Drug combating severe nausea in pregnancy begins clinical trial

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Guttuso and colleagues will begin to enroll pregnant women with hyperemesis gravidarum in the clinical trial this summer.

Pregnant women with hyperemesis gravidarum, the extreme and debilitating form of morning sickness that Kate Middleton, Duchess of Cambridge, famously experienced, may find relief from a medication prescribed for seizure patients.

The first randomized, double-blind, two-arm clinical trial to test gabapentin as a treatment for hyperemesis gravidarum, begins this summer, thanks to a four-year, $1.3 million National Institutes of Health

grant to Thomas J. Guttuso Jr, MD, associate professor of neurology and obstetrics and gynecology at the University at Buffalo School of Medicine and Biomedical Sciences. The drug is normally prescribed to treat seizures, pain and restless legs syndrome.

The incidence of hyperemesis gravidarum is not precisely known but estimates put it somewhere between 1 and 20 per 1,000 pregnant patients. Approximately 59,000 patients are hospitalized with the condition in the U.S. annually, but experts point out that the condition is very likely underreported.

"I think a lot of people don't appreciate just how sick and disabled these women can be," Guttuso says, noting that 15 percent of women with this condition end up having abortions even though they really want to have children.

"Some of the most severely affected end up having abortions because they have no hope of getting better," he says. "Ending the pregnancy is currently the only effective treatment for hyperemesis gravidarum. These women are so sick. They often retch every 15 to 30 minutes and it can go on all day and often at night as well."

Pregnant women with this condition have long sought relief; several social media sites deal with the condition and Guttuso has been contacted by some of them.

"We could never thank you enough for validating the severity of this debilitating, tormenting and life-threatening condition," one of them wrote upon hearing of the study. "These women who thought they would never be able to have another child are being given a renewed sense of hope."

For the upcoming study, UB and the University of Rochester each will

enroll approximately 40 women through Guttuso and Loralei L. Thornburg, MD, associate professor of obstetrics and gynecology, UR Medical Center.

The 80 women will be randomized to take either gabapentin or another anti-emetic drug, ondansetron. The women must have had moderate to severe refractory nausea and vomiting (i.e. hasn't responded to medication) before 16 weeks of gestation, causing them to lose at least five percent of their pre-pregnancy weight or having other signs of significant malnutrition or dehydration.

Guttuso is a Western New York neurologist and UB professor whose practice with UBMD, the practice plan of the UB medical school, focuses primarily on patients with movement disorders, such as Parkinson's disease. He originally became interested in gabapentin when he accidentally discovered that it appeared to be effective in treating hot flashes in postmenopausal women. Soon thereafter, a breast cancer patient undergoing chemotherapy informed him that gabapentin appeared to fully resolve her chemotherapy-induced nausea and vomiting.

Guttuso thought that it should be tried with patients suffering from hyperemesis gravidarum. He teamed up with several Buffalo obstetricians and UB professor of pediatrics Luther K. Robinson, MD, to do a pilot study on seven pregnant women who had not seen any improvement with other anti-emetic medications.

The pilot study examined the drug's safety, tolerability and effectiveness in treating hyperemesis gravidarum. After two weeks of gabapentin therapy, the seven women experienced an average 80 percent reduction in their nausea and a 94 percent reduction in their vomiting and near normal levels of eating and drinking.

"When they started with gabapentin, all of them showed a marked improvement," he says. "Within two hours of taking the first pill, most patients were feeling much better and several were able to start eating and drinking again. It was a pretty amazing thing to see."

About a year after Guttuso's results were published in 2010, the FDA put the study on clinical hold until further safety data was available; two of the seven infants had been born with birth defects. That clinical hold was removed in May 2012 when a subsequent study reported that the rate of congenital defects among 258 infants born to women taking gabapentin early in pregnancy was about the same as the rate of congenital defects in the general population. That allowed Guttuso to resume his research.

Guttuso says it's not clear how a seizure medication like gabapentin could help with symptoms of nausea and vomiting.

"Our theory is that in some women, particular brain cells become overactive in response to the very large increases in hormone levels that occur early in pregnancy," Guttuso says. "We theorize that this overactivity is partially mediated by too much calcium inflow and that leads to the symptoms of nausea and vomiting. Gabapentin most likely works by preventing the flow of calcium ions into particular brain cells that are involved with the generation of nausea and vomiting."

Guttuso is listed as an inventor on a patent owned by the University of Rochester covering the use of gabapentin for treating hot flashes.

Provided by University at Buffalo