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# International Journal of Geriatrics and Gerontology

Research Article

Hassen GW, et al. Int J Geriatr Gerontol 5: 125.
DOI: 10.29011/2577-0748.100025

# Synthetic Cannabinoid Receptor Agonists Abuse in Older Adults

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**Citation:** Hassen GW, Roffe E, Andreias L, Prospere E, Eng A, et al. (2021) Synthetic Cannabinoid Receptor Agonists Abuse in Elderly Patients. Int J Geriatr Gerontol 5: 125. DOI: 10.29011/2577-0748.100025

**Received Date:** January 28, 2021; **Accepted Date:** February 04, 2021; **Published Date:** February 11, 2021

## Abstract

**Background:** Abuse of substances including alcohol, heroin, and cocaine is common in older patients and is well reported. However, use of Synthetic Cannabinoid Receptor Agonist (SCRA) in this population is very rare and has not been well documented. Older patients with several age-related physiological changes, multiple comorbidities and the likelihood to use prescription drugs may encounter severe adverse effects from SCRA use.

**Objectives:** To review the clinical data and demographics of older adults who presented with SCRA intoxication to the emergency department (ED).

**Methods:** A retrospective chart review of older patients who presented with SCRA intoxication from January 1st, 2012 to December 31st, 2016 in an inner city ED.

**Results:** Seventy-seven patients presented with SCRA intoxication. Ninety seven percent of the patients were male and 3% were female. Fourteen patients made repeated visits for SCRA-related intoxication. Of the 67 patients who stayed in the ED, 7 patients spent more than 12 hours, 16 patients spent between 6 and 12 hours, and the remaining patients spent less than 6 hours in the ED. Of the 10 patients admitted to the hospital, 4 patients were admitted to the Intensive Care Unit setting (ICU) and 6 patients were admitted to the regular medical floor. One patient expired in the ED.

**Conclusion:** SCRA intoxication and abuse may result in serious adverse health effects and should be considered in the differential diagnostics of older patients who present to the ED with prolonged altered levels of consciousness. Male patients presented with SCRA-related intoxication and other adverse effects at a disproportionally higher rate than female patients did.

**Keywords:** Older patients; Emergency Department; Intoxication; SCRA

## Introduction

Recreational drugs such as K2 or Spice are a collection of SCRA that have become increasingly popular in recent years. Due to their relatively inexpensive cost and ease of accessibility, younger individuals tend to use them frequently. Compared to younger individuals, older patients use other substances such as cocaine, crack and heroin, more frequently [1-3]. In addition, older adults tend to abuse more alcohol and prescription drugs than SCRA [4,5]. Recently, abuse of SCRA among older adults has been reported [6]. One reason could be the relatively inexpensive cost of SCRA and its potential to induce a stronger high [6]. The fact that routine drug testing cannot detect SCRA could be another reason. Patients who are required to undergo drug testing for various reasons may prefer these types of drugs.

There are many adverse effects of SCRA. Depressed level of consciousness, seizures, and varying degrees of adverse cardiovascular events are some of the leading causes for ED visits.

These visits can result in prolonged ED stay, admission to the medical floor or ICU. There have been multiple media reports on mass intoxication of younger adults with serious adverse health effects, but only few reports on SCRA abuse and intoxication among older patients [7,8]. This study presents clinical data and demographics of older patients with presumed SCRA-induced intoxication. To date, we believe this report is the largest SCRA-related intoxication report on older adults.

**Methods**

We conducted a retrospective chart review of all patients who presented to an inner city ED from January 1st, 2012 to December 31st, 2016 with SCRA intoxication. The average annual number of patient visits to our hospital ranged from 65000 to 70000. The study was undertaken after obtaining a waiver from the corresponding Institutional Review Board (IRB). This report focused on patients above the age of 60 years at the time of presentation. Their clinical data, demographics, length of stay in the ED, and disposition types were analyzed. Descriptive statistics were performed using Microsoft Excel.

