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Management of Bonsai intoxication at emergency service: A review of 61 cases

Acil serviste Bonsai intoksikasyonu yönetimi: 61 olgunun incelenmesi

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Abstract

Aim: The aim of this study was to determine the effects of bonsai by assessing the correlation between the clinical and laboratory findings of cases diagnosed with bonsai intoxication who had been monitored in the emergency service.

Methods: This study was approved by ''Haseki Training and Research Hospital Ethical Committee of Non-Pharmacological Studies'' with approval number of:183 on 28.01.2015. A retrospective evaluation was performed on 61 bonsai intoxication cases who had been monitored and treated in the emergency service. The clinical findings of the pre- and post-treatment and laboratory findings of each case were evaluated.

Results: According to the initial clinical assessment of bonsai intoxication cases who were admitted to the emergency service, the Glasgow coma score (GCS) was found as 8 (E2, V2, M4), 9 (E2, V2, M5) and 4 (E1, V1, M2) in 87% (n=53), 10% (n=6) and 3.2% (n=2), respectively. The pupil reflex was fixed and dilated in 90% (n=52); whereas, it was normal in 10% (n=9). Although, the biochemical parameters (78.9%, n=49) and blood gas levels (98.6%, n=60) were within the normal physiological range in accordance with their age and gender, the elevated serum levels of creatine kinase (CK) and creatine kinase myocardial band (CK-MB) was determined in 21% of the cases (n=12). The pH value of venous blood gas of a case, in whom the elevated levels of CK-MB and CK were found to be directly proportional, was determined as 7.16. The level of troponin-I, electrocardiogram (ECG) findings, hemogram and coagulation parameters were also within the normal physiological range in accordance with their age and gender. The mean venous blood glucose levels were found as 120 ± 29 mg/dL (min: 78 mg/dL, max: 214 mg/dL), and a reverse correlation was detected between the hyperglycemic conditions of the cases and GCS scores on arrival. Of the bonsai intoxication cases, 60 had been treated with hydration therapy (0.9% NaCl solution, 15cc/min, 2000 cc), one was intubated by using midazolam, and monitored and treated in the emergency service.

Conclusion: Patients with different states of consciousness have been frequently encountered in the emergency service. This condition may depend on various factors such as alcohol, certain endocrine diseases (hypo-hyperglycemia, thyrotoxicosis, etc.), trauma, infections (central nervous system infections, sepsis, etc.), cerebrovascular disorders and intoxication. By considering the elevated synthetic cannabinoid (SC) abuse among the adolescents recently, the use of CB should be kept in mind for the pre-diagnosis of the juvenile patients who were brought to the emergency service with loss of consciousness.

Keywords: Bonsai intoxication, Cannabimimetic analogues, Emergency service

Öz

Amaç: Acil servisimizde takip edilen bonzai intoksikasyon vakalarının klinik ve laboratuar bulguları değerlendirilerek bonzainin etkilerinin belirlenmesi amaçlanmıştır.

Yöntemler: Bu çalışmada; 28.01.2015 tarihinde 183 onay numarası ile "Haseki Eğitim ve Araştırma Hastanesi İlaç Dışı Klınik Araştırmaları Etik Komitesi" tarafından onay alınarak acil serviste takip ve tedavi edilen 61 bonzai intoksikasyon vakası retrospektif olarak incelenmiştir. Her bir vakanın geliş klinik ve labovatuar bulguları ile takip ve tedavi sonrası klinik bulguları değerlendirilmiştir.

Bulgular: Acil servise getirilen bonzai intoxikasyon vakalarının ilk klinik değerlendirmesinde; glaskow koma skorları; % 87'sinde (n=53) 8 puan (E (eyes): 2, V(verbal): 2, M(motor): 4), %10 unda (n=6) 9 puan (E:2, V:2, M: 5), %3,2 (n=2) inde 4 puan (E:1, V:1, M:2) olduğu tespit edildi. Pupil reflexleri %90'ında (n=52) fixdilate iken, %10'unda (n=9) normal olarak değerlendirildi. Biyokimyasal değerlerinin %78,9 (n=49) kan gazı değerlerinin %98,6'sı (n=60) yaş ve cinsiyetlerine göre normal fizyolojik sınırlar içindeyken, vakaların %21,5'inde (n=12) CK ve CK-MB değerlerinin yüksek olduğu ve saptanan yüksek CK-MB değerleri ile CK değerlerinin doğru orantılı olduğu bir vakanın venöz kan gazı Ph değeri 7,16 olduğu görüldü. Troponin–I değerleri, EKG (elektrokardiyogram) bulguları, hemogram ve koagülasyon değerlerinin de vakaların yaş ve cinsiyetine göre normal fizyolojik sınırlarda olduğu tespit edildi. venöz kan glukoz değerleri ortalama 120 ± 29mg/dL olduğu (min:78mg/dL, max:214mg/dL) ve vakaların hiperglisemik durumları ile geliş glaskow koma skorları arasında da ters yönlü korelasyon ilişkisi olduğu saptandı. Gelen 60 bonzai intoksikasyonu vakasına hidrasyon tedavisi (%.0.9 NaCl solüsyonu, 15cc/dk, 2000 cc) verildiği, sadece bir vakanın da midazolam verilerek entübe edildiği ve acil servis yoğun bakımında takip ve tedavisinin yapıldığı görüldü.

