Supplement may prevent alcohol-related brain, skull defects

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The dietary supplement CDP-choline, sold as a brain-boosting agent and under study for stroke and traumatic brain injury, may block skull and brain damage that can result from alcohol consumption early in pregnancy, Medical College of Georgia researchers Drs. Erhard Bieberich and Guanghu Wang report. Credit: Phil Jones, Medical College of Georgia campus photographer

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Alcohol consumption in early pregnancy increases levels of a little-known lipid called ceramide, significantly increasing suicide among cells critical to skull and brain formation, Dr. Erhard Bieberich, biochemist in the MCG Schools of Graduate Studies and Medicine, reports in Cell Death *and Disease*.

Resulting neural crest damage includes the brain's "skin" - the multi-layered meninges that provides protection and nourishment - producing less TGF-β1, a growth factor critical for brain and bone development. That finding may help explain the cranial bone and cognitive defects that can result in fetal alcohol syndrome.

"There is just a little window," Bieberich said, about four weeks after conception when neural crest cells emerge for a few days before morphing into other cell types that help form numerous organs. This is often before a woman knows she is pregnant. The studies indicate the potential for lasting damage to the fetus if a woman drinks, for example, several glasses of wine within an hour during that window.

MCG researchers suspected ceramide, known to induce cell death and be activated by alcohol, as a culprit in the damage. They found high levels of ceramide both in mouse cells and pregnant mice exposed to alcohol along with a five-fold increase in apoptotic, or dying cells. "There is a clear correlation," he said.

Researchers thought neural crest cells were tough cells whose function could be replaced if they happened to get injured. Instead they found that 25 percent of mouse embryos exposed to alcohol during that critical period had defects in the fibrous joints that connect the skull. "You get a snowball effect: The neural crest is damaged, the meninges doesn't develop properly and tissue like bone and brain that are regulated by the meninges don't develop properly either," Bieberich said.

When they added ceramide-neutralizing CDP-choline to the mouse cells, cell death and ceramide levels were reduced. Alcohol prompts the body to produce more ceramide from the brain lipid sphingomyelin, a major component of cell membranes. They found that CDP-choline pushes back toward producing less ceramide, preventing damage providing the drinking stops.

"Ceramide can be bad or good," notes Bieberich, who has shown, for example, ceramide's role in helping early stem cells evolve into embryonic tissue. But alcohol upsets the natural balance.

Follow up studies, funded by the March of Dimes, include determining whether CDP-choline can rescue cells after the fact or whether it or a similar supplement would need to be taken preventively. "Hopefully we can rescue some of the cells by triggering or signaling the back reaction," Bieberich said.
He also wants to see if CDP-choline affords the same protection in pregnant mice that it does in laboratory cells.

Provided by Medical College of Georgia