Original Article

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Evaluation of the Changes in T Peak-T End Interval and T Peak-T End/QT Ratio in Tricyclic Antidepressant Intoxication

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Abstract

Objectives: Tricyclic antidepressant (TCA) intoxication can affect various systems including cardiovascular system. In recent years, the transmiyocardial repolarization parameters including T peak-Tend (Tp-Te) interval, Tp-Te dispersion and Tp-Te/QT have been shown to be associated with increased cardiac arrhythmia risk. The aim of this study was to evaluate the effect of TCA intoxication on transmyocardial repolarization parameters.

Materials and Methods: This study was a cross-sectional study including 124 patients (43 male and 81 female) who were followed up and treated for TCA intoxication and 37 volunteer controls. At admission, 6th hour and 24th hour, the electrocardiogram of the patients were evaluated and Tp-Te and QT interval were measured manually and Tp-Te/QT ratio was calculated.

Results: The mean age of the study group was 27.95±7.72. There were statistically significant difference in terms of Tp-Te ($p<0.001$), Tp-Te mean ($p<0,05$) and dispersion ($p <0,05$) in V2-6 derivations between patient and control groups. There were significant difference in the Tp-Te/QT values in V2-5 derivations ($p<0,05$). We found a statistically significant difference in maximum and minimum QT values, prolonged QTc, prolonged QTc dispersion and prolonged mean Tp-Te/QT values between patient and control groups ($p <0.05$); prolonged mean Tp-Te values were similar between groups ($p = 0,117$). In the ROC analysis performed to investigate the diagnostic value of Tp-Te and Tp-Te/QT data in predicting disease, we found that all leads except V2 derivation were diagnostic ($p <0.05$).

Conclusion: TCA intoxication significantly increased the transmiyocardial repolarization parameters compared to the healthy population.

Key words: tricyclic antidepressant intoxication, Tp-Te interval, QT interval, Tp-Te/QT ratio, electrocardiography

Özet

Giriş: Trisiklik antidepresan (TSA) zehirlenmesi, kardiyovasküler sistem dahil olmak üzere çeşitli sistemleri etkileyebilir. Son yıllarda, Tp-Te aralığı, Tp-Te dispersiyonu ve Tp-Te / QT gibi transmiyokardiyal repolarizasyon parametrelerinin artmış kardiyak aritmi riski ile ilişkili olduğu gösterilmiştir. Bu çalışmanın amacı, TSA intoksikasyonunun transmiyokardiyal repolarizasyon parametreleri üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntem: Bu çalışma, TSA intoksikasyonu için izlenen ve tedavi edilen 124 hasta (43 erkek ve 81 kadın) ve 37 gönüllü kontrolü içeren kesitsel bir çalışmadır. Başvuru anında, 6. saat ve 24. saatte hastaların elektrokardiyogramları değerlendirilerek Tp-Te ve QT intervali manuel olarak ölçülerek Tp-Te / QT oranı hesaplandı.

Bulgular: Çalışma grubunun yaş ortalaması 27.95 ± 7.72 idi. Hasta ve kontrol grupları arasında V2-6 derivasyonlarında Tp-Te ($p <0.001$), Tp-Te ortalaması ($p <0,05$) ve dağılımı ($p <0,05$) açısından istatistiksel olarak anlamlı fark vardı. V2-5 derivasyonlarında Tp-Te / QT değerlerinde anlamlı farklılık vardı ($p <0,05$). Hasta ve kontrol grupları arasında maksimum ve minimum QT değerleri, uzamış QTc, uzamış QTc dispersiyonu ve uzamış ortalama Tp-Te / QT değerlerinde istatistiksel olarak anlamlı fark bulundu ($p <0,05$); uzamış ortalama Tp-Te değerleri gruplar arasında benzerdi ($p = 0,117$). Tp-Te ve Tp-Te / QT verilerinin hastalığı öngörmedeki tanısal değerini araştırmak için yapılan ROC analizinde V2 derivasyonu dışındaki tüm derivasyonların tanısal olduğunu bulduk ($p <0.05$).

Sonuç: TSA intoksikasyonu, transmiyokardiyal repolarizasyon parametrelerini sağlıklı popülasyona göre anlamlı olarak artırmaktadır.

Anahtar kelimeler: Trisiklik antidepresan zehirlenmesi, Tp-Te aralığı, QT aralığı, Tp-Te / QT oranı, elektrokardiyografi

Introduction

Intoxication cases are among the most common reasons for admission to emergency services. In USA, the most common reason for drug intoxication at the age of 20 and above were analgesic drugs (13.1%), followed by sedative, hypnotic, antipsychotic drugs (11.2%) and antidepressant drugs with a rate of 6.2%. In the same report, sedative, hypnotic and antipsychotic drugs were the most common with 14.2% and antidepressant drugs were the fifth reason with 6.5% for drug intoxication-related deaths[1].

