Prosthetic Heart Valves and Pregnancy

To the Editor:

Pregnant women with mechanical heart valves are an ultra-high-risk group, in whom all anticoagulant options pose maternal and/or fetal risks. It is unclear why the authors of the recent update\(^1\) selected 4 studies, neither the most recent nor of the highest quality, to give a warfarin embryopathy rate of 1.6%. This anomaly rate is not supported by evidence in their Table 1 (3.9% of all pregnancies and 7.4% of livebirths) or by a recent systematic review (6.4% increasing to 10.2% in prospective studies).\(^2\) Furthermore, in the Vitale et al.\(^3\) study, which reported the low anomaly rate with warfarin doses of <5 mg, women in 43% of pregnancies required >5 mg warfarin, and among these 25 pregnancies, only 6 babies survived; of these 6 babies, 3 had anomalies. The clinician should be cognizant of the high rate of late fetal losses and neonatal deaths associated with warfarin, an issue of particular concern to women. In the systematic review, late fetal losses of neonatal deaths in warfarin-exposed pregnancies occurred in 8.8% of pregnancies and 11.7% of births, 10-fold that expected in a general population.\(^2\) A similar rate of 13.6% was found in 3 studies (n=103) published after the final date for inclusion in that review. Consequently, despite warfarin being associated with a lower rate of pregnancy-associated valve thrombosis, some women are reluctant to continue taking warfarin while pregnant.

Experience with low molecular weight heparin in pregnant women with mechanical valves is limited, and there are reports of case fatalities. We published a prospective case series of 14 pregnancies in women with mechanical valves treated with therapeutic enoxaparin (1 mg/kg twice daily).\(^4\) One nonfatal valve thrombosis occurred at 20 weeks’ gestation. Hung and Rahimtoola\(^1\) comment on the recent enoxaparin product warnings, pointing out, “This product . . . is not recommended for thrombotic prophylaxis in patients with prosthetic heart valves” (p 1241). In response to the restrictive labeling of enoxaparin, a recent cardiology consensus statement concluded that the role of enoxaparin in pregnant women with mechanical valves “should more appropriately be considered an unproven and imperfectly studied alternative among a trio of suboptimal and potentially unfavorable options (warfarin, unfractionated heparin, low molecular weight heparins)” (reference 5, p 16). Further, as enoxaparin does not cross the placenta, teratogenic effects are implausible. In our service, pregnant women with mechanical heart valves are provided with written information identifying the risks and benefits for all anticoagulant options. After the woman agrees to use an anticoagulant regimen, written consent is obtained. We agree with the consensus statement that “concern about efficacy and safety was justified for all agents” (p 16) and “the selective warning language about enoxaparin in pregnant patients with mechanical valves appears not to be justified” (reference 5, p 15). Finally, in our series of 41 women with homografts who became pregnant, 94% of the pregnancies resulted in a livebirth, and there were no cases of structural valve deterioration.\(^6\)

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Response

We thank McLintock and coworkers for their interest in our article. They have raised several issues.

1. They have dismissed 4 studies cited in our article as being not of “the highest quality” without providing criteria for their judgment. We presented actual data from each study and emphasized the importance of considering complications in live births.

2. Citing a review by Chan et al.,\(^1\) they state fetal loss or neonatal death in “warfarin-exposed pregnancies occurred in 8.8% of pregnancies and 11.7% of births, 10-fold that expected in the general population.” It was not possible in the review to discern the values of 8.8% and 11.7% or information about the general population.

Pregnancy and fetal loss varies considerably in the population. Two prospective studies have documented early pregnancy loss rates of 11.0% to 26.9% and spontaneous abortion rates of 9.5% to 12.5%.\(^2,3\) Moreover, mortality has steadily declined, and in 1991, perinatal (fetal/neonatal) mortality was 12.8%.

It is more appropriate to compare fetal loss in women with prosthetic heart valves receiving warfarin versus those who had no prostheses. In the European study,\(^4\) women with bioprostheses who received no warfarin had a stillbirth rate of 4%, whereas those with mechanical valves who received warfarin the first trimester and then warfarin had a stillbirth rate of 1.5% and neonatal death rate of 1.5%.

3. They present some data with homografts but not the 10- to 20-year outcomes of homografts.

4. They criticize the FDA warnings about use of low molecular weight heparin (LMWH). It is not for us to advise physicians in other countries to heed FDA warnings, but in the United States, it is important to do so. They agreed with a panel’s “consensus report.”\(^5\) Many panel members had disclosures about research grants, support, speakers bureau, and honoraria with many companies, including manufacturers of LMWH; some even had consultant status. In the spirit of disclosure, it would be appropriate to know the following: (1) Who directly and indirectly funded the meeting and publication of the report? (2) Who selected the panel members? (3) Did the panel members receive remuneration for the meeting and/or the publication and, if yes, from whom?

5. Finally, we wish to re-emphasize the need for a randomized trial of LMWH.\(^7\)

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Circulation. 2003;108:e159-e160
doi: 10.1161/01.CIR.0000102966.93922.B1
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/108/23/e159

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