



ACUTE INTOXICATION BY SYNTHETIC CANNABINOIDS: CLINICAL AND LABORATORY FINDINGS: A CASE SERIES

Ali Cem Yekdeş*

*Uzunköprü State Hospital, Department of Internal Medicine, Edirne, Turkey

Abstract: New psychoactive products (synthetic cannabinoids) which are subgroups of the cannabinoids began to be produced after prohibition and reduced accessibility of other cannabis in many countries. This psychoactive molecules act as an agonist of cannabinoid 1-2 receptors (CB1-2) resident central and peripheral nervous system. Many psychiatric symptoms such as euphoria, anxiety, agitation, irritability, paranoia, psychosis can be seen also physical symptoms like sweating, nausea, vomiting, appetite changes, hypertension, hypotension, chest pain, tachycardia, bradycardia, and respiratory depression can be seen. In our study we aimed to discuss clinical conditions of the cases which were brought to Emergency service(ER) with cannabinoid intoxication diagnosis after that followed up in intensive care unit (ICU). **Materials and Methods:** 25 patients with synthetic cannabinoid intoxication enrolled into the study between 2015-2016. Age, sex, neurological and cardiac examination during time of application, laboratory values such as pH, urea, creatinine, white blood cell counts, electrolyte levels, liver function tests were evaluated and statistically risk analysis was performed for each parameter. **Results:** The number of patients with synthetic cannabinoid intoxication was 25. Female/male ratio was 1/24. Ages of the cases were changes between 19 to 59, mean age was 26, 1. In neurological examination in ER 8 patients(%32) had unconsciousness, 2 patients(%8) had agitation, 5 patients(%20) had confusion, 8 patients(%32) had dizziness. 2 patients were normal for neurological examination, Glasgow coma scale were 15. In examination cardiological findings were 5 cases (%20) only tachycardia, one case (%4) hypertension, 10 cases (%40) hypotension and tachycardia together. Cardiological examinations were normal in 9 cases (%36). None of cases had bradycardia or other arrhythmic situations. In gastroenterologic examination we did not find nausea, vomiting or other gastroenterologic symptoms. 4 patients (%16) were followed up in ICU more than 48 hours. 4 patients (%16) were discharged from ICU less than 24 hours. Other 17 patients (%68) were followed up at least 24 hours that must be. Death did not occur in our cases. **Conclusion:** Synthetic cannabinoids square measure unsafe and harmful medicine of abuse; they'll even cause severe side effects. There's a necessity for a multidisciplinary approach for recognition and treatment of the clinical manifestation ensuing from synthetic cannabinoid use. Education of teachers, parents and adolescents about the potential health risks of victimization this product is important.

Key words: Synthetic cannabinoids, intoxication, psychoactive.

Introduction: Synthetic cannabinoids known as 'Bonzai' in Turkey have become common encountered abuse products nowadays. It's because cheaper and easy accessible than other addictive products (1).

Natural cannabis 'esrar' in Turkish produced from cannabis plant, is one of the most commonly used psychoactive molecule for abuse in the world (2). New psychoactive products (synthetic cannabinoids) which are subgroups of the cannabinoids began to produced after prohibition and reduced accessibility of other cannabis in many countries. It's also known as 'spice' or 'K2' in America and European countries (3). This psychoactive molecules act as an agonist of cannabinoid 1-2 receptors (CB1-2) resident central and peripheral nervous system. Central nervous system(CNS) effects like euphoria, hallucination, sleep disorders, visual problems, agitation, motor in coordination, vertigo and psychosis occurs by cannabinoid receptor 1 situated in the brain(4,5). As an intracellular second messenger cAMP concentration is decreased when G α subgroup of G protein is stimulated. As a result release of inhibitory and exhibitory synaptic cAMP dependent neurotransmitters decrease (6). On the other hand CB2 receptors are situated in CNS as well as immunity system cells like monocytes, macrophages, T-B lymphocytes. Many psychoactive molecules such as classical cannabinoids, non-classical cannabinoids, JWH products and benzoilindolles are available in synthetic cannabinoids group (7). The contents of the products sold on the market vary by product. Besides, most products contains JWH-018 molecule (John W. Huffmann) referring to person who found the substance.

Synthetic cannabinoids can be used by inhalation and orally but parenteral usage is

unknown (9). This lipophilic molecule can be quickly absorbed from the lung and distributed whole body when it is used by inhalation. On the contrary this effect is slower when it is used by orally. Although all active ingredients in the products have a different duration of influence, it is known that JWH-018 duration of influence is 1-2 hours.

Many psychiatric symptoms such as euphoria, anxiety, agitation, irritability, paranoia, psychosis can be seen also physical symptoms like sweating, nausea, vomiting, appetite changes, hypertension, hypotension, chest pain, tachycardia, bradycardia, respiratory depression can be seen(10,11). In addition, rarely acute renal failure and myocardial infarction cases had been reported in relation to cannabinoid usage (12).

In our study we aimed to discuss clinical conditions of the cases which were brought to Emergency service(ER) with cannabinoid intoxication diagnosis after that followed up in intensive care unit (ICU).

Materials and Methods: The cases diagnosed synthetic cannabinoid intoxication in the ER of Uzunköprü State Hospital in 2015-2016 and then followed up in the ICU, screened on the files and computer system retrospectively. Age, sex, neurological and cardiac examination during time of application, laboratory parameters such as pH, urea, creatinine, white blood cell counts, electrolyte levels, liver function tests(ALT,AST) were noted. Followed up time in ICU ant intubation need of the cases were taken into consideration. Data were analyzed.