Sonuç: Acil servislerde bilinç durum değişikliği olan hastalarla sıkça karşılaşılmaktadır. Bu durum; alkol, bazı endokrin hastalıklar (hipo-hiper glisemi, tirotoksikoz vb), travma, enfeksiyon (santral sinir sistemi enfeksiyonları, sepsis vb), serebrovasküler problemler ve zehirlenmeler gibi bir çok nedene bağlı olabilir. Son zamanlarda SK kullanımının toplumda gençler arasında yaygınlaştığı da bilinmektedir. Bu nedenle bilinç durum değişikliği ile Acil servise getirilen genç hastalarda SK kullanımının da ön tanıda akılda tutulması önemlidir.

Anahtar kelimeler: Bonzai intoksikasyonu, Sentetik kannabimimetik analoglar, Acil servis

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Introduction

Synthetic cannabinoids (SC) were first used in 2004 and became rapidly popular, especially among adolescents [1-5]. SCs have various names worldwide, with the most common one being "spice". However, in Turkey they are commonly known as "bonsai" [3]. Cannabinoids are classified into three groups as natural, endogenous and synthetic. The most well-known natural cannabinoid is delta 9-tetrahydrocannabinol (THC) which is the main ingredient of marijuana [6]. Endogenous cannabinoids consist of 2-arachidonoylglycerol and anandamide. However, SCs are made up of synthetic molecules in the laboratories to mimic the effects of THC [7,8]. SC are generally consumed in the form of cigarettes (with pipe, cigarette or hookah), however, vaporization, oral or rectal use were also reported [9]. The reported toxic symptoms of SC include agitation, seizures, hypertension, nausea, vomiting, hyperkalemia, anxiety, paranoia, tachycardia, nervousness, hallucination, paresthesia, somnolence and speech disorders [10-11].

Besides, there is certain evidence for an association between SC and psychiatric symptoms including psychosis [12]. In the present study, the state of consciousness of cases was evaluated by Glasgow coma score (GCS). GCS is an indicator which assesses the condition of central nervous system independently from the primary etiology. Drug intoxications and the use of narcotics may cause brain damage with loss of consciousness due to their effects on brain biochemistry [2,3]. The brain functions and the course of patient are evaluated according to the eye movements, verbal and motor responses in GCS. The GCS is scored between 3 and 15; 3 being the worst, and 15 the best. A score of 13 or higher is categorized as a recoverable brain injury, 9-12 as moderate, and 8 or below as severe brain injury [10].

A case was reported in whom the use of SC JWH-018 was considered to be associated with acute ischemic stroke [13]. Following the long-term use of SC, the syndromes of tolerance and abstinence are observed in patient. Tolerance has been developed rapidly which is thought to be relatively associated with high-addiction potential. Abstinence syndrome was defined as anxiety, increased sweating, excessive desire for drug abuse, tremor, headache, nightmares, insomnia, and irritability, difficulty in concentration, nausea and depression [9,10]. There were also various convulsion cases related to SC, and these are classified as tonic clonic seizure and they don't cause sequelae [5]. It is recommended to use benzodiazepine as an adjuvant therapy for the symptoms related to SC for the control of anxiety and agitation [14]. In the present study, the clinical and laboratory findings of bonsai intoxication cases who had been monitored in the emergency service were retrospectively evaluated.

Materials and methods

A retrospective evaluation was performed on 61 bonsai intoxication cases who were admitted to the emergency service of hospital by ambulance, between August and November of 2014. The cases were evaluated in terms of age, gender, arrival time to emergency service, GCS on arrival, physical examination findings, cardiac enzyme levels, ECG findings, biochemical parameters, hemogram and blood values levels, and pre-and-post therapy GCS and examination findings

Statistical analysis

SPSS 16.0 (Statistical Package for the Social Sciences) package program was used for the statistical analysis of the study data. Statistical descriptive methods were used for the assessment of the data (mean, standard deviation, median, frequency, ratio, minimum, maximum). The level of significance for the study was $p<0.05$.

