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Bulletin of Clinical Psychopharmacology 2015;25(Suppl. 1):S54-S5

[Abstract:0592] ***Addiction***

The effect of synthetic cannabinoids on P-wave dispersion: an observational study

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INTRODUCTION: Synthetic cannabinoids (SC) were first marketed as legal cannabis alternatives in Europe in the early 2000s. Consumption of SC has become widespread, despite law enforcement and regulatory control measures. The consumption of products containing SC may lead to serious adverse effects[1]. Psychiatric disorders may lead to an increased risk of cardiovascular disease (CVD). Previous studies have shown that P-wave dispersion (PD) is associated with increased risk of CVD[2]. PD is also associated with psychiatric disorders including hypochondriasis, depression and panic disorder[3,4]. The aim of the study is to investigate the effect of SC on PD in patients with SC consumption.

MATERIALS AND METHODS:

Study Population: The study population included 53 patients with SC consumption whose use of SC was admitted personally and/or detected in urine screening tests in Erenkoy Mental and Neurological Diseases Training and Research Hospital. Socio-demographic data was collected by using a questionnaire. Physical examination findings, medical history data, and resting 12-lead electrocardiograms (ECG) were obtained from the entire study population. PD was measured through 12-lead ECG obtained during patient admission. Patients with underlying cardiac conditions, abnormal ECG findings, or taking antidepressants or other medication that might interfere with ECG results were excluded. After exclusion criteria, the remaining 40 patients with SC consumption were included in the study. The control group consisted of 20 healthy age- and sex-matched volunteers. The study was approved by the local ethics committee and written informed consent was taken from all participants.

Addiction Profile Index (BAPI): The severity of addiction was determined by using addiction profile index (BAPI score). Total BAPI score was calculated as described previously[5]. BAPI has been validated by Ogel et al. in 2012. The cut-off point of the BAPI score was 10.7. BAPI score <12 was defined as low level of addiction, BAPI score 12-14 as moderate and BAPI score >14 as high level of addiction.

Electrocardiographic Measurements: Following a resting period of 20 minutes, 12-lead ECG was recorded at supine position at a paper speed of 50 mm/s and an amplitude of 20 mm/mV by using a Nikon Kohden ECG device (Japan). The onset of the P-wave was defined as the point of first downward departure from the top of the baseline for negative waves. The return to the baseline of the bottom of trace was considered to be the end of the P wave. The difference between the maximum and minimum P wave duration was calculated from any derivation of the 12-lead ECG and was defined as the PD (Pd=Pmaximum-Pminimum).

Statistical Analysis: Statistical analyses were performed using SPSS 20.0 statistical software package. Continuous data were expressed as mean±standard deviation while categorical data were presented as number and percentage of patients. Chi-square and Fisher's Exact test were used for comparison of categorical variables while student-t test or Mann-Whitney U test were used to compare parametric and nonparametric continuous variables, respectively. Correlation analysis was performed by Spearman's correlation test. Linear regression analyses were performed to determine the predictors of BAPI score. A value of $p<0.05$ was considered statistically significant.

RESULTS: The study population consisted of 40 patients with SC consumption and 20 age- and sex-matched healthy controls (26.9±7.3 years versus 26.2±6.4 years and 39 male versus 19 male, p=0.687, 0.611, respectively). The majority of patients was single (30 single versus 10 married) and graduated from primary school (35 patients). Mean duration of patients' SC consumption was 1.8±0.7 years. All patients completed BAPI scale for evaluation of addiction level. Mean BAPI score of study population was 13.8±2.8. Our study population had a moderate level of addiction according to BAPI score. Biochemical measurements were in normal range in the study population.

Heart rate was similar between the two groups (71.2±12.9 vs. 71.7±8.9, p=0.889). Patients with SC consumption had significantly higher

PD value than controls (41.2±13.8 ms versus 32.3±7.6, p=0.002). Correlation analysis revealed that BAPI score was significantly correlated with PD value (r=0.528, p=0.003). Linear regression analysis was performed to determine the predictors of BAPI score in patients with SC consumption. Among PD value, age and heart rate that were included in the linear regression model, PD value was shown to be significantly and independently affecting BAPI score (Beta: 0.477, t= 2.783, p=0.010).

DISCUSSION: Patients with SC consumption had significantly higher PD values than controls. BAPI score was significantly correlated with PD value. PD was an independent predictor of BAPI score. Our results demonstrated that SC consumption may lead to increased risk of CVD through increased PD. To the best of our knowledge, this is the first study to evaluate the effect of SC on PD in patients with SC consumption. Nowadays, there is an increased interest in consumption of SC in Turkey. Due to its ready accessibility and lower price compared to other cannabinoids, the usage of SC, especially the usage of bonsai, has been increasing among the young population. In accordance with the literature, the mean age of patients with SC consumption in our study population was 26.9±7.3 years. Due to its widespread usage, a lot of cases have attended to emergency clinics with a variety of symptoms ranging from dizziness to cardiac arrest. Therefore, clinicians should pay more attention to evaluating these patients in emergency clinics. Timely diagnosis and early treatment of those patients may save their lives. Although routine urine and blood samples are required for differential diagnosis, they are not sufficient for a diagnosis of SC consumption. Therefore, detailed medical history and more attention to environmental factors are important methods for an accurate diagnosis. Although all laboratory parameters were in the normal range for our study population, detailed medical history revealed the usage of SC by patients. Experimental research suggests that there is a strong relationship between psychiatric disorders and CVD. Due to increased risk of CVD, numerous clinical studies have been performed to this day. Therefore, we proposed a possible effect of SC on ECG parameters and designed the present study accordingly.

The 12-lead ECG is a common method for evaluation of CVD. As it is cheaper and more available than other diagnostic methods, clinicians firstly use it for the differential diagnosis of CVD. Previous studies have shown that PD is a non-invasive electrocardiographic marker that can be used to determine the increased risk of atrial fibrillation. Increased PD has been reported in several clinical settings such as coronary artery disease, hypertension, chronic renal disease, mitral stenosis, hypertrophic cardiomyopathy, and depression. Although there are several pathways leading to a prolongation of PD, the main mechanism of PD in these patients is thought to be based on structural and electrophysiological changes in the atrial myocardium. In our study, we found that patients with SC consumption have significantly higher PD than healthy controls. The PD value was also correlated with BASI score in these patients. Therefore, our results demonstrated that SC may lead to increased risk of CVD trough prolongation of the PD.

Study Limitations: There are several limitations for our study, such as small sample size. Therefore, large-scale studies should validate our results. Our study was designed cross-sectional. We did not follow up the patients prospectively. Therefore, we have no prognostic data for those patients. It would be better if we followed up the patients and documented new onset CVD in patients with SC consumption who have prolonged PD. The usage of the SC should be validated by novel urine tests. Further large-scale prospective studies are needed to validate our preliminary results.

CONCLUSIONS: Patients with SC consumption have higher PD values than healthy controls. The PD value was correlated with BASI score. PD was also independent predictor of BASI score in those patients. Our results demonstrated that SC consumption may lead to increased risk of CVD through prolonged PD. A simple and cheap ECG may help the clinician to assess cardiovascular risk in patients with SC consumption.

Keywords: cardiovascular risk, P-wave dispersion, synthetic cannabinoid

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Bulletin of Clinical Psychopharmacology 2015;25(Suppl. 1):S55-S6