VALVULAR DISEASES IN PREGNANCY

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SUMMARY

Important cardiovascular changes occur during pregnancy, labor and the postpartum period. Blood volume and erythrocyte mass increase, physiological anemia occurs and blood pressure decreases. Cardiac flow rate and stroke volume increase. Although healthy pregnant women can tolerate these changes, pregnant women with cardiac disease may get worse and the changes may cause risk for both the women and their fetuses. A valve disease with a favorable outlook before pregnancy may get worse when pregnancy is superimposed and pregnancy may have to be terminated. In such cases pregnancy plays an important part in selection of the type of treatment. Diagnostic methods and treatment alternatives should be appropriate for individual patients. Health professionals should give priority to maternal health rather than fetal health, mothers should be informed about possible risks and treatment alternatives should be discussed with them. Any treatment given to mothers may affect their fetuses and treatment should be selected accordingly. Mothers with a valve disease should undergo a thorough examination, should be informed about the risks of pregnancy and should be referred to tertiary health care centers before pregnancy and thereby they can give birth without problems. Management of valve diseases in pregnancy involves replacement of contraindicated drugs with safe ones, controlling conditions likely to cause cardiac loading, close follow-up and aggressive treatment of conditions aggravating the disease. Echocardiography should be performed to determine pulmonary pressure and all cardiac hemodynamics including the valves and when there are changes in symptoms, the patients should be evaluated in each trimester. Even if pregnancy is tolerated well, infections, anemia, arrhythmia, pulmonary embolus, pain and anxiety may worsen the condition. In these cases aggressive treatment is required. Physicians should know the maternal cardiovascular physiology well, should be equipped with latest relevant knowledge and should adopt a multidisciplinary approach during follow-up and labor.

Key words: *complication, pregnancy, valvular disease*

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GEBELİKTE KAPAK HASTALIKLARI

ÖZET

Gebelikte, doğum ve doğum sonrası süreçte önemli kardiyovasküler değişiklikler meydana gelmektedir. Kan hacmi ve eritrosit kitlesi artar, fizyolojik bir anemi meydana gelir, kan basıncı azalır. Kardiyak debi ve atım hacmi artar. Sağlıklı bir gebede bu değişiklikler iyi tolere edilirken, kardiyak hastalığı olan gebelerde hastalık ağırlaşabilir , anne ve fetus için risk teşkil edebilir. Gebelik öncesi klinik seyri normal olan bir kapak hastalığı gebeliğin eklenmesi ile birlikte ağırlaşıp gebeliğin sonlandırılması gerekebilir. Bu hastalarda gebeliğin varlığı yapılacak tedaviyi de etkilemektedir. Hastanın tanı ve tedavisinde izlenecek yol kişiye özel belirlenmelidir. Ancak anne sağlığı her zaman fetusunkinin üzerinde tutulmalı, anne doğabilecek riskler açısından bilgilendirilmeli ve tedavi seçeneklerinin kendisi ile tartışılmalıdır. Anneye uygulanacak tedavi fetusu da etkileyebileceği için tedavi seçeneklerinin buna göre düzenlenmesi gerekir. Kapak hastalığı olanlar,

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gebelik öncesi detaylı bir muayene, gebelik riskleri hakkında detaylı bir bilgilendirme ve takip için üçüncü basamak merkezlere yönlendirme ile sağlıklı bir şekilde doğum yapabilirler. Gebelikteki yönetim, kontrendike olan ilaçların güvenli olanlarla değiştirilmesi, yüklenmeye yol açacak durumların kontrol altına alınması, yakın izlem ve kapak hastalığını ağırlaştıran durumların agresif tedavisini içerir. Gebelik öncesi ekokardiyografi ile pulmoner basınçlar ve kapaklar dâhil tüm kardiyak hemodinami belirlenmeli, bu gebeler her trimesterde, semptomlarda değişiklik olduğunda tekrar değerlendirilmelidir. Gebelik iyi tolere edilse bile enfeksiyon, anemi, aritmi, pulmoner emboli, ağrı ve anksiete ile hastalar dekompanse olabilir. Dolayısıyla bu durumlarda agresif tedavi gerekir. Kalp hastalıklı kadınlara en iyi bakımı verebilmek için maternal kardiyovasküler fizyoloji iyi bilinmeli, literatür hakkında güncel bilgilere sahip olunmalı, izlem, eylem ve doğum sırasında multidisipliner bir yaklaşım sergilenmelidir.