**Results**

Between 2012 and 2016, there were 1045 patients with chief complaints related to SCRA abuse, of which 77 visits were by older patients. Forty-eight patients above the age of 60 years made the 77 visits. Fourteen patients made repeated visits for SCRA-related intoxication. The visits varied from two to ten visits per patient during the study period. For simplicity, each patient visit will be considered as an individual visit and it will be reflected in the analysis as such. Seventy-five patients (97%) were males and two patients (3%) were females. The clinical symptoms varied from agitation, depressed levels of consciousness, hypotension, sinus bradycardia, sinus tachycardia, syncope, and seizures. The first and single case of SCRA-related intoxication in elderly patient was documented in August 2013. The next case occurred in May 2014. Sixty-seven patients were discharged after their visit in the ED. Seven patients spent more than 12 hours, 16 patients spent between 6 and 12 hours, and the remaining 44 patients spent less than 6 hours in the ED. Ten patients were admitted to the hospital, of which 3 patients went to the Coronary Care Unit (CCU), 1 patient went to the Medical Intensive Care Unit (MICU), and the other 6 patients went to the regular medical floor. One patient who had a core temperature of 108.2 degrees Fahrenheit and cardiovascular instability expired in the ED. Seventeen Computed Tomography (CT) scans of the head were performed to rule out intracranial pathology. None of these images demonstrated evidence of intracranial bleeding or abnormal pathology.

The reason for the admissions to the CCU was symptomatic bradycardia. These patients reported dizziness and heart rates as low as 39 beats per minute. The reason for admission to the MICU was SCRA intoxication and diabetic Ketoacidosis (DKA). One patient presented after a fall with a hip fracture. Another patient was admitted due to recurrent seizures and hypotension. He had no known history of seizure disorder. This patient had experienced a couple of seizure episodes after smoking K2 in the past. He had one prior hospital admission for syncope. One additional patient with a known history of seizure disorder had a seizure while in the ED.

Two patients had positive tests for benzodiazepines and/or opiates in their urine. Both patients stayed less than 6 hours in the ED.

Table 1 Summarizes the Clinical Data and Demographics.

| Category | **Number of Patients** |
|---|---|
| Total number of patients | 77 |
| Male | 75 |
| Female | 2 |
| Admission to Hospital | 10 |
| Admission to ICU Setting | 4 |
| Length of Stay in hours in ED >6hours | 23 |
| Death in the ED | 1 |
| Seizure | 2 |
| Syncope | 2 |
| Fracture | 1 |
| Positive Urine toxicology | 2 |
| CT Head | 14 |
| Repeated ED visit for K2 intoxication | 14 |

**Table 1:** Clinical data and demographics of patients who presented to the emergency department with SCRA intoxication.

## Discussion

Synthetic Cannabinoid Receptor Agonists have the potential to cause several adverse health effects. Older adults are at higher risk for adverse effects for several reasons. During the aging process, older adults undergo a variety of physiological changes to their organ systems. This includes but is not limited to the cardiovascular, pulmonary, and renal systems. These changes may affect their ability to respond appropriately to environmental changes, disease conditions, and prescribed medications [9-11]. Similarly, the physiological response of an older adult to recreational drugs maybe different than the physiological response of younger individuals. Furthermore, older patients may have several comorbidities and maybe taking different classes of medications including prescribed and over the counter medications [11]. When taken alone, SCRA can have significant adverse effects, but when taken in conjunction with other medications or drugs, their adverse effects can be amplified. For example, patients who take beta-blockers may experience asymptomatic bradycardia, but when the beta-blocker is taken in conjunction with SCRA

the patient may develop severe symptomatic bradycardia with syncope. Similarly, patients who have seizure disorders may experience frequent seizures when smoking SCRA and patients with renal impairment may experience worsening of renal function from SCRA-induced rhabdomyolysis. Moreover, renal clearance of medications and drugs may be affected in older patients, leading to prolonged effects of medications and other drugs. Furthermore, opioids taken alone can affect the level of consciousness. Some older patients may have chronic pain from metastatic diseases, autoimmune diseases, and arthritis or from sequels of trauma for which opioid pain medication was prescribed. Others may take methadone for opiate maintenance therapy, which by itself can affect the level of consciousness [4,5,12]. Using SCRA while on opioid pain medications may worsen the level of impairment of consciousness. Patients, whose level of consciousness is affected by SCRA intoxication or combination of SCRA and prescribed medications or other recreational drugs, may forget to take their regular medications and may experience a variety of health complications such as diabetic ketoacidosis, or worsening of Congestive Heart Failure (CHF). They may fall and sustain head injury and/or long bone fractures. Chronic alcohol use disorder is another relevant problem in older patients [1,12-15]. Older adults can present with both alcohol intoxication, alcohol withdrawal and associated seizures. Additional or concomitant SCRA intoxication can be potentially fatal.

