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NEW-GENERATION ANTIPILEPTIC DRUGS DURING PREGNANCY AND THE RISK OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A SCOPING REVIEW

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Background:

Maternal antiepileptic drug (AED) use during pregnancy is associated with increased risk of cognitive adverse effects among the offspring. As new-generation AEDs continue to enter the market, evidence on the safety of these newer AEDs during pregnancy is scarce. To date, there are no published reviews summarizing the evidence of new-generation AED exposure in utero and the development of attention deficit-hyperactivity disorder (ADHD) in the offspring.

Objective:

The objective of this scoping review was to summarize the available evidence on the risk of ADHD after maternal exposure to new-generation AEDs during pregnancy.

Methods:

Using PRISMA Guidelines for scoping reviews we searched electronic databases (EMBASE and MEDLINE) for articles published between January 1, 1988, and July 22, 2019. New-generation AEDs were defined as any AED marketed after 1988. ADHD was defined as attention-deficit hyperactivity disorder, hyperkinetic disorder, hyperkinesis, or conduct disorder.

Results:

Out of 805 screened articles, a total of 8 publications met the inclusion criteria (7 cohort studies and 1 systematic review). Across the studies, the sample size of pregnant women exposed to AEDs ranged from 1 to 1383. AED monotherapy was examined in 6 studies (mostly lamotrigine), while only 2 studies examined AED polytherapy. The included studies reported a range of adjusted relative risks, from 0.84 [0.59-1.19] to 1.63 [0.41-6.06].

Conclusion:

Lamotrigine monotherapy holds the largest body of evidence among new-generation AEDS, with most studies concluding no significant risk of ADHD among the offspring. However, current available evidence is scarce, with several methodological limitations in the published studies. Disentangling the effect of AEDs from epilepsy itself and examining polytherapies that include new and old generation AEDs are challenges that merit additional investigations. Further comparative safety studies with longer follow-up periods and large sample sizes are needed to accurately quantify the true impact of new-generation AEDs exposure during pregnancy and ADHD.