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Original Article

ST-T segment changes in patients with tricyclic antidepressant poisoning

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ABSTRACT

Objective: Tricyclic antidepressant (TCA) poisoning is among highly prevalent and potentially dangerous toxicities. ST-T changes are observed in the electrocardiogram (ECG) of most of TCA poisoned patients. We aimed to study ST-T segment changes in TCA toxicity and its probable relationship with other ECG findings.

Methods: This retrospective study was carried out in Noor and Ali Asghar University Hospital, Isfahan (Iran) in 2012. Patients with TCA toxicity based on the patients' history who had not consumed any cardio-active drugs and did not have a past medical history of cardiovascular disease in the recent 5 years, were randomly selected and investigated. Their demographic and medical data on admission including ECG, age, sex, type and amount of ingested TCA, poisoning severity score, QRS changes, QT interval, heart axis position and R-wave were all recorded. ST-T changes and their relation with other ECG parameters have been determined using statistical analysis.

Findings: Medical records of 272 patients were analyzed. In symptomatic patients, ST change prevalence was 40.8% and T change prevalence was 9.5%. In asymptomatic patients, the frequency of ST and T changes were 4.8% and 0.8%, respectively ($P < 0.05$). The most common ST and T changes in baseline (on admission) ECG were non-significant elevation (15.4%), significant elevation (11%) in pre-cordial leads, and T-wave flattening (6.6%). A statistically significant correlation was documented between ST segment changes with QRS and R-wave in aVR. The correlation between T-wave changes and R-wave in aVR lead was also significant.

Conclusion: ST-T changes in TCA poisoned patients are more prevalent in symptomatic patients. Obviously for a more definite conclusion, it is necessary to design a prospective study with the control group. This may facilitate a better understanding of ST-T segment changes.

Keywords: Electrocardiogram; poisoning; toxicity; tricyclic antidepressant

INTRODUCTION

Tricyclic antidepressant (TCA) poisoning is among highly prevalent and potentially dangerous toxicities. TCAs are widely prescribed despite the availability of safer treatment alternatives.[1] In Britain, there are still death reports due to the overdose of these drugs.[2]

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TCAs block the reuptake of noradrenalin and serotonin and probably block the serotonin receptors in sympathetic nerve endings.[3,4] They also have anticholinergic, antialpha-adrenergic and quinidine-like (type Ia anti-arrhythmic) actions, i.e., through blockade of fast sodium channels.[3] It seems that in TCA poisoning, the major dangerous toxicological concerns are from selective inhibition of the re-uptake of serotonin.[4] The main cause of death after TCA overdose is reported to be cardiovascular toxicity.[5,6] In a research on 38 toxic patients with TCA overdose by Glauser and Fasoli, no cardiac arrhythmias except sinus tachycardia and rarely premature ventricular contraction were found in the first 24 h electrocardiogram (ECG).[7]

ECG has emerged as a useful tool for identifying toxicity with sodium channel blockade drugs[8] and is still considered as a screening tool for dangerous TCA exposures, therefore has a high prognostic indicator value.[9] The most common electrophysiological result of TCA poisoning is sinus tachycardia, PR interval prolongation, widened QRS complex (>0.1 s) and widened QT, AV block, ventricular ectopic, non-specific ST-T changes, right axis deviation and Brugada pattern changes (including Right Bundle Branch Block and downward elevation of ST segment in V_1-V_6 leads).[9,10] Among them, the important predictor ECG changes for this toxicity are generally considered as QRS prolongation, right axis deviation, $R > 3$ mm or R/S ratio > 0.07 in lead aVR.[3]

On the other hand, significant ST elevation[11,12] and non-specific ST changes[12,13] are also reported in some TCA toxicity studies. TCA effects can also be presented like cardiac ischemia with ST elevation and negative T-wave in ECG.[4]

Considering the high risk of mortality in TCA toxicity and its important value of ECG changes,[14] in this study we aimed to describe more about the ST and T-wave changes in TCA intoxicated patients and find out the probable relationship with other ECG findings during hospitalization period.