Tricyclic antidepressants (TCAs) show their therapeutic

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effects as negative allosteric modulators of neurotransmitter (serotonin and noradrenaline) reuptake[2]. It is reported that deaths caused by TCAs are most commonly seen with dotiepin and amitriptyline[3-4]. In Turkey, one of the most preferred TCA is amitriptyline (40-58%)[5].According to a review conducted in England and Wales death rate per 100.000 for all TCAs is 0.33 and for amitriptyline is 0,12[6]. TCAs are the most commonly prescribed antidepressants in the US after selective serotonin reuptake inhibitors and according to the report of the American Association for Poison Control Centers in 2003, among 12710 TCA intoxications, 0.6 % of them resulted in death while 64.7% of the patients had to be hospitalized[7].

The rate of life-threatening arrhythmia in TCA intoxications is known as 2.3% to 6% [8]. In these cases, electrocardiography (ECG) changes lead us to determine the severity of intoxication[9]. It has been reported that most patients develop major signs of TCA intoxication within 3 hours and severe rhythm disorders are seen in the first 6 hours[10]. The most common ECG change in these patients is sinus tachycardia. Also PR, QRS and QT prolongation, right axis deviation, right bundle branch block, AV blocks, changes that mimic acute myocardial infarction and Brugada syndrome, supraventricular tachycardia, premature ventricular extrasistoles, ventricular tachycardia, ventricular fibrillation, nonspecific ST-T changes and bradyarrhythmias can be seen in these patients[11]. T wave is the ECG finding of ventricular repolarization. In recent studies, transmyocardial repolarization parameters including T peak-Tend interval, Tp-Te dispersion and Tp-Te / QT ratio have been shown to be associated with increased risk of cardiac arrhythmias[12].

The aim of this study was to evaluate the effect of TCA intoxication on transmyocardial repolarization parameters and whether there is a relationship between these parameters and cardiac damage.

Materials and Methods

One hundred and twenty four patients who were admitted to our hospital between September 2011 and November 2015 and followed up and treated with TSA poisoning and thirty seven healthy control patients without any history of drug use were included to the study. The study was a cross-sectional clinical study.

Pregnant women, lactating women, those who were under 18 years of age, those with known or detected cardiac disease and those with additional diseases, those with electrolyte disorder, those with chronic medication use, patients whom the multidrug test was not performed were excluded from the study. Informed consent was taken from all study population. Ethical approval was obtained from the local ethics committee.

Age, gender, pulse, blood pressure, Glasgow coma scale (GCS), urea, creatinine, lactate and ECGs of all patients at the 6th and 24th hours were evaluated. In ECGs; QRS distance, ST elevation, ST depression, at aVR derivation R wave positivity, QT interval and corrected QT interval were measured and Tp-Te and Tp-Te/QT ratios were calculated. ECG recordings were measured by two experts who were completely blind about the condition of the patients. Prolonged QRS duration was defined as ≥100 msec. Tp-Te interval was measured by the tail method in the precordial leads. According to this method, the distance between the projection of the peak point of T wave on the isoelectric line and the point where the T wave ends was measured and defined as Tp-Te time. The QT interval was measured from the beginning of the QRS complex to the end of the T wave. In addition, corrected QT interval was calculated with the Bazett formula when the heart rate was not within normal range. In this way, abnormalities in heart rate were prevented from affecting the Tp-Te/QT ratio. The Tp-Te/QT ratio was calculated in the lead at which the Tp-Te interval was measured.

In the statistical evaluation, Chi-square or Fisher (in cases where the values observed in the cells did not provide the Chi-square test assumptions) was used. In the comparison of normal scattered numerical data between patient and control group, Student t test was used and Mann-Whitney U test was used for non-normal distribution. The change in rates in the data collected at the arrival, 6th and 24th hours was compared using the Cochran's Q test. Diagnostic characteristics of Tp-Te value and Tp-Te / QT ratio in chest leads were evaluated by ROC curve analysis. Sensitivity, specificity, positive predictive and negative predictive values of these limits was calculated in the presence of significant limit values. In the evaluation of the area under the curve, the cases with Type-1 error level below 5% were interpreted as statistically significant.

Results

The study included 124 patients who were followed up with TSA intoxication and 37 healthy volunteers as the control group.

The mean age of the patients was 27.95 ± 7.72 years and the mean age of the control group was 29.65 ± 6.76 years. There was no statistically significant difference between the age of the patients and the control group (p = 0.230). 43 (34.7%) of the males were in the patient group and 17 (45.9%) were in the control group. 81 (65.3%) of the females were in the patient group and 20 (54.1%) were in the control group. There was no statistically significant difference in terms of gender between the patient and control groups (p = 0.213).

