CV Risk Rises With Early-Preeclampsia History

BY PATRICE WENDLING
Chicago Bureau

DALLAS — Early cardiovascular risk-factor screening is warranted in women with a history of early-onset preeclampsia, according to results of a study in 617 women.

Significantly more women with a history of early-onset preeclampsia exhibited at least one major cardiovascular risk factor, as defined by the American Heart Association, when screened 6 months after delivery, and compared with healthy controls (89% vs. 71%).

The percentages of women exhibiting at least two and at least three cardiovascular risk factors were also significantly higher in the preeclampsia group, Dr. Bas Van Rijn said at the annual meeting of the Society for Maternal-Fetal Medicine.

Among women in the preeclampsia group 51% had two or more cardiovascular risk factors vs. 26% in the control group, and 19% had three or more risk factors vs. 6% in the control group.

"We advise using global risk estimations, such as the Framingham chart, to identify women that require lifestyle intervention programs aimed at primary prevention of cardiovascular disease," said Dr. Van Rijn of the division of perinatology and gynecology, University Medical Center Utrecht (the Netherlands).

The study included 243 women (mean age 30.5 years) admitted from 1995 to 2005 for early-onset preeclampsia and delivery before 34 weeks and a population-based control group of 374 healthy, nonpregnant women (mean 28.3 years). Women with chronic hypertension (greater than 140/90 mm Hg) were excluded. Outcomes were adjusted for age.

When compared with matched controls, women in the preeclampsia group had significantly higher rates of obesity (body mass index 26.1 vs. 24.3 kg/m^2); high blood pressure (126/79 vs. 120/70 mm Hg); and fasting glucose (5.1 vs. 4.8 mmol/L), LDL cholesterol (119 vs. 104 mg/dL), total cholesterol (198 vs. 186 mg/dL), and triglyceride (121 vs. 108 mg/dL) levels, Dr. Van Rijn and associates reported.

HDL-cholesterol levels were significantly lower among cases versus controls (55 vs. 61 mg/dL).

No significant differences were found for rates of diabetes mellitus and smoking.

In all, 15.2% of women with a history of preeclampsia met the criteria for metabolic syndrome, as formulated by the AHA and World Health Organization versus only 4.3% of controls (odds ratio 3.6).

The estimated 10-year risk of first cardiovascular disease events, as calculated by the Framingham CHD risk prediction scores, remained less than 10% for all of the women. This places the women in the AHA low-risk range, which is a 1%-3% absolute risk of developing a major cardiovascular event in the coming years, he said.

However, this is a bit deceptive, mainly because of the young age of the women, Dr. Van Rijn added.

For example, if one adds 10 years to the Framingham risk score (mean age 40 years), the risk category for the preeclampsia group would be 5%-10%, which is comparable to a woman who has experienced a myocardial infarction.

"Women with a history of early-onset preeclampsia exhibit many risk factors, but their relatively young age is masking their absolute cardiovascular risk," said Dr. Van Rijn, who disclosed no financial conflicts of interest.

The study was sponsored by the Netherlands Organization for Scientific Research. ■

Anticoagulation a Sticky Problem in Pregnant Patients Who Have Mechanical Heart Valves

BY BRUCE JANCIN
Denver Bureau

SNOWMASS, COLO. — When it comes to managing anticoagulation in the pregnant patient with a mechanical heart valve, there is simply no ideal solution, Dr. Carole A. Warnes stressed at a conference sponsored by the Society for Cardiovascular Angiography and Interventions.

'This is not the same as getting your patient through noncardiac surgery.'

DR. WARNES

"This is not the same as getting your patient through noncardiac surgery. It's very different. The blood is stickier than at any other time you'll have to manage a mechanical valve," cautioned Dr. Warnes, professor of medicine at the Mayo Clinic, Rochester, Minn.

Other normal physiologic changes in pregnancy that increase the risk of thromboembolic events in patients with mitral or aortic valve prostheses include a nearly 50% increase in circulating blood volume, accompanied by a 30% rise in cardiac output and a 10-20 beat-per-minute increase in resting heart rate. Also, uterine contractions can trigger sudden jumps in systolic and diastolic blood pressure.

What makes managing thromboembolic risk in pregnant patients with a mechanical heart valve so challenging is the need to trade off maternal versus fetal risk.

