Analytical confirmation of the Synthetic Cannabinoid Receptor Agonists (SCRAs) present in a cohort of presentations with acute recreational drug toxicity to an Emergency Department (ED) in London, UK

Prevalence of SCRA use

Synthetic cannabinoids are the main group of NPS present in the market

Fig. 1: Annual number of NPS reported by substance group, 2009-2014

- Tryptamines
- Synthetic cathinones
- Plant-based substances
- Piperazines
- Phenethylamines
- Other substances
- Ketamine & Phencyclidine-type substances
- Synthetic cannabinoids
- Aminooindanes

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Prevalence of SCRA use and toxicity

Limited use of novel psychoactive substances in South London nightclubs

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Synthetic Cannabinoid Exposures Reported to Texas Poison Centers

Mathias B. Forrester, BS
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A Characterization of Synthetic Cannabinoid Exposures Reported to the National Poison Data System in 2010

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From the Rocky Mountain Poison and Drug Center, Denver Health, Denver, CO (Hoyte, Jacob, Monte, Bronstein, Heard); University of Colorado School of Medicine, Department of Emergency Medicine, Aurora, CO (Hoyte, Jacob, Monte, Bronstein, Heard); the Department of Emergency Medicine, King Fahad Hospital of the University, Dammam, Saudi Arabia (Al-Jumaan).

Acute toxicity due to the confirmed consumption of synthetic cannabinoids: clinical and laboratory findings

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Objectives

Primary objective
- Prevalence of detection of SCRAs in a cohort of patients presenting to the ED with acute recreational drug toxicity

Secondary objective
- Better understand patterns of toxicity
Methods

- Prospective observational cohort study
- Inclusion criteria
  - ≥ 18y, acute recreational drug toxicity, plasma sample for renal function (U&E)
- Analysis of samples
  - High-resolution accurate mass-spectrometry with tandem liquid-chromatography (HRAM-LCMSMS)
- Demographic and clinical data collected
  - Age/gender, observations, disposition/length of stay
  - Palpitations/ chest pain/ seizures/ hallucinations/ agitation/ psychosis
Ethics (IRB) approval

- National UK Ethics (IRB) Approval

- Written informed consent not required
  - Plasma sample collected as part of routine care
  - Surplus plasma would otherwise have been discarded
  - Acellular material
  - Minimum clinical data collection
  - Anonymised sample and clinical data
Results

- Total of 179 patients included
- 18 (10%) positive for SCRA
- 14 male (78%) Median age: 31 years (IQR: 24 - 36) range 18 - 44 years
  - 2 (11%) insufficient plasma for wider drug screen
  - 7 (39%) no other drugs
  - 5 (28%) no other recreational drugs
  - 4 (22%) had significant co-ingestants
    - MDMA; Cocaine; MPA + PMMA; MPA + ethylphenidate
<table>
<thead>
<tr>
<th>SCRA</th>
<th>No. of cases</th>
<th>Concentration range (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5F AKB-48</td>
<td>13</td>
<td>50-7600</td>
</tr>
<tr>
<td>5F PB-22</td>
<td>7</td>
<td>30-400</td>
</tr>
<tr>
<td>MDMB-CHMICA</td>
<td>7</td>
<td>80-8000</td>
</tr>
<tr>
<td>AB-CHMI NACA</td>
<td>3</td>
<td>50-1800</td>
</tr>
<tr>
<td>Cumyl 5F PI NACA</td>
<td>1</td>
<td>800</td>
</tr>
<tr>
<td>BB-22</td>
<td>1</td>
<td>60</td>
</tr>
</tbody>
</table>
Self-reported drug use versus confirmed SCRA on analysis

- 9 (50%) patients were unaware/did not report SCRA use
- Self-report of cannabis use in 1 patient

