Letter to the Editor

Anticoagulation for prosthetic heart valves during pregnancy: the importance of warfarin daily dose

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We read with great interest the case by Leyh and associates on prosthetic valvular thrombosis in a pregnant patient anticoagulated with low-molecular-weight heparin (LMWH) [1]. Their case confirms once more the inefficacy of heparins to protect the mother from prosthetic valve thrombosis during pregnancy [2].

The usual management of anticoagulation in pregnant women is stopping warfarin administration and replacing it with either unfractioned or LMW heparin on the basis that warfarin has many untoward effects on the fetus [2]. According to our experience the untoward effects of warfarin are dose-dependent [3]. In our study 43 pregnant patients with mechanical valve prostheses were kept on warfarin continuously until the 38th week of gestation when a cesarean section was planned after warfarin administration had been stopped for 2 days. Patients were divided into two groups according to the daily warfarin intake (>5 mg or ≤5 mg); we found a significant increase in the number of fetal complications in the group of patients taking daily doses of warfarin >5 mg. We observed a total of two prosthetic valve thromboses.

In detail in the group of 33 gestations, with patients taking a warfarin dose ≤5 mg, there were 28 healthy babies and only five fetal complications (four spontaneous abortion and one fetal growth retardation). In the other group of 25 pregnancies, with patients taking a warfarin dose >5 mg, three full-term pregnancies and 22 fetal complications (18 spontaneous abortions, one stillbirth, one ventricular septal defect and two warfarin embriopathies) were observed. Furthermore, there was a very significant correlation between warfarin daily dose and fetal complications. The explanation for these findings is that warfarin has a molecular weight of approximately 1000 and readily cross the placenta to the fetus. The mother may therefore be within anticoagulation therapeutic range, but the fetus is considerably overdosed because of immature liver enzyme systems and low levels of vitamin K-dependent clotting factors [4].

These findings may confidently suggest a clinical approach to these patients. Those patients whose warfarin intake is ≤5 mg with an international normalized ratio (INR) within therapeutic range may continue to take warfarin during the entire pregnancy under strict medical surveillance, and consider a programmed cesarean section at the 38th week of gestation while briefly interrupting warfarin therapy. If the patients prefer to have vaginal delivery, heparin over the last 2 weeks of gestation should be offered as an option. On the other hand, those patients whose warfarin doses are >5 mg should be made fully aware of a likely much higher risk of fetal complications during pregnancy. If they decide to carry on pregnancy with warfarin and a have a bileaflet or an aortic valve prosthesis, the INR range may be lowered to 2.0–2.5 with the aim of bringing the warfarin intake down to 5 mg while still reaching a satisfactory antithrombotic effect. In those women who choose not to take warfarin and are at higher thrombotic risk (mitral prostheses, atrial fibrillation, first generation valves, previous thromboembolism), in-hospital heparin treatment, at least between weeks 6 and 12 and 2 weeks before delivery, seems justified.

It would have been very interesting to know the daily dose of warfarin of the patient treated by Leyh et al. to find out whether she would have benefited from warfarin administration during pregnancy. In pregnant patients with mechanical valves warfarin at a daily dose ≤5 mg seems to be the drug that provides the best antithrombotic effect with a reasonably low rate of untoward fetal complications.

References


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