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O0073

Pharmacovigilance analysis of the Vigibase on neonatal withdrawal syndrome following in utero exposure to antidepressants

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doi: 10.1192/j.eurpsy.2023.278

Introduction: Evidence on neonatal withdrawal syndrome following antidepressant intrauterine exposure is limited, particularly for antidepressants other than selective serotonin reuptake inhibitors (SSRIs).

Objectives: To ascertain whether maternal antidepressant treatment may be associated with withdrawal syndrome in neonates, investigating the comparative reporting between individual antidepressants and classes.

Methods: We performed a case/non-case pharmacovigilance study, searching reports of withdrawal syndrome in newborns in the Vigibase, the WHO database of suspected adverse drug reactions. Disproportionality analysis was performed, estimating reporting odds ratio (ROR) and the Bayesian information component (IC). Antidepressants were compared to all other medications, to methadone, and within each class of antidepressants (SSRIs, tricyclics (TCA) and other antidepressants). Antidepressants were ranked in terms of clinical priority, based on a semiquantitative score.

Results: We retrieved 406 reports of neonatal withdrawal syndrome in 379 neonates related to 15 antidepressants. Compared to all other drugs, disproportionate reporting was detected for antidepressants altogether (ROR: 6.18, 95%CI:5.45-7.01), for TCAs (10.55, 95%CI:8.02-13.88), other antidepressants (ROR: 5.90, 95%CI:4.74-7.36) and SSRIs (ROR: 4.68, 95%CI:4.04-5.42). All antidepressants showed a significant disproportionality, apart from bupropion (figure 1). We did not find any disproportionate reporting for any antidepressant compared to methadone. The clinical priority ranking showed moderate clinical priority for all antidepressants, with the exception four, that had a weak one (figure 1). Most frequently reported symptoms were respiratory symptoms

(n=106), irritability/agitation (n=75), tremor (n=52) and feeding problems (n=40).

Image:

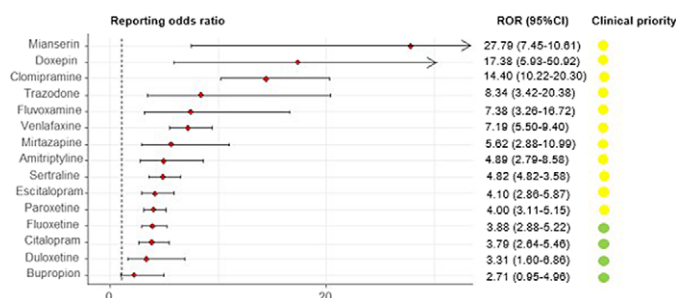


Figure 1. reporting odds ratios (RORs) with 95% Confidence intervals (95%CI) and clinical priority ranking. Yellow = moderate clinical priority; green = weak clinical priority

Conclusions: Exposure to antidepressants in utero is associated with moderate signals of disproportionate reporting for neonatal withdrawal syndrome for most antidepressants. Clinicians should pay extra attention to neonates with antidepressant-treated mothers.

Disclosure of Interest: C. Gastaldon: None Declared, E. Arzenton : None Declared, E. Raschi: None Declared, O. Spigset: None Declared, D. Papola: None Declared, G. Ostuzzi: None Declared, U. Moretti: None Declared, G. Trifirò Grant / Research support from: he was the scientific director of a Master program on pharmacovigilance, pharmacoepidemiology and real-world evidence which has received non-conditional grant from various pharmaceutical companies; he coordinated a pharmacoepidemiology team at the University of Messina until Oct 2020, which has received funding for conducting observational studies from various pharmaceutical companies (Boehringer Ingelheim, Daichi Sankyo, PTC Pharmaceuticals). He is also scientific coordinator of the academic spin-off "INSPIRE srl" which has received funding for conducting observational studies from contract research organizations (RTI Health Solutions, Pharmo Institute N.V.)., Consultant of: has served in the last three years on advisory boards/seminars funded by SANOFI, Eli Lilly, AstraZeneca, Abbvie, Servier, Mylan, Gilead, Amgen, Speakers bureau of: has served in the last three years on advisory boards/seminars funded by SANOFI, Eli Lilly, AstraZeneca, Abbvie, Servier, Mylan, Gilead, Amgen, C. Barbui: None Declared, G. Schoretsanitis Consultant of: Dr. Schoretsanitis has served as a consultant for HLS Therapeutics and Thermo Fisher Scientific.