Results

The mean age of the cases was 25.4 ±76 years (min: 15, max: 53), and it was determined that it was more frequently seen in age group of 20-30 years (44%, n=27) (Figure 1). The most common arrival time of the emergency service was between 8.00 pm and 2.00 am (86.6%, n=53), and they were all male except one case (98.6%, n=60).

According to the initial clinical assessment of bonsai intoxication cases, the pupil reflex was fixed and dilated in 90% (n=52); whereas, it was normal in 10% (n=9). The GCS scores on arrival were found as 8 (E2, V2, M4), 9 (E2, V2, M5) and 4 (E1, V1, M2) in 87% (n=53), 10% (n=6) and 3.2% (n=2), respectively (Table 1). The mean venous blood glucose level was 120±29 mg/dL (min: 78 mg/dL, max: 214 mg/dL) on arrival. A reverse correlation was detected between the hyperglysemic conditions of the cases and GCS scores on arrival (r=-0.25, p= 0.021). The most common symptoms and findings were determined as agitation (83%, n=51), vomiting (37%, n=23), dizziness/lethargy (98.6%, n=60), confusion (97%, n=59), changes in consciousness (98.1%, n=60), hypoglycemia (3.7%, n=2) and hyperglycemia (86.3%, n=53) (Table 2).

The ECG of the cases revealed no pathological findings on the emergency arrival. When the laboratory findings on arrival were evaluated, the level of troponin-I, hemogram and coagulation parameters were within the normal physiological range in accordance with their age and gender.

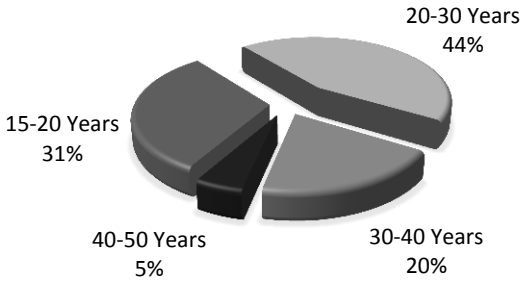

Figure 1: The age distribution of bonsai intoxication cases who were monitored and treated in the emergency service

Table1: The GCS scores of bonsai intoxication cases before the treatment

Number of cases	GCS scores
53 Cases (86.8%, n=53)	8 Point (E2, V2,M4)
6 Cases (1%, n=6)	9 Point (E2, V2, M5)
2 Cases (3.2%, n=2)	4 Point (E1, V1, M2)

Abbreviations: GCS: Glasgow Coma Scale, E:Eye Opening Response, V:Verbal Response, M:Motor Response

Table 2: The most common symptoms and findings of bonsai intoxication cases who were monitored and treated in the emergency service

Symptoms and findings of the cases at the initial assessment		
Agitation	51 Cases	87% (n=51)
Vomiting	23 Cases	37% (n=23)
Dizziness/lethargy	60 Cases	98, 6% (n=60)
Confusion	59 Cases	97% (n=59)
Changes in consciousness	60 Cases	98.1% (n=60)
Hypoglycemia	2 Cases	3.7% (n=2)
Hyperglycemia	53 Cases	86.3% (n=53)

Of the cases, 21.5% had elevated serum levels of creatine kinase (CK) and creatine kinase myocardial band (CK-MB), and the pH value of venous blood gas of one case, in whom the elevated levels of CK-MB and CK were found to be directly proportional, was determined as 7.16. The laboratory findings of the cases were summarized in Table 3. According to the anamnesis that was obtained from the patients and their relatives, none of the cases had a history of diabetes mellitus and elevated blood lactate levels in their blood gas values. All bonsai intoxication cases were monitored closely for 24 hours following their emergency department triage. The cases were treated by hydration therapy (0.9% NaCl solution, 15cc/min, 2000 cc), except one case, who was intubated by using midazolam as a result of respiratory depression and metabolic acidosis (pH of venous blood gas: 7.16), and monitored and treated in the emergency service.

The pupil reflexes of the cases were able to be measured after 3.7 ± 2.1 hours in average during their follow-up and treatment. The mean GCS scores was 14.38 at the 12th hour; it was scored as 15, 14 and 13 in 39% (n=24; E4, V5, M6), 59% (n=36; E4, V4, M6) and 2% (n=1; E4, V4, M5) of the cases, respectively (Table 4).

