PT705
Therapeutic Drug Monitoring (TDM) in maternal serum, amniotic fluid and umbilical cord blood during pregnancy and delivery

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Abstract

Introduction: Treatment of psychiatric diseases during pregnancy is complicated by the concern for the safety of the unborn child because all psychotropic medications more or less cross the placenta. Fetal outcome is influenced by various factors and - among others - the effects of a specific drug itself depend on the concentration in maternal and fetal serum as well as on its concentration in amniotic fluid.

Method: The present study is a naturalistic prospective investigation of different psychotropic drug concentrations in maternal serum (MS) and amniotic fluid (AF) of 14 women and umbilical cord blood (UC) of nine newborns. The women were treated with different doses of psychotropic drugs such as antidepressants, antipsychotics, anticonvulsants and others.

Results: Patients received thirteen different psychotropic drugs. Results are available for five antidepressants (citalopram, paroxetine, sertraline, fluoxetine and venlafaxine), 3 anticonvulsants (valproic acid, levetiracetam, lamotrigine), 2 benzodiazepines (diazepam, clobazam), as well as for olanzapine, methadone and methylphenidate. Concentrations of different psychotropic drugs were found in maternal plasma, amniotic fluid and umbilical cord blood in highly variable concentrations suggesting that fetal exposure is continual and may occur through a variety of paths accounting for increased fetal exposure.

Conclusion: The preliminary data of this ongoing study highlight the penetration of different psychotropic drugs into the amniotic fluid as another way of fetal exposure. Of particular interest in this context is the observation that the well known teratogenic valproic acid does not accumulate in AF in approximately the same way as other anticonvulsants do, however valproic acid has the highest penetration ratio into umbilical cord blood with potentially negative effects on the offspring. Understanding the current data and their limitations will allow providers to guide their patients in choosing treatment options. Consistent and simple strategies should be used when discussing the risk-benefit analysis with the patient.

PT707
Transcriptome analysis in Tsc2 heterozygous knockout mice

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Abstract

Tuberous sclerosis complex (TSC) is an inherited autosomal dominant disorder caused by mutations in either TSC1 or TSC2. TSC patients display severe neurological symptoms such as epilepsy and autism spectrum disorder (ASD). We previously reported that Tsc2 heterozygous knockout (Tsc2+/−) mice exhibited ASD-like social impairment which were improved by mTOR inhibitor administration. In the present study, whole-genome gene expressions were analyzed in the Tsc2+/− brains for elucidating the molecular mechanism of ASD.

Total RNAs were prepared from whole brains of male Tsc2+/− and wild-type mice administrated with rapamycin or saline. Whole-genome expression assay was performed using Illumina MouseRef-8 Expression BeadChips. The list of candidate transcripts obtained from the whole-genome expression assay was subjected to gene ontology analysis with MetaCore.