Folate prevents alcohol-induced congenital heart defects in mice

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A new animal study has found that high levels of the B-vitamin folate (folic acid) prevented heart birth defects induced by alcohol exposure in early pregnancy, a condition known as fetal alcohol syndrome.

Researchers at the University of South Florida College of Medicine and All Children's Hospital report that the protection was afforded only when folate was administered very early in pregnancy and before the alcohol exposure. The dose that best protected against heart defects in mice was considerably higher than the current dietary recommendation of 400 micrograms (0.4 milligrams) daily for women of child-bearing age.

The findings were published online earlier this month in the *American Journal of Obstetrics and Gynecology*.

While more research is needed, the study has implications for re-evaluating folate supplementation levels during early pregnancy, said principal investigator Kersti Linask, PhD, the Mason Professor of Cardiovascular Development at USF and Children's Research Institute/All Children's Hospital.

"Congenital heart defects can occur in the developing embryo at a time when women typically do not even know they are pregnant - 16 to 18 days following conception. They may have been drinking alcohol or using prescription drugs without realizing this could be affecting embryonic development," Dr. Linask said.

"We found that we could prevent alcohol-associated defects from arising in the mice -- provided folate was given in relatively high concentrations very early in pregnancy around conception."

In the USF study, two randomly assigned groups of pregnant mice were fed diets supplemented by folate in adjusted doses known from epidemiological studies to rescue human embryos from craniofacial birth defects. From the day after conception, one group received a high dose of folate supplementation (10.5 milligrams/kilogram) and the second received a moderate dose (6.2 mg/kg). A third control group ate a normal folate-supplemented diet (3.3 mg/kg) determined to maintain the general health of the pregnant mice, but not to rescue embryos from birth defects.

During the first week of pregnancy, the mice in all three groups were then administered injections of alcohol simulating a single binge drinking event in humans.

Following this alcohol exposure, Doppler ultrasound confirmed that 87 percent of the embryos of pregnant mice in the third group - those not receiving folate supplementation beyond what was present in their normal diets - had developed heart valve defects. The affected embryos were also smaller in size and their heart muscle walls appeared thinner.

Between days 15 and 16 of pregnancy in the mice - equal to 56 days of gestation in humans -- ultrasound also showed that the high-folate diet protected heart valve development against lasting defects and restored heart function and embryonic size to near-normal levels. The moderate-folate diet provided only partial protection; in this group 58 percent of the mouse embryos developed heart valves that functioned abnormally, with a back flow of blood.

The researchers suggest that folate fortification may be most effective at preventing heart birth defects when administered at significantly higher levels than the doses currently recommended to prevent pregnancy complications -- both in normal women (0.4 milligrams recommended daily) and even in women who have delivered an infant with a spinal birth defect (4 milligrams daily).

Although higher folate levels did not cause adverse side effects in the pregnant mice, Dr. Linask notes, the safety and effectiveness of higher doses must be proven with human trials.

The heart is the first organ to form and function during embryonic development of vertebrates. The USF researchers suggest that folate supplementation thwarts alcohol's damaging effect on an important early signaling pathway that plays a vital role in early heart development and subsequently in valve formation.

Provided by University of South Florida