The median GCS at the arrival of the patients was 15. The most common used drug was amitriptyline and followed by opipramol, imipramine and clomipramine, in the specified order. The median amount of drug taken by the patients was determined as 500 mg. The most common symptom was nausea and vomiting. The other commons symptoms were tachycardia, agitation, confusion, secretion,

Table 1. Comparison of mean arterial pressure, pulse, pH and lactate values of the patient group with the 6th hour and 24th hour data

	Admission	6th hour	24th hour	p
MAP,mean±SD, mmHg	83.19±13.64	81.03±12.69	84.40±10.75	0.009
Pulse, mean±SD	100.5±28.78	90.98±12.73	83.69±8.83	<0.001
pH, mean±SD	7.372±0.458	7.394±0.032	7.390±0.018	<0.001
Lactate,median(IQR)	1.15(0.93)	0.91(0.34)	0.85(0.49)	<0.001

Abb. IQR, interquartile range; MAP, mean arterial pressure; SD, standart deviation

dry mouth, hypertension, hypotension, tremor, mydriasis, seizure, delirium, coma, and myositis, respectively. All patients underwent gastric lavage, activated charcoal and fluid treatment. 79 (63.7%) patients underwent NaHCO3 treatment and 26 (20.9%) patients underwent other treatments. Median duration of hospitalization was 2 days. 121 (97.6%) patients were discharged with cure, 3 (2.4%) patients were transferred to another service and no patient died.

Mean arterial pressure, pulse, pH and lactate parameters were recorded at admission, the 6th hour and 24th hours. There was a statistically significant difference in the follow-up values of mean arterial pressure, pulse, pH and lactate values of the patients (p <0.05). (Table 1)

ECG findings were recorded at admission, the 6th hour and 24th hours. There was a statistically significant difference in the follow-up of the ratio of ECG parameters like normal sinus rhythm, sinus tachycardia, QRS complex enlargement, R wave at aVR derivation, supraventricular tachycardia, ST segment changes and ventricular extra systole (p <0.05). There was no statistically significant difference in QTc prolongation, right bundle branch block, right axis deviation, first degree atrioventricular block, Wolf Parkinson White and Brugada syndrome findings (p> 0.05).

There was no statistically significant difference between the Tp-Te values at V1 derivations at admission, the 6th hour and 24th hours of ECG (p = 0.289); There was a statistically significant difference in Tp-Te values in V2-6 derivations (p <0.001). There was also a statistically significant difference in the mean and dispersion of Tp-Te values (p <0.05) (Figure 1).

There was a statistically significant difference in Tp-Te / QT values in V1-5 derivations at admission, the 6th hour and 24th hour ECGs of the patients (p <0.05). There was no statistically significant difference in the follow-up of Tp-Te / QT at V6 derivation (p = 0.163) (Figure 2).

Figure 1. Tpeak - Tend intervals of the patient group at admission, 6th hour and 24th hours

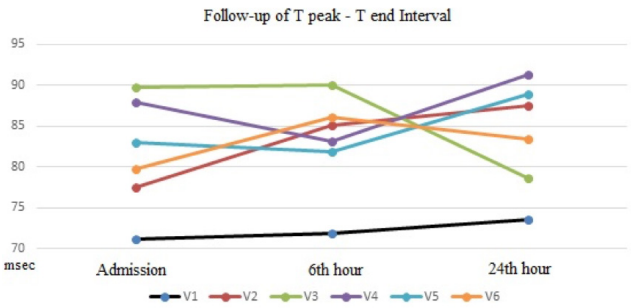
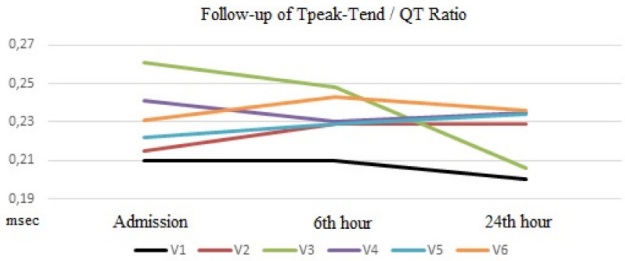


Figure 2. Tpeak - Tend / QT ratio of the patient group at admission, 6th hours and 24th hours



There was a statistically significant difference in the maximum and minimum QT values of the patients' ECGs at admission, the 6th hour and 24th hours (p <0.001); There was no statistically significant difference in QT dispersion, maximum and minimum QTc, QTc dispersion values (p> 0.05).