Anahtar kelimeler: *gebelik, kapak hastalıkları, komplikasyon*

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INTRODUCTION

Valvular diseases in young women are generally congenital or related to previous endocarditis or rheumatic heart diseases. Maternal and fetal risks have increased in these patients. Results depend on type, severity, functional capacity, left ventricular function and pulmonary pressure of the valvular disease[1,2]. Mothers with a valve disease should undergo a thorough examination, should be informed about the risks of pregnancy and should be referred to tertiary health care centers for the follow-up and thereby they can give birth without problems. Close follow-up should be performed in pregnant women with valvular diseases, contraindicated drugs used before pregnancy should be changed with safe ones, incidents that may cause overload should be kept under control. Aggressive management is needed for the cases that will aggravate the valvular disease.

HEMODYNAMIC CHANGES IN PREGNANCY

Important cardiovascular changes occur during pregnancy, labor and postpartum period. While these are well tolerated in a normal woman, pregnant women with cardiac disease may get worse and they, may pose a risk for the mother and fetus[3].

Growing fetus causes an increase in blood flow up to 19 times in the last trimester[4]. As a result, serious changes occur in maternal hemodynamia. Increase in blood volume starts as early as the 5th week, reaches to maximum in twenty-twenty four weeks and then makes a plateau phase[4]. At the end of the pregnancy, blood volume is 30-50% more than pre-pregnancy. This increase is more in multiple pregnancies. Erythrocyte mass increases 20-30% compared to pre-pregnancy. Disproportion between the increases of blood volume and erythrocyte mass causes physiologic anemia of pregnancy. Both systemic vascular resistance and blood pressure decrease and resting pulse rate increases 10-20 per minute. Cardiac output increases by 30-50%. Increase in blood pressure causes the pre-load to increase and decrease in systemic vascular resistance causes the pre-load to decrease. Cardiac output increases according to these two incidents and the increase in heart rate. Heart rate volume increases in the first two trimesters and decreases in the trimester according to the suppression that uterus performs on vena cava.

Cardiac output and blood pressure increase with uterus contractions during labour. Pain and anxiety increase the blood pressure and heart rate more. In the early puerperal period, low pressured vascular bed disappears with the separation of placenta, suppression on vena cava ceases and blood volume flowing into circulation increases. As a result, pre-load and cardiac output increase. In the patients at risk, pulmonary edema progresses in this period. Hemodynamic changes generally turns back to normal in postpartum 2-6 weeks.

Hemodynamic changes seen in pregnancy may imitate the heart disease. Tiredness, dyspnea and reduced exercise capacity are seen in normal pregnancy. Peripheric edema and jugular venous distension is seen in pregnancy. Midsystolic murmurs may be heard during pregnancy in all the women. In diastolic or continuous murmurs, severe systolic murmurs, in the presence of symptom or abnormal EKG, echocardiography is needed[5]. In healthy pregnant women, changes in the sizes of diastole and systole of the right and left ventricle and slight insufficiencies may be seen[6].

RESULTS OF VALVULAR DISEASES IN PREGNANCY

Although clinically significant maternal heart diseases are less than 1% in pregnancy[7], when they are present, they are associated with poor maternal, fetal and neonatal results[8]. A valvular disease with normal clinic course before pregnancy, may deteriorate with pregnancy and it may be needed to terminate the pregnancy. Presence of pregnancy also affects the treatment to be administered to these patients[9]. The path to follow in the diagnosis and treatment of the patient should be determined individually. But, some specific principles should be observed: 1) Mother's health should always be regarded as above the health of the fetus. 2) It is required to inform the mother about the risks that may arise and treatment options should be discussed with her. 3) Because the treatment performed on the mother may also affect the fetus, treatment options should be arranged according to this.

