Could NCM-3S Be Used In The Intubation Decision of Patients Showing Toxicity Findings After Synthetic Cannabinoid Abuse?

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Abstract

Objective: We aimed to evaluate the need for endotracheal intubation of patients with NCM scoring system by using findings of examinations, vital parameters, and results of blood gas tests of the patients coming to the emergency room (ER) with acute toxicity caused by synthetic cannabinoid.

Material and Methods: Information regarding the 140 patients (out of all 319905 patients coming to the ER in 1 year) between the ages of 15-65, showing findings of acute toxicity caused by synthetic cannabinoid, such as complaints at first admission, sex, demographic characteristics, vital signs, examination findings, results of performed imaging and lab tests, administered treatments, information on the service in which the patients stay or are referred are all retrospectively reviewed. The ones who need intubation are evaluated under risky patient group (RPG) while the ones that have been discharged from the ER are evaluated as non-risk group (NRPG).

Results: When the intubation need of the patients is reviewed, it has been seen that there is statistically significant difference in the respiratory rate measured in the ER, systolic blood pressure, O2 saturation, Glasgow coma score, PCO2 values and pulse rate of patients in the risk group. NCM-3S scoring has been created to evaluate the intubation need of patients showing acute toxicity of synthetic cannabinoid.

Conclusion: It has been concluded that NCM-3S score, which we created using pulse rate, systolic blood pressure, respiratory rate, fingertip oxygen saturation, mental state and PCO2 values of patients showing signs of acute toxicity of synthetic cannabinoid in the ER, can be used in projecting the intubation need of patients.

Key words: Synthetic cannabinoid, emergency service, symptom and findings

Özet

Amaç: Acil servise sentetik kannabinoid akut toksisitesi ile başvuranlarda; muayene bulguları, vital parametreleri ve kan gazı test sonuçlarına göre geliştirdiğimiz NCM skorlama sistemi ile hastaların endotrakeal entübasyon ihtiyacını değerlendirmeyi amaçladık.

Metod: Acil servise 1 yıl boyunca başvuran 319905 hastadan sentetik kannabinoid akut toksisite bulguları gösteren 15- 65 yaş aralığındaki 140 hastanın başvuru şikayetleri, cinsiyeti, demografik özellikleri, vital bulguları, muayene bulguları, yapılmış olan görüntüleme ve laboratuar testleri, uygulanan tedavi, yattığı veya sevk edildiği bölüm bilgileri retrospektif olarak incelendi. Entübasyon ihtiyacı olan hastalar riskli hasta grubu olarak, acil servisden taburcu olan hastalar riskli olmayan grup olarak değerlendirildi.

Bulgular: Hastaların entübasyon ihtiyacını değerlendirmek için Riskli hasta grubunda acil serviste ölçülen solunum sayısı, sistolik kan basıncı, saturasyon O², Glaskow koma skoru, PCO² değeri ve nabız dakika sayısında istatistiksel olarak anlamlı fark tespit edildi. Sentetik kannabinoid akut toksisitesi gösteren hastaların entübasyon ihtiyacını değerlendirmek için NCM-3S skorlaması oluşturuldu.

Sonuç: Acil serviste Sentetik kannabinoid akut toksisite bulguları gösteren hastalarda ölçülen nabız dakika sayısının, sistolik kan basıncının, solunum sayısının, parmak ucu sat O² değerinin, mental durumunun, PCO² değeri ile oluşturduğumuz NCM-3S skorunun hastaların entübasyon ihtiyacını öngörmede kullanılabileceği sonucuna varılmıştır.

Anahtar kelimeler: Sentetik kannabinoid, acil servis, semptom ve bulgular

Sutaşır
Could NCM-3S Be Used In The Intubation Decision of
16 Patients Showing Toxicity Findings After Synthetic Cannabinoid Abuse?

