SOCIETÀ ITALIANA DI FARMACOLOGIA

RELAZIONE DI FINE PERIODO

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TIPOLOGIA DI BORSA RICEVUTA: Borsa di Studio SIF per l'estero

TIPOLOGIA DI RELAZIONE: fine periodo

TITOLO DELLA RELAZIONE: Behavioural teratogenicity of psychotropic drugs: a study of the Francophone Mother-Baby Units database

RELAZIONE:

Introduction. Women with severe mental disorders may not discontinue their treatments during preganacy because of the high risk of relapse [1]. Over the last decades, a large body of literature has been focused on the risk of birth defects and poor neonatal outcome related to fetal exposure to psychotropic drugs, whereas studies investigating the neurobehavioural development of babies with prenatal exposition to those drugs remain extremely limited.

In the present study we evaluated the develompent of babies jointly hospitalized with their mothers in psychiatric Mother-Baby Units (UMBs), by using weekly and interaction-focused evaluations which permit to collect more detailed informations compared to the classic and more global develomental scales.

The aim of the present investigation was to explore the independent impact of prenatal exposure to psychotropic drugs (antipsychotics, antidepressants, mood stabilizers, anxiolytics-hypnotics) on infant interactive skills from birth to 6 months of age.

Methods. We used data on maternal demographic and clinical characteristics, prenatal exposure to psychotropic drugs and neonatal outcome collected in the database of the MBUs of the Francophone Network between 2001 and 2007. All data stored in this database were collected by using the French version of the Marcé Clinical Checklist [2], which is a standardized tool originally developed in the United

Kingdom in order to promote multi-site research among MBUs. Infant interactive patterns were assessed using the 0-1 month and 2-6 months Bobigny scales, which are usually rated weekly during the hospital stay by nurses [3]. These scales assess the 3 following dimentions: physical interactions, visual interactions and vocal interactions; the 2-6 month scale further assesses facial interactions as this dimension cannot be reliably assessed in younger babies. For each dimension, a total score was calculated by adding the individual items scores; this total score was subsequently categorized for each interactive dimension according to the distribution in the sample. Two independent samples of mother-baby dyads were distinguished according to the age of the baby at the time of mother-baby interaction assessment with Bobigny scales. All procedures were in accordance with the standards of the French National Data Protection Authority.

Logistic Generalized Estimating Equation (GEE) regression models giving odds ratios (ORs) and 95% confidence intervals (CIs) were used to explore the independent associations between prenatal exposure to psychotropic drugs and Bobigny scales scores in the two samples of babies. The same modeling strategy was used for each interactive dimension of the Bobigny scales and all models were a priori adjusted for the following maternal variables: presence of partner, educational level, parity, ICD-10 psychiatric maternal diagnoses categorized into (i) mood disorders: bipolar affective disorders and depressive disorders, (ii) psychotic disorders: schizophrenia, schizoaffective disorders, and other nonaffective psychotic disorders, and (iii) other disorders (substance use, personality disorders, and anxiety disorders), exposure to tobacco during pregnancy. The models were also adjusted for the following infant variables: prematurity and sex of the baby. For the scale 2-6 months, duration of hospitalization of the mother in the MBU was also adjusted for as a proxy of severity of maternal psychiatric disorder. Statistical analyses were carried out using SAS® 9.4.

Results. Of the 92 babies asssessed with the 0-1 month Bobigny scale, more than half were exposed to antipsychotics during pregnancy; nearly one out of 10 babies were exposed to antidepressants, whereas exposure to mood stabilizers was less frequent (17%). Nearly half of babies were exposed to anxiolytics-hypnotics with a majority (79.5%) exposed to benzodiazepines. Nearly all babies (93.5%) were exposed to more than one psychotropic medication, the most frequent combination was exposure to antipsychotics and anxiolytics (33.3%). Of the 225 babies assessed with 2-6 months scale, exposure to antipsychotics was found in 30.7% of cases; 16.0% of babies were exposed to antidepressants. Less then one out of ten baby was exposed to mood stabilizers; babies exposed to anxiolytics-hypnotics were mainly (93%) exposed to benzodiazepines. The majority of babies were exposed to a single psychotropic medication (54.7%).

Among babies assessed with the 0-1 month scale, those prenatally exposed to lithium were five times more likely to have better visual interactions compared to those without (adjusted Odds Ratio (aOR)=0.18,

95%CI=0.04-0.85). No association was found between exposure to the other psychotropic drugs and infant interactive patterns in the first month of age.

Among babies assessed with the 2-6 months scale, exposure to antidepressants was associated with poorer visual (aOR=2.60, 95%CI=1.10-6.12) and facial interactions (aOR=2.86, 95%CI=1.43-5.69). No association was found between exposure to the other psychotropic drugs and babies' interactions in this sample.

Conclusions. We found no major impairment in developmental skills of babies exposed to psychotropic drugs; however, the alteration we detected in babies' interactions after exposition to antidepressants need to be further investigated. A number of publications recently suggested a link between prenatal exposition to antidepressants and risk of autism spectrum disorders [4]; moreover, a warning call on the risk of neurodevelopmental impairment for antidepressants exposure was recently published by the French National Health and Medicines Agency [5] and safety procedures were undertaken by the Pharmacovigilance Division of the European Medicines Agency [6] on this topic.

References

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