RISK CLASSIFICATION IN PREGNANCY

Cardiac diseases that are regarded as low risk in pregnancy; atrial septal defect, ventricular septal defect, patent ductus arteriosus, low gradient (<50 mm Hg) asymptomatic aortic stenosis, mitral valve prolapse, mitral insufficiency, slight or mild mitral stenosis and repaired acyanotic heart diseases without cardiac dysfunction.

Mild risk group consists of; big left-to-right shants, coarctation of aorta, Marfan syndrome with normal aortic root, mild or severe mitral stenosis, slight or mild aortic stenosis and severe pulmonary stenosis.

Eisenmenger syndrome, severe pulmonary hypertension, complex cyanotic heart disease (Fallot tetralogy, Ebstein anomaly, truncus arteriosus, transposition of the arteries, tricuspid atresia), Marfan syndrome with aortic valve or root involvement, severe aortic stenosis, aortic or mitral valve disease accompanied by mild or severe left ventricle dysfunction (ejection fraction<40%), myocardial infarction, aortic dissection, pulmonary hypertension and peripartum cardiomyopathy compose the high risk group[10].

Pregnancy should not be recommended in high risk patients. These patients should understand the damage that pregnancy may cause to their health well. In case of pregnancy, each patient should be assessed according to the severity of the illness and symptoms based on the patient's personal state.

EVALUATION

Ideal evaluation of the patient with a clinically significant valvular disease should be started before pregnancy. A whole cardiac evaluation including echocardiography, chest radiograph and electrocardiogram (ECG) should be performed. In ECG, left axis deviation may be seen resulting from the uterus pushing the diaphragm up. All cardiac hemodynamics including pulmonary pressure and valves should be determined with echocardiography.

Pregnant women with valvular disease should be reevaluated each trimester and when there is a change in the symptoms[5]. Even if the pregnancy is well tolerated, infection, anemia, arrhythmia, pulmonary embolus, pain and anxiety may decompensate the patients. Therefore aggressive management is required in these cases.

FOLLOW-UP OF THE PREGNANT WOMEN WITH VALVULAR DISEASE

Exercise is restricted in the pregnant women with valvular disease. Diuretic treatment is performed in the cases in which volume load is required to be reduced. Diuretic and vasodilators reduce the afterload. Preferred vasodilators are calcium canal blockers and nitrates. β-blockers control the increase in heart rate and corrects the symptoms by extending the diastolic filling time[11-13]. In the pregnant women with atrial flutter and fibrillation, procainamide[14]. and quinidine[15,16]. are preferred for the antiarrhythmic treatment. If atrial fibrillation is present, anticoagulant treatment is required to reduce the embolism risk [17,18].

DELIVERY METHOD IN PREGNANT WOMEN WITH VALVULARY DISEASE

Vaginal birth is recommended in patients with mitral stenosis whose mitral valve area is over 1,5 cm^2or aortic stenosis, in the cases with mitral insufficiency and mitral

valve prolapse. Epidural anesthesia should be used in order to provide efficient pain control. Because systemic vascular resistance increases and venous return decreases with the mother's push in the second stage, assisted vaginal birth is preferred in order to shorten this stage. Caesarean is only performed for obstetric indication reasons because blood loss and changes in hemodynamic parameters occur more often in caesarean delivery. In the cases with severe mitral stenosis, it may be required to place a pulmonary artery catheter in order to perform a close hemodynamic monitorization during the delivery[19]. Right after the delivery, pulmonary congestion, edema and atrial arrhythmia may develop. Therefore, it is necessary to continue the hemodynamic monitorization for another 24 hours.