Eurasian J Tox. 2020; 2 (1):15-22

Introduction

Psychoactive substances (Psychotropic) are chemicals that essentially affect the central nervous system and cause temporary changes in perception, mental state, level of consciousness and behavior by changing the functions of the brain. Over the last years, there has been a massive increase in new psychoactive substances which are also called legal highs, designer drugs, herbal highs, and research chemicals[1]. Even though synthetic cannabinoids (SC) are generally consumed in the form of cigarettes (with pipes, cigarettes or hookahs), rectal or oral (in vapor) have also been reported[2]. These chemicals show their effect by activating the cannabinoid receptors in the body. Cannabinoid receptors have two known sub-groups which are Cannabinoid 1 (CB1) receptor and Cannabinoid 2 (CB2) receptor. The CB1 receptor is more localized in the brain while the CB2 receptor can be found within the immune system. Synthetic cannabinoids typically have a full agonist effect on CB1 receptors hence causing maximum effect even with low doses[3].

Even though resembling cannabis, since SCs do not have any record in any mass spectrometer system and do not have reference standards, they cannot be identified[4,5]. The patients generally apply to hospital with neurological, psychiatric, cardiac, and respiratory disorder findings[6]. Among the cases, serious conditions such as acute coronary syndrome (ACS), seizure, stroke, rhabdomyolysis, acute renal failure, and respiratory depression have also been notified. A significant number of cases were monitored in the ICU, some of them even reported to have died during their stay[7,8,9,10]. For an emergency physician, it is not easy to manage a case that is thought to be SC toxicity. The reason for this is the obligation to make a timely and correct decision about a patient with somnolence and vomiting and who cannot be communicated or have any other relatives except for hospital staff and of whom it is utterly difficult to obtain any medical history or information. In this study, we aimed to evaluate the need for endotracheal intubation (ETI) of patients applying to ER after SC abuse, through NCM-3S scoring system (respiratory rate, systolic blood pressure, O_2 saturation (satO_2), Glasgow Coma Score (GCS), PCO2 value and pulse rate) we developed using first examination findings, vital signs and results of blood gas test.

Materials and Methods

The study is initiated with the approval (number 1058) of the 3rd step Training and Research ethics committee, dated 01/09/2015. The study, which was planned retrospectively, included 140 cases between the ages 15-65 with statements of synthetic cannabinoid abuse in their story, out of 319905 patients applying to the ER between the dates July the 1st, 2014 and June the 30th, 2015. The study is performed as per the principals of the "World Medical Association Declaration of Helsinki".

The hospital automation records, judicial reports, and ambulance records of patients coming to the ER either by walking or by ambulance and who have statements (either by themselves or by their relatives) of synthetic cannabinoid abuse, have retrospectively been reviewed (for 1 year). Patients' complaints at first admission, sex, demographic characteristics, vital signs, examination findings, results of performed imaging and lab tests, administered treatments, information on the service in which the patients stay or are referred are all retrospectively reviewed through patient files or automation system of the hospital, and the information of patients who qualify to be included in the study is registered in the form we created.

Vital signs of the patients (arterial blood pressure, pulse, fever, oxygen saturation), Glasgow Coma Score points, effects after substance exposure (palpitation, sweating, nausea, vomiting, xerostomia, fatigue, edginess, chest pain, dyspnea, headache, uneasiness, itchiness, eye redness, drowsiness, blurred vision, eye burning, skin redness, dizziness, somnolence, spasm, hand numbness) are reviewed. Physical examination findings which can be related to substance use such as wakefulness, somnolence, stupor, coma, agitation, hallucination, anxiety, confusion, euphory, convulsion, increased muscular tonus, flushing, tachypnea, cyanoses, arrhythmia, conjunctival hyperemia, nystagmus, mydriasis, myosis, hyperpyrexia, salivation, lacrimation, urinary incontinence, erection, diarrhea, emesis, hyperreflexia and, hypoventilation, and hyperventilation.

In lab tests, pH, pO_2, pCO_2, HCO_3, BE levels are checked from the blood gas samples drawn in the ER. Results such as the applied intubation, referral to ICU and exitus are retrospectively reviewed via patient files and hospital automation system and registered in patient forms. The patients who need intubation and are referred to the ICU are evaluated as risky patient group (RPG), and the patients who are discharged from the ER are evaluated as non-risky patient group (NRPG). In light of the study, we created NCM-3S scoring to evaluate patients' need for intubation. The scoring system, which is created as per respiratory rate, systolic blood pressure, O_2 saturation (satO_2), Glasgow Coma Score (GCS), PCO2 value and pulse rate is shown in Table 1.

