DOSE NORMALIZED PLASMA CONCENTRATIONS OF SERTRALINE AND N-DESMETHYLSERTRALINE THROUGHOUT PREGNANCY AND POSTPARTUM

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INTRODUCTION
Depression impacts 10 to 20% of individuals during pregnancy and postpartum [1], and 6-8% of pregnant individuals receive a prescription for a selective serotonin uptake inhibitor (SSRI). Sertraline, the most commonly prescribed SSRI during pregnancy [2], is extensively metabolized to N-desmethylsertraline (DMS) which contributes 5-10% of the pharmacological effect [3]. Changes in physiology during pregnancy can result in significant changes in drug exposure that can lead to unpredictable changes in response [4]. In order to effectively treat pregnant individuals with depression and balance maternal health against the possibility of obstetrical and neonatal adverse outcomes, one must be able to anticipate needed dose changes.

OBJECTIVE
Our objective was to characterize changes in sertraline and N-desmethylsertraline concentrations throughout pregnancy and postpartum in individuals with depression collected in the Women’s Mental Health Program (WMHP) biorepository.

METHODS

- Prospectively collected data (WMHP) from an observational clinical study (1992 – 2011)
- Inclusion criteria: (1) 16 – 46 years; (2) diagnosed with depression; (3) on a stable dose of sertraline before sampling ≥ 7 days; (4) planning pregnancy, or < 16 weeks gestation.
- Exclusion criteria: (1) non-verified maternal daily dose (mg/day); (2) dose prior to sampling > 36 hours, or missing/not clinically interpretable data (i.e., < 0 hours).
- Medication adherence was assessed via self-report and recorded weekly via interview with study personnel.
- Enrolled patients were followed at 4-8 week intervals during pregnancy, delivery, and throughout 12 months postpartum (Figure 1).
- Differences in sertraline and DMS dose normalized concentrations (DNC) throughout pregnancy and postpartum were characterized using a repeated measures ANOVA with Tukey’s post-hoc test (p<0.05).
- Analysis was performed using R Software (v.3.5.2).

RESULTS

Table 1. Distribution of pregnancies and serum concentrations across pre-pregnancy, pregnancy and postpartum. *Median (range)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-preg</th>
<th>1st Trimester</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
<th>Delivery</th>
<th>Early PP</th>
<th>Late PP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (weeks)*</td>
<td>38.7 (29 – 43)</td>
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<td></td>
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<tr>
<td>Maternal age (years)*</td>
<td>34.1 (18.7 – 46.8)</td>
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<td></td>
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<td></td>
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<tr>
<td>Pregnancies (n)</td>
<td>24</td>
<td>81</td>
<td>132</td>
<td>129</td>
<td>133</td>
<td>106</td>
<td>60</td>
</tr>
<tr>
<td>Sertraline/DMS concentrations (n)</td>
<td>36</td>
<td>134</td>
<td>281</td>
<td>229</td>
<td>134</td>
<td>147</td>
<td>126</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- A total of 219 individuals (243 pregnancies) were included in the analysis. (Table 1)
- Median sertraline daily dose used was 100 mg (range 12.5 – 300).
- There were no differences in the reported time after dose at any time point (p<0.0592).
- Sertraline DNC were significantly lower at delivery compared to pre-conception (p<0.01), and between delivery and all other periods (i.e., 1st, 2nd, 3rd, early and late postpartum) (p<0.0001) (Figure 2).
- There was some evidence that DMS differed by period (overall p<0.012), but after adjusting for multiple comparisons no pairwise differences between periods were statistically significant (all p>0.05) (Figure 2).

Figure 2. Sertraline (red) and N-desmethylsertraline (blue) dose-normalized concentrations (DNC) (geometric mean with 95% confidence interval) by pregnancy period *p<0.01, **p<0.001 comparing to the delivery time point.

REFERENCES