ENDOCARDITIS PROPHYLAXIS

Endocarditis prophylaxis in pregnancy is based on the suggestion given by American Heart Association (AHA) in 1997. These suggestions are being updated currently. Patients with rheumatic heart disease are in the mild risk group regarding bacterial endocarditis. Patients with; mechanical valve or infective endocarditis history, pulmonary shunts formed with surgery, congenital heart malformation (especially with acquired valve dysfunction such as bicuspid aortic valve and rheumatic valve disease), valve repair history, hypertrophic cardiomyopathy and of the patients with mitral valve prolapse, the ones with valve insufficiency related murmur and patients with thickened valves in echocardiography take place in the high risk group. It is recommended that prophylaxis should be given to these patients and mild risk patients of the low socio-economic status[9] (Table I). In the first 30 minutes of the operation, ampicillin 2g IM/IV and gentamicin 1.5 mg/kg (not more than 120 mg) and 6 hours later ampicillin 1 gr IM/IV or amoxicillin 1 gr oral are given to the patients that are at high risk in prophylaxis. Amoxicillin 3 gr oral or ampicillin 2 gr IM/IV is given to the mild risk patients in the first 30 minutes of operation. Vancomycin is recommended for the patients who are allergic to ampicillin and amoxicillin (Table II).

Table I: *Patients whose infective endocarditis prophylaxis is required.*

- Patients with prosthetic heart valve and infective endocarditis.
- Pregnant women who have complex cyanotic heart disease (single ventricle presence, transposition of the the arteries, Fallot tetralogy).
- Patients with pulmonary shunts formed by surgery.
- Patients with congenital heart malformation (especially patients with acquired valve dysfunction such as bicuspid aortic valve and rheumatic valve disease).
- Patients with valve repair history.
- Patients with hypertrophic cardiomyopathy.
- Of the patients with MVP, the ones with valve insufficiency related murmur and patients with thickened valves in echocardiography

According to ACC/AHA 2006 suggestions, if there is no vaginal hysterectomy, vaginal birth, caesarean or the tissues aren't infected, prophylaxis isn't required during urethral catheterization, dilatation and abortion, therapeutic abortus, sterilization operations, IUD insertion and removal.

POOR MATERNAL AND FETAL OUTCOME IN THE PREGNANT WOMEN WITH VALVULAR DISEASES

In a study conducted in Canada with 562 women with congenital or acquired heart disease and 599 pregnancies, poor maternal and fetal outcome were examined[5]. 40% of the women enrolled in this study

Table II: *Endocarditis prophylaxis for genitourinary interventions.*

State	Agent	Regime
High risk patients	Ampicillin+gentamicin	In the first 30 minutes of the operation; Ampicillin 2g IM/IV + gentamicin 1.5 mg/kg (not more than 120 mg) and 6 hours later; Ampicillin 1 gr IM/IV or amoxicillin 1 gr oral
High risk patients allergic to ampicillin	Vancomycin+gentamicin	Vancomycin 1 gr IV in 1-2 hours + gentamicin 1.5 mg/kg (not more than 120 mg) in the first 30 minutes of the operation
Moderate risk patients	Amoxicillin or ampicillin	Amoxicillin 2 gr oral or ampicillin 2 gr IM/IV 1 hour before starting the operation, in the first 30 minutes of operation
Moderate risk patients allergic to ampicillin	Vancomycin	Vancomycin 1 gr IV in 1-2 hours. Finish the procedure in the first 30 minutes of the operation.

had a primary valve disease. Poor maternal outcome (pulmonary edema, bradyarrhythmia requiring treatment and tachyarrhythmia, cardiac arrest and death) were seen in 13% of the completed pregnancies. Poor outcome were found to be associated with reduced left ventricle systolic function (EF<40%), left heart obstruction (aortic stenosis with a valve area of below 1,5 cm^2 or mitral stenosis below 2cm^2), previous cardiac incidences (heart failure, permanent ischemic attack or paralysis), and functional class II[20] and above. These results were determined in 4% of the patients with no risk factor; 27% with one risk factor and 62% with two or more risk factors. It was reported that one of each three women who died carried two or more heart diseases and left heart obstruction are also determinant factors of fetal complications such as premature birth, intrauterine growth restriction, respiratory distress syndrome, intraventricular bleeding and death. Other determinant factors of the poor perinatal outcome are anticoagulant usage in pregnancy, smoking and multiple pregnancy. Fetal mortality is 4% in the patients carrying one or more of these risk factors and 2% in the ones who don't carry risk factors. When similar risk factor carrying patients were examined, fetal results were worse in the ones over the age of 35 and under 20[5].

