Progesterone fails to avert preterm birth of twins in women with short cervix

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SAN FRANCISCO – Prophylactic progesterone does not decrease and may even increase the rate of preterm birth in women with a twin pregnancy who have a short cervix but no symptoms of complications, a study has shown.

Among the 165 women in a randomized open-label trial conducted in France, the rate of birth before 37 weeks' gestation did not differ significantly between those who were and were not given 17-alpha hydroxyprogesterone caproate (Makena), Dr. Philippe Deruelle reported at the annual meeting of the Society for Maternal-Fetal Medicine, on behalf of the Groupe de Recherche en Obstétrique et Gynécologie in France.

In addition, in results that he characterized as surprising, the progesterone group in fact had a higher rate of birth before 34 weeks and before 32 weeks.

"We could say that the clinical implication of our study is that 17-hydroxyprogesterone is not effective in women with an asymptomatic twin pregnancy and a short cervix for prevention of preterm delivery, and it might even be harmful," he commented. "Preterm delivery in twin pregnancies is probably due to uterine distension and contraction, with no effect of progesterone for prevention."

One session attendee said, "My issue is that you gave progesterone at 24 weeks and after. I wonder if you have a subanalysis seeing maybe if you give it earlier, you get a different effect, and if you give it later, you see more of the harm. And I thank you for reminding all of us that scope creep should not be done, and we shouldn't use an intervention before it's proven to work."

The investigators have not done such a subanalysis, Dr. Deruelle replied.

Another attendee questioned the relatively high dose of progesterone used – 500 mg twice weekly – and the fact that the investigators used the caproate formulation, which may have effects different from those of other formulations. "We really have to look at perhaps other progesterones. I think with caproate, specifically, we really have to be very cautious" about dosing, he said.

"We assumed with the higher doses, it might be more powerful than the dose previously published," which was ineffective, Dr. Deruelle explained.

Women from 10 university hospitals in France with twin pregnancies and a short cervix were enrolled in the trial between the 24th and 31st weeks of gestation.

They were assigned evenly to a progesterone group or a control group, with treatment continued until 36 weeks or preterm delivery.

The mean gestational age at enrollment was about 28 weeks. On average, cervical length was 15 mm in the progesterone group and 17 mm in the control group, said Dr. Deruelle of Hôpital Jeanne de Flandre, Lille, France.

Results reported at the meeting showed that the mean time between randomization and delivery – the trial's primary outcome – did not differ significantly between the progesterone and control groups (45 vs. 52 days, *P* = .09).

Women in the progesterone group did not have a lower rate of birth before 37 weeks (80% vs. 77%) and in fact had higher rates of birth before 34 weeks (40% vs. 28%, *P* = .019) and before 32 weeks (29% vs. 12%, *P* = .0002), reported Dr. Deruelle.

The mean gestational age at birth was younger in the progesterone group (34 $^{6}/_{7}$ vs. 35 $^{3}/_{7}$ weeks, *P* less than .03). Rates of other adverse pregnancy outcomes were similar.

The two groups also were statistically indistinguishable with respect to most adverse neonatal outcomes as well, but neonates in the progesterone group had a lower birth weight (2,090 vs. 2,230 g, *P* less than .03).

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