For statistical analysis, SPSS for Windows software is used. In descriptive statistics of the data, values such as mean, standard deviation, median lowest, highest, frequency, and proportion are used. Variable distribution is measured with the Kolmogorov-Smmirnov test. In the analysis of quantitative data, the Mann-Whitney test and unpaired t-test are used. In the analysis of qualitative data, the chi-square test is used, and when chi-square conditions are not ensured, the Fischer test is used. The effect level is reviewed through univariate and multivariate logistic regression analysis. In the survival analysis, SPSS 22.0 software is used. The statistical alpha significance level is accepted as $p < 0,05$.

Eurasian J Tox. 2020; 2 (1):15-22

Sutaşır
Could NCM-3S Be Used In The Intubation Decision of
Patients Showing Toxicity Findings After Synthetic Cannabinoid Abuse? 17

Table 1. NCM-3S scoring system

NCM- 3S	0	1	2	3
Respiratory Rate	12-16	<12 / >16		
Systolic blood pressure	90-140	60-90 >160	<60	
O$_2$ Saturation	95 and above	90-94	85-90	<85
Glasgow coma score (Mental)	14-15	9-13	7-8	<6
P CO$_2$	<45	45-60	61-80	80>
Pulse rate	60-100	30-59 100-120	<30 >120	

Results

The mean age of participating 140 patients was 27,2 ± 8,1 and 129 of the patients (92,1%) were male. 77 of the patients (55%) were brought to the ER by an ambulance, 49 of them (35%) by walking and 14 of them (10%) are brought by being carried by their relatives.

Patients on SC only form 67,1% of the participants while patients on both alcohol and SC form 11,4% and patients on other pleasure-inducing substances along with SC form 21,4%. When the method of SC abuse is reviewed, the most frequent abuse method was with hand-rolled cigarettes by 76 patients (54,3%). When the symptoms of the first admission of patients in ER are reviewed, the most frequent symptom is somnolence with 42 patients (30%), vomiting with 38 patients (27,1%) and palpitation with 37 patients (26,4%) (Table 2). Admission vital signs, fingertip saturation, and GCS values and admission blood gas parameters of patients at the time of the first admission to ER are stated in Table 3. When RPG and NRPG patients are evaluated, among all patient groups, 24 patients (17.14%) underwent ETI and there was statistical significance between blood pressure, respiratory rate, pCO2, SpO2, GCS, pH, pO2 and NCM-3S scores of these patients (Table 4,5). In the ROC analysis performed for the decision of applying ETI for the patients admitted to the ER following SC abuse, NCM-3S score, age, diastolic BP, pulse, mean arterial pressure, systolic BP, pCO2, SpO2, GCS, pH, pO2 values of 24 patients underwent ETI (17.14%) are reviewed and the highest AUC values were NCM score (AUC: 0.932) and pCO2 (AUC: 0.909), respectively (Figure 1).

Discussion

It has been seen that the majority of the patients admitted to the ER due to SC abuse were male and a part of the young patient population. When the patients are evaluated as per their SC abuse along with alcohol and other pleasure-inducing substances; it was seen that the majority went to the ER due to sole SC abuse however substances such as cannabis, extasy, alcohol, heroin, cocaine, cigarettes, energy drinks,

Table 2. Effects following SC abuse and distribution of ER finding

Symptoms following abuse	n	%
Somnolence	42	30,0%
Vomiting	38	27,1%
Palpitation	37	26,4%
Fainting	30	21,4%
Nausea	27	19,3%
Chest pain	25	17,9%
Dyspnea	20	14,3%
Drowsiness	20	14,3%
Spasm	19	13,6%
Fatigue	15	7,1%
Uneasiness	12	10,7%
Seizure	13	9,3%
Other (Eye redness, sweating, tremor, edginess, skin redness, dizziness, hot flash, blurred vision, eye burning, xerostomia, itchiness, hand numbness)	66	47,1%
Findings of Examination		
Somnolence (Lethargy)	36	25,7%
Wakefulness	31	22,1%
Confusion	28	20,0%
Arrhythmia	26	18,6%
Mydriasis	25	17,9%
Agitation	24	17,1%
Hypoventilation	23	16,4%
Tachypnea	21	15,0%
Stupor	17	12,1%
Euphoria	12	8,6%
Emesis	10	7,1%
Other neurological findings (increased muscular tonus, coma, convulsion, hyperreflexia, myosis, nystagmus, anxiety, fixed dilated pupils)	43	31,4%
Other (conjunctival hyperemia, cyanoses, salivation, erection, flushing, lacrimation, diarrhea, hyperpyrexia, urinary incontinence, hyperventilation)	31	22,1%