In a study involving 64 women with valvular disease, bad results such as heart failure and arrhythmia were monitored in the patients with severe mitral or aortic stenosis (valve area<1,5 cm^2). Premature birth, intrauterine growth restriction and low birth weight were more in the babies of women in this group[21].

If maternal heart disease is congenital then there is increased risk also in the fetus regarding congenital heart disease[22].

COMMON VALVULAR DISEASES

1. Mitral stenosis

Rheumatic mitral stenosis is the most frequent valvular disease seen in pregnant women. It may be single or concomitant with aortic and tricuspid disease[21]. Fluid retention and related increased volume load increase the cardiac outcome, left atrium volume and pressure, pulmonary venous filling pressure and dyspnea. It decreases the exercise tolerance. Increase in mother heart rate decreases the diastole filling time and increases the left atrium pressure more. In 25% of these patients, deterioration occurs in their clinical condition during pregnancy. Mortality is less than 1% in the women with minimal symptoms[23]. This rate is about 5% in the women with a severe deterioration in functional capacity. It goes up to 17% in the cases with atrial fibrillation in addition[19]. Due to the increase in heart rate and cardiac output, pulmonary edema manifestation, which may be fetal, might occur especially as the left ventricle filling time decreases. Pulmonary congestion findings become clear between 20 weeks and term mostly.

In a study done among women with mitral stenosis, bad results were found as reduced mitral valve area (<1,5 cm^2) and abnormal functional class before pregnancy[23]. As the maternal functional class deteriorates, fetal mortality increases. When the mother becomes functional class IV, fetal mortality is 30%[25].

Drug treatment in the women with slight or mild cardiac symptoms is aimed at decreasing the volume load and is composed of diuretic treatment, limitation of salt and exercise. Diuretic treatment may decrease the uteroplacental flow so should be used with attention. β-blockers control the increase in heart rate and correct the symptoms by extending the diastolic filling time[15-17]. Cardio-selective β-blockers such as metoprolol and atenolol should be preferred. Increasing left ventricle volume may cause atrial flutter and fibrillation. Development of atrial fibrillation requires urgent treatment involving cardioversion. β-blockers and digoxin are used for the control of rate. If antiarrhythmic treatment is needed, procainamide[14] and quinidine [15,16] are the drugs with most experience. In the patients with mitral stenosis and atrial fibrillation, due to the risk of systemic embolism increase, anticoagulant treatment is required[17,18].

Of the patients with severe mitral stenosis (valve area <1 cm^2) and at functional class III, IV with severe symptoms, the ones who had mitral valvuloplasty or valve surgery before pregnancy tolerate the pregnancy better compared to the ones medically treated[26]. In the patients who attended with severe symptoms in pregnancy, maternal and fetal results of the ones who had percutaneous mitral valvuloplasty in the second trimester are quite good[27]. By avoiding operations in the first trimester, risk of radiation on the fetus can be decreased[28]. Abdomens of the women exposed to radiation should be protected with lead shirt and these

patients should be informed about the possible risks. In order to avoid radiation risk, mitral valvuloplasty may be done under the guidance of transesophageal echocardiography. Open heart surgery can be performed in the patients with severe mitral stenosis in pregnancy. Maternal results are similar to the ones who aren't pregnant but fetal loss is monitored in 10-30% of these cases[29]. Therefore, this method should be the last option.