There was a statistically significant difference between prolonged QTc, prolonged QTc dispersion and prolonged mean Tp-Te / QT values between the patient and the control groups (p <0.05). There was no statistically significant difference between prolonged mean Tp-Te values between the groups (p = 0,117).

The patients were divided into 4 groups according to the active ingredient of the drugs they received. Prolonged QTc was seen in 66 (71.7%) patients, prolonged QTc dispersion in 45 (48.9%), prolonged mean Tp-Te in 8 (8.7%) and prolonged mean Tp-Te / QT was seen in 26 (28.3%) patients receiving amitriptyline. Prolonged QTc was seen in 18 (100%) patients, prolonged QTc dispersion in 13 (72.2%) patients, prolonged mean Tp-Te / QT was seen in 2 (11.1%) patients receiving opipramol. No prolonged mean Tp-Te / QT were detected in opipramol patients. Prolonged QTc was detected in 12 (100%) patients, prolonged QTc dispersion in 10 (83.3%), prolonged mean Tp-Te / QT in 3 (25%) patients and prolonged mean Tp-Te was seen in none of the patients who received imipramine. Prolonged QTc and prolonged mean Tp-Te / QT were detected in 2 (100%) patients receiving clomipramine. No prolonged QTc dispersion and prolonged mean Tp-Te was detected in clomipramine patients.

According to the comparison of the chest derivations of the ECGs taken at admission, the 6th hour and 24th hours;

there was a statistically significant difference in Tp-Te, the mean Tp-Te, the Tp-Te dispersion and the Tp-Te / QT (except the value of Tp-Te / QT at V3 derivation at the 24th hour) values between patient and control groups ($p < 0.05$). Only in V3 derivation at 24th hour, there was no statistically significant difference between the Tp-Te / QT values of the patient and control groups ($p = 0.236$).

In the ROC analysis performed to investigate the diagnostic value of Tp-Te data in chest derivations, all derivations except V2 were found to be diagnostic for predicting the pathology ($p < 0.05$). The highest AUC value was present in V4 derivation. The cut-off value for V4 derivation was ≥ 73.5 msec, the sensitivity 83.1% specificity was 78.4%, the positive predictive value was 92.8% and the negative predictive value was 58% (Figure 3).

In the ROC analysis performed to investigate the diagnostic value of T peak-T end / QT data in chest derivations, all derivations except V2 were considered to be diagnostic for predicting the pathology ($p < 0.05$). The highest AUC value was present in lead V6. The cut-off value for the V6 diversion was ≥ 0,216, the sensitivity was 71.8%, the specificity was 86.5%, the positive predictive value was 94.7% and the negative predictive value was 47.8% (Figure 4).

Discussion

Intoxication is one of the most common causes of emergency service admissions and it constitutes 0.07-0.7 % of all patients admitted to emergency clinics[13]. The studies conducted in Turkey showed this ratio to be in the range from 0.7 to 1.5%[14-17]. GCS is widely used to determine the severity of the patient's condition during the initial evaluation and follow-up of patients brought for intoxication. Arranto et al.[18] reported that they had an average GCS score of 11 in antidepressant intoxications. In another study, the mean GCS of patients was found to be 14[19]. In our study, GCS median was 15.

In the USA, amitriptyline (40%) is the most common cause of intoxications with TCAs. Imipramine second and doxepin have been reported in the third place[11]. In our study, it was found that most common cause for TCA intoxications were amitriptyline (74.2%), the second most frequent opipramol (14.5%), then imipramine and clomipramine. Amitriptyline, which is known as a sleep pill among the population, is frequently seen in intoxication cases because it is cheap in our country and widely prescribed by physicians.

There are few studies showing the rate of high dose drug intake in suicidal attempts. In a study performed by Makk et al., 498 (79.3%) of the 628 patients received high dose medication, and 130 (20.7%) received non-high dose medications[20]. The median value of the drug taken in our study was 500 mg.

Clinical signs and symptoms of TCA intoxication are altered state of consciousness, meaningless speech, mydriasis, and decrease in bowel sounds, nausea, vomiting, dry mouth, ataxia, and tachycardia[11]. The fact that the clinical findings of TCA poisoning are variable and the absence of specific findings cause difficulties in diagnosis and follow-up. However, the most common disturbed organs are heart and brain and especially central nervous system depression and cardiovascular findings are important so it is important to follow-up these findings[21]. In our study, nausea, vomiting, tachycardia, agitation, confusion, dry mouth and mydriasis were common symptoms and findings consistent with the literature. One of the clinical conditions of anticholinergic drugs due to the effects of postsynaptic muscarinic receptor antagonism is seizure. In some studies, the rate of convulsion has been reported to be 4 - 24% in severe antidepressant intoxication[22]. Several studies stated that the percentage of seizures in anticholinergic drug intoxications is 3.5-25 %[19, 21-23]. In our study, seizures were observed in 2 patients (2.4%).