Unfractionated heparin doesn't cross the placenta. It is often considered safer for the fetus than warfarin in pregnancy. But unfractionated heparin is a poor anticoagulant in pregnancy. The response to the standard dosage varies widely because of the background increases in factor VIII and fibrinogen. As a result, the risk of a thrombosed valve or other thromboembolic event with prolonged heparin is about 10%. The maternal hemorrhage risk is increased as well.

Warfarin is far more effective than unfractionated heparin at preventing valve thrombosis in pregnancy. However, it crosses the placenta, and fetal exposure during gestational weeks 6-9 can result in warfarin embryopathy. The risk is approximately 6% but might be dose dependent. In one older Italian study involving 58 pregnancies, no cases of embryopathy occurred at warfarin doses of 5 mg/day or less, compared with a 9% rate at doses above 5 mg/day (J. Am. Coll. Cardiol. 1999;33:1637-41).

"The fetal risk is probably not as high with warfarin as you might think, but for medicolegal reasons you probably want to avoid it in most circumstances," Dr. Warnes observed at the conference, which was cosponsored by the American College of Cardiology.

Some advocate low-molecular-weight heparin throughout pregnancy as the best approach, but Dr. Warnes is leery. The supporting data are extremely limited. Moreover, she has seen thromboembolic complications occur even when LMWH dosing was guided by monitoring of factor Xa levels rather than relying on fixed-dose therapy.

The most popular management strategy in the United States entails a switch from warfarin to unfractionated heparin as soon as pregnancy is diagnosed, with a switch back to warfarin at 13 weeks' gestation, after the risk of embryopathy is over.

This is followed by yet another switch back to heparin at about 35 weeks in anticipation of delivery, because the fetus can't safely pass through the birth canal while anticoagulated.

The heparin is stopped for as short a time as possible around delivery. Heparin is resumed 6-12 hours post partum, because that's still a high-risk period for valve thrombosis.

If this strategy is employed, it's important to give heparin at an adequate intensity. This means maintaining the activated partial thromboplastin time at greater than twice control. If factor Xa monitoring is used, aim for 0.35-0.7 U/mL of anti–factor Xa, Dr. Warnes urged.

The highest-risk situation in pregnancy in terms of thromboembolism involves a tilting disc prosthesis in the mitral position. This is a situation in which continued use of warfarin throughout pregnancy is a reasonable strategy up until the switch to intravenous heparin at week 35, even though the Physicians Desk Reference lists warfarin as contraindicated in pregnancy, the cardiologist said.

Warfarin throughout pregnancy is a particularly attractive strategy in a high-risk woman who was well controlled on the anticoagulant at 5 mg/day or less prior to pregnancy, which might lessen the risk of warfarin embryopathy, she continued.

Whatever anticoagulation strategy is used in pregnancy, a daily baby aspirin during the second and third trimesters is safe and probably beneficial. It should be used routinely, according to Dr. Warnes. ■

β-Blockers Can Be Continued Through Entire Pregnancy

SNOWMASS, COLO. — Don't hesitate to continue β-blocker therapy throughout pregnancy when the situation calls for it, Dr. Carole A. Warnes urged at a conference sponsored by the Society for Cardiovascular Angiography and Interventions.

"In practice I have been using β-blockers in pregnancy for 30 years. I've never had a significant problem with a baby after the mother has had a β-blocker," declared Dr. Warnes, professor of medicine at the Mayo Clinic, Rochester, Minn.

"Do we worry about the growth of the fetus? Yes, and it needs to be monitored. At the time of delivery the baby may be bradycardic or may have hypoglycemia, but we can deal with that very easily. So for the woman who needs a β-blocker—for example, a patient with hypertrophic cardiomyopathy, or perhaps hypertension with a dilated aorta—we can use them and use them safely, and if it's better for the mother to continue then we do so," she added at the conference, which was cosponsored by the American College of Cardiology.

There are four key principles to keep in mind when prescribing cardiovascular drugs in pregnancy: Stick to the ones with a long safety record, use the lowest effective dose and shortest duration, avoid multidrug regimens, and steer clear of agents labeled category D or X by the Food and Drug Administration, the cardiologist said.

In addition to many of the β-blockers, other cardiovascular drugs she listed as relatively safe in pregnancy include digoxin, calcium channel blockers, procainamide, hydralazine, methyldopa, and furosemide.

Agents that are not safe to use during pregnancy include statins, ACE inhibitors, angiotensin receptor blockers, phenytoin, and folic acid antagonists, including some antibiotics, Dr. Warnes said.

—Bruce Jancin