Spotlight: New Prescription Drugs of Abuse and Their Opioid Interaction Risks

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4th Human Abuse Liability & Abuse-Deterrent Formulations
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Conflict of Interest Statement

- Most manufacturers of prescription opioids or stimulants subscribe to RADARS System.
- RADARS System is the property of Denver Health and Hospital Authority, a political subdivision of the State of Colorado.
- Subscribers receive information, but do not participate in developing the System, data collection, or analysis. They do not have access to the raw data.
- Employees are prohibited from personal financial relationships with any company.
Roadmap

• Why nonopioid prescription drug misuse and abuse is increasingly common
• Framework for identifying nonopioid drug misuse and abuse
• Highlights of drug classes
Why is nonopioid prescription drug misuse and abuse increasingly common?
Nonopioid Prescription Drugs

- Potentiate effects of opioids
- “Smooth out” effects of other drugs
- Used as substitution or replacement when drug of choice not available
Framework for identifying nonopioid drug misuse and abuse
Surveillance Data

- National Poison Data System
<table>
<thead>
<tr>
<th>Generic Code</th>
<th>Intentional Abuse</th>
<th>Single Substance</th>
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</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td>51275</td>
<td>15895</td>
</tr>
<tr>
<td>Dextromethorphan</td>
<td>18182</td>
<td>12852</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>13833</td>
<td>7402</td>
</tr>
<tr>
<td>Carisoprodol</td>
<td>8633</td>
<td>3375</td>
</tr>
<tr>
<td>Atypical Antipsychotics</td>
<td>8556</td>
<td>2982</td>
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<tr>
<td>Other Sedative/Hypnotic/Anti-Anxiety or Anti-Psychotic</td>
<td>8150</td>
<td>3700</td>
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<tr>
<td>Diphenhydramine</td>
<td>5927</td>
<td>3163</td>
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<tr>
<td>Other SSRI</td>
<td>5185</td>
<td>1329</td>
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<tr>
<td>Other Antihistamines</td>
<td>5155</td>
<td>2208</td>
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<tr>
<td>Other Anticonvulsant (Excluding Barbiturates)</td>
<td>3931</td>
<td>1371</td>
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<tr>
<td>Methylphenidate</td>
<td>3662</td>
<td>2116</td>
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<tr>
<td>Other Antidepressant</td>
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<td>1133</td>
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<tr>
<td>Trazodone</td>
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<td>868</td>
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<td>Ibuprofen</td>
<td>3017</td>
<td>1057</td>
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<td>Other Muscle Relaxant</td>
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<td>1257</td>
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<tr>
<td>Cyclobenzaprine</td>
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<td>853</td>
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<td>Gabapentin</td>
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<td>379</td>
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<td>Phenothiazines</td>
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<td>642</td>
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<td>Amitriptyline</td>
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<td>365</td>
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<tr>
<td>Clonidine</td>
<td>1159</td>
<td>389</td>
</tr>
</tbody>
</table>
Surveillance Data

• National Poison Data System
• General population surveys
Lifetime Nonmedical Use

Prevalence (95% CI)

- Cannabis: 40%
- Loperamide: 2%
- Heroin: 2%
- Benzodiazepines: 2%
- Non-pharmaceutical fentanyl: 2%
- GABA Analougues: <1%
Surveillance Data

• High risk groups
  o Department of Corrections, Jails
  o Teenagers and young adults
  o Substance abuse treatment programs
  o Diversion
Highlights of Commonly Abused Nonopioid Pharmaceuticals
GABA Analogs

- Gabapentin, pregabalin
- 10-15% prescribed opioids also prescribed gabapentin
- Misuse common in opioid use disorders (15-28%)
- Increased mortality when combined with opioids
  - Likely synergistic respiratory depression
Diversion of GABA Analogs

Rates of gabapentin diversion (per 100,000) by quarter, 2002-2015
Gabapentin and Mortality

Loperamide

- Antidiarrheal
- Prescription and OTC
- Intestinal mu agonist
- Poor systemic absorption due to p-glycoprotein
- Abused alone or in combination with opioids
Loperamide Abuse

Miller H et al. JAPHA 2017, 57(2): S45–S50
Loperamide Abuse

Reported toxicities categorized by organ system:

<table>
<thead>
<tr>
<th>Organ system</th>
<th>1985-2013 (n = 21)</th>
<th>2014-2016 (n = 33)</th>
<th>Total, 1985-2016 (n = 54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal(^a)</td>
<td>6</td>
<td>1</td>
<td>7</td>
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<tr>
<td>Cardiovascular(^b)</td>
<td>4</td>
<td>15</td>
<td>19</td>
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<tr>
<td>Respiratory(^c)</td>
<td>2</td>
<td>2</td>
<td>4</td>
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<tr>
<td>Neurological(^d)</td>
<td>4</td>
<td>5</td>
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<tr>
<td>Death</td>
<td>10</td>
<td>17</td>
<td>27</td>
</tr>
</tbody>
</table>

Miller H et al. JAPHA 2017, 57(2): S45–S50
Antipsychotics

- Atypical antipsychotics commonly abused both alone and in combination with other drugs
- Especially popular in incarcerated population
- Quetiapine often drug of choice
Antipsychotic Abuse

• 429 patients from detox and rehab units
• 73 (17%) abuse atypical antipsychotics with alcohol, opioids, cocaine/crack, methamphetamine, and/or cannabis
• Quetiapine most common (84.9%)
• Other antipsychotics - olanzapine (17.8%), risperidone (24.7%), aripiprazole (20.5%), ziprasidone (8.1%), and asenapine (2.9%)
• Goals: "getting mellow", "slowing down”, or enhancing effects of other drugs

American Academy of Addiction Psychiatry (AAAP) 24th Annual Meeting & Symposium
Quetiapine DAWN ED visits

Antidepressants

- Reports of abuse of all classes
- May have higher rates with SNRI
  - Stimulant effects due to norepinephrine reuptake inhibition
  - When used with opioids, pharmaceutical “speedball” effect
  - Adverse effects include seizures and dysrhythmias
Cyclobenzaprine

- Reported via NPDS
- Few studies of misuse/abuse
- Anticholinergic effects
- Structural similarity to tricyclic antidepressants
- Anticipate synergistic CNS and respiratory depression with opioids
Other Antiepileptics

- Nearly all have been reported both in single substance and polysubstance abuse cases
- Levitiracetam may be on the horizon
- Synergistic CNS depression with opioids
- Cardiac effects also possible
Gaps in Knowledge

• What interventions are needed to decrease polysubstance abuse?
• Is postmarketing surveillance needed for nonopioid drugs?
• What education should be given to prescribers regarding risks?
Summary

• Nonopioid pharmaceutical drug abuse is becoming more common
• Many likely to be co-abused with opioids
• Synergistic CNS and respiratory depression most common interaction
• Need methods for surveillance and early warning
Questions?

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