Table 3: Laboratory findings on arrival of bonsai intoxication cases who were monitored and treated in the emergency service

Test	Parameter	Min	Max	Mean	Normal range
Venous Blood Gas	Ph	7.1	7.5	7.35±0.07	7.31 - 7.41
	pO_2 mmHg	15.9	92.8	54.1±32.6	35 - 45
	pCO_2 mmHg	29	80	54.1±32.6	41 - 51
	HCO_2 mmol/L	19.7	42	27.9±4.3	24 - 28
	SO_2 %	19	99.50	73.3±20.5	55 - 70
Biochemisty	Glucose mg/dL	78	214	120±29	74 - 106
	CK U/L	57	3700	149	<145
	CK-MB ng/mL	0.6	121	2	0.6-6.3
	Troponin-l ng/mL	0.01	0.03	0.01±0.004	0 - 2.00
	Urea mg/dL	14	54	30.0±8.4	17 - 43
	Creatine mg/dL	0.5	1.3	0.8±0.1	0.51-0.95
	AST U/L	14	171	25	<35
	ALT U/L	6	262	17.5	<35
	LDH U/L	72	645	236	<247
	Ca mg/dL	7.8	10.5	9.2±0.6	8.4 - 10.5
	Na mg/dL	132	145	136±3.0	136 - 145
	K mg/dL	3.3	5.8	3.9±0.4	3.3 - 5.1
	Cl mg/dL	92.6	100.8	100±12	98 - 107
Complete Blood Count	Wbc 10e9/ul	4.5	18.3	9.9±4.4	4.00 - 10.00
	Hgb g/dL	12.4	17.6	14.7±1.3	11.0 - 16.0
	Hct %	37	53	44.1±3.4	37.0 - 54.0
	Platelet 10e9/ul	148	431	258±65	100 - 300 l
Bleeding Time	INR	0.8	1.5	1.0±0.1	0.8 - 1.2
	APTT sn	19.8	27.7	23.0±7.0	23 - 35
	Prothrombin time sn	10.3	14.6	11.8±1.2	10 - 14

Abbreviations: CK: creatine kinase, CK - MB: creatine kinase myocardial band

Table 4: The GCS scores of bonsai intoxication cases who were monitored and treated in the emergency service at the 12th hour

Number of cases	GCS scores
24 Cases (39.3%, n=24)	15 Point (E4, V5,M6)
36 Cases (59%, n=36)	14 Point (E4, V4, M6)
1 Case (1.7%, n=1)	13 Point (E4, V4, M5)

Abbreviations: GCS: Glasgow Coma Scale, E:Eye Opening Response, V:Verbal Response, M:Motor Response

During the follow up of the cases in the emergency service for 24 hours, the clinical and laboratory findings were completely improved and none of them developed any complications. Therefore, they were discharged from the hospital by informing them and their relatives about the drug addiction and by referring them to the addiction control centers.

Discussion

SCs were initially noticed in European Union, however the recent reports on the abuse of these compounds spread all around the world [15-20]. The most common form of natural cannabinoid is 9-THC [3,6]. Cannabinoids affect the CB1 and CB2 receptors in the body and they show these effects generally based on a CB1 like mechanism of action, impaired consciousness, sleep changes and cardiovascular effects. Whereas the role of CB2 is poorly understood, it is known that THC acts only through CB1. This is different than SC's, which act both through the CB1 and CB2 receptors and are more effective than THC [15,17]. The binding affinity, and thereby the effects of the SCs to the CB1 receptors show variations; it has higher affinity and stronger effect than 9-THC [16]. The clinical findings of the SCs may be different due to the variations in their composition. These drugs can cause anxiety or panic as well as opposing effects like repressed anxiety. The most frequent cardiovascular effects are hypertension and tachycardia, but effects such as bradycardia and hypotension have also been reported [4,6]. In a study performed by Hoyte et al., the most common symptoms were detected as tachycardia (40%), agitation (23.4%), vomiting (15.3%), dizziness/lethargy (13.5%), confusion (12%), nausea (10%), hallucination (9.4), hypertension (8.1%), drowsiness (7.3%), chest pain (4.7%), syncope (2.1%), hypotension (1.3%) and bradycardia (1.3%) in 1,353 patients who were exposed of a single component of SC [1]. The reason of variations in the clinical findings is still unknown; however, the type of SCs, the amount of toxic substances, the frequency of use, personal liability and the chronic toxicity effect of SC might cause these variations [5,18].

