ARE SOME ANTIEPILEPTIC DRUGS PREFERRED DURING PREGNANCY? – NO

Ettore Beghi
Istituto di ricerche Farmacologiche Mario negri, Milano, Italy

The treatment decisions in women with epilepsy during pregnancy imply a compromise between maternal and fetal risks associated with uncontrolled seizures and the adverse effects of drugs on the newborn, including teratogenesis and neurodevelopmental delay. Seizures may be harmful during pregnancy both to the mother and the fetus and prompt adequate control with antiepileptic drugs to prevent morbidity and even mortality (AEDs). However, there is no evidence in the literature to inform drug choice and eventual changes because there are no randomized trials of the comparative efficacy, safety and tolerability of AEDs during pregnancy. Pregnancy is associated with several pharmacokinetic alterations leading to a decrease of plasma levels of most AEDs. However, variations of drug plasma levels and other aspects of the pharmacokinetic profile are not sufficient to suggest treatment changes. Although infants exposed to antiepileptic drugs (AEDs) *in utero* present an increased risk of malformations, and valproate is the drug with the highest teratogenic risk, data from the EURAP registry suggest that, at a daily dose of 600mg or lower, the teratogenicity of the drug is comparable to that of phenobarbital given at less than 150mg/day and carbamazepine between 400mg/day and 1000mg/day. Intrauterine exposure to valproate has been considered of major concern because of the purported effects of the drug on brain development. However, published reports on valproate (and other AEDs) present serious methodological flaws which complicate any attempt to correlate intra-uterine exposure to AEDs with neurodevelopmental delay. For these reasons, there is no drug to be preferred *a priori* during pregnancy. The choice of the drug should be tailored to the individual patient keeping into account epilepsy syndrome, the severity of the disease, and the safety and teratogenetic profile of each drug.

***References**:*

1. Battino D & Tomson T. management of epilepsy during pregnancy. Drugs 2007;67:2727-46; 2. Nicolai J et al. Neurodevelopmental delay in children exposed to antiepileptic drugs in utero: A critical review directed at structural study-bias. J neurol Sci 2008;271:1-14; Tomson T et al. Dose-dependent risk of malformations with antiepileptic drugs: an analysis of data from the EURAP epilepsy and pregnancy registry. Lancet Neurol 2011;10:609-17; 4; Tomson T & Battino D. Teratogenic effects of antiepileptic drugs. Lancet Neurol 2012;11:803-13.