Serum Sertraline and N-Desmethylsertraline Levels in Breast-Feeding Mother-Infant Pairs

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Objective: The authors' goal was to study the serum sertraline levels of breast-feeding mothers and their infants. Method: They obtained serum levels of sertraline and N-desmethylsertraline in nine mother-infant pairs. Results: Sertraline levels were very low (less than 2 ng/ml) in seven of the nine infants and low (3 ng/ml) in one. N-Desmethylsertraline levels were also low (6 ng/ml or less) in seven of the nine infants. One infant had a high level of N-desmethylsertraline, and one infant had unusual serum sertraline and N-desmethylsertraline values (half of its mother's levels). All infants were thriving. Conclusions: Most breast-feeding infants whose mothers were taking sertraline had very low serum levels of both sertraline and N-desmethylsertraline, consistent with published reports. The authors discuss in detail the one infant with unusually high levels.

(Am J Psychiatry 1998; 155:690–692)
TABLE 1. Serum Concentrations of Sertraline and N-Desmethylsertraline in Nine Pairs of Nursing Mothers and Infants

<table>
<thead>
<tr>
<th>Case</th>
<th>Infant’s Age (weeks)</th>
<th>Infant’s Sex</th>
<th>Infant’s Weight (lb, oz)</th>
<th>Maternal Dose of Sertraline (mg/day)</th>
<th>Number of Days Dose Was Given</th>
<th>Maternal Serum Level (ng/ml)</th>
<th>Infant Serum Level (ng/ml)</th>
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</thead>
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<tr>
<td>1</td>
<td>22</td>
<td>F</td>
<td>6,10</td>
<td>100</td>
<td>2</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>M</td>
<td>7,03</td>
<td>100</td>
<td>7</td>
<td>60</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>M</td>
<td>7,11</td>
<td>100</td>
<td>4</td>
<td>62</td>
<td>96</td>
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<td>5</td>
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<td>5</td>
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<tr>
<td>5</td>
<td>15</td>
<td>M</td>
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<td>M</td>
<td>6,10</td>
<td>100</td>
<td>2</td>
<td>117</td>
<td>114</td>
</tr>
</tbody>
</table>

**a**At serum sampling.  
**b**<2 denotes that the serum concentration was below the limit of quantifiability; 0 denotes that it was not detectable.

DISCUSSION

The sertraline levels of eight out of nine breast-fed infants whose mothers were taking sertraline were very low. Our study of nurslings revealed nonquantifiable levels (less than 2 ng/ml) in seven of nine infants and a very low level (3 ng/ml) in one. These data are consistent with those of Mammen et al. (3), Epperson et al. (4), and Stowe et al. (5), who found sertraline levels below 2 ng/ml, 2.5 ng/ml, and 3 ng/ml or less, respectively, in nursing infants.

N-Desmethylsertraline was found in most of our nurslings. Trace amounts (2–6 ng/ml) were found in the sera of five of nine infants, and a substantial amount (24 ng/ml) was found in a sixth. The mothers of these infants typically had the highest serum levels in the series, particularly of N-desmethylsertraline. The infant with the N-desmethylsertraline level of 24 ng/ml had the mother with the highest sertraline dose and N-desmethylsertraline serum level. Mammen et al. (3) and Epperson et al. (4) found infant serum levels of N-desmethylsertraline below 2 and 5 ng/ml, respectively. However, the maximum dose used by these investigators was 100 mg/day of sertraline. Four of our mothers required doses greater than 100 mg/day for response, which accounts for our higher levels.

Our N-desmethylsertraline findings are similar to those of Stowe et al. (5), who found that nine of 11 infants had detectable N-desmethylsertraline levels of 10 ng/ml or less. However, N-desmethylsertraline does not contribute to antidepressant activity in behavioral models. In vitro data suggest that N-desmethylsertraline has about one-eighth of the serotonin reuptake blockade potency of sertraline (6).

We evaluated our final case carefully because the infant’s N-desmethylsertraline levels were unusual in that they were half the values for its mother. We checked the values twice. The infant was clinically thriving before blood was drawn. We considered several questions.

Could the infant develop this level with the dose delivered in breast milk? We can draw inferences about our case from data provided by Altshuler et al. (2) for sertraline breast milk concentrations. Their case
mother was the same age as our mother and took the same sertraline dose (100 mg/day). Our case mother had her serum level drawn 2 hours after receiving sertraline. According to Altshuler’s data, the breast milk concentration 2 hours after dose administration is about half that at 5 hours, when peak breast milk concentration occurs. If we assume that our case mother’s concentration at 2 hours after dose administration was half the maximal concentration achieved and double it, our infant received $2 \times 117 \text{ ng/ml}$, or $234 \text{ ng/ml}$ of sertraline in breast milk. If we assume that sertraline is fully unbound, which is unlikely, we can conclude that the baby received a maximum of $0.234 \text{ mg/day}$ of sertraline (and probably N-desmethylsertraline) if 1000 ml/day of breast milk was consumed. This very low oral dose makes the development of infant serum levels similar to those of directly treated mothers exceedingly unlikely.

Was there another source of sertraline? We wondered if this mother gave the infant sertraline. We were unable to contact her after the serum levels were drawn. Sur-reptitious administration of antidepressant to an infant has been described (8).

Might there be another source of error? The serum is hand-pipetted and sent frozen for analysis. We cannot completely rule out processing contamination.

We believe that this infant’s serum level was a spurious finding. The 18 published cases (3–5) plus our eight cases add up to 26 cases of low serum levels of sertraline and N-desmethylsertraline in infants, which supports our contention that our final case is highly atypical.

In our opinion, sertraline use during breast-feeding is acceptable; however, a safe level of exposure to any agent is difficult to establish. Although these infants were thriving, chronic exposure to very low doses of antidepressants could affect infant neurodevelopment, which has not been systematically studied.

REFERENCES