There is no special antidote to be used in the treatment of anticholinergic intoxications[24]. TCAs show their primary cardiotoxic effects by blocking sodium and potassium chan-

Figure 3. ROC curve of Tpeak-Tend data at chest derivations

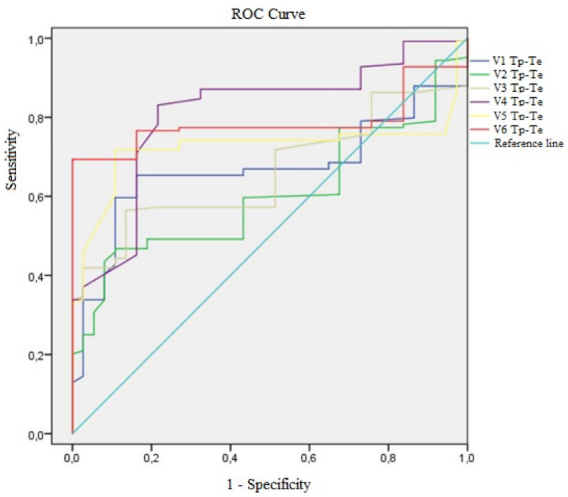
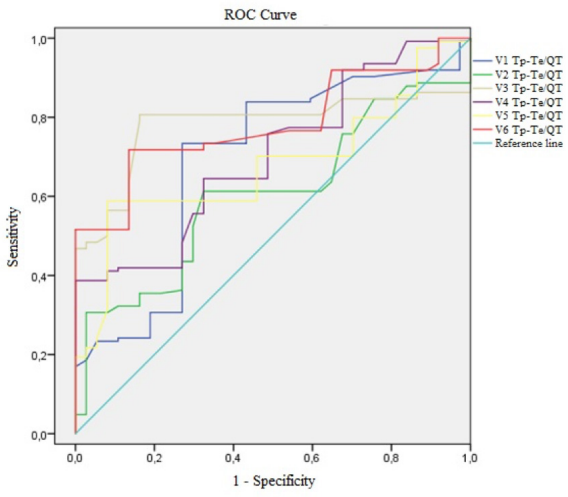


Figure 4. ROC curve of Tpeak-Tend / QT ratio at chest derivations



nels[25, 26]. NaHCO3 has been shown to regulate the conduction, increase cardiac contraction and suppress ventricular ectopia. Therefore, it is recommended that patients with QRS duration of longer than 100 msec, fluid therapy resistant hypotension and ventricular arrhythmias should be treated with NaHCO3[10]. Unverir et al.[27] reported that 6.5% of their patients were treated with sodium bicarbonate, 2.2% with diazepam and 1.6% had dopamine. In our study, 100% of the patients were treated with fluid and 63.7% of them were treated with sodium bicarbonate. The reason for these high rates is the fact that the patients were hospitalized in intensive care and most of the patients had cardiac involvement.

The duration of hospital stay is also an important factor. Graudins et al.[19] reported an average length of stay of 14 hours in antidepressant intoxication. In a study conducted in our country, the duration was reported as 0.7 days[14]. In another study, patients with antidepressant, intoxication had a mean stay of 1 day in the intensive care unit[18]. In our study, the median duration of stay in intensive care unit was 2 days. Considering the patients in our study were serious intoxication cases with cardiac involvement, the duration of hospitalization of our patients were similar with the previous studies.

The incidence of ECG abnormalities in TCA intoxications was reported to be 37%[28]. These ECG findings include: heart rate changes, rhythm disturbances and conduction delays[29]. Unverir et al.[27] evaluated the ECG findings after TCA intake in their study and normal sinus rhythm was observed in 41% of patients, sinus tachycardia in 40.7%, right axis deviation in 10.7%, prolongation of QRS in 7.9%, R> S in aVR was observed in 7.3% of the patients. In addition, it has been reported that right bundle branch block, prolongation of QT duration, left bundle branch block, left axis deviation, premature atrial contraction, sinus bradycardia, ST depression, second degree atrioventricular block, atrial tachycardia, ventricular fibrillation and asystole were also seen in these cases. In our study, 29.8% of patients had normal sinus rhythm, 33.1% had sinus tachycardia, 8.9% had right axis deviation and 47.6% had +R wave in aVR derivation.

