Thrombophilia of Pregnancy: Heparin Doesn’t Improve Outcomes

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Daily injections of low-molecular weight heparin (LMWH) do not improve outcomes for mother or child in thrombophilia of pregnancy, according to findings of the Thrombophilia in Pregnancy Prophylaxis Study (TIPPS), a multinational, open-label randomized trial published online July 24 in the *Lancet*.

"While I wish we could have shown that LMWH prevents complications, we actually proved it doesn't help," lead author Marc A. Rodger, MD, professor of the Faculty of Medicine at the University of Ottawa, Ontario, Canada, said in a news release. "However, I'm very glad that we can now spare these women all those unnecessary needles."

Adverse outcomes of thrombophilia include pregnancy-associated venous thromboembolism, pregnancy loss, severe preeclampsia, small-for-gestational-age infants, and placental abruption. Although use of LMWH to treat pregnant women with thrombophilia first became widespread in the 1990s, no large, multisite randomized clinical trial had ever been performed to prove its effectiveness.

The goal of this study was to see whether antepartum dalteparin would lower the rate of these complications in pregnant women with thrombophilia.

Between February 28, 2000, and September 14, 2012, the researchers enrolled 292 pregnant women with thrombophilia at increased risk for venous thromboembolism or with previous placenta-mediated pregnancy complications from 36 tertiary care centers in 5 countries. They randomly assigned the women 1:1 to receive antepartum LMWH (dalteparin) (5000 IU once daily up to 20 weeks' gestation, and twice daily thereafter until at least 37 weeks) or to a control group not receiving dalteparin. The researchers excluded 3 women (2 in the dalteparin group and 1 in the no dalteparin group) after randomization because of ineligibility. The outcome adjudicators, but not patients and study personnel, were blinded to treatment assignment.

In both intention-to-treat analysis and on-treatment analysis, dalteparin did not reduce the incidence of the primary composite outcome (independently adjudicated severe or early-onset preeclampsia, small-for-gestational-age infant, pregnancy loss, or venous thromboembolism).

"These findings allow us to move on, to pursue other, potentially effective, methods for treating pregnant women with thrombophilia and/or complications from placenta blood clots," Dr. Rodger said in the news release.

Safety analysis showed that the 2 groups did not differ in the occurrence of major bleeding, but that minor bleeding was more common in the dalteparin group (28/143 [19.6%]) than in the control group (13/141 [9.2%]; risk difference, 10.4%; 95% confidence interval, 2.3% - 18.4%; *P* = .01).

"Antepartum prophylactic dalteparin does not reduce the occurrence of venous thromboembolism, pregnancy loss, or placenta-mediated pregnancy complications in pregnant women with thrombophilia at high risk of these complications and is associated with an increased risk of minor bleeding," the study authors write.

In an accompanying editorial, Paul S. Gibson, MD, from the Department of Medicine and the Department of Obstetrics and Gynecology, University of Calgary, Alberta, and Kara A. Nerenberg, MD, from the Department of Medicine, University of Ottawa, Ontario, Canada, call TIPPS "methodologically rigorous" but note study limitations of low event rates (18.9% events observed vs 49% anticipated in the control group), differential use of aspirin between the study groups, slow recruitment rate, and small subgroup sizes.

TIPPS "shows that [LMWH] is ineffective in preventing a wide range of clinically important adverse pregnancy outcomes in women with thrombophilia," the editorialists write. "Hopefully, these results will finally tip clinicians away from using the drug in this setting and motivate researchers to pursue other potentially effective preventive interventions."

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