ORIGINAL ARTICLE
FREQUENCY OF QTc PROLONGATION IN PATIENTS WITH HEMORRHAGIC STROKE

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Background: Acute cerebral events play an important role in generating autonomic imbalance especially cardiac rhythm disturbances. This forms the basis of significant lethal abnormalities of heart rate and rhythm like QTc prolongation, ventricular fibrillation, asystole, and ultimately death. This study was conducted to determine the frequency of QTc prolongation in patients presenting with acute haemorrhagic stroke at a tertiary care hospital. **Methods:** This descriptive case series was conducted at Medical Unit-I, ward-5, Jinnah Postgraduate Medical Centre (JPMC), Karachi, from 13 October, 2009 to 12 April, 2010. Patients of either gender and age >18 years who presented within 48 hours of onset of acute hemorrhagic stroke for the first time, confirmed by computerized tomography (CT) scan of brain were included. A 12 lead electrocardiogram (ECG) was performed. Lead III and VI were used for this due to their importance in this aspect. QTc was then calculated by using Bazetts formula. Data was analysed using SPSS-12. **Results:** Among 95 patients of acute haemorrhagic stroke, 48 (50.5%) had prolonged QTc in lead III, 47 (49.5%) had prolonged QTc in lead VI. The average QTc interval in lead III was 440.4±45.2 (Range=364–571). Proportion of prolonged QTc in lead III was higher in males than females. Frequency of QTc III prolongation was higher in comparatively younger age groups than older age groups. **Conclusion:** The frequency of prolonged QTc interval among patients of acute hemorrhagic stroke is alarmingly higher in our setup. Prolonged QTc is a useful predictor of impending clinical deterioration and provide an opportunity for early intervention to reduce severe loss like mortality.
Keywords: Haemorrhagic stroke, QTc prolongation

INTRODUCTION

Stroke is the third leading cause of morbidity and mortality worldwide.[1] According to the recent World Health Organization (WHO) estimates, developing countries account for 85% of deaths from stroke worldwide.[2] The annual incidence of stroke in developed countries is about 2/1000 people, but the correct figure depends on the age structure of the population as the incidence rises sharply with increasing age. According to WHO estimates for the year 2020, stroke will stay the second leading cause of death along with ischemic heart disease (IHD) both in developing and developed countries.[3] During the last three decades there is decline in the incidence of the disease in the western population, whereas the burden of the disease in South Asian countries (India, Pakistan, Bangladesh, and Sri Lanka) is expected to rise.[4] In Pakistan exact epidemiological data is lacking, still stroke is the commonest reason for admission in neurology and medical wards.[5] Rapid intervention after onset of a stroke can limit neurological damage and improves patient recovery of functioning.[6] Only 25% of patients return to the level of every day physical functioning of community-matched persons who have not had a stroke.[7]

Pathologically stroke has been divided into two types: infarction and haemorrhage.[8] Acute cerebral events play an important role in generating autonomic imbalance especially cardiac rhythm disturbances.[9,10] This forms the basis of significant lethal abnormalities of heart rate and rhythm like QTc prolongation, ventricular fibrillation, asystole, and ultimately death.[11] Although association between increased QT dispersion and ventricular rhythm has been evaluated extensively, but use of this electrocardiographic marker with the incidences of acute haemorrhagic stroke is relatively less studied.[12] Studies show repolarization abnormalities, manifesting as prolonged QTc in 44.2–68.29% of the patients having haemorrhagic stroke.[13,14] QTc prolongation is one of the prognostic markers of hemorrhagic stroke along with lower Glasgow Coma Scale (GCS) and brain stem involment.[15]

This study was conducted to know QTc prolongation in patients suffering from haemorrhagic stroke so that appropriate early intervention could be instituted to prevent cardiac arrhythmias and death. Prolonged QTc may be a useful predictor of impending clinical deterioration and provide an opportunity for early intervention to reduce severe loss like mortality.

MATERIAL AND METHODS

This was a descriptive case series, conducted at Medical Unit - I, ward-5, JPMC, Karachi, from 13 October, 2009 to 12 April, 2010. It included 95 patients admitted with acute haemorrhagic stroke by calculating sample size with presumed proportion of 44.5%[8,9], 10% absolute precision and 95% confidence level. Patients were selected through purposive sampling. Patients who were more than 18 years old, first time presenting within 48 hours of onset of acute haemorrhagic stroke, were included in the study. Diagnosis was confirmed by non-enhanced CT scan of brain showing hyperdense area consistent with intracerebral haemorrhage, as reported by expert radiologist. Those patients who were excluded from the study included: ischemic stroke, transient ischemic attack, subdural and epidural haematoma, subarachnoid haemorrhage diagnosed on non-contrast CT scan brain; patients with atrial fibrillation, atrial flutter, bigeminy, on pace maker, and bundle branch or AV block diagnosed on ECG, patients using antiarrhythmic drugs, tricyclic and tetracylic antidepressant agents, and patients with hypocalcaemia.

An informed consent was obtained either from patients or from their attendants. A 12-lead ECG was performed by qualified ECG technician under the supervision of the principal investigator. ECG was analyzed by a cardiologist who was blinded to the clinical data. Lead III and VI were used for this due to their higher importance in this aspect. QTc was then calculated by using Bazetts formula.[9]

$$QTc = \frac{QT}{\sqrt{R-R}}$$

A QTc value of >430m sec is labelled as prolonged.[9] Data was collected on a *pro forma*. Statistical analysis was performed by using SPSS-12. Data was described and is presented in tabulated forms.