18 Sutaşır
Could NCM-3S Be Used In The Intubation Decision of
Patients Showing Toxicity Findings After Synthetic Cannabinoid Abuse?

Eurasian J Tox. 2020; 2 (1):15-22

Table 3. Patients' admission parameters and first blood gas measures

Admission Parameters	Median	Min-Max
Systolic Pressure	110,0	60 - 160
Diastolic Pressure	63,5	40 - 100
Mean Pressure	80,0	47 - 120
Pulse	92,0	30 - 140
Respiratory Rate	14,0	0,0 - 25,0
Fever	36,5	35 - 37
SPO_2	94,0	57 - 100
GCS	15,0	3,0 - 15,0
Ph	7,3	6,5 - 7,5
PO_2	80,0	52 - 102
PCO2	50,0	37 - 148
BE	-1,0	-9,2 - 11,0
HCO_3	23,0	15,8 - 31,0

Table 4. Comparison between patients who underwent endotracheal intubation and who did not undergo endotracheal intubation as per values

	ETI N/A		ETI Applied		
	Median	Mean ± SD	Median	Mean ± SD	p
Blood gas pH,	7.3	7.3±0.1	7.2	7.1±0.2	0.000
pO_2,	80.0	79.7±10.7	81.5	82.3±4.6	0.697
pCO_2,	48.0	50.7±11.3	75.0	82.9±33.0	0.000
Systolic pressure	110.0	114.0±15.6	92.5	94.8±17.9	0.000
Diastolic pressure	70	67.1±11.5	50.0	53.7±9.1	0.000
Mean pressure	83,3	82.7±12.1	66.7	67.4±11.5	0.000
Pulse	91.5	92.9±13.8	101.0	92.7±30.4	0.337
Respiratory rate	15.0	15.6±4.1	10.0	9.4±2.9	0.000
Sat O_2	95.0	94.6±4.7	86.0	84.8±8.3	0.000
GCS	15.0	13.6±2.5	5.0	6.3±3.2	0.000

ETI; endotracheal intubation

Table 5. RGP and NRGP evaluation as per age, diastolic BP, pulse, mean arterial pressure, systolic BP, pCO2, SpO2, GCS, pH, pO2

			Asymptotic 95% Confidence Interval	
Test Result Variable(s)	Area	Asymptotic Sig.[b]	Lower Bound	Upper Bound
Age	,594	,147	,467	,721
Diastolic BP	,244	,000	,142	,346
MBP	,222	,000	,116	,328
Pulse	,551	,434	,403	,699
Respiratory Rate	,047	,000	,015	,079
Systolic BP	,238	,000	,124	,352
pCO_2	,909	,000	,830	,988
SpO_2	,087	,000	,010	,165
GCS	,101	,000	,018	,184
pH	,078	,000	,011	,146
pO_2	,158	,000	,048	,268
Total Score	,932	,000	,863	1,000

