

## Common preterm labor drug has more side effects than alternative

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The drug most commonly used to arrest preterm labor, magnesium sulfate, is more likely than another common treatment to cause mild to serious side effects in pregnant women, according to a study from researchers at Lucile Packard Children's Hospital and Stanford University School of Medicine. Their findings suggest that, since the effectiveness of the two drugs appears similar, physicians should consider side effects more strongly when choosing which drug to prescribe.

Newborns whose mothers had received magnesium sulfate were also more likely to be admitted to the neonatal intensive care unit than those whose mothers had received the alternative treatment, although the data do not offer an explanation for this finding and more research needs to be conducted to rule out other causes. What is clear is that currently available treatments for preterm labor are far from perfect.

"There is no free lunch with any of these drugs," said Deirdre Lyell, MD, a specialist in high-risk obstetrics at the hospital's Johnson Center for Pregnancy and Newborn Services. "But magnesium sulfate has some particularly unpleasant side effects, including vomiting, lethargy and blurry vision. The alternative treatment, nifedipine, often leaves women feeling better."

Side effects are particularly important for women struggling with the risk of premature birth and the rapid medical decisions that might need to be made about the care of their newborn. Lyell, assistant professor of



obstetrics and gynecology at the medical school, and Yasser El-Sayed, MD, associate professor of obstetrics and gynecology at the medical school, are the lead and senior authors respectively of the research, which will be published in the July issue of Obstetrics & Gynecology. The study is the largest multicenter trial that randomized the use of the preterm labor drugs to compare outcome.

Preterm labor is defined as labor before 37 weeks' gestation. Although it's not always possible to prevent premature birth, physicians strive to delay delivery for at least 48 hours. The extra time allows a doctor to arrange to transfer the woman to a medical facility experienced in treating premature infants and helps maximize the effectiveness of steroids used to help the fetus to prepare for the harsh outside world.

Magnesium sulfate, nifedipine and other preterm labor treatments, called tocolytics, are thought to work by relaxing overactive uterine muscles and halting ongoing cervical changes that may lead to delivery. But it's not been clear if one is better than the others. Force of habit has dictated the use of magnesium sulfate by many physicians in the absence of a compelling reason to choose an alternative.

Lyell and El-Sayed and their collaborators randomly assigned 192 patients at Packard Children's or Santa Clara Valley Medical Center who were in preterm labor to receive either magnesium sulfate, which is an intravenous treatment, or nifedipine, an oral treatment. They found that magnesium sulfate was more effective in achieving the study's primary outcome - preventing delivery for 48 hours with uterine quiescence. But there were no significant differences in the treatments' ability to delay delivery, in the gestational age of the newborn or in the birth weight of the infants. The researchers speculate that this seeming contradiction could be explained if nifedipine, rather than stopping a woman's contractions, simply renders them clinically ineffective.



However, two-thirds of the women who received magnesium sulfate experienced mild to severe side effects such as shortness of breath and fluid build-up in the lungs during the treatment. In contrast, one-third of the women who received nifedipine experienced side effects of the treatment, including headaches. Nifedipine is commonly used to treat high blood pressure and heart disease.

"The take-home message is that we saw no differences in relevant outcomes between the two groups," said Lyell, "but there was a significant difference in the side effects experienced by the women, and some of these were very serious."

Lyell and El-Sayed emphasized that magnesium sulfate is still an appropriate treatment for preterm labor. It continues to be used regularly both at Packard Children's and Santa Clara Valley Medical Center. But they believe it may be time for physicians to give more weight to expected side effects when considering what to try first.

"It's been my experience that women who have had magnesium sulfate remember it; they don't like it," said Lyell. "Those who receive nifedipine don't feel as bad. These drugs are prescribed under what are already very difficult circumstances for the patients, and side effects are very important to them."

Source: Stanford University Medical Center

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