RESULTS

In our study, out of 95 patients of acute hemorrhagic stroke, 65 (68.4%) were males and 30 (31.6%) were females with male to female ratio as 2.17: 1. Age of patients was 58.7±13.1 (ranging from 25–90) years. Majority age group was 51–60 years (31.6%). The average QTc interval in lead III was 440.4±45.2 (Range=364–571). Out of 95 patients, 48 (50.5%) had prolonged QTc interval in lead III while 47 (49.5%) had normal QTc interval in lead III. The average QTc interval in lead VI was 439.7±44.1 (Range=364–602). Data is shown in Table-1. Frequency of QTc prolongation in lead III was higher in comparatively younger age groups than older age groups and similar pattern was found regarding the frequency of QTc prolongation in lead VI in various age groups (Table-2).

Table-1: Frequency of QTc prolongation in lead III and VI by gender (n-95)

Outcome	Male (n=65) No. (%)	Female (n=30) No. (%)	Total
QTc prolongation in III			
Yes	37 (56.9)	11 (36.7)	48
No	28 (43.1)	21 (63.3)	47
QTc prolongation in VI			
Yes	37 (56.9)	10 (33.3)	47
No	28 (43.1)	20 (66.7)	48

Table-2: frequency of QTc prolongation in lead III and VI by age (n=95)

Outcome	Age groups (years) No (%)				
	≤40	41–50	51–60	61–70	>70
QTc prolongation in III					
Yes	4 (66.7)	12 (52.2)	14 (46.7)	11 (44)	8 (72.7)
No	2 (33.3)	11 (47.8)	16 (53.3)	14 (56)	3 (27.3)
QTc prolongation in VI					
Yes	4 (66.7)	12 (52.2)	15 (50)	9 (36)	7 (63.6)
No	2 (33.3)	11 (47.8)	15 (50)	16 (64)	4 (36.4)

Values given in parentheses are percentages

DISCUSSION

Intra-cerebral haemorrhage (ICH) accounts for around 10–15% of all strokes worldwide, with a higher proportion of it in Asian countries.[16] Principal finding of this study has shown that half of the subjects had prolonged QTc interval in lead III and lead VI. Findings of the present study were consistent with most of the reported studies. A retrospective study conducted in Belgium by Sakr *et al*, in subarachnoid haemorrhage (SAH) patients, 34% of the patients had a prolonged QTc.[17] A prospective study conducted by Bergh *et al*, in a consecutive series of 62 patients with aneurysmal SAH, admitted within 72 hours, 61% of the patients had a prolonged QTc.[18] A study carried out by Maramattom on 110 patients with supra-tentorial intracerebral haemorrhage, changes in ECG were observed in 64% of the patients and 8% patients had prolonged QTc interval.[19] Another study done by Akbar *et al* at Multan on 84 patients suffering from acute hemorrhagic stroke 63.4% and 68.29%, had prolongation of QTc in lead III and VI respectively.[14]

In a study done by Schuiling WJ *et al*, QTc prolongation was found 13%.[20] In a retrospective cohort study (n=122), a combination of a pathological Q wave, ST depression and T inversion was the most powerful risk factor for in hospital mortality in a multivariate model also including Hunt and Kosnik, QTc interval, age and sex.[21] Subarachnoid haemorrhage in particular induces a wide variety of ECG changes, such as QT prolongation, changes of ischemia, and life-threatening arrhythmias such as ventricular fibrillation or flutter and occasionally *torsade de pointes*.[22–24]

Several electrophysiological mechanisms for the conductance abnormalities and impaired cardiac contractility have been suggested, which include

reduced beta-adrenoceptor density, post receptor signal defects, abnormal excitation-contraction coupling, and molecular abnormalities. Our study may provide sufficient evidence to support the statement as previously reported in literature that QTc prolongation is independent predictors of a poor outcome, but the relation of these individual ECG parameters with poor outcome is not explained by the occurrence of DCI. The additional value of ECG abnormalities to baseline characteristics in prognosticating outcome appeared to be limited. The frequency of prolonged QTc interval among patients of acute hemorrhagic stroke is alarmingly higher in our setup as consistent with the reported literature. It might be more if ECG was performed immediately after onset. An earlier presentation of the patients immediately after onset of stroke may reduce the severe loss. Facilitated ambulances with ECG for cardiac events or stroke may provide a more reliable frequency of prolonged QTc done immediately after onset by expert mobile technicians.

This study may act as a catalyst for future researchers to measure QTc interval in cases of stroke or cardiac events. Ambulance services may be enhanced on the basis of requisition of the services as per condition of the patient described during the basic inquiry.

A most important strength of the study is that ECG abnormality like prolonged QTc may be a useful and cost effective predictor of impending clinical deterioration and may provide an opportunity for early intervention to reduce severe loss like mortality.

CONCLUSION

In conclusion it can be said that males are affected more in terms of strokes and QTc prolongation. Frequency of QTc prolongation in lead III was higher in younger age groups. Prolonged QTc is a useful predictor of impending clinical deterioration and may provide an opportunity for early intervention to reduce severe loss like mortality.

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