Pharmacogenetic testing for CYP2D6 and CYP2C19: Can it offer guidance for pregnant women taking SSRIs?

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Clinical Problem

- Depression affects 10-15% of pregnant women.
- Guidelines recommend supporting women to make an informed treatment decision based on the (≈equal) risks of antidepressants versus untreated depression in pregnancy.
- how to modify SSRI prescribing when pharmacogenetic test results for CYP2D6 and CYP2C19 are available.

BUT

- Pharmacogenetic guidelines were based on research in non-pregnant cohorts.

Research Question & Hypothesis

Research question:
For women taking selective serotonin reuptake inhibitors (SSRIs) during pregnancy, do scores measuring depression symptoms differ significantly depending on which variations they have in the genes CYP2D6 and/or CYP2C19?

Hypothesis:
Women with deleterious variants in the genes CYP2D6 or CYP2C19, taking SSRIs prenatally, would have more depression symptoms than women whose genetic variants have been associated with normal SSRI metabolism

Methods

Secondary analyses of two longitudinal cohort studies including women taking SSRIs (N=83)
- Included participants for whom DNA and depression score (Edinburgh Postnatal Depression Scale) were available

Analysis
- Comprehensive CYP2D6 and CYP2C19 genotyping, include copy number variation
- Variant classification
- Statistical hypothesis testing using the Kruskal-Wallis Test

Not yet.

Findings from this study do not support the use of pharmacogenetic testing (of CYP2D6 and/or CYP2C19) to guide SSRI prescribing during pregnancy.

Results

- Age: M=31.69 years (SD=5.41)
- Highly educated (M=15.91 years of education; SD=2.96).

Discussion

Possible explanations for our finding:
1. These enzymes function differently in pregnancy, thus our metabolizer predictions (based on evidence in non-pregnant cohorts) were inappropriate for these pregnant samples.
2. Our metabolizer predictions were invalid because they couldn’t account for the influence of both genes (or any other genes in the SSRI metabolic pathways). Currently, there are no holistic prediction algorithms for pharmacogenetic test results applied to SSRI prescribing (even outside the context of pregnancy).

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