Anticoagulation in pregnancy with mechanical heart valve prosthesis


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Women with a well-functioning mechanical heart valve (MHV) tolerate pregnancy well. A challenge lies in achieving safe and effective anticoagulation. The hypercoaguable changes in pregnancy begin early and persist for at least 6 to 12 weeks postpartum. In pregnancy, mechanical prostheses pose additional problems because of the risk of thromboembolism and the need for the higher level of anticoagulation, which might lead to maternal bleeding or fetal hemorrhage. Anticoagulation regimens in pregnant women with MHV have not been sufficiently studied, and the current guidelines of the European Society of Cardiology (ESC) are based on weak scientific evidence (level of evidence C). In a large review, the risk of valve thrombosis was 3.9% with vitamin K antagonists (VKAs) throughout pregnancy, 9.2% when unfractionated heparin (UFH) was used in the first trimester and VKAs in the second and third trimesters, and 33% with UFH throughout pregnancy. Maternal death occurred in these groups in 2%, 4%, and 15% of the patients, respectively, and was usually related to valve thrombosis.

The exact percentage of women of reproductive age with MHV is unknown. In the European Registry on Pregnancy and Cardiac Disease (ROPAC) initiated in 2008, among 2966 pregnancies with structural cardiac disease (patients included in the registry up to April 1, 2014), it was found that 32% of the women had valvular heart disease, of which 212 women had MHV, 134 had a tissue heart valve (THV), and the remaining 2620 had no prosthetic valve. In that prospective observational worldwide multicenter registry, van Hagen et al analyzed data by valve type and by emerging or developed country status. Maternal mortality was defined as death during pregnancy and up to 1 week after delivery. In women with MHV, they reported high risk of maternal mortality (1.4%), hemorrhage (23%), and fetal loss (18.4%). Valve thrombosis occurred in 4.7% of the patients, regardless of the position (mitral vs aortic) and was associated with high maternal mortality (20%). A half of the valve thrombosis events occurred during the first trimester, and in all patients, switching from a VKA to some form of heparin was revealed. These data indicate that the first trimester may be a particularly vulnerable time in this population.

The current ESC guidelines indicate that a change of anticoagulation regimen during pregnancy should be implemented in the hospital (class I, level C). In the first trimester, continuation of VKAs throughout pregnancy should be considered (class IIa, level C) when the warfarin dose is lower than 5 mg/d (or phenprocoumon <3 mg/d or acenocoumarol <2 mg/d) because the risk of embryopathy is low (<3%), while VKAs are in large series the most effective regimen to prevent valve thrombosis. The international normalized ratio level is the cornerstone of anticoagulation monitoring.

For women with a warfarin dose exceeding 5 mg/d (or phenprocoumon >3 mg/d, or acenocoumarol, >2 mg/d), the guidelines suggest (class IIa, level C) discontinuation of VKAs between weeks 6 and 12 and replacement by adjusted-dose UFH under a PTT ≥2 × control and applied as intravenous infusion or low-molecular-weight heparin (LMWH) twice daily with dose...
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In women with an MHV, van Hagen et al.\(^1\) reported a significantly lower percentage of pregnancies ending with a live mother and child than in those without prosthetic valve (81.6% vs 97.7%, \(P < 0.001\)) and a significantly lower chance of an event-free pregnancy with a live birth (58.0% vs 78.1%, \(P < 0.001\)). Despite the bleeding complication, which also occurred more frequently in women with MHVs and around the delivery period, it did not induce other adverse events. Also no cases of warfarin embryopathy were reported, which supports the safety of VKAs in the first trimester in women with a warfarin dose of less than 5 mg/d (or phenprocoumon, <3 mg/d, or acenocoumarol, <2 mg/d).

As reported by van Hagen et al.,\(^2\) cesarean deliveries and preterm cesarean deliveries were more common in developed countries and associated with a much greater risk of hemorrhage during delivery and postpartum. The current guidelines state that the mode of delivery should be guided by standard obstetric indications with the exception in women on VKAs at the time of delivery.\(^1\)

In summary, in daily practice, there is a lack of standard care in pregnant women with MHV. It is well known that current anticoagulation regimens including VKAs or heparins may be associated with serious maternal and fetal complications. However, warfarin is still the most effective anticoagulant for preventing thromboembolic events during pregnancy with the above limitations in the first trimester. Although there are no randomized controlled trials comparing the different anticoagulation strategies, the risk of thromboembolic events using warfarin throughout pregnancy is lower than 4%, compared with 33% with the use of UFH throughout pregnancy.\(^1\) The ROPAC investigators examined the largest group of pregnant women with MHV in a prospective analysis and revealed serious complications in more than 40% of this population. It is emphasized for pregnant women with MHV that integrated care by a heart valve team of cardiologists, surgeons, anesthesiologists, and obstetricians with expertise in the management of high-risk cardiac patients is needed.\(^1,8\) But what should an internist, general practitioner, or general cardiologist do in a small center? I completely agree that therapeutic anticoagulation with frequent (weekly) monitoring is crucial for all pregnant women with MHVs and that the knowledge of reasonable anticoagulant management strategies is necessary. Also a clinical follow-up including echocardiography should be performed monthly and the advantages and disadvantages of different anticoagulation strategies should be discussed with the mother and her partner.\(^1\)

REFERENCES