Eurasian J Tox. 2020; 2 (1):15-22

Sutaşır
Could NCM-3S Be Used In The Intubation Decision of
Patients Showing Toxicity Findings After Synthetic Cannabinoid Abuse? 19
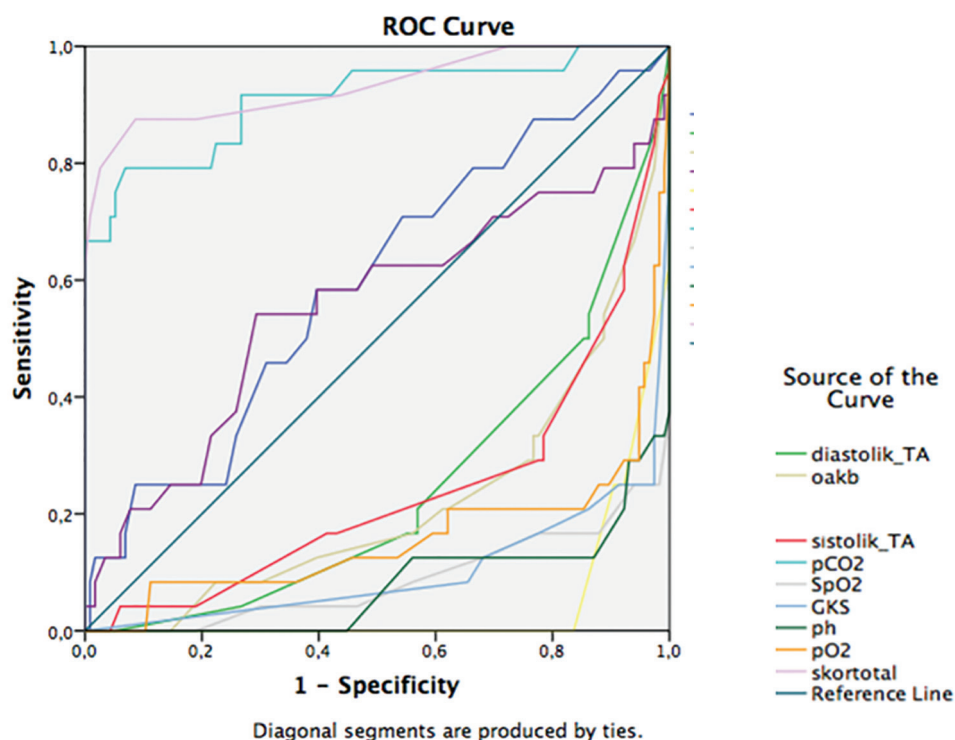
Figure 1. Roc analysis performed to define the need for ETI as per age, diastolic BP, pulse, mean arterial pressure, systolic BP, pCO2, SpO2, GCS, pH, pO2 and NCM-3S score values

and methylenedioxymethamphetamine are frequently used together[6,11,12]. The fact that in this study, the percentage of alcohol consumers with SC is 11,4% and other pleasure-inducing substance users' is 21,4% show that just as the literature suggests, other psychotropic substances can be used along with SC. Usage of other substances along with SC is a topic that requires consideration especially during emergency interventions of intoxication cases and when planning a course of treatment against substance abuse. As stated in the literature, the acute physical effects of SCs vary from sweating, nausea, vomiting, hypertension/hypotension, chest pain, dyspnea, tachycardia/bradycardia, respiratory depression, mental fog, confusion, psychomotor agitation, somnolence and sedation[11,12,13]. Yoshito Kamijo et al carried out a multicenter retrospective study in Japan and saw 24,9% vomiting, 23,6% uneasiness, 15,6% nausea, 14,5% palpitation, 9,3% confusion[14]. And in our study, we have seen 30% somnolence, 27,1% vomiting, 26,4% palpitation. When the examination findings following SC abuse are reviewed, we have seen sweating, nausea, vomiting, tachycardia, arrhythmia, hypotension, hypertension, anxiety, clonus, hypertonicity, fasciculations, ataxia, mydriasis, nystagmus, tremor, somnolence, hallucination, decreased motor coordination, confusion, stupor, and state of coma[4,6,11,13,15]. All these findings suggest that what is stated in literature coincide with the examination results in our study and that when patients come to the ER with SC abuse, psychological, neurological, cardiac, metabolic, gastrointestinal, muscular, ocular findings can be seen.

