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Title of Project:

Identifying the Clinical Presentation of Adolescents Presenting to the Emergency Department Related to Synthetic Cannabinoid Overdose

A) Study Proposal and Rationale:

Use of synthetic cannabinoids is growing in consumption due to their accessibility, affordability and minimal regulation. These compounds are produced in massive amounts through underground laboratories commonly found in China and other countries (1). After production, they are imported en masse to small American markets such as delis and gas stations. Marketing specifically targets children and adolescents with names including: K2, Spice, Black Mamba, Mr. Nice Guy and Skunk. Whereas the active component of marijuana is a partial agonist of cannabinoid receptors, synthetic cannabinoids are full agonists and are often mixed with additional chemicals making these compounds particularly dangerous in the pediatric population (2).

Preliminary studies from Europe and Australia have shown that young adults are more likely to seek treatment for SCRA use and its effects (2) . Thus, supporting the crucial need for pediatric providers to understand and safely predict factors that will lead to worse outcomes in pediatric users. Between 2010 and 2011, the rate of ED visits involving synthetic cannabinoids had a statistically significant doubling for patients aged 12 to 17 (3). Even more dramatically, the rate per 100,000 population for those aged 18 to 20 had a statistically significant increase of more than four times (3). Overall, patients aged 12 to 20 made 55 percent (15,796 visits) of all ED visits involving synthetic cannabinoids in 2011. (3). In contrast, the rate of ED visits involving synthetic cannabinoids did not increase significantly for patients aged 21 or older indicating that adolescents are particularly susceptible to adverse outcomes from SCRA use (3). Therefore, I will focus my research on identifying the factors that confer worse health outcomes in pediatric patients with SCRA ingestion.

Project Aims:

Specific Aim 1: Characterization of Presentation Signs Associated with ED Visits for Synthetic Cannabinoid Use

- SCRA intoxication is increasing in incidence amongst adolescents (ages 12-21) and first presentation is commonly seen in the Emergency Department. Using clinical information from the American College of Medical Toxicology's Toxic Registry, which houses ED intake data from multiple sites nationally, my aim is to identify demographic and clinical factors associated with SCRA use, intoxication and adverse events.

Specific Aim 2: Predictive Risk Modeling for Severe Adverse Outcomes of Synthetic Cannabinoid Use in Children and Adolescents

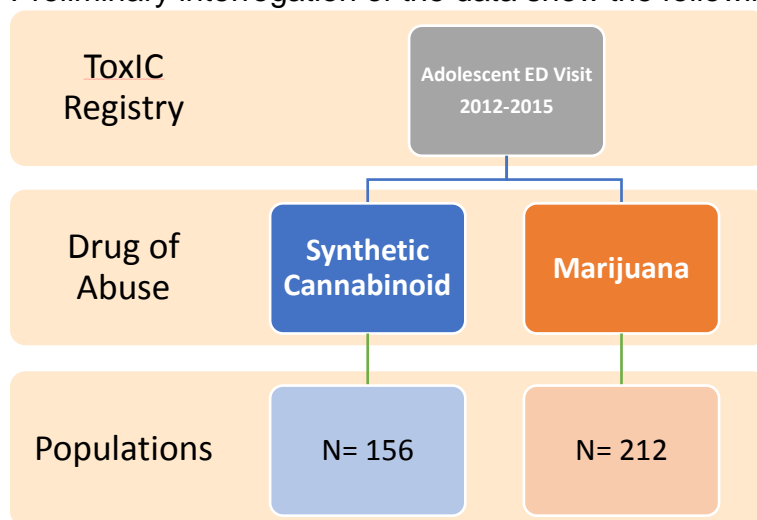
- For predictive model development, several of the clinical and utilization measures identified in specific aim 1, will serve as variables for being at risk of SCRA toxicity on presentation to the pediatric ED.

B) Study Design and Statistical Analysis

Study Design

This study will be a retrospective multicenter descriptive analysis that will define the clinical presentation, demographic information and medical complications of pediatric patients who present to the emergency department after SCRA use. De-identified data will be derived from cases ages 13-21 from the 45 national participating sites of the Toxicology Investigators Consortium (ToxIC) Case Registry. The registry exclusively compiles cases that have been consulted and managed by a medical toxicologist and is used as a surveillance tool. All adolescent reports originating from an Emergency Department (ED) which included self reported SCRA intoxication will be analyzed in the study. For a comparison, all adolescent reports with THC intoxication will also be analyzed from this registry. Clinical data collected on each patient include: Age group, location of initial encounter, substances involved, presenting signs and symptoms and treatment provided. As part of the assessment, reported clinical symptoms including the presence of: Agitation, Hallucinations, Coma/CNS depression, Seizures, Delirium/Toxic Psychosis and Extrapyrimal symptoms will be assessed.

Preliminary interrogation of the data show the following numbers for each group:



Statistical Analysis

Data Analysis: Subject characteristics, including age, gender, race/ethnicity, acute vs chronic exposure, other drugs consumed and treatment parameters will be summarized and compared between SCRA and Marijuana groups. The categorical outcome

variables (i.e. number of reported symptoms of agitation) will be summarized as percentages and in 2x2 contingency tables to compare group. Given that this is a retrospective cohort study, this data will be analyzed for relative risk. Univariate and multivariate regression modeling to explore the relationship between selected risk factors (i.e. age, gender, multi drug use and other identified factors) for predicting association between the covariates and clinical presentation in our relative risk analyses

Statistical packages to be used include: R and JMP.

Determining Effect Size

- Determined based on Zaurova, M et al, 2016 "Clinical Effects of Synthetic Cannabinoid Receptor Agonists Compared with Marijuana in Emergency Department Patients with Acute Drug Overdose"
 - Found 40% of subjects with SCRA intoxication presented with agitation compared to 16% in the Marijuana Group, and this finding is statistically significant with a $p < 0.05$
- Using biomath.info/stat, calculated effect size is **$p^2 > 0.34$**
 - If the proportion of agitation in the SRCA group is at least 34% then I have 80% power to find significance $p < 0.05$

Resources:

1. Brodwin, Erin. Production of dangerous synthetic marijuana is soaring and the DEA can't keep up. Business Insider. May 15, 2015.
2. Synthetic Cannabinoids 2015: An update for pediatricians in clinical practice. World J Clin Pediatr. 2016 Feb 8; 5(1): 16–24
3. Donna M. Bush, Ph.D., F-ABFT and David A. Woodwell, M.P.H. UPDATE: DRUG-RELATED EMERGENCY DEPARTMENT VISITS INVOLVING SYNTHETIC CANNABINOIDS. Substance Abuse and Mental Health Services Administration (SAMHSA)
4. Zaurova, M et al. J. Med. Toxicol. (2016). doi:10.1007/s13181-016-0558-4