The Egyptian Journal of Critical Care Medicine xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

The Egyptian Journal of Critical Care Medicine

journal homepage: www.sciencedirect.com

Original article

Evaluation of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in critical care patients with synthetic cannabinoid (bonzai) intoxication

Mustafa Kaplan [a], Alpaslan Tanoglu [b], Tolga Duzenli [b], Muhammet Yildirim [a], Yusuf Serdar Sakin [c,*], Musa Salmanoglu [a], Yalçin Önem [a]

[a] GATA Haydarpasa Training Hospital, Internal Medicine Department, 34668 Uskudar-Istanbul, Turkey
[b] GATA Haydarpasa Training Hospital, Gastroenterology Department, 34668 Uskudar-Istanbul, Turkey
[c] Gulhane Military Medical Academy, Gastroenterology Department, 06018 Kecioren-Ankara, Turkey

ARTICLE INFO

Article history:
Received 20 August 2016
Revised 2 January 2018
Accepted 28 March 2018
Available online xxxx

Keywords:
Synthetic cannabinoid
İntoxication
İntensive care unit
Neutrophil to lymphocyte ratio
Platelet to lymphocyte ratio

ABSTRACT

Objective: Synthetic cannabinoid drug abuse has been dramatically increasing among young individuals in many countries. There have been reports of serious side effects with SC abuse in these patients. Previous researches have exhibited that neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are associated with mortality and morbidity in many chronic diseases. The aim of this study was to evaluate PLR and NLR in critical care patients with synthetic cannabinoid (bonzai) intoxication.

Materials and methods: One hundred and seven synthetic cannabinoid intoxication patients requiring intensive care and 40 healthy controls were included in the study. Patients characteristics and the complete blood count (CBC) variables, including white blood cell (WBC), hemoglobin (Hb), platelet count, NLR, PLR as well as AST, ALT, albumin total bilirubin, and other routine biochemical parameters were tested. Data analyses were conducted with SPSS-15 software (SPSS Inc., Chicago, Illinois, USA). Statistical significance was set at a p-value of <0.05.

Results: All participants were male, and the mean age of the patients was 21.74 ± 1.57 and healthy controls was 22.62 ± 2.9 years ($p > 0.05$). All the routine laboratory tests and inflammatory markers (Erythrocyte sedimentation rate and C-reactive protein) were similar between groups. As complete blood cell count; mean WBC values were $9.43 \pm 3.27 \times 10^3/mm^3$ vs $7.05 \pm 2.12 \times 10^3/mm^3$ ($p < 0.001$), mean platelet counts were $237.33 \pm 60 \times 10^3/mm^3$ vs $263.90 \pm 65.98 \times 10^3/mm^3$ ($p = 0.022$), NLR counts were 3.17 ± 1.95 vs 2.32 ± 1.27 ($p = 0.003$) and PLR values were 114.43 ± 36.39 vs 133.94 ± 45.27 ($p = 0.008$), in patients and controls, respectively. Cardiac side effects were observed among 36 patients but nobody was died.

Conclusion: Our results exhibited a significant increase of NLR values and decrease of PLR counts among critical care patients with synthetic cannabinoid (bonzai) intoxication. After at least 24 h of intensive care stay without side effects, the patients might transfer out to inpatient clinic for ongoing follow up period and psychiatric consultation.

1. Introduction

The use of synthetic cannabinoids has been dramatically increasing among young individuals in many countries. The reasons of the rise in synthetic cannabinoid (SC) abuse are its cannabis-like effects, easy supply, cheap price and detection difficulties with routine toxicological screening methods [1,2]. Substances containing synthetic cannabinoids are named such as spice, K2, Bonzai and Jamaica in different countries They are typically consisted of several different SCs that mixed with herbal

* Corresponding author.
E-mail addresses: serdarsakin78@yahoo.com (Y.S. Sakin), msalmanoglu@gata.edu.tr (M. Salmanoglu).

Peer review under responsibility of The Egyptian College of Critical Care Physicians.

Production and hosting by Elsevier

https://doi.org/10.1016/j.ejccm.2018.03.002
2090-7303/

Please cite this article in press as: Kaplan M et al. Evaluation of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in critical care patients with synthetic cannabinoid (bonzai) intoxication. Egypt J Crit Care Med (2018), https://doi.org/10.1016/j.ejccm.2018.03.002

ingredients and smoked alike cannabis [2–4] and SCs produce cannabis-like effects in humans [2]. Although SCs show their effects by activating cannabinoid receptors in the body, they do not include cannabis or herbal products and formed from chemicals mixed with plant parts.). The exact number of the SC addiction is not known according to difficulties in detecting synthetic cannabinoid. In a survey study which include 14,966 participants, 17% of participants was reported to take SCs, and 7.2% of patients reported preference for SC over cannabis for reasons such as accessibility, cost, non-detection and effects [5]).

There are two cannabinoid receptor subgroups currently which are Cannabinoid 1 (CB1) receptors (mostly in the brain) and cannabinoid 2 (CB2) receptors (mostly in the immune and enteric nervous system). SCs typically make full agonist effects on CB1 receptors, thereby they cause maximum effect even at very low doses [6–9]. Sympathomimetic effects such as sweating, agitation and restlessness can be seen in synthetic cannabinoid toxicity in addition to marijuana's psychoactive effects [10]. In recent years, there have been reports of serious side effects with SC abuse such as rhabdomyolysis, renal failure, acute myocardial infarction, respiratory depression [1]. For diagnosis of intoxication; there must be suspicion and a good knowledge of signs and symptoms of this intoxication [10,11]. The main therapy of synthetic cannabinoid intoxication is supportive treatment for symptoms and benzodiazepines for agitation and anxiety [8–10].