One of the most important signs of heart involvement in TCA intoxications is the arrhythmias. The rate of ventricular arrhythmias in TCA intoxications was reported to be 2.7% and 6% in previous studies[8, 30]. In another study, the rate of life-threatening arrhythmias in TCA intoxications was reported to be 2.3%[31]. According to Foulke et al.[22], the rate of arrhythmias in antidepressant intoxications was 57% and by Arranto et al. the rate was 15%[32]. In our study, supraventricular tachycardia was found to be 8.1% and ventricular extra systoles were detected in 9.7% of the patients. All of these arrhythmias were completely recovered after treatment with NaHCO3 without any use of antiarrhythmic drugs. This shows that NaHCO3 treatment may alone be enough for arrhythmias caused by TCA intoxications since it suppresses ventricular ectopic beats.

The prolongation of QRS duration is an important parameter indicating cardiac influences in TCA intoxications. In the studies conducted by Bosch et al.[33], the rate of prolongation of QRS in TCA intoxications was 19% and Arranto et al. reported as 18%[32]. In our study, the rate of QRS prolongation was found to be 76.6%. The high rate of QRS prolongation in our study can be explained by the fact that we included intoxication patients with cardiac involvement and in need for intensive care.

It is known that antipsychotic drugs cause A-V block, PR-QRS-QT and T wave changes in ECG by suppressing contraction of heart with especially quinidine-like effects[13]. Of the patients included in the study, 2.4% had first degree AV block, 37.9% had right bundle branch block, 79% had QTc prolongation, 47.6% had +R wave in aVR, 3.2% had nonspecific ST changes and 1.6% had Brugada syndrome. This suggests that there may be a wide variety of ECG findings in anticholinergic drug intoxications and that the clinician should be alert to the development of almost all kinds of ECG findings in such intoxications.

It is known that TCA drugs can increase the risk of sudden cardiac death in intoxication patients due to the adverse cardiac effects[34]. These drugs are thought to lead to sudden cardiac death by increasing cardiac arrhythmogenicity[35]. The ECGs are often used to evaluate the increased arrhythmia risk. In surface ECG, QT interval, QTc interval, QT dispersion measurements show the heterogeneity of cardiac repolarization and are the parameters used to identify patients with increased risk of cardiac arrhythmia. In our study, maximum and minimum QT, QT dispersion, maximum and minimum QTc, QTc dispersion values were calculated at admission, the 6th and 24th hours. There was a statistically significant difference in maximum and minimum QT values and there was no statistically significant difference in QT dispersion, maximum and minimum QTc, QTc dispersion values.

In the ECG, the range from the top to the end of the T wave (Tp-Te) corresponds to the repolarization dispersion and the increase in the Tp-Te interval and Tp-Te / QT ratio has been shown to be related to life-threatening ventricular arrhythmias like in QT dispersion[36]. There are a limited number of studies in the literature about the Tp-Te / QT ratio in TCA drug intoxications.

The importance of Tp-Te as an indicator in the prediction of Torsades de Pointes (TdP) in patients with long QT syndrome (LQTS) was highlighted by Yamaguchi et al[37]. These investigators concluded that Tp-Te is more valuable than QTc and QT dispersion as a predictor of TdP in patients with acquired LQTS. Shimizu et al. showed that not QTc but Tp-Te predicts sudden cardiac death in patients with hypertrophic cardiomyopathy[38]. Topilski et al. showed that QT, QTc and Tp-Te are strong predictors of TdP. They also stated that the elongated Tp-Te alone was the best indicator [39]. Also Watanabe et al. reported that the long Tp-Te interval was associated with the development of spontaneous and inducible ventricular tachycardia in individuals with organic heart disease[40].

The ratio of Tp-Te / QT was significantly increased in patients with risk for arrhythmic events such as LQTS, Brugada syndrome, short QT syndrome, and organic heart diseases such as acute myocardial infarction. Functional reentry is the underlying mechanism in arrhythmias associated with an increased Tp-Te / QT ratio. Gupta et al. reported that Tp-Te / QT ratio is more sensitive than Tp-Te is an arrhythmogenic indicator[41]. Tp-Te duration and Tp-Te / QT ratio have been investigated in many diseases, but there are few studies on Tp-Te duration and Tp-Te / QT ratio in TCA drug intoxications. In our study, in the follow-up of Tp-Te values in V2-V6 leads, in Tp-Te mean and dispersion follow-up, Tp-Te / QT values in leads V1-V5 were found to be statistically significant as a result of the comparison between TCA intoxication patient group and control group. Similarly, there was a statistically significant difference between prolonged QTc, prolonged QTc dispersion and prolonged mean Tp-Te / QT values between the groups. In the ROC analysis to investigate the diagnostic value of Tp-Te / QT data in predicting the disease, other leads except V2 derivation were found to be valuable in predicting the disorder. These findings have also shown that Tp-Te and Tp-Te / QT have a high diagnostic value in TCA intoxications.

