Anticoagulation With Pregnancy In Prosthetic Valves:* A Review Paper

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Summary:

Pregnancy in women with valvular heart diseases having prosthetic cardiac valves and on anticoagulants pose a special problem. These women should be aware of the extra risks of pregnancy to them and of the limited opportunity to give birth to healthy children.

The normal oral anticoagulant measures and control should be maintained until the third trimester of pregnancy, then gradually it should be tapered. During the third trimester, aspirin or subcutaneous heparin could be used. After delivery the standard anticoagulant regimen can be started after two to three days. There will be, perhaps, a higher incidence of spontaneous abortion with woman on anticoagulants. In the case of fertility problems, where it is difficult for the woman to become pregnant, a tissue valve prosthesis should be considered. There are very good published reports which suggest that an open heart operation can be performed in pregnant woman with an acceptable risk for the mother and fetus.

Pregnancy in women with valvular heart diseases having prosthetic cardiac valves and on anticoagulants pose a special problem. These women should be aware of the extra risks of pregnancy to them and of the limited opportunity to give birth to healthy children. It is still difficult to answer these questions definitely. The pregnancy and deliveries do occur uneventfully however there are cases of atrial fibrillation, pulmonary edema, bleeding, heart failure, thromboembolism, maternal deaths and more often fetal loss.

The functional results of valve replacement are not uniform. In most patients with aortic valve prosthesis myocardial contractility is close to normal, while in patients with mitral and multiple valve prosthesis it is commonly disturbed; the patients of latter two groups often develop atrial fibrillation. Pregnant woman with prosthetic cardiac valves are exposed to increased risk of subacute bacterial endocarditis, bleeding tendencies and thromboembolic complications; there is also a threat of an adverse effect of anticoagulant therapy on the fetus. In addition, there is irrespective of pregnancy, the risk of suture incompetence and prosthetic destruction.

Clinical manifestation of endocarditis caused by infectious lesions of any valve prosthesis are the same as in natural valve lesions but outcome is worse. With normal functioning of ball prosthesis metallic sounds that are not accompanied by any murmurs are auscultated. Fever combined with appearance of murmurs mediated by paravalvular leaks, is indicative of endocarditis development. The murmur sometimes is heard sometimes after the onset of fever. The risk of endocarditis is particularly high in the intra and postpartal periods, when transitory bacteremia is not uncommon. Endocarditis entails a number of complications. Bacterial colony growth on the valves can increase valvular obstruction, leading to haemodynamic disturbances up to a gradual onset of heart failure. There is also hazard of embolism with the colonies of microorganisms. The development of an abcess in the valvular ring area can entail prosthesis rejection. Adequate antiseptic and aseptic measures and

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preventive treatment make it possible, as a rule to avoid the risk of subacute bacterial endocarditis.

There is increase risk of thromboembolism with pregnancy. It ranges usually between 5% — 20% and in pregnancy 17.9%. Anticoagulant therapy protects the pregnant woman from thrombo embolic complications, but on the other hand, indirect-acting anticoagulants (coumarin and indendione preparations) cross the placental barrier and pose double risk for the fetus. Fetal loss in the mothers who received coumarin derivatives before conception and in the first trimester of pregnancy significantly increases as compared with the fetal losses in women with prosthetic cardiac valves who did not receive such therapy because of hemorrhagic complications in the fetus and intraplacental hemorrhages. The use of indirect anticoagulants throughout pregnancy until term is threatened with the development of fetal hemorrhagic complications during vaginal delivery. By term, blood coagulation in fetus is normalized and perinatal hemorrhages don't develop if indirect-acting anticoagulants are discontinued a few days before labor. Heparin doesn't cross the placental barrier and therefore it is quite safe for the fetus; however its constant parenteral administration is rather burdensome. Thus heparin substitution from indirect-acting anticoagulants at least two weeks before terms seems optimal. However this is impossible in case of premature labor.

The second hazardous aspect of coumarin anticoagulant application is the threat of teratogenic effect on the fetus (chondroplasia, nasal hypoplasia, optic nerve atrophy etc.). Indirect-acting indendione anticoagulant (phenindione) seems safe in this respect although the long term administration exposes the mother to the risk of renal and hepatic failure. A certain risk of teratogenic effect of coumarin derivatives cannot be discarded. The experience of Phenindione use in 51 pregnant women proved to be encouraging, neither mother nor children revealing any hemorrhagic complications[1].

Sago Y et al[2] in their series of 30 patients with Starr Edward cardiac valve, 14 patients who were taking warfarin gave rise to three neonatal anomalies and five fetal losses with spontaneous abortions. It is suggested that the best plan is to use long acting oral anticoagulants during antenatal period and heparin over the periods of labor. Larrea J L et al[4] in their series of 38 women with 47 pregnancies showed a high incidence of complications in the mothers and fetuses, 23% had spontaneous abortions and two of the 36 new born had chondroplasia pnunctata, 3 women (7.9% acute valvular thrombosis, one died after replacement of thrombosed valve with mortality of 2.6%. More complications have been observed in fetuses and infants of women treated with oral anticoagulants during pregnancy than treated with heparin. However, the mother had more complications with heparin anticoagulation. Neither heparin nor oral anticoagulants clearly proved superior as the anticoagulant regimen of choice for pregnant women with mechanical valves. Counselling before conception occurs and avoidance of pregnancy are recommended for women with mechanical valve prosthesis because of the high risk of serious fatal complications in the mother and fetus. Use of tissue valves in women of childbearing age who desire to have children also seems advisable, even with the possibility of having to undergo another operation as a result of degeneration of the valve tissue.

