Editorial
Άρθρο σύνταξης

Psychotropic medication in pregnancy: The cost-benefit ratio revised

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The use of drugs during pregnancy and breast-feeding is a long-lasting debate among scientists. Many of them support the view that the risks are minimal, since the anomalies in fetuses due to chemical compounds are approximately 1%,[1] while others argue that the effects of drug delivery in this special period of life has largely unknown delayed consequences.[2] In clinical practice the dilemma is to prescribe or not to prescribe a drug during pregnancy.

Recent scientific data indicate direct adverse effects due to the state of the mental health of the mother to the fetus and, possibly, an increased risk of developing serious mental disorders in children whose mothers did not receive medication during pregnancy.[3] Given the uncertainty of the data, the optimal way of managing the problem is to educate the clinicians regarding available research data, to develop an individualized risk-benefit analysis, and finally to inform the mother and, where feasible, the father.

Currently, the choice is based on a five category classification A, B, C, D and X. Regulatory authorities such as the EMA, FDA, etc. have established the five categories to indicate the potential of a drug to cause birth defects if used during pregnancy. The categories are determined by the reliability of documentation and the risk to benefit ratio. They do not take into account any risks from pharmaceutical agents or their metabolites in breast milk. An extra category N has been adopted where there are no data available.

In reality this classification has certain limitations. For example we have two antipsychotic drugs. The first drug is classified as B and the second one as C. How certain is that the first is safest than the second one? The answer is we don't really know. A drug with studies in animals and reports in humans can be classified in category C, while another drug just because it has limited studies or use, which did not show relevant problems, can be classified in category B and then after data accumulation can be re-classified as C or D.

In general, summarized data for all the categories of the psychotropics do not show significant teratogenic effects. There are cautions for tricyclic antidepressants, some anticonvulsant and lithium (until completion of the organogenesis of the heart).[4,5] The administration of psychotropic drugs during breast-feeding is clearly more restrictive, due to the potential toxicity in the newborn and the infant, and the existence of the safer alternative of the human-like milk. Furthermore, a drug is rarely falls within the exclusion category (x) without figures to support this restriction.

In practice a lot of information is collected from the traditional pregnancy registries, i.e. prospect observational studies, which monitor pregnant women from the time of entry in the registry until a short time after birth and detect major teratogenic incidents. These registries have significant limitations, such as small samples, inability to control the population, and limited follow-up. The presence of confounders such as tobacco use, alcohol consumption, and folic acid prescription during pregnancy can complicate the interpretation of the results.

The traditional classification of the five categories is simplistic and often confuses over the complexity and ambiguity of the final choice. The limitations have led to the development of alternative methods for the assessment of the risk of medication use in pregnant women. The broader cooperation of regulatory authorities worldwide is fundamental. Since December 2014, FDA published the New Pregnancy and Lactation Labelling Rule (PLLR),[6] which has already been implemented for all new drugs by June 30, 2015, and gradually retroactively for drugs that have been licensed from 2001 and beyond. The new classification is based, like the previous one, in the traditional pregnancy registries, but also in the design of larger cohort studies, databases

of civil claims of persons who have suffered damage, and the wider cooperation of the parties involved (regulatory agencies, scientists, users etc.). Finally this new PLLR forms a new parameter, which relates to the effect of drugs on the females and males reproductive potential.

The landscape in the use of drugs in pregnancy is significantly altered after the accumulation of research. Data show that the risks from the use of drugs in pregnancy and lactation are probably overestimated, while the various diseases and conditions may have multiple adverse effects both on mothers and children.[3,7] The administration of any psychotropic drug during pregnancy is based on an integrated risk assessment plan. Parents are required to have an active role in the final decision, helped by a clear and comprehensive cost-benefit analysis from their physicians.

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