Conclusion

In conclusion, according to our study; there is significant prolongation in transmyocardial repolarization parameters in TCA intoxication cases compared to healthy population. These group of patients should be hospitalized, monitored carefully for life threatening arhytmias and cardiac injury.

Conflict of Interest

The authors declare that that have no conflict of interest. No funding was taken for the study. All authors participated in data collection, data analysis, writing and final manuscript control processes of the study. Informed consent was taken from all study population. Ethical approval was obtained from the local ethics committee.

References

1. Bronstein AC, Spyker DA, Cantilena JRM, Louis R, Green JL, Rumack BH, et al. 2009 Annual report of the American Association of Poison Control Centers' national poison data system (NPDS): 27th annual report. Clinical Toxicology. 2010;48:979-1178.
2. Small GW. Treatment of geriatric depression. Dep Anx Supp 1998; 1: 32–42.
3. Deegan C, O'Brien K. Amitriptyline poisoning in a 2-year old. Pediatric Anesthesia. 2006;16(2):174-7.
4. Nelson, JC, Spyker, DA. Morbidity and Mortality Associated With Medications Used in the Treatment of Depression: An Analysis of Cases Reported to U.S. Poison Control Centers, 2000–2014. American Journal of Psychiatry.2017;174,438–50.
5. Biçer S, Sezer S, Çetindağ F, Kesikminare M, Tombulca N, Aydoğan G, et al. Acil Çocuk Kliniği 2005 Yılı Akut Zehirlenme Olgularının Değerlendirilmesi. Marmara Medical Journal 2007;20;12-20
6. Hawton K, Bergen H, Simkin S, Cooper J, Waters, K, Gunnell D, et al. Toxicity of antidepressants: rates of suicide relative to prescribing and non-fatal overdose. British Journal of Psychiatry. 2010; 196: 354–358.
7. McKenzie MS, McFarland BH. Trends in antidepressant overdoses. Pharmacoepidemiol Drug Saf 2007; 16:513-23.
8. Liebelt EL, Francis PD, Woolf AD. ECG lead aVR versus QRS interval in predicting seizures and arrhythmias in acute tricyclic antidepressant toxicity. Annals of emergency medicine. 1995;26:195-201.
9. Singh N, Singh HK, Khan IA. Serial electrocardiographic changes as a predictor of cardiovascular toxicity in acute tricyclic antidepressant overdose. American journal of therapeutics. 2002;9:75-9.
10. Woolf AD, Erdman AR, Nelson LS, Caravati EM, Cobaugh DJ, Booze LL, et al. Tricyclic antidepressant poisoning: an evidence-based consensus guideline for out-of-hospital management. Clinical Toxicology. 2007; 45: 203–233.
11. Mills KC. Tricyclic antidepressants. In Tintinalli JE, Kellen G, Stapczynski JS, editors. Emergency Medicine A Comprehensive Study Guide. 6th ed. New York: McGraw-Hill; 2004. pp. 1025-33
12. Hevia JC, Antzelevitch C, Bárzaga FT, Sánchez MD, Balea FD, Molina RZ, et al. Tpeak-Tend and Tpeak-Tend dispersion as risk factors for ventricular tachycardia/ventricular fibrillation in patients with the Brugada syndrome. Journal of the American College of Cardiology. 2006;47(9):1828-34.
13. Linden C, Burns J. Poisoning and drug overdosage. In Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, editors. Harrison's Principles of Internal Medicine. 16th ed. New York: McGraw-Hill; 2006. pp. 2581-93.
14. Özköse Z, Ayoglu F. Etiological and demographical characteristics of acute adult poisoning in Ankara, Turkey. Human & experimental toxicology. 1999;18:614-8.
15. Goksu S, Yildirim C, Kocoglu H, Tutak A, Oner U. Characteristics of acute adult poisoning in Gaziantep, Turkey. Journal of Toxicology: Clinical Toxicology. 2002;40:833-7.
16. Yavuz S. Aydın S. Zehirlenme olgularının profili. Toksikoloji dergisi. 2003;1:47-52.
17. Akköse Ş, Fedakar R, Bulut M, Çebiçci H. Zehirlenme olgularının beş yıllık analizi. Acil Tıp Dergisi. 2003;3:8-10.
18. Harrigan RA, Brady WJ. ECG abnormalities in tricyclic antidepressant ingestion. The American journal of emergency medicine. 1999;17:387-93.
19. Graudins A, Dowsett RP, Liddle C. The toxicity of antidepressant poisoning: is it changing? A comparative study of cyclic and newer serotonin-specific antidepressants. Emergency Medicine. 2002;14:440-6.
20. Mak KK, Ho CS, Zhang MW, Day JR, Ho RC. Characteristics of

overdose and non-overdose suicide attempts in a multi-ethnic Asian society. Asian journal of psychiatry. 2013;6:373-9.

