



PROSTHETIC VALVES

Background

Mechanical Valves

Pregnancy in women with mechanical prosthetic heart valves must be considered high risk for both the mother and the fetus. The hypercoagulable state of pregnancy and the inherent thrombogenicity of a mechanical prosthetic valve exposes the pregnant woman to a high risk for prosthetic valve thrombosis or thromboembolism. Unfortunately, there is no ideal anticoagulant treatment that will fully protect a pregnant woman from such events. Fetal risk varies depending on the type of anticoagulant used during pregnancy [vitamin K antagonist e.g. warfarin, unfractionated heparin (UFH) or low molecular weight heparin (LMWH)].

Tissue Prostheses

Tissue valves (bioprosthetic, homograft, or autograft) may be preferable in women of childbearing age, as these do not usually require anticoagulation during pregnancy. However, a tissue prosthesis has a limited lifespan because of progressive structural degeneration. The issue of accelerated bioprosthetic valve degeneration during pregnancy remains a matter of debate in the literature. Pregnancy is safe if the tissue prosthetic valve function is normal, the left ventricular function is normal and there is no pulmonary hypertension. A tissue valve with significant stenotic degeneration raises similar problems during pregnancy as does a diseased native valve. This section will focus mainly on the issues related to mechanical valve during pregnancy.

Anticoagulant Treatment

1. **Warfarin** can cross the placenta and is associated with an increased risk of fetal wastage (spontaneous abortion, stillbirth), prematurity, bleeding in the fetus, and teratogenicity. The most common fetal anomaly is the characteristic warfarin embryopathy, consisting of nasal hypoplasia and/or stippled epiphyses after in utero exposure during the first trimester of pregnancy (between 6th and 12th weeks). The incidence of warfarin embryopathy is reported to be between 4% and 10%. Central nervous system abnormalities after exposure to warfarin during any trimester of pregnancy have also been described; however they are rare (less than 1%). The risk of clinically important embryopathy seems to be lower in patients whose required therapeutic dose of warfarin is ≤ 5 mg per day. Fetal coagulopathy is an issue if the mother remains on warfarin at the time of delivery as the combination of the anticoagulant effect and delivery trauma increases the risk of bleeding in the neonate. Warfarin is not contraindicated in postpartum mothers who breast feed.
2. **Unfractionated heparin (UFH)** does not cross the placenta, so does not have the potential to cause fetal bleeding or teratogenicity. Heparin can cause thrombocytopenia (although this seems to be rare in pregnancy) or osteoporosis. UFH has a short circulating half time, and activated partial thromboplastin time (APTT) is difficult to achieve. During pregnancy factor VIII and fibrinogen levels increase, which leads to a decrease in APTT. UFH is not an optimal anticoagulant treatment during pregnancy, as subtherapeutic heparinization is quite common and consequently thromboembolic event rate high. If subcutaneous UFH is used, it should be initiated in high doses (17500-20000 U every 12 hours) and adjusted to a 6-hour post-injection aPTT in the therapeutic range; mid-interval aPTT level should be at least twice control or an anti-Xa heparin level of 0.35-0.70 U/ml should be attained (1). UFH is not contraindicated in postpartum mothers who breast feed.

3. **Low molecular weight heparin (LMWH)** is an alternative anticoagulant treatment to warfarin or UFH. LMWH does not cross the placenta, has more predictable bioavailability and has a lower incidence of thrombocytopenia and osteoporosis than UFH. During pregnancy LMWH should be administered 2 times a day (bid), and the dose must be adjusted based on the anti Xa level 4 hours after subcutaneous injection; the recommended anti Xa target level is approximately 1.0 U/ml. LMWH is not contraindicated in postpartum mothers who breast feed.

A pregnant woman with mechanical valve is at high risk for thromboembolism. In addition to the anticoagulant treatment low-dose *Aspirin* (75-100mg) has been recommended (1). Aspirin is considered safe in pregnancy. However, the addition of aspirin imparts an increased risk of bleeding. *Dipyridamole* should not be considered as an alternative antiplatelet agent because of its harmful effects on the fetus.