METHODS

This descriptive and retrospective study was carried out in Noor and Ali Asghar University Hospital, Isfahan (Iran) in 2012. Medical records of 272 patients who had referred to the poisoning department of this hospital for the management of their TCA toxicity (based on ICD-10 coding) were randomly selected. Patients with TCA toxicity who had not consumed any cardio active drugs and did not have a past medical history of cardiovascular disease in the recent 5 years were investigated. Their demographic and medical data on admission including ECG, age, sex, type and amount of ingested TCA, poisoning severity score (PSS),[15] QRS changes, QT interval, heart axis position and R-wave were all recorded. The research protocol was approved by the institutional board for human studies and the privacy of all data for all patients was highly considered.

To determine the severity of toxicity, PSS index was used. Based on this classification, the patients were categorized into five categories:[15]

- Asymptomatic (0): Without any symptoms or signs of toxicity.
- Mild (1): Transient, mild and self-limiting symptoms and signs.
- Moderate (2): Long-standing symptoms and signs.
- Severe (3): Severe or life-threatening symptoms and signs.
- Lethal (4): Death.

To make the methodological comparison easy, patients were classified in two groups: Without clinical symptoms (PSS = 0) and with symptom (PSS > 0). In the evaluation of QT interval, QTs > 0.45 s in men and QTs > 0.47 s in women were considered as prolonged.[16] In order to classify the rate of ST segment elevation, in cases in which ST 0.04 s after QRS complex were elevated > 0.2 mV in pre-cordial leads and > 0.1 mV in limb leads, they were recorded as significant elevation and less than these values were recorded as non-significant elevation.[12] The evaluation of ST segment depression was also done in the same way. In the cases that ST segment depression was > 0.1 mV from isoelectric line, 0.08 s after QRS complex ending, they were categorized as significant depression, and fewer rates were classified as non-significant depression.[17] ST segment changes were categorized in 9 classes: No change, significant elevation in pre-cordial leads, significant elevation in limb leads, elevation in both of the leads, depression in pre-cordial leads, depression in limb leads, depression in both of the leads, non-significant depression and elevation.

The existence of correlation for each of the ECG findings with ST-T changes were determined by RO-spearman correlation analysis and Chi-square statistical tests. Data were analyzed using the Statistical Package for the Social Sciences for windows (SPSS, Chicago, IL, USA) version 16.0. $P < 0.05$ was considered as a significant difference.

RESULTS

A total of 272 eligible patients (110, 40.4% male) who were hospitalized due to TCA poisoning in the recent 5 years were studied. They aged 13-75 years old (Mean ± standard deviation [SD]: 28.2 ± 10.14). Nortriptyline (41.5%) and amitriptyline (41.2%) toxicity were the most prevalent kind of poisoning, whereas doxepin (0.04%) was the least. The time elapsed from drug consumption to hospital referral varied from 5 to 22 h (Mean ± SD: 4.51 ± 3.2). Maximum ST Changes were non-significant elevations (15.4%) and significant elevation (11%) in pre-cordial leads [Table 1] and the most common (6.6%) change of T-wave was flattened T-wave [Table 2].

A total of 38 patients (14%) had no clinical symptoms on admission and during hospitalization period. However, 13 (34.2%) of them (4.8% out of the total studied patients) as indicated in ECG, had ST changes on admission. Only 0.8% of patients had abnormal T-wave on admission [Table 3]. Two patients died

Table 1: Frequency distribution of ST segment changes in study patients

ST changes (leads)	*N* (%)
Normal	148 (54.4)
Elevation of pre-cordial	30 (11.1)
Elevation of limb	12 (4.4)
Elevation of pre-cordial+limb	9 (3.3)
Depression of pre-cordial	5 (1.8)
Depression of limb	2 (0.7)
Depression of pre-cordial+limb	4 (1.5)
Non-significant elevation	42 (15.4)
Non-significant depression	20 (7.4)

Table 2: Frequency distribution of T-wave changes in study patients

T-wave changes	*N* (%)
Normal	244 (89.7)
Flattened	18 (6.6)
Tall (in some leads)	8 (3)
Invert (negative)	2 (0.7)

Tall T: >0.5 mV in limb leads and >1 mV precordial leads, Flattened T: <0.1 mV limb leads or <0.2 mV precordial leads

Table 3: Frequency distribution of abnormal ST segment and T-wave of the study patients on admission

Poisoning severity	Abnormal ST (%)	Abnormal T-wave (%)	Total (%)
PSS=0	13 (4.8)	2 (0.8)	38 (14)
PSS>0	111 (40.8)	26 (9.5)	234 (86)

PSS=Poisoning severity score

because of TCA poisoning. One of them had ST elevation in limb leads; while the other had ST depression in precordial leads. None of them had the changes we have considered for T-wave.

