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Opinion Article

Raising Awareness of Acetaminophen Risk in Pregnancy and Developmental Concerns

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ABOUT THE STUDY

Pregnant women receiving the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) vaccines are recommended to opt for Acetaminophen (APAP) over nonsteroidal anti-inflammatory drugs as a safe medication for managing adverse effects, including local pain and fever. Despite the prevalent use of Over-The-Counter (OTC) APAP in Japan for vaccine-associated side effects, including pain and fever, awareness regarding its safety during pregnancy is limited.

In recent years, the number of children with developmental disabilities has increased owing to, in part, an increased awareness of these conditions, allowing those who were previously undiagnosed to be diagnosed [1]. Its causes are multifactorial and include genetic, infectious, and environmental factors. A recent study showed that higher APAP metabolites levels in the cord blood are associated with the subsequent development of Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) in a dose-dependent manner [2]. According to one study, APAP exposure during pregnancy increases the risk of ADHD diagnosis in children at 7 years of age [3]. Currently, the U.S. Food and Drug Administration discourage the usage of APAP at all stages of pregnancy [4].

Potential mechanisms linking prenatal APAP exposure to ADHD/ASD include the following:

- The role of APAP as an endocrine disruptor in the developing brain has been extensively studied [5]. During pregnancy, APAP decreases estrogen synthesis in the uterus [6]. Estrogen is essential for regulating apoptosis, synaptogenesis, and morphometry of neurons in the developing brain [7].
- Prenatal APAP exposure during prenatal development adversely affects the hippocampus of the fetal brain. This is manifested as a reduction in the expression of genes related to sex-determining region Y-box 2/notch signaling, leading to a diminished proliferation of neural progenitor stem cells [8]. Moreover, APAP directly causes neurotoxicity in cortical neurons by inducing apoptosis [9].
- Cord blood analysis suggests that unmetabolized APAP disrupts the homeostatic balance of glutathione synthesis, thereby increasing oxidative stress in the central nervous system. Elevated glycine levels lead to the activation of N-methyl-d-aspartate receptors, contributing to the pathogenesis of ADHD [10].
- A molecular database and literature mining study suggested that APAP, along with maternal exposure to pesticides, increases the risk of ASD by affecting apoptosis and the metabolism of reactive oxygen species and carbohydrates [11].

CONCLUSION

When addressing pain and fever, (a concern not exclusive to the SARS-CoV-2 vaccine), pregnant women should exercise caution with medications and dietary supplements. Whenever possible, opting for cryotherapy modalities, like ice packs, is advisable. Emphasizing the risk associated with analgesic-antipyretic drugs during pregnancy is essential unless a causal relationship between APAP and developmental problems can be ruled out. Physicians should consider providing detailed explanations of the risks of APAP using easy-to-understand pamphlets with illustrations. Delayed safety education on the use of any medication during pregnancy may negatively impact maternal and infant health. Moreover, the rise in OTC medication overdoses is a recent concern, as many common cold remedies contain APAP, and many women are unaware of its content and associated side effects. Therefore, providing information during prenatal examinations is important. Epidemiological studies on the association between APAP use during pregnancy and developmental outcomes that consider variations based on race, dose, and duration of use are needed globally.

CONFLICT OF INTEREST

This article is a personal opinion, and the responsibility lies with the author.

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REFERENCES

1. T Hirota, King BH. Autism spectrum disorder. JAMA. 2023;329(2023):157-168.
2. Ji Y, Azuine RE, Zhang Y, Hou W, Hong X, Wang G, et al. Association of cord plasma biomarkers of in utero acetaminophen exposure with risk of attention-deficit/hyperactivity disorder and autism spectrum disorder in childhood. JAMA Psychiatry. 2020;77(2):180-189.
3. Cooper M, Langley K, Thapar A. Antenatal acetaminophen use and attention-deficit/hyperactivity disorder: An interesting observed association but too early to infer causality. JAMA Pediatr. 2014;168(4):306-317.
4. US Food and Drug Administration. FDA Drug Safety Communication: FDA has reviewed possible risks of pain medicine use during pregnancy. FDA official site. 2015.
5. Bauer AZ, Swan SH, Kriebel D, Liew Z, Taylor HS, Bornehag CG, et al. Paracetamol use during pregnancy-A call for precautionary action. Nat Rev Endocrinol. 2021;17(12):757-766.
6. Addo KA, Palakodety N, Fry RC. Acetaminophen modulates the expression of steroidogenesis-associated genes and estradiol levels in human placental JEG-3 cells. Toxicol Sci. 2021;179(1):44-52.
7. McCarthy MM. Estradiol and the developing brain. Physiol Rev. 2008;88(1):91-134.
8. Xie L, Qin J, Wang T, Zhang S, Luo M, Cheng X, et al. Impact of prenatal acetaminophen exposure for hippocampal development disorder on mice. Mol Neurobiol. 2023;60(12):6916-6930.
9. Posadas I, Santos P, Blanco A, Munoz-Fernandez M, Cena V. Acetaminophen induces apoptosis in rat cortical neurons. PloS One. 2010;5(12):e15360.
10. Anand NS, Raghavan R, Wang G, Hong X, Azuine RE, Pearson C, et al. Perinatal acetaminophen exposure and childhood Attention-Deficit/Hyperactivity Disorder (ADHD): Exploring the role of umbilical cord plasma metabolites in oxidative stress pathways. Brain Sci. 2021;11(10):1302.
11. Furnary T, Garcia-Milian R, Liew Z, Whirledge S, Vasiliou V. *In silico* exploration of the potential role of acetaminophen and pesticides in the etiology of autism spectrum disorder. Toxics. 2021;9(5):97.