Effects of Pregnancy-Related Hemodynamic Changes

With the increase in blood volume and heart rate with the progression of pregnancy, prosthetic valves may hemodynamically mimic a stenotic valve (gradient increase) with the consequent risk for adverse cardiac events (example: new onset of atrial tachyarrhythmia or pulmonary edema in the presence of mitral prosthetic valve). (see Cardiovascular Changes During Pregnancy)

Maternal Cardiac Complications

Maternal cardiac complications in women with mechanical heart valves depend on the type of mechanical valve, the function of the valve and the anticoagulation regime used.

Warfarin throughout pregnancy with or without heparin near term. In a large systematic review of pregnancy outcomes in women with mechanical valves, the rate of thromboembolic events in women with mechanical valves using oral anticoagulants throughout pregnancy was 3.9 % and death from all causes was 1.8% (mostly valve thrombosis). (3) Another series of 61 pregnancies reported only 2 minor thromboembolic events during pregnancy. (7) In high risk women, this regimen has been proved be the safest anticoagulation regime for the mother.

UFH 1st trimester/ warfarin 2nd, 3rd trimester, with or without UFH near term. In the review of pregnancy outcomes in women with mechanical valves, the rates of thromboembolic events and death in women with this combined regime were 9.2% and 4.2% respectively (mostly valve thrombosis). (3) All 21 women with thromboembolic events were on heparin (10 women were on low dose heparin). Another series reported on 31 pregnancies in women using dose adjusted subcutaneous heparin (APTT twice the control level at 4 hours after dosing) in the 1st trimester. Four minor transient cerebral events were documented. There were no obstructive valve thrombosis. (7)

UFH throughout pregnancy. In the review of pregnancy outcomes in women with mechanical valves, women treated with UFH throughout pregnancy had overall rates of thromboembolic events and death of 33% and 15% respectively (mostly valve thrombosis). (3) When women were on adjusted dose heparin the thromboembolic event rate decreased to 25% and the death rate decreased to 6.7%. In contrast, when women were on low-dose heparin, the thromboembolic event rate was 60% and death rate was 40%.

LMWH throughout pregnancy. A review of studies of women with mechanical valve treated with LMWH during pregnancy (81 pregnancies) demonstrated rates of valve thrombosis of 8.6% and rates of thromboembolic events of 12.3%. (8) All thromboembolic events occurred in women with mitral mechanical valves. There was a lower event rate when the dose was adjusted to anti Xa level (2%

thromboembolic events), and a much higher event rate when the dose was fixed (30% thromboembolic events).

Fetal Complications

Fetal complications in women with mechanical prosthetic valves can be related to the anticoagulation regime used. Rates of miscarriage in women treated with warfarin throughout pregnancy, UFH throughout pregnancy or with UFH/Warfarin combination are 25%, 24% and 25% respectively. (3)

In the large systematic review of pregnancies in women with mechanical valves, warfarin throughout pregnancy was associated with *embryopathy* in 6.4% of live births; however, when heparin was used between 6 and 12 weeks of pregnancy the risk of embryopathy was minimized. There was a higher risk of fetal embryopathy for women who require more than 5 mg warfarin to have therapeutic anticoagulation and when warfarin is used between 6-12 weeks gestation.

In a review of pregnancies in women with mechanical valves treated with LMWH, the live birth rate was 87.6%. No congenital anomalies were detected. (8)

Management Strategies

Preconception Counseling/Contraceptive Methods

Ideally, a comprehensive cardiovascular examination should be undertaken before embarking on pregnancy. This includes a careful history and physical examination, an echocardiogram and an electrocardiogram. The additional prognostic benefit of cardiopulmonary exercise testing has not been defined, but may be helpful in some cases.

