Maternal Antidepressant Use Linked to Infant Brain Malformations

Maternal antidepressant use may be associated with structural brain changes in infants, according to new imaging research.

A study of 33 children showed that the offspring of mothers who used selective serotonin reuptake inhibitors (SSRIs) during pregnancy were nine times more likely to develop Chiari type I brain malformation (CIM) than the offspring of nondepressed, nonmedicated mothers.

Most children with this type of malformation, defined by cerebellum brain tissue extending into the spinal canal, do not have significant problems. However, some experience headaches and problems with balance severe enough to require surgery.

Rebecca C. Knickmeyer, PhD, assistant professor of psychiatry at the University of North Carolina (UNC) School of Medicine in Chapel Hill, told *Medscape Medical News* that although the study suggests that the increased risk for these brain changes in infants may be caused by maternal use of SSRIs, it could also be due to factors such as severity of the depressive disorder itself.

"We just don't know very much about the causes of Chiari malformations right now," said Dr. Knickmeyer.

The investigators add that the study findings are not a call for clinicians to change their prescribing practices for pregnant patients.

"There is no definitive answer to the optimal treatment of women with depression during pregnancy....Potential risks of pharmacotherapy must be weighed against the potential risk of active, untreated depression," they write.

The study was published online May 19 in *Neuropsychopharmacology.*

Common but Not Well Understood

CIM is believed to result from the "underdevelopment of the posterior cranial fossa and overcrowding of the normally developing hindbrain," report the researchers.

"It is not present at birth but emerges postnatally," they write, adding that although it is "somewhat common," very little is known about the condition.

"We were interested in getting at least an initial look at whether [CIM] could be related to medication vs other factors associated with depression during pregnancy," she said.Dr. Knickmeyer added that the investigative team wanted to look at how depression during pregnancy affects child brain development.

Drawing from ongoing neuroimaging studies at UNC, the researchers evaluated data for 33 children (60% boys) of mothers who had been diagnosed with depression and who were taking SSRIs for the condition during pregnancy, as well as 66 age-matched children of mothers with no history of depression or antidepressant use.

The most common SSRI used by the first group's mothers was sertraline (*Zoloft*, Pfizer Inc), followed by fluoxetine and citalopram.

All of the children underwent MRI scans at the age of 1 and/or 2 years. CIM was defined as having tonsillar herniation of -6 mm or greater.

Malformations

Results showed that CIM was found in 18% of the children of mothers who took SSRIs during pregnancy vs 2% of the children of healthy mothers ($P = .003$; odds ratio [OR], 10.32).

The percentage was even higher for those with mothers who also had a family history of depression ($P = .002$; OR, 38.08), "suggesting an important role for genes as well as environment," note the investigators in a release.

Other risk factors for the malformations included maternal use of SSRIs at conception ($P = .01$) and exposure to SSRIs by the offspring in all 3 trimesters ($P = .002$).

The cohort who had been exposed to SSRIs also had significantly earlier gestational age at birth ($P < .001$), shorter birth length ($P < .001$), and longer overall stays in the neonatal intensive care unit ($P = .003$) than did the healthy control group.

In further analysis, the researchers looked at 90 additional children, including 30 whose mothers had been diagnosed with depression but who did not take any antidepressants during pregnancy and 60 from healthy mothers.

There were no significant differences in occurrence of CIM between these groups (7% vs 5%, respectively).

Overall, "this study found a striking increase of CIM in children with prenatal SSRI exposure," write the investigators.

However, Dr. Knickmeyer noted that it is a small trial that needs to be replicated.

"We also need to figure out the mechanism. It's a tough area because taking any medications during pregnancy, whether it's for depression or diabetes or heart disease, is always about risk vs benefits," she said.

"And the risk and benefits are going to be different for each individual woman. Untreated, uncontrolled depression clearly has negative consequences for babies and moms. So the question becomes about treatment. Psychotherapy gives good results for some but not for others," noted Dr. Knickmeyer.

"It really is a personal decision to be made between a woman and her healthcare providers using the best information that we have at the time."

Three of the study authors report no relevant financial relationships. Dr. Knickmeyer reports being a collaborator on 2 grants from Pfizer. A list of the 3 other investigators' potential conflicts is given in the original article.

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