial in terms of reducing the incidence of preeclampsia in women at high risk of developing preeclampsia" [38].

When acute thrombotic events occur, pregnant women should be delivered by a specialist team. Therapeutic doses of low molecular weight heparins (LMWH) may be used, while prophylactic doses of LMWH should be used to reduce the risk of recurrent thromboembolic events in pregnancy [37].

Stroke and pregnancy

Stroke can occur during pregnancy, the puerperium, or postpartum. Incidence of pregnancy-related stroke varies between 11 and 26 per 100,000 deliveries, with the greatest risk in the postpartum period and the 3 days around birth [39].

Women with ischemic stroke or transient ischemic attack (TIA) and high-risk for thromboembolic complications should be treated with unfractionated heparin (UFH) or low molecular weight heparin (LMWH) with monitoring of anti-factor Xa. Alternatively the use of UFH or LMWH until week 13 is recommended, followed by warfarin until week 32. After week 32 UFH or LMWH are re-administered until delivery. Women with ischemic stroke or TIA and low-risk for thromboembolic events should be treated with UFH or LMWH till week 12 followed by aspirin until delivery [39].

Conclusion

There are many alterations in hemodynamic parameters during pregnancy, resulting the occurrence of non-prediagnosed diseases, or the deterioration of already diagnosed ones. In both situations, prompt detection and treatment according to the latest international guidelines is required, aiming the reduction of morbidity and mortality to mother and fetus respectively.

Address correspondence to: Dr. Apostolos I Hatzitolios, Aristotle University of Thessaloniki, 1st Medical Propedeutic Department, AHEPA Hospital, Stilponos Kyriakidi 1, PC 54636, Thessaloniki, Greece. Tel: 00302310993480, Fax: 00302310-994918, E-mail: axatzito@med.auth.gr

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