A Retrospective Analysis of Fentanyl-Positive Detection in Meconium

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BACKGROUND

- Opioid abuse among pregnant women is on the rise, with the national prevalence of opioid use disorder increasing from 1.5 per 1,000 delivery hospitalizations in 1999 to 6.5 in 2014.¹
- In utero opioid exposure can lead to serious adverse neonatal outcomes, including neonatal abstinence syndrome (NAS).
- Recently, fentanyl has been recognized as the leading drug responsible for rapid increases in overdose death in the United States.
- During labor and delivery, fentanyl is routinely administered in the epidural as an analgesic. Therefore, it can be difficult to differentiate analgesic use from maternal abuse when fentanyl is detected in meconium.

OBJECTIVE

This study aims to describe the fentanyl detection rate in meconium drug testing, compare it with urine, and correlate it with relevant negative clinical outcomes.

METHODS

- We retrospectively analyzed our laboratory database of 766 positive meconium drug testing conducted between July 2017-Dec 2019.
- The database contains results for positive meconium drug testing, corresponding urine drug testing results from mother and baby, prescribed medications, and drug abuse history (Figure 1).
- Based upon medication and drug abuse history, the patients with fentanyl detected in their meconium drug testing were divided into two groups:
  - (1) non-abuse group- identified fentanyl prescription(s) and no history of abuse
  - (2) abuse group – a current detection or history of fentanyl abuse.
- Relevant clinical information was acquired through manual chart review.
- Both meconium and urine drug testing were performed by quantitative LC-MS/MS assays.
- Statistic data analysis was performed using R software (version 3.6.2).

RESULTS

- Fentanyl was detected in 79 out of 766 positive meconium specimens.
  - Of these 79, 44 (55%) were in the non-abuse group and 35 (44 %) were in the abuse group.
  - The abuse group displayed significantly higher concentrations (fentanyl: mean 63 ng/g, n=35, norfentanyl: mean 136 ng/g, n=27) than those in the non-abuse group (fentanyl: mean 17 ng/g, n=41, norfentanyl: 32 ng/g, n=16). (See Figure 2)
  - The positive detection rate by parent drug fentanyl, metabolite norfentanyl were compared between meconium and urine. Results were listed in Table 2.
  - The ratio of fentanyl/norfentanyl in meconium was compared with that in urine. The ratio in meconium is much higher (mean 1.23, n=40) than that in urine (mean 0.48, n=19). (See Figure 3)
  - The relevant clinical outcomes including gestational age, birth weight and length of hospital stay of all 79 patients were listed in Table 1.
  - In all 79 cases, NAS was diagnosed in 37 cases, among which 67% (24) was in the abuse group.
  - In the 37 patients diagnosed with NAS, fentanyl concentration in the meconium was associated with clinical severity indicated by its correlation with the length of hospital stay. (See Figure 4)

FIGURES AND TABLES

- Figure 1. Example of Meconium Drug Testing Database.
- Figure 2. Distribution of Fentanyl and Norfentanyl Concentration in Meconium. The boxplot displays the comparison of fentanyl and norfentanyl distribution in two groups (*P value<0.01). (For visual purposes, the boxplot has 4 outliers removed for fentanyl, 1 outlier removed for norfentanyl).
- Figure 3. Ratio of Fentanyl/Norfentanyl in Meconium vs. Urine. The ratio of fentanyl/norfentanyl in meconium is much higher than that in urine. (For visual purposes, the boxplot has 4 outliers removed for meconium, 2 outliers removed for urine).
- Figure 4. Correlation of Fentanyl Concentration in Meconium with Length of Stay in NAS Patients (n=37). For these patients, the fentanyl concentration in the meconium was correlated with clinical severity indicated by length of hospital stay.

<table>
<thead>
<tr>
<th>Positive detection rate</th>
<th>Urine</th>
<th>Meconium</th>
</tr>
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<tbody>
<tr>
<td>65% (47/72)</td>
<td>100% (79/79)</td>
<td></td>
</tr>
<tr>
<td>Detection by fentanyl only</td>
<td>13% (6/47)</td>
<td>46% (36/79)</td>
</tr>
<tr>
<td>Detection by norfentanyl only</td>
<td>45% (21/47)</td>
<td>4% (3/79)</td>
</tr>
</tbody>
</table>

Table 1. Relevant Clinical Outcomes of Fentanyl-Positive Patients.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational Age (weeks)</td>
<td>25</td>
<td>42</td>
<td>36</td>
<td>37</td>
</tr>
<tr>
<td>Length of Stay (hours)</td>
<td>1</td>
<td>2348</td>
<td>438</td>
<td>348</td>
</tr>
<tr>
<td>Weight (grams)</td>
<td>0</td>
<td>3860</td>
<td>2597</td>
<td>2595</td>
</tr>
</tbody>
</table>

Table 2. In meconium, the positive detection rate of fentanyl alone is 46% (36 out 79), and of norfentanyl alone is 4% (3 out of 79). In contrast, in urine the detection rate is 13% (6 out of 47) and 45% (21 out of 47) for fentanyl and norfentanyl respectively.

CONCLUSIONS AND SIGNIFICANCE

- Among patients with positive screens for fentanyl in meconium, more patients had measurable parent drug compared to higher detection fentanyl metabolite in corresponding urine drug screens.
- Fentanyl detection in meconium is common, and its concentrations correlates with poor outcomes for infants.
- To our knowledge, this is the first time fentanyl incidence in meconium and its correlation with clinical outcomes have been reported.

REFERENCES