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Study shows no benefit from drug widely used to prevent premature births

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When a pregnant woman goes into early labor, her obstetrician may give her drugs to quiet the woman's uterus and prevent premature birth.

New research shows, however, that one popular drug works no better than a placebo at maintaining pregnancy after the initial bout of preterm labor is halted, say scientists at the Stanford University School of Medicine, Lucile Packard Children's Hospital and Santa Clara Valley Medical Center. The new trial is the first-ever placebo-controlled test of nifedipine, a muscle relaxant originally developed to lower blood pressure, and its effect on premature delivery with prolonged treatment.

"Medication use should be minimized in pregnancy unless it's clearly indicated," said Deirdre Lyell, MD, assistant professor of obstetrics and gynecology at Stanford and the study's lead author. Serious side effects of nifedipine in pregnancy are rare, Lyell said, but even a low risk isn't worthwhile if the drug has no benefit. "We all want to prevent preterm birth, but prolonged treatment with nifedipine doesn't appear to be an answer."

The findings will appear in the December issue of the journal *Obstetrics and Gynecology*.

Preterm births, defined as deliveries before 37 weeks of pregnancy, are on the rise in the United States. Pregnancy normally lasts 40 weeks. A report released earlier in November by the March of Dimes gives the United States a "D" grade for its rate of preterm births, which increased

between 1981 and 2005 from 9.4 to 12.7 percent of all births. Smoking, lack of insurance and early intervention by physicians were cited as major contributing factors.

"The scope of the problem is enormous," Lyell said.

In early life, preemies face health problems such as respiratory distress, bleeding on the brain and tissue-destroying intestinal infections. Long-term complications of prematurity include neurological disorders, chronic lung disease and vision and hearing problems. The earlier the delivery, the greater the risks. That means doctors are very motivated to help women in early labor stay pregnant as long as possible. A recent survey by the Society for Maternal-Fetal Medicine found 29 percent of obstetricians prescribed drugs to keep such patients from re-entering early labor. Of those, 79 percent said nifedipine was their first-choice therapy.

Lyell's team recruited 71 women who had been successfully treated for preterm labor between 24 and 34 weeks of pregnancy. The women were then randomly assigned to receive doses of nifedipine or placebo every six hours until 37 weeks of pregnancy or until delivery, whichever came first. The researchers hoped nifedipine would prevent preterm labor from re-starting. They evaluated whether subjects' pregnancies lasted to 37 weeks and measured how long delivery was delayed. They also noted the babies' gestational age at delivery, birth weight and complications of prematurity.

The team saw no differences between nifedipine and placebo for any measurement. About 40 percent of women in both groups reached 37 weeks of pregnancy, with delivery delayed an average of a month. Babies' average health was the same in both groups, too.

Lyell cautioned that the study was designed to detect a 50 percent

improvement in delayed deliveries. If nifedipine confers a smaller advantage, it would not have been spotted in this study, she said. Lyell thinks a larger study of nifedipine is warranted. "A small benefit would be especially significant at early gestational ages, and less so later on. But overall, there's no benefit to prematurity."

Based on the current lack of data to support this drug, Lyell believes obstetricians should proceed with caution. "All medications have side effects," she said. Though nifedipine has a fairly good safety record, a few case reports link it to dangerously low blood pressure in pregnant women.

"If something has not been shown to be of benefit, it shouldn't be used," Lyell concluded. "Every now and then, there will be a patient who has an unusual side effect.

"It's important to distinguish between acute treatment, which is given to a woman in preterm labor, and maintenance treatment, which is given to a woman following an episode of preterm labor that has ended," she added. "This study addresses maintenance treatment. We still use nifedipine for acute treatment of preterm labor."

Source: Stanford University Medical Center