3,4 Dimethoxyamphetamine (DMA): hallucinogen and CYP2D6 inhibitor? A case report.

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Background

• The amphetamine 3,4 Dimethoxyamphetamine (MDMA) is a common recreational drug of abuse.
• In 2008, the United Nations estimated that 10-25 million people had used MDMA in the previous year.
• MDMA is commonly referred to as “Ecstasy” ("E", "X", "XTC") and is associated with dance parties ("raves") and electronic music.
• "Ecstasy" marketed products may contain other psychoactive designer amphetamine derivatives that produce clinical effects similar to MDMA.
• Some MDMA marketed products contain no psychostimulant substance.
• We present a case of MDMA intoxication and subsequent detection of an amphetamine derivative 3,4 dimethoxyamphetamine (DMA) with limited published information in the medical literature.
• We hypothesize DMA inclusion in an “Ecstasy” labeled product to prolong the effects of MDMA through CYP2D6 inhibition.

Case Report

• A 19-year-old female college student with witnessed tonic clonic seizure presents to ED.
• She was accompanied by her boyfriend who stated that she had taken “E” approximately 1.5-2 hours prior to the seizure.
• In ED, confused, somnolent and minimally responsive to stimuli
• Heart Rate 95, Blood Pressure 137/92, Respiratory Rate 10, O2Sat 100%, Temp 37.5°C
• Physical Examination is unremarkable
• Laboratory Studies remarkable for:
  - Serum Sodium of 114mEq/L, Urine Drug Screen: Amphetamine Positive
  - Head CT revealed no abnormalities
• 12 hours after admission, second tonic-clonic seizure observed, Serum Sodium of 114mEq/L.
• Administered Lorazepam 2mg intravenously, cessation of seizure
• MRI reveals diffuse cerebral edema
• Administered 3% hypertonic saline with normalization of serum sodium.
• 48hour following admission, patient had clearing of altered mental status
• Admitted to ingestion of tablet marketed as “Ecstasy” in order to determine if other drugs were involved, liquid chromatography-time-of-flight mass spectrometry (LC-TOF/MS) of serum and urine was performed. Results are shown in Table 1. The first tested serum was obtained ~14 hours from ingestion. Subsequent times of serum and urine draws are recorded

Table 1

<table>
<thead>
<tr>
<th>Drug</th>
<th>Serum 1 1220</th>
<th>Serum 2 1523</th>
<th>Serum 3 1715</th>
<th>Urine 1 0910</th>
<th>Urine 2 1221</th>
<th>Urine 3 1753</th>
</tr>
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<tbody>
<tr>
<td>MDMA</td>
<td>148</td>
<td>130</td>
<td>132</td>
<td>4051</td>
<td>3726</td>
<td>3341</td>
</tr>
<tr>
<td>MDA</td>
<td>12</td>
<td>10</td>
<td>10</td>
<td>634</td>
<td>263</td>
<td>84</td>
</tr>
<tr>
<td>HMA</td>
<td>221</td>
<td>170</td>
<td>144</td>
<td>1949</td>
<td>905</td>
<td>151</td>
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<tr>
<td>3,4-DMA</td>
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<td>125</td>
<td>121</td>
<td>2532</td>
<td>2245</td>
<td>1825</td>
</tr>
</tbody>
</table>

Discussion

• Very little known about clinical effects or metabolism of 3,4 DMA.
• Other dimethoxyamphetamine are inhibitors of CYP2D6.
• Not previously reported as co-formulant in Ecstasy products.
• MDMA is metabolized via CYP2D6 to 3,4-dihydromethamphetamine (HHMA).
• Subsequent metabolism to 4-hydroxy-3-methoxymethylamphetamine (HMA).
• A secondary pathway via CYP2B6 to 3,4-methylenedioxyamphetamine (MDA) and 4-hydroxy-3-methoxyamphetamine (HMA).
• Absence of HHMA and HMA, persistently elevated serum MDMA, and MDA suggests inhibition of the major pathway of MDMA metabolism (CYP2D6).
• Unknown reason for DMA addition to this product.
• Previously described minimal clinical effects of DMA.
• We propose the addition of 3,4 DMA as a CYP2D6 inhibitor in an attempt to prolong or intensify the clinical effects of MDMA. Health care providers should be aware of this potential adulterant.