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The relationship between use of antipsychotics, anticonvulsants and other mood stabilisers in pregnancy and poor neonatal adaptation syndrome: A literature review

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Introduction

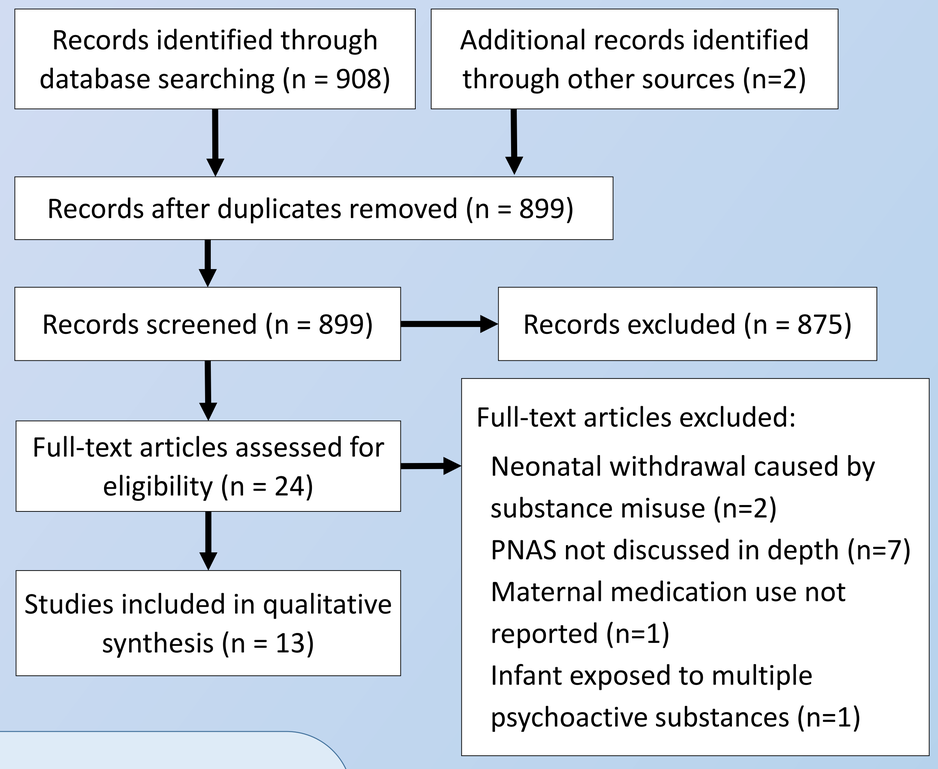
Psychotropic medications are commonly prescribed to women in the perinatal period to support maternal mental health; around 10-13% of foetuses are exposed to a psychotropic drug(1).

In-utero exposure to psychotropic drugs are associated with a risk of developing poor neonatal adaptation syndrome (PNAS) in the neonate, often presenting with neurological, autonomic, respiratory and gastro-intestinal symptoms(2). Although PNAS is generally self-limiting, there is a paucity of information regarding its management, including the optimal duration of the neonatal observation period, diagnostic tools, and treatment of symptomatic neonates.

Method

A literature search in line with the PRISMA guidelines was conducted in Cochrane, EMBASE, Medline and Web of Science databases. Studies reporting on neonates exposed to antipsychotics, anticonvulsants, and/or mood stabilisers for any duration of the pregnancy and assessed for PNAS were included. Studies published before 2010, or where there was in-utero exposure to illicit drugs or multiple psychotropic medicines were excluded. Articles were screened for eligibility as shown in Figure 1.

Fig.1 – Screening of literature



Results

Thirteen articles (seven case studies and six cohort studies) were included in the review, involving a total of 139,175 mothers and 139,163 infants.

The exposure of infants to multiple psychotropic medicines during pregnancy is common.
Five studies reported the exposure of infants to benzodiazepines, hypnotics, antidepressants (SSRI, SNRI, mirtazapine) in combination with antipsychotics, although the exact number of infants was unknown.

Incidence of PNAS in neonates:

- **366 (11%)** of 3,310 infants with in-utero exposure to psychotropic medications (antipsychotics, mood stabilisers, antiepileptic medications, alone or in combination with antidepressants)
- **1,564 (1.2%)** of 135,435 unexposed infants

Commonly reported symptoms of PNAS are presented in figure 2.
However, it was not possible to ascertain contributing factors leading to the development in PNAS in the control group, as data on other concurrent medications and physical health conditions were unavailable.

Fig. 2 - PNAS Symptoms reported

- Sneezing,
- Irritability, agitation
- Loose stools
- Breathing difficulties
- Feeding difficulties, regurgitation
- Sleepiness
- Jitteriness, tremor,
- Abnormal muscle movements
- Muscle hyper/ hypotonicity
- High-pitched cry
- Yawning

A total of **1,005 infants (30.3%)** exposed to antipsychotics, anticonvulsants and mood stabilisers, either alone or in combination with antidepressants, required specialist management in a neonatal unit.

However, due to the lack of data, and presentation of other birth complications, it was not possible to define the exact number of infants who were admitted to neonatal units solely for the management of PNAS, and the degree of intervention they required (e.g. postnatal observation period, supportive or medical management of PNAS).

Limitations of study

- There may be an overrepresentation of cases of PNAS due to reporting bias.
- The symptoms observed in neonates are not specific to PNAS and may be indicative of other neonatal complications. This highlights the importance of using validated assessment tools such as the Finnegan score to aid diagnosis.
- There is a lack of uniformity in the way clinicians approach the assessment and management of infants at risk of developing PNAS, including the neonatal observation period and use of validated assessment tools such as the Finnegan score.

Conclusion

In-utero exposure to psychotropic medication may be associated with increased risk of symptoms related to PNAS, amongst other complications, however our findings may have been skewed towards an overrepresentation of cases of PNAS due to reporting bias. This risk may be increased if the infant was exposed to more than one psychotropic medication.

It is not possible to conclude a direct relationship between individual psychotropic medications and PNAS, due to the lack of data on individual drugs, the use of psychotropic polytherapy and other concomitant medications in pregnancy. More research is required to establish optimal strategies to monitor and manage at-risk infants.

Raising awareness amongst maternity and neonatal team members on the importance of data capture within electronic health records can complement research studies with real world treatment patterns, compliance and outcomes across a diverse patient population.

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2. Kieviet N, Dolman KM, Honig A. The use of psychotropic medication during pregnancy: how about the newborn? Neuropsychiatr Dis Treat 2013;9:1257–66. https://doi.org/10.2147/NDT.S36394.