Variable and Potentially Fatal Amounts of Nicotine in E-Cigarette Nicotine Solutions

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BACKGROUND
• Experimental research on electronic cigarettes (e-cigarettes) is sparse.
• Regulated as “tobacco products” by the U.S. Food and Drug Administration (FDA), e-cigarette safety has not been determined.
• Enables sale of e-cigarettes and tobacco-derived nicotine solution without rigorous safety regulations that would be required if the products were regulated as drug delivery devices (e.g., transdermal nicotine patches).
(U.S. Department of Health and Human Services, 2011)
• Consumers currently have no information on nicotine concentration levels or whether nicotine solutions are safe.

PURPOSE
• The present study aimed to gather preliminary data on the amount of nicotine contained in e-cigarette nicotine solutions.

METHODS
• Seven e-cigarette nicotine solution samples (A-G) ranging from “low” to “super high” were analyzed
• Samples ranged from pre-packaged and sealed vials with concentration levels printed on the labels to blank bottles with handwritten labels reading “high nicotine” with no concentration level, warning statements, or directions for use.
• Samples A and G were marked as 24 mg/mL (marked)
• Unmarked samples (B-F) were analyzed using suggested manufacturer ranges of nicotine concentration.
• Triplicate 0.05 mL aliquots were taken from each sample of nicotine solution and then serially diluted with Milli-Q water.
• Samples were analyzed by liquid chromatography-electrospray ionization-tandem mass spectrometry (methodology described in Miller, Norris, Rollins, Tiffany, & Wilkins, 2010).

RESULTS
• All e-cigarette nicotine solutions assayed contained nicotine, as advertised.
• Results of replicate nicotine concentration analyses and mean nicotine concentration for each sample (A-G) are presented in Table 1.
• For all samples, amount of nicotine present (mg/mL) was equivalent to or lower than what was marked or expected given the manufacturer concentration ranges provided.
• Even at lower levels of nicotine than expected given manufacturer specifications, these nicotine solutions could be toxic or lethal if taken in larger doses than directed.

Table 1. Replicate and Mean Nicotine Concentration Analyses for E-Cigarette Nicotine Solutions

<table>
<thead>
<tr>
<th>Sample</th>
<th>Brand</th>
<th>Expected Concentration Level</th>
<th>Replicate Analyses</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID</td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>A</td>
<td>Vapor Liquid (High)</td>
<td>24 mg/mL (marked)</td>
<td>19.8</td>
<td>21.2</td>
</tr>
<tr>
<td>B</td>
<td>No Brand, Hand-labeled Liquid (High)</td>
<td>25-36 mg/mL (est.)</td>
<td>12.4</td>
<td>12.1</td>
</tr>
<tr>
<td>C</td>
<td>Smart Smoke Liquid (High)</td>
<td>25-36 mg/mL (est.)</td>
<td>13.2</td>
<td>13.5</td>
</tr>
<tr>
<td>D</td>
<td>Smart Smoke Liquid (Med)</td>
<td>10-18 mg/mL (est.)</td>
<td>12.7</td>
<td>11.2</td>
</tr>
<tr>
<td>E</td>
<td>Smart Smoke Liquid (Low)</td>
<td>6.14-14 mg/mL (est.)</td>
<td>8.29</td>
<td>8.60</td>
</tr>
<tr>
<td>F</td>
<td>BE112 Pre-filled Cartridge (Super High)</td>
<td>25-36 mg/mL (est.)</td>
<td>19.8</td>
<td>20.4</td>
</tr>
<tr>
<td>G</td>
<td>Vapor Pre-filled Cartridge (High)</td>
<td>24 mg/mL (marked)</td>
<td>22.4</td>
<td>22.7</td>
</tr>
</tbody>
</table>

SIGNIFICANCE AND CONCLUSIONS
Variability in Nicotine Concentration
• The nicotine concentration range of e-cigarette solutions vary by manufacturer, as does amount of nicotine advertised to be contained in each strength range (e.g., low, medium, high, extra high, super high).
• Results of the present study indicate a consumer purchasing nicotine solution marked as “high” could receive a solution with significant variability in nicotine concentration (present results ranged from 12.3 mg/mL to 22.2 mg/mL) depending on where the product is purchased.
• Consumers should be aware that there is no standardized naming convention for nicotine concentration levels and that concentrations may vary by manufacturer, as does amount of nicotine expected given the manufacturer concentration ranges presented.

Potential Safety and Lethality Issues
• Future research needs to determine other chemicals or compounds present in e-cigarette nicotine solutions and to analyze nicotine absorption during e-cigarette smoking.
• Existing data on cigarette smoking has indicated that a heavy cigarette smoker may consume 40-60 mg of nicotine/day (Fagerstrom, Heatherton, & Kozlowski, 1990), a dose (0.5-1.0 mg/kg) that could be lethal if taken in bolus fashion rather than over the course of a day. (U.S. Department of Health and Human Services, 1988)
• Our preliminary results indicate that a 5cc vial of 20mg/mL nicotine solution could be potentially lethal in an adult, and less solution would be required to be potentially fatal if ingested by a child.
• Nicotine exposure via the use of an e-cigarette may be within acutely safe levels.
• However, because of the potential for nicotine induced toxicity and even fatality if these products are used in a manner other than directed (e.g., ingested orally, absorbed transdermally), we believe nicotine solutions should be regulated and accurately labeled with appropriate warnings.

ACKNOWLEDGEMENTS
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