If the mitral valve is bigger than 1,5 cm^2 and the patient isn't symptomatic, vaginal birth isn't contraindicated. In order to provide efficient pain control, epidural anesthesia should be used. Because systemic vascular resistance increases and venous return decreases with the mother's push in the second stage, assisted vaginal birth is preferred in order to shorten this stage. Caesarean is only performed for obstetric indication reasons because blood loss and changes in hemodynamic parameters occur more frequently in caesarean delivery. In the cases with severe mitral stenosis, it may be required to place a pulmonary artery catheter in order to perform a close hemodynamic monitorization during the labor[30]. Right after the labor, pulmonary congestion, edema and atrial arrhythmia may develop. Therefore, it is necessary to continue the hemodynamic monitorization for another 24 hours.

2. Mitral insufficiency

Mitral insufficiency is generally related with mitral valve prolapse in young women and is well tolerated because the systemic blood pressure decreases during pregnancy[31]. Pregnancy results are perfect in the patients with mitral valve prolapse. Increase in blood volume and cardiac systemic vascular resistance decreases the blood flow running back. So, even severe insufficiencies are well tolerated in pregnancy. Patients have the risk of heart failure development in the third trimester. Diuretics and vasodilators are required to reduce the afterload. Only vasodilators to be used in pregnancy are calcium canal blockers and nitrates because angiotensin receptor blockers are contraindicated with ACE inhibitors and hydralazine can't be used in the first two trimesters.

Surgery should be avoided in pregnancy. Only in the heart failure cases that don't respond to treatment and acute rupture of chordae, surgery may be considered. Repair should be done if possible. But, even if the patient is operated, mitral insufficiency related left ventricle dysfunction generally doesn't recover after the surgery[32].

Even though heart failure is present, vaginal birth isn't contraindicated. Hemodynamic monitoring is only required in severe cases.

3. Mitral valve prolapse

Its frequency in pregnancy has been reported as 1,2%[33]. Among the complications that may develop in pregnancy are; hemodynamic problems related to generally slow-progressing mitral insufficiency that develop on mitral valve prolapse (MVP) floor, additional tissue damage related to infective endocarditis, mechanical complications, septic embolization, arrhythmias, teratogenic effects of antiarrhythmic and vasodilator agents. Risk increase in MVP cases without complications is related with the level of mitral insufficiency. But, close follow-up is required in the cases with advanced MY level and carrying infective endocarditis and severe arrhythmia risk.

Vaginal birth isn't contraindicated. Care should be taken in the cases with an impaired left ventricle function, because pulmonary edema may develop due to the immediate increase in venous return after caesarean[34].

4. Aortic stenosis

It is rarer compared to mitral stenosis. It is generally congenital[35]. Delivery is safe in women with good function capacity. Severeness of the stenosis is evaluated by mean valve area or peak gradient of flow passing through the valve. Because severe aortic stenosis cases can't provide the blood flow increase required for pregnancy, it is recommended that these patients be operated before pregnancy[36]. Mortality can reach up to 17% in these patients. If the patient gets symptomatic before the end of first trimester, termination is recommended. Even after the termination mortality rates are about 40%[9]. In the cases with mild stenosis, there is conservative approach. In rare cases, if heart failure is present, percutaneous balloon aortic valvulotomy may be required. It shouldn't be forgotten that these operations are dangerous for the mother and baby and provide a temporary solution.

Preferred delivery method is normal birth with epidural anesthetics. It is beneficial on the shortening of the second stage.

5. Aortic Insufficiency

Aortic insufficiency in young women is related to artic root enlargement seen in Marfan syndrome, bicuspid aortic valve and previous endocarditis. Pregnancy related reduced systemic vascular resistance decreases the blood flow running back. Isolated aortic insufficiency can be controlled by diuretics and vasodilators[7]. Course of the pregnant women with left ventricle dysfunction or bad functional capacity seem deteriorating. But there is little data to support this. A detailed assessment should be performed in the women with severe aortic insufficiency related to Marfan syndrome in pregnancy. Surgery is performed only to the functional class III - IV patients and if there is no response to the treatment.

6. Pulmonary Stenosis

Pulmonary stenosis may be seen isolated or as a part of congenital anomalies such as Fallot tetralogy. It is well tolerated as long as there is no other anomaly changing the hemodynamics. If required, percutaneous balloon valvulatomy may be performed.