Many other studies performed on patients with SC abuse show us that following evaluation in which the first examination and treatment were performed in ERs, the patients who underwent intubation were followed in ICUs[7,9,15]. There are scoring systems used in evaluating the severity and discharge of patients of risk groups in ERs and ICUs[16]. It is possible to define the risk status of patients with simple bedside flow diagrams which include respiratory, cardiac and mental status evaluations[17]. Acute Physiology and Chronic Health Evaluation (APACHE), is the first model of scoring systems developed to have an idea about the prognosis of patients. However, as this system was too complicated for routine usage, the APACHE II system was created[18]. The calculation is made with the worst values of the results of biochemical analyses which are done with the blood tests performed in the first 24 hours following the admission of patients. For this reason, APACHE II is not a suitable system to be performed swiftly in the ERs[19]. Another scoring system is called Mainz Emergency Evaluation Score (MEES) and is a descriptive scoring system, also including GCS[20]. In this system, in addition to GCS, 7 other parameters such as arterial systolic blood pressure, pulse, respiratory rate, oxygen saturation value, EKG changes, and pain measurement are included in the evaluation[16]. Modified Early Warning Score (mEWS) is another validated bedside flow diagram used in emergency service admissions. In this system, five basic physiological parameters are evaluated. These are systolic arterial blood pressure, pulse, respiratory rate, body temperature measurement, and AVPU scale and they are

Sutaşır
Could NCM-3S Be Used In The Intubation Decision of
Patients Showing Toxicity Findings After Synthetic Cannabinoid Abuse?

20

Eurasian J Tox. 2020; 2 (1):15-22

used to evaluate consciousness (21,22). Many early warning systems are developed by taking pulse, blood pressure, respiratory rate, fever and level of consciousness as basis. In our study, the values stated in the literature have been considered as well. Pulse, blood pressure, respiratory rate and mental state at the first admission to the ER are evaluated and saturation and blood gas PCO_2 (of which results come out in short notice) values which are taken in the ER are added to the evaluation. However, there could not be found any study related to the planning of the need for ETI, based on the combined evaluation of the physiological and clinical state of the patients at the time of admission along with the first blood gas test results, as can be seen in our study. As can be seen in the literature, in the evaluations of blood gas of intubated patients after SC abuse, respiratory acidosis, hypoxia and pCO^2 values of patients are above normal (7,9,15). In our study, it has been seen that compared to the NRPG, RPG had lower pH and higher pCO_2 values. The topic of respiratory depression after SC abuse is a debated issue. In experimental studies, a decrease in respiratory rate, hypoxia, hypercapnia, acidosis effects have been proven (23,24). Nevertheless, there is not adequate information regarding its direct effect leading to respiratory depression on patients. It is suggested that SCs could cause an increase in resistance in bronchia and a decrease in respiratory rate. And in some cases, it is known to need mechanical ventilation due to respiratory failure (23,25). It is likely to see the effects on the respiratory system being created through the central nervous system and cardiovascular system. Other studies of literature have also shown acute respiratory acidosis and acute metabolic acidosis in patients (25,26,27). It is seen both in our study and in the literature review that in SC toxicity cases, hypoventilation results in respiratory acidosis and this leads to respiratory depression and ETI is applied to these patients. It is also seen that in RPG, systolic blood pressure, GCS value, pulse rate, respiratory rate, saturation and pCO2 value measured in the ER, as a part of the NCM-3S scoring system we developed, are significant in determining the need for ETI in SC toxicity cases.

Factors such as illegal supply of SCs, difficulty in running lab analysis due to their unpredictable and constantly changing structure, inadequate anamnesis from patients after SC abuse, change in consciousness and confusion, neurological changes that can lead to stupor and coma and finally the fact that the study was prepared in a single center thus having a limited number of patients are the constraints of our study.

Conclusion

A patient coming to the ER with SC abuse is one of the difficult cases to manage for ER physicians. The reasons behind this difficulty can be said to be patients coming to the ER with an ambulance, thus the ability to obtain very limited anamnesis, most frequently not having any relative with them except for medical personnel, difficulty in respiration and changes in consciousness level. SCs are known to have hypoxia, hypercapnia and acidosis effects. Many patients require mechanical ventilation due to respiratory failure. All these situations led us to the conclusion that NCM-3S score we created by using pulse rate, systolic blood pressure, respiratory rate, fingertip O^2 saturation, mental state and PCO^2 value measured in ER at first admission, can be used in projecting the need for intubation of patients in SC toxicity cases.

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Sutaşır
Could NCM-3S Be Used In The Intubation Decision of
Patients Showing Toxicity Findings After Synthetic Cannabinoid Abuse? **21**

Eurasian J Tox. 2020; 2 (1):15-22

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