Preconception counseling in women with mechanical heart valves receiving anticoagulant treatment should include a discussion about the potential fetal and maternal risk associated with each of the possible anticoagulant regimes. The following issues should be understood by the mother: fetal risk associated with warfarin (congenital malformation and fetal loss rate) and maternal risk associated with heparin or LMWH, primarily thromboembolic events, and rarely thrombocytopenia or osteoporosis.

When counseling regarding anticoagulant options, consider the following factors associated with higher maternal thromboembolic risk: presence of mitral mechanical valve (highest risk in older style mechanical valve), prosthetic valve dysfunction (higher than normal baseline gradient across the valve), atrial fibrillation/flutter, previous thromboembolic event, left ventricular dysfunction, or elevated pulmonary pressure.

Women on warfarin should be warned that pregnancy tests have to be done as soon as a period is missed in order to avoid progression of pregnancy beyond 6 weeks while on and consequent fetal embryopathy. Switching of the warfarin to LMWH before pregnancy it is not recommended given the higher rate of thromboembolic events with LMWH.

Woman of childbearing age with tissue valves should be counseled about the lower pregnancy related risks; however, such a woman faces increased risk of redo surgery. Redo-surgery is almost inevitable. Mortality risk at the time of redo surgery varies among cardiac centers.

For women with congenital heart disease, transmission of congenital heart disease to offspring should be discussed. The risk of transmission is approximately 5-10% and varies with the maternal cardiac lesion.

A discussion about contraceptive methods is appropriate in all women with prosthetic heart valves. Combined (estrogen and progesterone) oral contraceptive pills can usually be used in women with tissue prostheses; however, caution is recommended in women with mechanical bileaflet valves or previous thromboembolism. In women with older types of mechanical valves (Starr Edwards and Bjork Shiley) estrogen-containing pills should be avoided, because of the higher thrombogenic risk (9). (see Contraception)

Medication use should be reviewed if a woman is contemplating pregnancy or is pregnant. The MOTHERISK website (<http://www.motherisk.org>) is an excellent resource.

Ante-partum Care

Coordinated care between a heart disease specialist, a hematologist, and a high-risk obstetrician at a high-risk pregnancy center should be implemented. The frequency of follow-up visits (clinical and echocardiographic) is dictated by the type of heart valve and the clinical status of the woman at time of conception. There is an expected increase in prosthetic valve gradients by the time of peak cardiac output (28-32 weeks gestation). However, significant or unusual changes in gradient or valve area may indicate valve thrombosis. If there is suspicion of mechanical valve thrombosis, a transesophageal echocardiogram should be performed.

Based on the available guidelines, (1,2) and our centre experience the following scheme of anticoagulation during pregnancy is proposed:

1. Before the 6th week of gestation, switch warfarin to LMWH (2 times a day). Measure anti Xa level frequently to a target of 1.0 U/ ml. We recommend aspirin (81mg) in addition to LMWH.
2. Strategies between the 13th and 36th weeks of gestation depend on the regime chosen:
 - 2.a. Maintain the LMWH with careful follow-up; in patients with higher thromboembolic risk the anti Xa level may be targeted between 1 and 1.2 U/ml.
 - 2.b. Switch back to warfarin; target an INR of approximately 3 (range 2.5- 3.5). In patients with lower thromboembolic risk (bileaflet aortic valve without atrial fibrillation or LV dysfunction) the INR range may be targeted between 2 and 3.
3. At 36 weeks gestation warfarin must be switched back to LMWH.

Women who develop mechanical valve thrombosis are at high risk for death. Changes in the anticoagulation regime, thrombolysis and cardiac surgery have all been used to treat women with valve thrombosis. The approach should be based on the individual case. Cardiac surgery carries a high risk for the fetus (10-11). There is limited data available regarding the use of thrombolytics in pregnancy, although successful cases of treatment of mechanical valve thrombosis with thrombolytics have been reported (12).

Fetal echocardiography can be offered to mothers with congenital heart disease. A fetal echocardiogram is done at approximately 20 weeks gestation.