In the present study, symptoms and findings were similar to those reported in the literature and the results were presented in Table 2 and 3.

According to the laboratory findings, the serum levels of CK-MB was determined as normal in 92% (n=5); whereas it was elevated in 8% (n=6) of the cases. The serum levels of CK-MB and CK were found to be directly proportional. These elevated serum values might be related to the initial medical approaches that were performed in the emergency service. Although, the action time is shorter than 8 hours in most the SC intoxication cases, it has reported that it might take more than 24 hours in certain individuals [2]. It is recommended to use benzodiazepine as an adjuvant therapy for the symptoms related to SC for the control of anxiety and agitation [9]. In the present study, only hydration therapy was performed on cases and they were closely monitored for 24 hours. Only one patient was intubated for 3 hours and monitored under the conditions of intensive care. It was determined that the duration of confusion did not proceed more than 24 hours in none of the cases during their 24-h follow-up in the emergency service, and the consciousness was completely recovered after 5.7 ± 2.2 hours in average.

The number of abusers of synthetic cannabinoids and cathinones has increased remarkably worldwide. The chemical structures of the distributed drugs are skillfully changed so that the drugs may pass through screenings for detection. Simple screening methods are required for detection of these drugs in seized and biological materials. There are currently no commercial kits or devices for the routine screening of these drugs. Colorimetric, immunochemical, and chromatographic methods have been introduced in reviews; a suitable method

must be chosen for each laboratory. Although various human sample matrices are available for testing, urine and blood are of the first choices. However, many of these drugs, especially unchanged synthetic cannabinoids, exist in urine and blood for only a short period. Therefore, other matrices that can prove the consumption of these drugs, such as hair and saliva, are likely to receive more attention in the future [21].

The diagnoses of bonsai intoxication is done according to the information obtained from patient's relatives and ambulance personnel who make the first intervention and transfer, physical examination and clinical findings of the cases. The routine screening tests for SCs have not yet been performed in hospitals connected to Ministry of Health, and it was determined that SC screening test was not applied to 61 cases included in our study. It is required to include SC screening test to the routine procedures, and to perform more detailed studies regarding the detection of connection between the symptoms and findings in these cases by means of determining the metabolites of SC. Recently, SC has become the widely consumed substance worldwide. The age range of the users is pretty wide and bonsai has become popular especially among adolescents. It is predicted that the number of users will continue to increase gradually due to its cheaper price and ease of accessibility. The legal arrangement directed to these substances should be reviewed, and it is necessary to apply criminal sanction especially to the dealers, to determine the profile of the users, to educate the individuals who are fitting to this profile about drug abuse and to take precautions as soon as possible. In collaboration with the Ministry of Education and the Ministry of Health, educational seminars should be organized about the use of bonsai and other addictive substances for children in the primary and secondary education period and their families. Moreover, the conditions of rehabilitation centers should be improved by the Ministry of Health and the awareness of the society should be raised by means of organizations including the Ministry of Health, media and nongovernmental organizations.

These substances are affecting all body systems and cause psychiatric disorders in addition to the loss of physical health in juvenile population. Besides, it raises the crime rate, it also hinders education and causes loss of job and educational power, and the chronic use of these substances may result with death in the end.

Patients with different states of consciousness have been frequently encountered in the emergency service. This condition may depend on various factors such as alcohol, certain endocrine diseases (hypo-hyper glycaemia, thyrotoxicosis, etc.), trauma, infection (central nervous system infections, sepsis, etc.), cerebrovascular disorders and intoxication. By considering the elevated synthetic cannabinoid (SC) abuse among adolescents recently, the use of CB should be kept in mind for the pre-diagnosis of the juvenile patients who were admitted to the emergency service with loss of consciousness. As an early diagnosis, the possibility of using SC should be considered in all juvenile cases who are admitted to the emergency service and are suffering from changes in consciousness due to the proliferation of SCs among the adolescence.

The limitation of our study is the lack of bonsai screening tests in the monitored individuals due to the currently available facilities of the hospitals. The screening tests may identify the metabolites of the SC along with their associated signs and symptoms. Therefore, further studies, which will be conducted with larger study populations and which will provide results evidenced by laboratory tests are warranted in order to elaborate a clearer insight on the effects of bonsai use.

In conclusion, it is certain that Bonsai use is gradually increasing and it will continue to be a health problem. Therefore, the need for the identification of the chemicals contained in these substances and the necessary examination, equipment and experience for reporting will also increase day by day.

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