21. Whyte IM, Dawson A, Buckley N. Relative toxicity of venlafaxine and selective serotonin reuptake inhibitors in overdose compared to tricyclic antidepressants. Qjm. 2003;96:369-74.

22. Foulke GE. Identifying toxicity risk early after antidepressant overdose. The American journal of emergency medicine. 1995;13:123-6.

23. Henry JA, Antao CA. Suicide and fetal antidepressant poisoning. Eur J Med 1992; 458–65.

24. Høegholm A, Clementsen P. Hypertonic sodium chloride in severe antidepressant overdosage. Journal of Toxicology: Clinical Toxicology. 1991;29:297-8.

25. DeBattista C. Antidepressant agents. In Katzung BG, Masters SB, Trevor AJ, editors. Basic & Clinical Pharmacology,12th ed. NY: McGraw Hill; 2012. pp.521-40.

26. Benowitz NL. Tricyclic Antidepressants In Olson KR, editor. Poisoning and Drug Overdose. USA: Appleton and Lange; 1999. pp:310-12.

27. Unverir P, Atilla R, Karcioglu O, Topacoglu H, Demiral Y, Tuncok Y. A retrospective analysis of antidepressant poisonings in the emergency department: 11-year experience. Human & experimental toxicology. 2006;25:605-12.

28. Stern TA, O'gara PT, Mulley AG, Singer DE, Thibault GE. Complications after overdose with tricyclic antidepressants. Critical care medicine. 1985;13:672-4.

29. Groleau G, Jotte R, Barish R. The electrocardiographic manifestations of cyclic antidepressant therapy and overdose: a review. The Journal of emergency medicine. 1990;8:597-605.

30. Phillips S, Brent J, Kulig K, Heiligenstein J, Birkett M, Group AS. Fluoxetine versus tricyclic antidepressants: a prospective multicenter study of antidepressant drug overdoses. The Journal of emergency medicine. 1997;15:439-45.

31. Dökmeci İ.Trisiklik antidepresanlar. In Dökmeci İ, editor. Toksikoloji. 3rd ed. İstanbul: Nobel Tıp Kitapevleri; 2001. pp:414-5.

32. Arranto C, Mueller C, Hunziker P, Marsch S, Eriksson U. Adverse cardiac events in ICU patients with presumptive antidepressant overdose. Swiss Medical Weekly. 2003;133:479–83

33. Bosch TM, van der Werf TS, Uges DR, Ligtenberg JJ, Fijen Jw, Tulleken JE, et al. Antidepressants self-poisoning and ICU admissions in a university hospital in The Netherlands. Pharmacy World and Science. 2000;22:92-5.

34. Hennekens CH, Hennekens AR, Hollar D, Casey DE. Schizophrenia and increased risks of cardiovascular disease. American heart journal. 2005;150:1115-21.

35. Hennessy S, Bilker WB, Knauss JS, Margolis DJ, Kimmel SE, Reynolds RF, et al. Cardiac arrest and ventricular arrhythmia in patients taking antipsychotic drugs: cohort study using administrative data. BMJ. 2002;325:1070.

36. Acar G, Akkoyun M, Nacar A, Dirnak I, Yıldırım ÇG, Nur YM, et al. Evaluation of Tp-e interval and Tp-e/QT ratio in patients with rheumatoid arthritis. Turk Kardiyoloji Dernegi arsivi. 2014;42:29-34.

37. Yamaguchi M, Shimizu M, Hidekazu I, Terai H, Uchiyama K, Kotaro O, et al. T wave peak-to-end interval and QT dispersion in acquired long QT syndrome: a new index for arrhythmogenicity. Clinical Science. 2003;105:671-6.

38. Shimizu M, Ino H, Okeie K, Yamaguchi M, Nagata M, Hayashi K, et al. T peak to T end interval may be a better predictor of high risk patients with hypertrophic cardiomyopathy associated with a cardiac troponin I mutation than QT dispersion. Clinical cardiology. 2002;25:335-9.

39. Topilski I, Rogowski O, Rosso R, Justo D, Copperman Y, Glikson M, et al. The morphology of the QT interval predicts torsade de pointes during acquired bradyarrhythmias. Journal of the American College of Cardiology. 2007;49:320-8.

40. Watanabe N, Kobayashi Y, Tanno K, Miyoshi F, Asano T, Kawamura M, et al. Transmural dispersion of repolarization and ventricular tachyarrhythmias. Journal of electrocardiology. 2004;37:191-200.

41. Gupta P, Patel C, Patel H, Narayanaswamy S, Malhotra B, Green JT, et al. Tpe/QT ratio as an index of arrhythmogenesis. Journal of electrocardiology. 2008;41:567-74.