Synthetic Cannabinoid Receptor Agonists exert their effect via Cannabinoid (CB) receptors. There are two types of CB receptors (CB1 and CB2). These receptors are distributed within the Central Nervous System (CNS) as well as peripherally (immune system and the heart) [16-24]. The behavioral symptoms and seizures appear to be mediated via CB1 receptors in the CNS. The cardiovascular effects of SCRA appear to be either tachycardia or bradycardia. These effects seem to be mediated through different mechanisms, including several ion channels and CB receptors [25-27]. The proposed mechanism for renal effect is believed to be thrombotic microangiopathic disease [28]. The presumed mechanism for seizures is SCRA-mediated glutamate-induced excitotoxicity and/or reduction of inhibitory GABA effects [23,29-31]. Animal studies have demonstrated that SCRA lead to induction of seizures, whereas THC does not [32]. Hyperthermia may result from SCRA abuse, but the exact mechanism is unknown.

Our chart review revealed that some admissions were for worsening medical conditions such as DKA and falls with hip fracture. Other patients experienced syncope, some seizures, while few exhibited symptomatic cardiovascular effects from SCRA. Most patients experienced Altered Mental Status (AMS) of various durations. The reason for the prolonged length of AMS as well as length of stay in the ED is not clear. This may be attributed to SCRA's effect, or to the sedative medications given in the ED for agitation and violent behavior. Prolonged length of stay can also be from non-convulsive seizures/status, which can also be because of SCRA intoxication. A portable Electro Encephalogram (EEG) monitoring device could be helpful in these patient groups with prolonged AMS who required longer observation time, particularly those who did not receive sedative medications [33-36].

Older adults may frequently present to the ED with a range of issues including medical complaints and socioeconomic concerns. Not all ED physicians are familiar with or have adequate resources to appropriately address the needs of geriatric patients or complicated geriatric presentations. These patients may have multiple comorbid conditions, may be on several classes of medications, be on opioid pain medications for the treatment of chronic pain, and/or may be on methadone maintenance therapy.

In light of the physiological changes with aging and the complexity of the older patient's presentation to the ED possibly compounded by using SCRA, the medical team with geriatric training could optimize the level of care offered to this patient population. To adequately address the different aspects of older patient's problems, a designated Geriatric section in the ED may also be beneficial. This should positively impact patient care, length of stay, and disposition.

## Limitations

This is a single site study in an inner city hospital ED, therefore, the results may not be generalizable or applicable to other settings. The population of our study may not be representative of older patients who use SCRA elsewhere. In addition, there might have been several missed SCRA intoxication cases that were triaged for other medical symptoms despite their K2 use and intoxication. For example, sinus bradycardia can have several causes, one of which is methadone use. Some patients who were on Methadone and used SCRA may have presented with intoxication, but the triage documentation may have only listed Methadone overdose. Some patients could have been missed if they presented with other symptoms such as vomiting, dizziness, or fever and were subsequently diagnosed with a gastrointestinal or infectious process.

There was no standardized toxicology test for the detection of SCRA to determine whether SCRA are present in body fluids. This information was obtained from patient's self-report, or from a report by others. Another limitation of the study is incomplete data in the patient's charts. Chart review revealed that all medications and comorbidities were not documented in all patients. Prolonged stay may partly be attributed to sedative medications, concomitant alcohol use, or other recreational drug use as well as non-convulsive seizure/status.

## Conclusion

Older adults can often present with adverse effects related to SCRA intoxication. Synthetic Cannabinoid Receptor Agonists can lead to serious adverse health effects and their abuse should be considered in the differential diagnosis of older patients who present to the ED with prolonged altered level of consciousness. Male patients may present to the ED with signs and symptoms of SCRA-related intoxication at a disproportionally higher rate than female patients.

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