Synthetic Cannabinoids: User Profiles and Clinical Picture Author: William Fox, MD // Editor: Larissa Velez, MD

Designer drugs are hardly new "players" in the toxicology world, but their recent popularity and media exposure have enabled them to reach a wider population with greater consequences for emergency department (ED) practitioners. Synthetic cannabinoids, with names such as Spice, K2, and "potpourri", are becoming increasingly common. They are often advertised as "legal highs", or psychoactive substances that thwart drug regulations due to minute variations in their chemical structure that make them marginally different from banned substances. The lack of regulation not only means that the substances can be freely bought or sold, but that there is little oversight into the synthesis and purification processes involved in their creation. In the ED, an increasing number of patients are arriving with a history of K2 or Spice usage and a clinical picture that **does not fit known toxidromes**. Patients I have seen after suspected ingestion present hypertensive and tachycardic, but at times somnolent and difficult to arouse. Often, they can alternate between these two, causing many problems in trying to predict behaviors in the ED that can be dangerous to the patient and the health care providers. A number of studies have attempted to characterize this new trend and assist practitioners in diagnosing and treating ingestions that arrive in the ED. One such study was the STRIDA project designed and managed by the Karolinska University Laboratory, the Karolinska Institutet, and the Swedish Poisons Information Centre.

The STRIDA project (STRIDA being the Swedish-language acronym) began in January 2010 and was designed to help define and differentiate what the project termed "new psychoactive substances (NPS)," which included synthetic cannabinoids. The study analyzed blood and urine samples of patients with suspected or admitted substance use who presented to ED and coupled the analysis with the patient's clinical appearance based off of the Poison Severity Score (PSS). The PSS utilizes a grading scale from 0-4, with zero being no abnormal signs or symptoms and four being fatal, and one through three representing increasing levels of organ dysfunction. The score has twelve subsections based on the different organ systems examined. Of the 189 subjects analyzed in the study population, the vast majority of people using NPS were **young** (<30 years old, median male/female age of 21/19 years, respectively) and overwhelmingly **male** (~80%). Synthetic cannabinoids were most popular in high-school aged adolescents, and the study notes relatively low (1-1.5) mean PSS scores.

The study does not comment on exact clinical presentation or course of either synthetic cannabinoid or NPS ingestion as a whole, mainly due to the high frequency of substance coingestion and the relatively nonspecific clinical course discussed in other research on the topic. The authors use the lack of a clear clinical picture (and relatively high frequency of coingestion) to bolster support for the use of laboratory testing as an aid in the correct diagnosis of NPS ingestion. Additionally, the authors comment on a number of cases (~17% of samples received) in which no drugs were detected based on their reference library of chemicals. They propose a number of reasons for the undetected substances, including rapid excretion time, chemical structure instability, symptoms not related to substance use, or presence of substances not in the reference library. The legislative status of synthetic cannabinoids also changed during the course of the study, with a decrease in ingestion frequency after Sweden classified one of the chemicals (known as JWH-081) as a "Narcotic drug". The implications of NPS are **co-ingestions**, and a broad differential may be necessary to interpret patients with nonspecific or even seemingly contradictory clinical appearances. Additionally, by understanding the lack of regulation surrounding the manufacture of these substances, one can hypothesize that in a case with a convincing history, the patient may have ingested a chemical (either intentionally or unintentionally) whose structure (and, by extension, effects) are unknown. Despite the valuable data and perspective provided in the paper, one may be left questioning how these patients actually appear clinically, especially in isolated exposures. Further reading led me to another recent paper documenting the clinical findings of confirmed synthetic cannabinoid consumption in Freiburg, Germany.

In the paper, the authors combine rigorous laboratory analysis with clinical presentation in a patient population of 29 individuals with confirmed synthetic cannabinoid ingestion. Based on the data, the clinical appearance of synthetic cannabinoid ingestion is varied. The summation of all the synthetic cannabinoids studied reveal that a number of users will experience **tachycardia (76%, n=22), restlessness/agitation (41%, n=12), changes in perception/hallucinations (38%, n=11), mydriasis (38%, n=11), and hypertension (34%, n=10)**. Though it may appear that the majority of patients consuming synthetic cannabinoids will experience a hyperactive state, careful analysis of the table reveals that **almost an equal amount can experience somnolence or unconsciousness followed by somnolence** (17%, n=5 for both). The authors comment on the wide distribution of the CB₁ receptor in both the central and peripheral nervous system and the variety of effects that can be elicited by either the selective or general activation of receptors in these different areas.

Despite the advances made by these papers and the growing number of case studies of synthetic cannabinoid ingestion in medicine, abuse of these chemicals continue to present a confusing clinical picture for practitioners. **Supportive care** continues to be the mainstay of treatment.. Continued advancement in research and publications will help further delineate more specific management options for this now common aspect of toxicology in EM.

References // Further Reading:

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