Recently, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been evaluated as new prognostic indicators for various malignancies [12–15]. Additionally, previous researches have exhibited that NLR and PLR are associated with mortality and morbidity in many chronic diseases, such as diabetes, hypertension and many other cardiac problems [14,16,17]. Currently, NLR has been accepted as a sign of subclinical inflammation, and used in combination with other inflammatory markers to determine inflammation in many diseases [13–16].

Abuse of SC has become a serious problem for public health institutions due to growing prevalence, variety of dosage/content and the lack of regulations for these drugs [18]. The aim of this study was to evaluate NLR and PLR in critical care patients with SC (bonzai) intoxication.

2. Materıals and methods

2.1. Patients

This was a retrospective case-control study assessing patients with SC (bonzai) intoxication between November 2015 and January 2016. Permission for the study was obtained from the local ethics committee of GATA Haydarpasa Training Hospital.

The study included 107 male patients who were stayed critical care because of synthetic cannabinoid 'Bonsai' intoxication and age and sex matched 40 healthy controls in GATA Haydarpasa Training Hospital. Due to the difficulties in detecting synthetic cannabinoids in laboratory tests, we include the patients due to their anamnesis, or their relatives' declarations. Age, gender, duration and frequency of abuse, complete blood count and routine blood tests (alanine aminotransferases, urine tests, blood creatinine level, erythrocyte sedimentation rate, C-reactive protein etc.), electrocardiographies (ECGs), physical examination findings were analyzed.

Patients with diseases such as diabetes, cardiac diseases, renal disorders, acute or chronic infections, celiac disease, inflammatory bowel disease, atherosclerotic disease, history of hypertension, malignancy, autoimmune disorders, hematological disorders, rheumatic diseases, and chronic obstructive lung diseases, as well as patients taking drugs such as aspirin, steroids, warfarin, heparin, antidiabetics, hyperlipidemics and antihypertensives, and patients with other addictions such as alcohol abuse were excluded from the study.

2.2. Laboratory analysis

The complete blood count (CBC) parameters such as white blood cell (WBC), hemoglobin (Hb) level, platelet count, mean platelet volume, NLR and PLR were recorded. The blood samples were obtained by vacutainer through the brachial vein into tubes containing dipotassium ethylenediaminetetraacetic acid (EDTA) in the intensive care unit on admission. It should be noted that, the CBC studies were performed within 45 min of the blood samples being drawn as a routine procedure of our hospital.

Complete blood count analysis was performed by using a fully automated hematologic analyzer (Abott, Cell-dyn Sapphire, USA) in biochemistry clinic. Serum levels of AST, ALT, albumin, total bilirubin and other routine biochemical parameters were evaluated by standard automated techniques (Abbott Architect C16000, USA). Although difficulty of detecting of SCs are well known, all the patients' blood and urine analysis for toxicology screen were performed for exact diagnosis.

2.3. Statistical analysis

Statistical analyses in this study were performed using SPSS ver. 15 software (SPSS Inc., Chicago, Illinois, USA). Demographic and clinical characteristics of patients, laboratory parameters, duration and frequency of abuse were determined with mean ± standard deviation, median, range and percentages (%). The variables were investigated using Kolmogorov-Smirnov/Shapiro Wilk's test to determine whether or not they are normally distributed. Independent samples t-tests were used to compare two groups. Receiver operating characteristic (ROC) curve analysis was used to identify optimal cut-off values of NLR and PLR.

3. Results

The mean age of the patients was 21.74 ± 1.57 and healthy controls was 22.62 ± 2.9 years ($p > 0.05$). All the patients and healthy controls were smokers (3 to 7 packages/week), and didn't have regular alcohol consumption. The patients in both group didn't have any comorbid disease. According to complaints; 10 patients (% 9.34) had sudden aggression, 36 patients (% 33.6) had dyspnea and chest pain and cardiac effects (mainly bradycardia), 24 patients had (% 22.4) confusion and fainting, 14 patients had (% 13) dizziness and drowsiness, 8 patients had (% 7.4) hallucinations (Table 1). Fortunately, none of the patients died as a result of drug abuse.

We couldn't detect the type of SCs in all patients, due to the abundant form of SCs and undetectable property of SCs in blood and urine tests. When comparing SCs intoxication with healthy control group, we found significant differences for platelet count, WBC count, NLR and PLR. The mean WBC value of the patients and healthy controls was $9.43 \pm 3.27 \times 10^3/mm^3$ and 7.05 ± 2.12

Table 1
Patient percentages according to complaints (n: number of patients, %: percentage value).

Complaint	n	%
Cardiac side effects	36	33.6
Sudden aggression, meaningless movements	10	9.34
Fainting, confusion	24	22.4
Nausea, vomiting	16	14.9
Drowsiness and dizziness	14	13
Hallucinations	8	7.4

Please cite this article in press as: Kaplan M et al. Evaluation of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in critical care patients with synthetic cannabinoid (bonzai) intoxication. Egypt J Crit Care Med (2018), https://doi.org/10.1016/j.ejccm.2018.03.002