7. Pulmonary Insufficiency

Pulmonary insufficiency is generally seen in patients operated for Fallot tetralogy. Arrhythmia risk is high in these patients. Pulmonary insufficiency is normally tolerated provided that patient is asymptomatic, right ventricle isn't dilated and functions normally. Patients with symptoms, right ventricle enlargement and dysfunction benefit from surgery before pregnancy[37,38]. Symptoms arising in pregnancy respond to diuretic and antiarrhythmic treatment.

8. Tricuspid valve disease

It may be congenital or acquired. The ones with rheumatic origin generally occur with mitral and aortic valve involvement. Isolated tricuspid insufficiency doesn't create a problem. In the presence of other valves' involvement, treatment is performed by assessing the other lesions[9].

PREGNANCY IN WOMAN WITH VALVE PROSTHESIS

Cardiovascular inspection and echocardiography should be performed on the patients with a valve replacement history when they learn that they are pregnant. In this inspection, artificial valve function, sufficiency of the valve repair, ventricle function, states of the other valves and inspection frequency should be determined. Drugs that the patient takes should be reviewed. If there is a slight insufficiency following the valve repair, its effect on the left ventricle function should be determined by performing a echocardiography at specific intervals during pregnancy. Diuretics and vasodilators may be required. Hydralazine should be preferred to ACE inhibitors because of their negative effects on the fetus[39]. If the insufficiency increases, left ventricle function is impaired, patient becomes symptomatic, then mother's benefits should be regarded as above those of the fetus and surgical treatment should be performed. If the development of fetus is enough, caesarean can be performed in the same session with cardiac surgery[40].

Bioprosthesis don't require anticoagulants but they are more labile compared to mechanical prosthesis. In a study in which 232 patients with prosthetic heart valve were examined, it was reported that thromboembolism and 10 year mortality ratios of mechanical valves are higher compared to those of bioprothesis but valve loss and related reoperation and operation related mortality are less in these patients[41]. Pregnancy doesn't seem to affect the loss rate of mechanical prosthesis, homografts and bioprothesis[41-43]. If there is need for valve repair, it should be performed before pregnancy and bioprothesis should be preferred. Because it takes 3 months to recover after bioprothesis, the patient should take warfarin and shouldn't get pregnant. In the patients with prosthesis but also previous emboli, atrial fibrillation and left atrium dilated, heparin should be taken in the first trimester and the last 2 weeks of the pregnancy and warfarin should be taken in the remaining times. If the patients with bioprothesis want pregnancy, they should undergo a clinical and echocardiographic inspection. If heart failure or any impairment is determined in the prosthetic valve, pregnancy should be recommended by no means[44].

In women with valve replacement; despite the anticoagulation, maternal mortality related to valve thrombosis is 1-4%. With the increase in procoagulant factor levels, decrease in anticoagulant factor levels, resistance improvement and decrease in fibrinolysis, tendency to thrombosis increases[45].

There is no consensus regarding anticoagulation in the first trimester. The most efficient preventive drug on thrombosis for the women with prosthetic heart valve is warfarin[36,45]. Warfarin goes through placenta and increases the risks of spontaneous abortus, embryopathy, prematurity and intracranial bleeding related stillbirth. Most frequently it causes bone hypoplasia, chondrodysplasia punctate, cleft palate and lip. Embryopathy risk in the women taking X 5 mg K vitamin antagonist daily is quite little (about 5%). This risk decreases to zero with taking heparin in between the 6th and 12th weeks but thrombosis risk increases. The safest method also for the mother is to use warfarin in the first trimester. Drug concentrations change in pregnancy due to the change in intravascular volume and body weight. Efficiency of anticoagulation should be followed both by warfarin and unfractionated heparin. The target is the same in INR pregnancy, too.