Labour and Delivery

Labour and delivery should be planned carefully with a multidisciplinary team well in advance. It is important to communicate the delivery plan to the woman and to other physicians involved in her care. The best delivery plan is not useful if information is not readily available when needed.

A planned induction of labour is the safest option in pregnant women on anticoagulation.

Vaginal delivery is recommended in most instances. Good pain management for labour and delivery is very important in order to minimize maternal cardiac stress. To decrease maternal expulsive efforts during the second stage of labour, forceps or vacuum delivery is often utilized. To decrease potential harmful complications from difficult mid cavity-assisted delivery, uterine contractions are often utilized to facilitate the initial descent of the presenting part.

When women go into labour while still on warfarin or have only recently discontinued warfarin, cesarean delivery is necessary in order to avoid bleeding complications in the neonate, who will be secondarily anticoagulated.

The need for maternal monitoring is dictated by the functional status of women. In general, invasive monitoring is not required.

In general, endocarditis prophylaxis at the time of labour and delivery is not recommended. However, some experts continue to administer antibiotics because they feel that the risks of adverse reactions to antibiotics are small and the risk of developing endocarditis has major health consequences.

Post-partum Care

The hemodynamic changes of pregnancy may take up to six months to normalize. Women should be seen early after pregnancy (usually within 6-8 weeks). The frequency of additional follow up visits should be dictated by the clinical status of the women.

References:

1. Bates SM, Greer IA, Pabinger I. et al. Venous Thromboembolism, Thrombophilia, Antithrombotic Therapy, and Pregnancy. American College of Chest Physicians Evidence- Based Clinical Practice Guidelines (8th Edition) Chest 2008; 133:844S–886S
2. Bonow RO, Carabello BA, Chatterjee K et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease. JACC 2006; 48(3):e1-148.
3. Chan WS, Anand S, and Ginsberg JS. Anticoagulation of Pregnant Women With Mechanical Heart Valves A Systematic Review of the Literature Arch Intern Med. 2000;160:191-196
4. Nassar AH, Hobeika EM, Abd Essamad HM et al. Pregnancy outcome in women with prosthetic heart valves. Am. Journal of Obstetrics and Gynecology (2004) 191, 1009 e13
5. Kawamata K, Neki R, Yamanaka K et al. Risks and Pregnancy Outcome in Women With Prosthetic Mechanical Heart Valve Replacement. Circ J 2007; 71: 211 – 213.
6. Elkayam U. and Bitar F. Valvular Heart Disease and Pregnancy. Part II: Prosthetic Valves. JACC 2005, Vol. 46, No. 3, 403–10.
7. Meschengieser SS, Fondevila CG, Santarelli MT, and Lazzari MA. Anticoagulation in pregnant women with mechanical heart valve prostheses. Heart 1999;82:23-6.
8. Oran B, Lee-Parritz A, and Ansell J. Low molecular weight heparin for the prophylaxis of thromboembolism in women with prosthetic mechanical heart valves during pregnancy. Thromb Haemost. 2004;92:747-51.
9. Thorne S, Nelson-Piercy C, MacGregor A et al. Pregnancy and contraception in heart disease and pulmonary arterial hypertension. J Fam Plann Reprod Health Care. 2006. 32 (2): 75-81(7)
10. Weiss BM, von Segesser LK, Alon E et al. Outcome of cardiovascular surgery and pregnancy: a systematic review of the period 1984-1996. Am J Obstet Gynecol 1998;179:1643-53.
11. Arnoni RT, Arnoni AS, Bonini RC et al. Risk factors associated with cardiac surgery during pregnancy. Ann Thorac Surg 2003;76:1605-8.
12. Sahnoun-Trabelsi I, Jimenez M, Choussat A, and Roudaut R. Prosthetic valve thrombosis in pregnancy. A single-center study of 12 cases. Arch Mal Coeur Vaiss 2004;97:305-10