The correlation between ST or T-wave changes and PR, QRS, QT, R-wave width in aVR, heart axis and heart rate changes in the ECG during hospitalization period was evaluated with statistical analysis (data not shown). ST changes had statistically significant correlation with QRS and R-wave width in aVR (P = 0.001 and P < 0.0001, respectively). Furthermore, T-wave changes had statistically significant correlation with R-wave width in aVR (P = 0.007).

DISCUSSION

Our demographical findings show that TCA poisoning was more prevalent in women. Dianat *et al.*,[18] in their local epidemiologic study (n = 1582) on TCA poisoning in Tehran, Iran found the prevalence ratio of TCA poisoning as 1.6/1 (females/males), which is very consistent with our findings. This may be due to the availability of antidepressant drugs for the treatment of depression (which seems to be more prevalent in females) and the probability of choosing a painless way for suicidal gesture. Accordingly, the most widespread TCA drugs that were misused for suicidal purpose in our study were nortriptyline and amitriptyline, which is consistent with Dianat study and maybe due to the widely usage and prescribing of these two drugs for different psychiatric indications including major depression in Iran.

Our research indicated that in TCA toxicity, the prevalent changes in ST-T, non-significant and significant elevation in pre-cordial leads and flat T-wave were the most common T-wave changes. Non-specific ST-T changes were prevalent and these can be seen in each lead of ECG. In non-symptomatic patients, abnormalities of flat T-wave and ST segment depression were non-specific. Electrolyte imbalances, anemia, fever, acidosis, alkalosis or the release of androgenic catecholamines may probably be considered among its causes.[19]

ST-T changes in TCA toxicity were previously mentioned as non-specific changes,[20] but to our best of knowledge, no study has been done yet to find the most prevalent changes of ST-T changes in TCA poisoned patients' ECG. In our study, the most common ST changes were seen with normal QRS and normal R-wave in aVR lead. This may be due to the lower poisoning severity of our patients. However, the probability of earlier occurrence of ST changes comparing to QRS widening or positive R in aVR should also be considered. Accordingly, ST changes may foreshadow the next occurrence of QRS interval complex or positive R in aVR although this needs more clinical evidence.

Our findings showed that 34.2% of the patients who had no clinical toxicity symptoms on admission, showed at least one form of ST changes in their ECG. In addition to the existence of normal variance in these people, we suppose that the occurrence of ST changes in ECG is observed before the outbreak of clinical toxicity symptoms. In Daviglus *et al.*, study on 1673 men aged between 40 and 55 who had no sign of heart problem or important changes in ECG in recent 5 years, 10% of them had ST changes in their ECG taken while relaxing, at least once in a year. Furthermore, 12% of 40-59 years old people had some light abnormalities in T-wave.[13] It seems unlikely that such changes in patients under our scrutiny be the normal finding of TCA poisoned patients' ECG. On the other hand, in our study, the ST changes were followed by changes in QRS width and positive R-wave in aVR. It is possible that the identified

changes in the ECG of the TCA poisoned patients and the most common ST changes (ST elevation in our study) be observed simultaneously.

An epidemiologic research on 9139 men aged 4-24 years old was accomplished by Sigurdsson *et al*., to specify ST-T change prevalence. Among the men who had no recognized heart disease, the prevalence of these changes increased from 2% in 40-year-old people to 30% in people aged 80. These changes were observed more often in old people and those who had high blood pressure, glucose intolerance, high serum triglyceride and left heart dilatation.[21]

In this study, the relationship between T-wave changes and each of PR, QRS, QT, R-wave width in aVR, heart axis and heart rate changes were scrutinized by statistical calculation and a close correlation between T-wave changes and R-wave changes in aVR was obtained. Obviously for a more definite conclusion, it is necessary to design a prospective study which includes a control group (normal general population) and to take serial ECGs and check serum troponin from hospitalized patients. This may facilitate a better understanding if the changes are normal or could be considered as side-effect of drugs, by comparing ST-T segment changes.

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AUTHORS' CONTRIBUTION

All authors have contributed in design, experiments, manuscript preparation and final proofreading.

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