Child and Adolescent Psychiatry

O0074

Claudin-5, occludin, zonulin and tricellulin levels of children with attention deficit/hyperactivity disorder

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doi: 10.1192/j.eurpsy.2023.279

Introduction: Accumulating studies have pointed out that gut-blood and blood-brain barrier dysfunctions due to the alterations in permeability may play a role in the pathophysiology of neurodevelopmental disorders. Tight junctions are crucial components of these barriers and some peptides including claudin-5, occludin, zonulin and tricellulin are important components of these structures.

Objectives: This study aimed to investigate the relationship between these molecules and attention deficit hyperactivity disorder (ADHD) in children and adolescents.

Methods: A total of 57 children with ADHD and 60 controls aged between 6 and 12 years were included in the study. The severity of ADHD symptoms was assessed through a parent-rated questionnaire and Conner's Continuous Performance Test. Serum levels of biochemical variables were measured using enzyme-linked immunosorbent assay kits.

Results: Serum claudin-5 and tricellulin levels were significantly lower in the ADHD group compared to the control group. The difference between the groups in terms of serum claudin-5 and tricellulin levels remained significant after controlling for confounding factors such as age, gender and autistic characteristics. There was no significant difference between the groups in terms of serum zonulin and occludin levels. (Table 1)

Table 2. Serum claudin-5, occludin, zonulin and tricellulin levels of ADHD and controls

	ADHD (n=57)	Controls (n=60)	Statistical Analysis	ANCOVA ^c p	F	p	η_p^2
	Mean \pm SD	Mean \pm SD	z/t				
Claudin-5 *(ng/mL)	2,14 \pm 0,71	2,47 \pm 0,71	-3,702	P< 0,001 ^a	10,196	0,002	0,083
Occludin *(ng/mL)	3,75 \pm 7,17	2,99 \pm 2,75	-0,136	p= 0,892 ^a	0,264	0,608	0,002
Zonulin *(ng/mL)	4,82 \pm 5,89	5,06 \pm 5,53	-0,076	p= 0,939 ^a	0,008	0,930	< 0,001
Tricellulin (ng/mL)	3,04 \pm 0,56	3,34 \pm 0,71	-2,552	p= 0,012 ^b	6,650	0,011	0,56

Conclusions: These results suggest that claudin-5 and tricellulin may be involved in the etiopathogenesis of ADHD. Alterations in these peptides may affect the brain by leading a dysregulation in intestinal or blood-brain barrier permeability that eventually affects the gut-brain axis. The causal relationship between these peptides and ADHD requires further investigation.

Disclosure of Interest: None Declared

O0075

Do children with ADHD symptoms become socially isolated? Longitudinal within-person associations in a nationally-representative cohort

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doi: 10.1192/j.eurpsy.2023.280

Introduction: Social isolation in childhood can be detrimental to physical and mental health. Children with neurodevelopmental disorders, such as attention deficit hyperactivity disorder (ADHD), may be particularly at risk for becoming socially isolated. Similarly, isolated children have limited opportunities to observe, model, and learn age-appropriate interpersonal interactions with other children which could increase ADHD behaviours.

Objectives: This study examined longitudinal associations between ADHD symptoms and social isolation across childhood. We tested the direction of this association across time, while accounting for pre-existing characteristics, and assessed whether this association varied by ADHD presentation, informant, sex, and socioeconomic status.

Methods: Participants included 2,232 children from the Environmental Risk (E-Risk) Longitudinal Twin Study. ADHD symptoms and social isolation were measured at ages 5, 7, 10, and 12. We used random-intercept cross-lagged panel models to assess the directionality of the association across childhood.

Results: Children with increased ADHD symptoms were consistently at increased risk of becoming socially isolated later in childhood, over and above stable characteristics ($\beta=0.05-0.08$). These longitudinal associations were not bidirectional; isolated children were not at risk of worsening ADHD symptoms later on. Children with a hyperactive ADHD presentation were more likely to become isolated, compared to an inattentive presentation. This was evident in the school setting, as observed by teachers, but not by mothers at home.

Conclusions: Our findings highlight the importance of enhancing peer social support and inclusion for children with ADHD, particularly in school settings. We add explanatory value over and above traditional longitudinal methods as our results represent how individual children change over time, relative to their own pre-existing characteristics.

Disclosure of Interest: None Declared

O0076

Effects of geography on risk for suicidal ideation and suicide attempts among commercially insured children and youth in the US

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doi: 10.1192/j.eurpsy.2023.281

Introduction: To study the effects of geography on risk for suicidal ideation and suicide attempts among commercially insured children and youth in the US

Effects of geography on risk for suicidal ideation and suicide attempts among commercially insured children and youth in the US