<table>
<thead>
<tr>
<th>SELF-REPORT</th>
<th>SCRA</th>
<th>Other recreational drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>MDMB-CHMICA</td>
<td>-</td>
</tr>
<tr>
<td>Pills</td>
<td>MDMB-CHMICA</td>
<td>-</td>
</tr>
<tr>
<td>Unknown</td>
<td>5F AKB-48</td>
<td>-</td>
</tr>
<tr>
<td>5F PB-22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>5F AKB-48</td>
<td>-</td>
</tr>
<tr>
<td>5F PB-22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown Alcohol</td>
<td>5F AKB-48</td>
<td>-</td>
</tr>
<tr>
<td>MDMB-CHMICA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cocaine Cannabis</td>
<td>5F AKB-48</td>
<td>Cocaine</td>
</tr>
<tr>
<td>5F PB-22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White powder</td>
<td>5F AKB-48</td>
<td>Ethylphenidate MPA</td>
</tr>
<tr>
<td>5F PB-22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mephedrone</td>
<td>5F AKB-48</td>
<td>MPA PMMA</td>
</tr>
<tr>
<td>MDMA</td>
<td>5F AKB-48</td>
<td>MDMA</td>
</tr>
</tbody>
</table>
### Clinical features

- Observations at time of ED presentation:

<table>
<thead>
<tr>
<th></th>
<th>HR (bpm)</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
<th>Temp (°C)</th>
<th>GCS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median (IQR)</strong></td>
<td>87 (72.5 - 120.3)</td>
<td>128 (124.3 - 135.5)</td>
<td>80 (68.5 - 83.5)</td>
<td>36 (35.5 - 36.9)</td>
<td>15 (14 – 15)</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td>52 – 130</td>
<td>110 – 147</td>
<td>55 – 118</td>
<td>34.5 – 38</td>
<td>6 – 15</td>
</tr>
</tbody>
</table>

- One (6%) patient had temperature of 38° C
  - SCRAs: 5F AKB-48; with MDMA and mirtazapine
Cardiotoxicity

- Chest pain in 1 (6%) patient
  - SCRAs: 5F AKB-48, 5F PB-22
  - MPA and ethylphenidate
- No hypertension (SBP > 160 mmHg) or palpitations

**TACHYCARDIA (HR > 120 bpm)**

- YES: 5 (28%)
- NO: 13 (72%)

**Substances and Compound Groups**
- MDMB-CHMI CA
- AB-CHMI NACA
- 5F AKB-48, 5F PB-22
- AB-CHMI NACA
- MDMB-CHMI CA (insufficient plasma)
- 5F AKB-48 (MPA and PMMA)
Neurological Features

- One (6%) patient had GCS < 8
  - SCRAs: 5F AKB-48, MDMB-CHMICA; no other drugs detected

Seizure

- N = 4
  - 22% Seizure

- N = 14
  - 78% No Seizure

MDMB-CHMICA
5F AKB-48
AB-CHMI NACA
MDMB-CHMICA (insufficient plasma)
5F AKB-48, 5F PB-22 (COCaine)
Neuropsychiatric features

- No reported hallucinations
- Psychosis in 1 (6%) patient
  - SCRAs: 5F AKB-48, 5F PB-22, with cocaine

Agitation/Aggression

N = 14
78%

N = 4
22%

AB-CHMI NACA
5F AKB-48
5F PB-22
AB-CHMI NACA
5F AKB-48,
MDMB-CHMI CA
AB-CHMI NACA
5F AKB-48
(MDMA)
Disposition

Median LOS: 3.5 hours (IQR 2.65 – 6)
Range: 1.7 - 14.8

- ED N = 13, 72%
- Short-stay N = 3, 17%
- Critical care N = 1, 6%
- Self-discharged N = 1, 6%
- MDMB-CHMICA (insufficient sample)
- 5F AKB-48 (MDMA)
- AB-CHMI NACA
Limitations

Advantages

- Analytical confirmation
- Study design
- Internal validity

Disadvantages

- Limited clinical data
- No biochemical data
- No treatment data
- External validity
Conclusion

- SCRAs are a more common reason (than expected) for drug-related ED visits
  - 18/179 patients (10%)
  - 50% of patients did not report SCRA use
- SCRAs are associated with
  - Cardiotoxicity, neurotoxicity, neuropsychiatric complications
- Future research
  - Larger cohort of patients, triangulation with other local data-sets
Thank you

Co-investigators

- Dr Natalie Thurtle, Dr James Ho, Dr George Bailey, Dr Takahiro Yamamoto, Alison Dines, Dr David Wood, Dr John Archer and Professor Paul Dargan
  - Guy’s and St Thomas’ NHS Foundation Trust, London, UK
- Dr Simon Hudson
  - LGC Health Sciences, Fordham, UK
- Dr Michelle Wood
  - Waters Corporation, Wilmslow, UK