Results: Totally 25 different patients followed up in the ICU of Uzunköprü State Hospital in 2015-2016 with cannabinoid intoxication diagnosis were found. All 25 patients files were included in the study. According to demographic features of the cases, we found one of them 1 (%4) was female, the rests 24 (%96) were male. Ages of the cases were changes between 19 to 59, mean age was 26, 1. We found that two patients were hospitalized twice between dates taken to the study. For these patients first hospitalization data were

For Correspondence:

alicemyekdese@hotmail.com.

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included in the study. Second hospitalization data were excluded. In neurological examination in ER 8 patients(%32) had unconsciousness, 2 patients(%8) had agitation, 5 patients(%20) had confusion, 8 patients(%32) had dizziness (table 1). 2 patients were normal for neurological examination, Glasgow coma scale were 15. Five of 8 unconscious patients were intubated due to superficial respiration and respiratory acidosis found in blood gas tests. All other patients were monitored in ICU with nasal oxygen supply. In examination cardiological findings were 5 cases (%20) only tachycardia, one case (%4) hypertension, 10 cases (%40) hypotension and tachycardia together. Cardiological examination was normal in 9 cases (%36). None of cases had bradycardia or other arrhythmic situations. In gastroenterological examination we did not find nausea, vomiting or other gastroenterologic symptoms. According to laboratory findings one case (%4) had minimal AST elevation (44U/L). Although other cases had normal liver function tests results. We found renal function tests such as urea and creatinine normal for all cases. We saw hypokalemia in one case (%4) (3,1mmol/L). All other cases had no electrolyte imbalance. We found minimal leukocytosis in 13 cases (%52). On the contrast in 12 cases (%46) hemogram test were normal (table 2). We did not see leucopenia in any cases. 4 patients (%16) were followed up in ICU more than 48 hours. 4 patients (%16) were discharged from ICU less than 24 hours. Other 17 patients (%68) were followed up at least 24 hours that must be. All the patients were consulted with a psychiatrist. Death did not occur in our cases.

Discussion: In recent years synthetic cannabinoids have become most popular intoxication product admitted ER in hospitals. Prediction of symptoms for cannabinoid intoxication is quite difficult because of the variety and different amounts of active ingredients provided illegally in the market. Clinical progresses of patients have a wide spectrum depending on the neurological,

gastroenterological, renal and cardiac signs and symptoms.

According to CDC (Centers for Disease Control and Prevention) reports in 2015 in America, synthetic cannabinoid usage increased %330 in comparison with previous year. They found most of the cases were male (%80) mean age were 26. The most common symptoms were agitation (%35), tachycardia (%29), lethargy (%26), vomiting (%16) and confusion(%4,2). The death occurred in %0,05 cases (13).

In a study on 158 cannabinoid usage cases, Bozkurt *et al.* (14) studied sociodemographic features of cases. In the study %5,1 of cases were female, the rests were male, mean age was 26,1. Özer *et al.* (15) reported three cases. According to neurological examination one case was normal, one of them had agitation and the other had hallucination and psychotic changes. Elevated liver function tests were determined two of 3 cases. In the other case cardiac arrest and death occurred when laboratory tests had not been resulted yet. In another study Küçük *et al.* (16) included 11 cannabinoid overdose cases. One of them was female the rest were male. They found %25 cases had agitation, %14 cases had nausea and vomiting, %13 cases had unconsciousness, %16 had palpitation, %3,5 had hallucination. %24 of all cases were followed up in ICU. Altınışık *et al.* (17) studied on 12 cases. One case were intubated. Average of duration of ICU stay was 72 hours. In our study distribution of cases according to sex were %4 female, %96 male. Mean age was calculated 26,1. We determined abnormal liver function test in only one case and also we did not face with death. We didn't see any gastroenterological symptoms. On the contrast almost all cases had neurological symptoms. Five patients were intubated and mean duration of ICU stay was 36 hours.

Ergül *et al.* (18) studied on six cases. Three of them were applied renal replacement therapy (haemodialysis) due to severe acute renal failure. Additionally they found compartment syndrome in two cases and faciotomy were

processed. They saw the decrease in creatine kinase (CK) levels with the treatment. In another study Oğuz *et al.* (19) identified rhabdomyolysis in two cases needed haemodialysis treatment for once. In our study we did not reach CK levels of patients. We didn't find any pathology in renal function tests which are urea and retaining.

Kane *et al.*(20) introduced three cases in their study. Vasopressor treatment were admitted the cases due to hypotension and bradycardia. Vasopressor treatment needs took 48 hours. Besides in the literature two ischemic stroke cases due to synthetic cannabinoid usage were reported (21, 22). Also Keskin *et al.* (23)

reported a case observed ischemic stroke and myocardial infarction concomitantly. We didn't see any major neurological or cardiological outcomes.

In conclusion, illegally launching 'bonzai' has become one of the most important problems for ER and ICU due to rise of usage rates in Turkey like the entire world. According to both cases in literature and our study, however mortality rates are low and mortal complications are only at the level of case reports for the time being, we believed to increase these rates by finding new active ingredients unless inhibiting usage and distribution of them.

Table1: Neurological symptom rates of patients

	Patient count(n)	Rate (%)
Confusion	5	%20
Dizziness	8	%32
Agitation	2	%8
Unconsciousness	8	%32
Normal	2	%8

Table 2: Other Physical examination and laboratory findings

		Patient count(n)	Rate (%)
Cardiovascular symptoms and signs	Tachycardia	15	%60
	Hypertension	1	%4
	Hypotension	10	%40
	Other symptoms	0	0
Gastrointestinal symptoms and signs	Elevated liver function test	1	%4
	Other symptoms	0	0
Renal signs	Renal impairment	0	0
	Hypokalemia	1	%4
Haematological signs	leukocytosis	13	%52
	Other	0	0

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