Prenatal exposure to paracetamol may increase autism spectrum and hyperactivity symptoms in children

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Tylenol 500 mg capsules. Credit: Wikipedia

A new study has found that paracetamol (acetaminophen), which is used extensively during pregnancy, has a strong association with autism spectrum symptoms in boys and for both genders in relation to attention-related and hyperactivity symptoms.

The findings were published this week in the *International Journal of Epidemiology*. This is the first study of its kind to report an independent association between the use of this drug in pregnancy and autism spectrum symptoms in children. It is also the first study to report different effects on boys and girls. Comparing persistently to nonexposed children, the study has found an increase of 30 per cent in the risk of detriment to some attention functions, and an increase of two clinical symptoms of autism spectrum symptoms in boys.

Researchers in Spain recruited 2644 mother-child pairs in a birth cohort study during pregnancy. 88 per cent were evaluated when the child was one year old, and 79.9 per cent were evaluated when they were five years old. Mothers were asked about their use of paracetamol during pregnancy and the frequency of use was classified as never, sporadic, or persistent. Exact doses could not be noted due to mothers being unable to recall them exactly.

43 per cent of children evaluated at age one and 41 per cent assessed at age five were exposed to any paracetamol at some point during the first 32 weeks of pregnancy. When assessed at age five, exposed children were at higher risk of hyperactivity or impulsivity symptoms. Persistently exposed children in particular showed poorer performance on a computerised test measuring inattention, impulsivity and visual speed processing.

Boys also showed more autism spectrum symptoms when persistently exposed to paracetamol. Lead author Claudia Avella-Garcia, researcher at CREAL, an ISGlobal allied centre in Barcelona, explained that, "although we measured symptoms and not diagnoses, an increase in the number of symptoms that a child has, can affect him or her, even if they are not severe enough to warrant a clinical diagnosis of a neurodevelopmental disorder."

Co-author Dr. Jordi Júlvez, also a researcher at CREAL, commented on the possible reasoning for the effects of paracetamol on neurodevelopment: "Paracetamol could be harmful to neurodevelopment for several reasons. First of all, it relieves pain by acting on cannabinoid receptors in the brain. Since these receptors normally help determine how neurons mature and connect with one another, paracetamol could alter these important processes. It can also affect the development of the immune system, or be directly

toxic to some fetuses that may not have the same capacity as an adult to metabolize this drug, or by creating oxidative stress."

There could also be an explanation for why boys are more likely to have autism spectrum symptoms: "The male brain may be more vulnerable to harmful influences during early life", said Claudia Avella-Garcia. "Our differing gender results suggest that androgenic endocrine disruption, to which male brains could be more sensitive, may explain the association."

The study concluded that the widespread exposure of infants to paracetamol in utero could increase the number of children with ADHD or autism spectrum symptoms. However, they stressed further studies should be conducted with more precise dosage measurements, and that the risks versus benefits of paracetamol use during pregnancy and early life should be assessed before treatment recommendations are made.

More information: "Acetaminophen Use in Pregnancy and Neurodevelopment: Attention Function and Autism Spectrum Symptoms"; Claudia B. Avella-Garcia, Jordi Julvez, Joan Fortuny, Cristina Rebordosa, Raquel García-Esteban, Isolina Riaño Galán, Adonina Tardónf, Clara L. Rodríguez-Bernal, Carmen Iñiguez, Ainara Andiarena, Loreto Santa-Marina, Jordi Sunyer; *International Journal of Epidemiology*; DOI: 10.1093/ije/dyv

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