Observations on the Urine Metabolic Ratio of Oxymorphone to Oxycodone in Pain Patients

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Oxycodone Metabolism

metabolic ratio = $\frac{\text{oxymorphone mg/g creatinine}}{\text{oxycodone mg/g creatinine}}$
Glucuronidation of Oxycodone and Oxymorphone

### Percent Glucuronidated Oxycodone and Oxymorphone from 115 Subjects

<table>
<thead>
<tr>
<th></th>
<th>Oxycodone</th>
<th>Oxymorphone (oxycodone use)</th>
<th>Oxymorphone (oxymorphone use)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td>3.05</td>
<td>93.16</td>
<td>99.11</td>
</tr>
<tr>
<td><strong>Median</strong></td>
<td>4.49</td>
<td>97.32</td>
<td>100.00</td>
</tr>
<tr>
<td><strong>Skewness</strong></td>
<td>−1.68</td>
<td>−4.33</td>
<td>−1.97</td>
</tr>
<tr>
<td><strong>75th percentile</strong></td>
<td>10.83</td>
<td>100.00</td>
<td>100.00</td>
</tr>
<tr>
<td><strong>25th percentile</strong></td>
<td>−3.59</td>
<td>94.70</td>
<td>98.77</td>
</tr>
<tr>
<td><strong>Standard deviation</strong></td>
<td>12.92</td>
<td>16.97</td>
<td>1.65</td>
</tr>
</tbody>
</table>
Sample Selection

235,634 samples from routine clinical testing with creatinine levels higher than 20mg/dL

Selected for samples with reported use of oxycodone but not oxymorphone

68,834 samples that have reported oxycodone use
49,176 samples above lower limit of quantitation (28.8% non-consistent)

Selected samples reporting oxymorphone use but not oxycodone

1,607 subjects representing oxymorphone use

32,563 subjects representing oxycodone use

Used the first sample from subjects with more than one visit
Oxycodone Distribution

- geometric mean = 1.9 mg/g
- 75th percentile = 6.3 mg/g
- 25th percentile = 0.7 mg/g
Oxymorphone Distribution

geometric mean = 0.8 mg/g
75th percentile = 2.7 mg/g
25th percentile = 0.3 mg/g
Distribution Statistics

### Table 1
Statistical Data Generated from Population Distributions of Both Urine Concentrations and their Corresponding Values Normalized Using Creatinine Values

<table>
<thead>
<tr>
<th></th>
<th>Oxycodone (ng/mL)</th>
<th>Oxymorphone (ng/mL)</th>
<th>Oxycodone (mg/g) Creatinine corrected</th>
<th>Oxymorphone (mg/g) Creatinine corrected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of non-zero measurements</td>
<td>30,455</td>
<td>31,473</td>
<td>30,455</td>
<td>31,473</td>
</tr>
<tr>
<td>Mean</td>
<td>9,015</td>
<td>3,092</td>
<td>7.8</td>
<td>2.8</td>
</tr>
<tr>
<td>Geometric mean</td>
<td>1,998</td>
<td>846</td>
<td>1.9</td>
<td>0.8</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>35,040</td>
<td>6,858</td>
<td>50.4</td>
<td>5.9</td>
</tr>
<tr>
<td>Geometric standard deviation</td>
<td>6.2</td>
<td>5.5</td>
<td>5.6</td>
<td>5.4</td>
</tr>
<tr>
<td>Median</td>
<td>2,244</td>
<td>876.3</td>
<td>2.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Skewness</td>
<td>-0.2</td>
<td>-0.1</td>
<td>-0.4</td>
<td>-0.2</td>
</tr>
<tr>
<td>75th percentile</td>
<td>71,067</td>
<td>2,816</td>
<td>6.3</td>
<td>2.7</td>
</tr>
<tr>
<td>25th percentile</td>
<td>607.3</td>
<td>257.6</td>
<td>0.7</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Oxycodone vs. Oxymorphine

Specimen with 100 fold less oxymorphone than expected

log (amount oxymorphone mg/g) = 0.60 x log(amount oxycodone mg/g) – 0.19, R² = 0.39, p < 0.0001
Oxycodone vs. Metabolic Ratio

MR = –0.45 \log(\text{amount oxycodone mg/g}) – 0.19, R^2 = 0.25, p < 0.0001
Estimation of the Proportion of Poor Metabolizers

possible deception

(2.4 + 2.1%)
Estimation of the Proportion of Ultra-Rapid Metabolizers

(1.8+1.1%)
Oxymorphone from Metabolism Compared to Oxymorphone as a Medication

![Graph showing the distribution of oxymorphone per gram of creatinine (mg/g) due to metabolism and due to oxymorphone use. The x-axis represents log(oxymorphone per gram of creatinine (mg/g)), and the y-axis represents the normalized number of subjects. The graph shows a comparison between the two sources of oxymorphone.]
Limitations

• This was a retrospective analysis conducted on urine specimens submitted for “medication” monitoring from “physicians’ offices”.
• Dose and time after dose were unknown.
• Liver and renal status of subjects in the population is unknown.
• Reported medications are listed by physicians that may, if not accurate, misrepresent subjects.
• Although these factors will affect metabolism and excretion of oxycodone, the data set was used to represent the pain patient population as a whole and no inferences about individual subjects were made.
• More clinical data is needed for interpretation of clinical effects of results presented.
Acknowledgements

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Questions