Heparin doesn't go through placenta so doesn't have a risk regarding fetal bleeding and teratogenicity. Side effects are osteoporosis and thrombocytopenia. The most important factor limiting its usage is insufficient anticoagulation and thromboembolism risk. Thrombosis risk related to heparin usage in the first trimester in up to 25%[45]. It is recommended to perform heparinization about 2-3 times of normal aPTT. There is no data for now proving that intravenous heparin usage is superior to subcutaneous. Because intravenous heparin should be applied in hospital it is not useful. But there are people claiming that it should be used in the last 2 weeks of pregnancy. Subcutaneous heparin dose should be started with 17.500-20.000 units in every 12 hours and dose should be set by making an aPTT control 6 hours later. aPTT control should be performed once a week[36,45]. Patients should start heparin treatment in the 36th week and close monitorization should be done by using antifactor Xa activity. The target is 0,55mU/ml. If the antifactor Xa activity can't be performed, dose should be set so that aPTT is 2.

It is difficult to manage unfractionated heparin treatment in pregnancy and it significantly increases the thromboembolism risk. In a study conducted among 976 patients with mechanical heart valve and their 1234 pregnancies, though treatment doses were monitored, it was shown that thrombosis risk significantly increased with unfractionated heparin usage. Warfarin usage was found to be much safer with 3.9% thromboembolism and 1.8% death risk. But fetal loss in the patients who used warfarin was 30%. Major bleeding (especially during pregnancy) was reported in 2,5 % of the patients in this group[46]. There is consensus on warfarin usage in patients with valve prosthesis in the second and third trimester. In order to decrease the intracranial bleeding risk in the baby, it is recommended that intravenous heparin should be started or elective caesarean should be planned in the 36 the gestational week.

Because the low molecular weighted heparin provides a more stable anticoagulation, it is preferred to unfractionated heparin. Its reliability in venous thromboembolism has been proved[47] but it has been used in few patients with mechanical valve. Its thrombocytopenia[48] and osteopenia[49] risks are less compared to unfractionated heparin and it appears to be safe for the fetus as well[50]. It can't be recommended to the patients with mechanical valves currently because there aren't enough studies performed yet[20,51].

If valve thrombosis occurs despite all these precautions, mother's benefits should be regarded as above those of the baby and urgent operation should be planned. If the patient is stable, doesn't take oral anticoagulation when the action starts and if there is no other additional cardiovascular disease such as another valve or left ventricle dysfunction, aortic dilatation, then normal birth can be performed under epidural anesthetics. They benefit from the shortening of the second stage. Hemodynamic monitorization is only recommended in patients with severe valve stenosis or heart failure developed recently. Caesarean helps to avoid the stress of the normal birth. But hemodynamic effects of anesthesia and assisted ventilation and increased thrombosis risk should be taken into consideration. Obstetricians, cardiologists and patient should decide on the delivery method, planned delivery should be performed. In the patients with anticoagulant treatment, heparin should be stopped 4 hours before the caesarean or at the beginning of the birth, and it should be started 12 hours after the vaginal or surgical delivery. Because coagulation system of the fetus isn't mature, the effect of warfarin finishes 7-10 days after it is stopped. If the action starts when the patient is in oral anticoagulation, elective caesarean should be performed when INR is below 2 in order to decrease fetal intracranial bleeding risk. Infective endocarditis prophylaxis should be given to the high risk patients with previous endocarditis and mechanical heart valve.

Patients using heparin and warfarin can breast-feed.

RECOMMENDATIONS

In order to determine left ventricle and valve dysfunction in the patients with valvular disease, echocardiography should be performed before pregnancy. Patient should be informed about the risks if the functional capacity isn't normal or she has left ventricle dysfunction, valve stenosis, heart failure or embolism history. Pregnancy isn't recommended for the patients with more than 1 risk factor. Patient should be seen by a cardiologist every trimester. Patients with artificial valve should be informed about the need and risks of anticoagulation.

Patients with valvular diseases can give a healthy birth with a detailed inspection before pregnancy, detailed informing of the patients with severe valvular disease about the pregnancy risks and redirection to tertiary healthcare services for the follow-up.

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