**EDITORIAL**

# Neurotropic Drugs in Pregnancy and Lactation from the Point of View of the Clinical Teratologist

Generally, most drugs ingested by the pregnant mother cross the placental barrier and reach the developing embryo and fetus. Hence, drugs taken in pregnancy for maternal treatment may affect the course of pregnancy as well the embryo. While most drugs are not teratogenic, those that have the potential to cause damage to the developing conceptus may, in most severe cases cause fetal death or abortions, or interfere with the normal development of single or multiple organs causing congenital malformations. Sometimes these drugs only interfere with fetal growth causing intrauterine growth retardation or induce premature birth and increased rate of perinatal complications [1, 2]. Neurotropic drugs may affect the embryonic and fetal developing brain causing various degrees of neurodevelopmental, neuropsychiatric or neurological disorders. This area of neuroteratology has been expanding over the three decades with the introduction of animal models and epidemiological human studies [3]. Lately exposure to environmental agents during pregnancy are considered by many investigators to be an important contributor to the increased rate of autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD) as well as psychiatric diseases [4, 5]. The teratogenic or neuroteratogenic effects of most drugs are dose and time dependent.

Drugs taken by the nursing mother may appear in the milk, possibly affecting the nursing infant. These effects depend on the type of the drug, dosage, its elimination half - life and on the amount secreted in the milk [6].

The reviews in this mini-thematic selection of papers discuss the possible effects of drugs used for the treatment of ADHD and of antiepileptic drugs. The authors summarize the data related to the possible teratogenic and neurodevelopmental effects of these drugs and the possible effects on the nursing infant if taken by the nursing mother. These neurotropic drugs are generally used daily due to the underlying maternal illness.

In the review by Ornoy and Koren [7] the authors first discuss the effects of stimulants: methylphenidate and amphetamines, which are the first line drugs for this disorder, and then all other non- stimulant drugs. Methylphenidate and amphetamines do not seem to be teratogenic, but there is insufficient data including lack of data related to possible neurodevelopmental effects. As for non-stimulant drugs (atomoxetine, clonidine, guanfacine) there are very little data and it is therefore preferable not to use them. As for bupropion there are more reassuring data from studies on its use for other indications. There are very few data on neurodevelopmental outcome except for amphetamines following recreational use. There are some data on breastfeeding and nursing following the use of amphetamines which suggests them to be contraindicated. Due to the general paucity of data it is advised not to use ADHD medication during pregnancy. If treatment is needed, methylphenidate seems to be the preferred drug, as it is to continue breast feeding

The review by Bromley and Bluet-Duncan [8] summarizes the data related to long-term neurodevelopment of children exposed in utero to various antiepileptic drugs (AEDs). Of the AEDs valproic acid seems to be definitely associated with a significant increase in neurodevelopmental problems among the offspring, including language impairment, reduced cognitive abilities and increased rate of ASD. As for the other AEDs, there is limited evidence for possible neurodevelopmental problems. Carbamazepine and phenobarbital seem to be associated with postnatal neurodevelopmental problems, as apparently does phenytoin. There are limited data for the newer antiepileptic drugs such as lamotrigine, levetiracetam and oxcarbazepine.

In the review by Kaplan and Demir [9], the authors discuss the possible effects of phenytoin, phenobarbital, carbamazepine and valproic acid as well as of the newer AEDs levetiracetam and lamotrigine on embryonic and fetal development. They describe the organ specific teratogenic effects of the “older”, classical, AEDs as opposed to the newer ones. Generally, there is a 2-3 - fold increase in congenital malformations following the use of these AEDs, with valproic acid apparently being the most teratogenic of these drugs. On the other hand, lamotrigine and levetiracetam do not seem to be significant teratogens. The authors also discuss issues such as dose response effects, polytherapy versus monotherapy and the use of the newer AEDs over the elder, classical ones. The authors suggest to use, whenever possible, the newer AEDs – lamotrigine and levetiracetam as they do not seem to be teratogenic. They also conclude that women treated with AEDs may nurse their infants, except those treated with lamotrigine as lamotrigine appears in high concentrations in the milk.

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