The decision on the permissibility of pregnancy in woman with prosthetic cardiac valves in individual in each case: it is always necessary to differentiate between the two extreme points "pregnancy is inadmissible" and "pregnancy is not dangerous". The decision is based on the evaluation of the cardiac function. The result of surgical intervention, and the presence of concomitant disease. The percentage of the complications both in the mother and fetus being high during pregnancy in woman with mechanical prosthetic cardiac valves, it seems preferable to recommend woman who intends to undergo valve replacement first to give birth, (in the absence of contraindications) and then to undergo surgery. After the operation an optimal way of contraception should be selected. Pregnancy in patients with the biological prosthetic cardiac valve seems permissible, because the danger associated with anticoagulants treatment is absent. Bortolotti U et al[3] in their study of seven patients with bioprosthetic valve for eight pregnancies have concluded that bioprosthetic valves

can be considered the most suitable devices employed in women of the childbearing age because the anticoagulants can be avoided. Therefore eliminating the risks related to in appropriate administration of oral anticoagulants as well as the hazards associated with the potential teratogenic effect of coumarin drugs; and pregnancy might favour calcification of porcine hetero grafts, leading to bioprosthetic failure. Close follow up and repeated echocardiography is needed to further evaluate the problem.

In pregnant woman with prosthetic cardiac valves Heparin should be substituted for indirect-acting anticoagulants at very beginning of the gestation period. In the second trimester of pregnancy it is preferable to continue heparin. In the third trimester indirect-acting anticoagulants are possible, but they should again be replaced by heparin two weeks before term.

Iturbe-Alessio I et al[7] conclude that in the second and third trimester of pregnancy, derivatives provide effective protection against thromboembolism while causing few fetopathic effects, but that these agents are contraindicated from the 6th to 12th weeks of gestation. Low dose heparin does not protect against prosthetic valve thrombosis, and possibility that a larger dose might be more effective requires further exploration.

Anticoagulant therapy[8] during pregnancy is problematic because both heparin and oral anticoagulants can potentially produce adverse maternal and fetal effects. Reviewing the relevant literature makes it clear that the heparin is safer for the fetus over oral anticoagulants. For the prophylaxis and treatment of venous thromboembolic disease in pregnant patients, heparin is the preferred anticoagulant because its efficacy and safety is established. However because the efficacy of heparin in preventing systemic embolism in patients with prosthetic heart valve is not established, either adjusted dose of heparin or a combination of heparin and oral anticoagulants can be used. Schivizappa L et al[4] in their study have highlighted the need for maintaining an adequate anticoagulation in pregnant women with mechanical prosthesis. There is a potential risk of teratogenicity in first trimester and fetal hemorrhages in second and third trimester. They had shown that there is lack of effective pharmacological alternatives to coumarin drugs.

Pavankumar P et al[9] in their series of 37 women had 47 pregnancies. Full term delivery of normal infants was achieved in 40 cases. There were 3 premature births, 2 spontaneous abortions, one still birth and one ectopic pregnancy. The fetal mortality was 8.5%, valve thrombosis developed in 2 cases which was treated successfully. Oral anticoagulants were continued throughout pregnancy. Heparin was substituted before labor began, but discontinued after delivery, when effective oral anticoagulants was resumed. Their experience showed that pregnancy in women with mechanical heart valve prosthesis and continued oral intake of anticoagulants is safe and successful in most cases. We are currently following this practice in our unit and we are having satisfactory results. At the moment we are collecting the data in this regard to highlight this very serious problem.

Two successful[10] cases of mitral valve replacement with cardiopulmonary bypass and myocardial protection are reported. Post-operative anticoagulation was obtained with oral anticoagulants. These patients delivered two healthy newborns. The report suggests that an open heart operation can be performed in pregnant women with an acceptable risk for the mother and fetus. The patients with valvular heart disease, who become pregnant should be carefully assessed. If continuation of pregnancy poses extra risks and danger to the life of mother, therapeutic abortion is desirable in first trimester. In latter months especially if pregnancy is essential for different reasons the patient can be operated upon (both for close heart and open heart procedures) with acceptable risks for the mother. There are always increased chances of abortion and fetal abnormalities in such cases and the patients and relatives should be informed of this before surgery is done.

Acknowledgement:

I acknowledge the excellent secretarial help of my secretaries Mrs. Zahida Anwar and Amjad Rehman. My sons Badar, Haris and Suhaib also helped me in typing the manuscript.

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