Synthetic Cannabinoids

Update for Healthcare Professionals

Dayne Laskey, PharmD, DABAT

Objectives

- Describe the epidemiology of recreational drug use
- Explain the pharmacologic and health effects of synthetic cannabinoid use
- Discuss trends associated with synthetic cannabinoid use in the U.S.
- Communicate effective strategies that support pharmacy’s role in recreational drug abuse prevention and education

Disclosure

- “Dr Laskey has no actual or potential conflict of interest associated with this presentation”

I. RECREATIONAL DRUG USE

Recreational Drug Use in the US

“Classic” Recreational Drugs
**Synthetics: Alexander Shulgin**

- American pharmacologist, chemist
- 1961: Develops Zectran (mexacarbate) for Dow Chemical
- DEA schedule 1 license
- “Godfather of psychedelics”
- PIHKAL (1991), TIHKAL (1997) – Together describe synthesis of over 250 psychoactive compounds

**Phenethylamines**

![Chemical Structure](image)

**“Bath Salts”**

- In 2014, 101 new recreational substances were identified by EMCDDA.
  - 31 of these were cathinones
  - 30 were cannabinoids
- Mechanism(s)
  - ↑ presynaptic release of catecholamines
  - Inhibit breakdown of neurotransmitters (e.g. MAOIs)
  - Inhibit catecholamine reuptake (DAT, NAT, SERT)
- Clinical effects
  - Paranoia, agitation, psychosis, tachycardia, hypertension, hyperthermia, seizures, coma, death.
II. PHARMACOLOGY AND EFFECTS

Marijuana

- Mechanism
  - Complex combination of 86 active components
    - Δ9-Tetrahydrocannabinol (THC), Cannabidiol (CBD), cannabinol (CBN), cannabavarin (THCV), cannabinol (CBN), cannabichromene (CBC), delta-8-THC, cannabicyclol (CBL)
  - Partial agonist
    - CB1: CNS
    - CB2: Peripheral NS, immune cells
- Legal status
  - 7 states recreational (plus D.C.)
  - 14 states decriminalized
  - 29 states allow medical (plus D.C.)

Marijuana - Potency

Unintentional Pediatric Exposures

- Clinical Effects
  - Lethargy, ataxia, irritability, vomiting, respiratory depression, bradycardia, hypotension
  - Several cases requiring hospitalization and admission to ICU
- Contrast with adults
  - Agitation, paranoia, tachycardia, nausea/vomiting


Cannabinoid hyperemesis syndrome

- Occurs in users with regular cannabis use > 1 year (74.8%)
- Severe n/v with accompanying abdominal pain, cycling over months (100%)
- Compulsive hot baths (92.3%)
- Pathology is unclear


Synthetic Cannabinoids - History

- Structurally unrelated to THC
  - CB1/CB2 agonists
  - Many times more potent
- First synthesized in the 1960s for research into the endocannabinoid system
  - JWH-XXX – John William Huffman
  - AM-XXX – Alexandros Makriyannis
  - HU-XXX – Hebrew University
  - CP-XXX – Pfizer

Synthetic Cannabinoids - History

- 2004 – Internet, head shop sales begin in Europe
- 2008 – First law enforcement seizure in US
- 2011 – 15 synthetic cannabinoids placed on Schedule I
- 2012 – Synthetic Drug Abuse Prevention Act
  - Defines SCs pharmacologically rather than structurally
- 2015 – Largest outbreak of SCs in history
  - DEA estimates there are at least 75 additional synthetic cannabinoids that remain unscheduled
  - Some may still be subject to prosecution under Federal Analogue Act of 1986

Synthetic Cannabinoids – Clinical Effects

- Excited delirium
- Acute kidney injury
- Seizures
- Psychosis
- Hallucinations
- Cardiotoxic effects
- Respiratory depression
- Coma
- Death

Sources

Clinical effects by type

- JWH Series (11/2010)
  - AMS, seizures, hyperthermia, tachycardia
- XLR-11 (5/2013)
  - Tachycardia, hypertension, psychosis, AKI
- AB-FUBINACA (1/2014)
- MAB-CHMINACA (10/2015), AB-CHMINACA (1/2015)
  - Bradycardia, hypotension, obtundation
- ADB-PINACA (1/2015),
  - Hallucinations, psychosis, tachycardia, agitated delirium
- AMB-FUBINACA
  - Severe CNS depression in absence of other features

Synthetics: Treatment

- Supportive care
  - Intravenous fluids
  - Treatment of hyperthermia
- Talkdown measures, calming environment
- Monitoring
  - Vitals, EKG, renal function, CK
- Sedation (benzodiazepines preferred)
  - Role for neuroleptics?

Synthetics: Why the demand?

- Curiosity
- Feeling good/getting high
- Lack of toxicological screening
- Availability – Internet and retail stores
- Perceived legality
- Cost – Fraction of the price of conventional marijuana
- Poor perception of the risk

A Growing Public Health Threat

- 644 NPS identified by UN Office of Drugs and Crime 2008-2015
  - Synthetic cannabinoids are the fastest growing class
  - >177 novel SCs identified in 2014 alone
- Second most common illicit substance among US high school students in 2014 and 2015
  - Third most common in 2016

Timeline

- Affinity and Potency of Novel Synthetic Cannabinoids
- Timeline of key events

References:

Laboratory Trends

Timeline

Laboratory Trends

Poison Center Trends

Outbreaks occur in clusters

IV. OUR ROLE
### Clinical Challenges

- No clear toxidrome
- No readily available diagnostic tools
- No antidote
- No pharmacologic/pharmacokinetic data
- Unpredictable and severe effects
- Unknown long-term effects

### Other Challenges

- Difficult for law enforcement to track
- Cases are often underreported
- Baseline use patterns are difficult to track

### Challenges in the Laboratory

- Takes weeks-months to complete
- Requires collaboration between healthcare providers, law enforcement, clinical laboratories, organic chemists,

### NPDS

- National Poison Data System
- >62 million exposures dating back to 1983
- The only real-time public health surveillance tool in the US

### What is the role of the pharmacist?

- Prevention
- Education
- Assistance
References


References