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QT_C INTERVAL PROLONGATION AND ITS EFFECT ON OUTCOME OF THE SEPTIC ICU PATIENTS

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ABSTRACT
Aim to correlate QTc prolongation and its effects on APACHE score, SOFA score, length of stay and outcome of the septic ICU patients. In a prospective observational study conducted in single tertiary hospital between March-December 2013. Patients with sepsis admitted to our ICU were included. These septic patients were divided into two groups, one group having normal QTc interval on ECG (electrocardiogram) and other group with prolonged QTc interval. The APACHE score, SOFA score, ICU duration of stay and associated mortality has been observed during their ICU stay. Our study included 155 patients with sepsis. Among these patients, 129 patients had normal where as 26 patients had prolonged QTc interval on 12 lead ECG. The incidence of QTc prolongation was 16.7% (26/155). The APACHE (8.67 ± 5.53 Vs 13.46 ± 5.88), SOFA (2.35 ± 2.08 Vs 5.42 ± 3.26) and ICU duration of stay (92.92 ± 19.84 Vs 157.26 ± 52.53 hours) were statistically significant ($p<0.05$) in patients with prolonged QTc interval whereas the ICU mortality (14 deaths / 129 patients Vs 5 deaths / 26 patients) was not statistically significant. Drug induced QTc prolongation was common risk factor in our study. Prolonged QTc interval can be considered as one of the severity and morbidity indicator in critically ill septic patients with other established scores like APACHE-II and SOFA. Older age and female sex has been associated with high incidence of QTc interval prolongation.

INTRODUCTION

Cardiac conduction abnormalities are seen more commonly in ICU patients. Critically ill patients are at an increased risk of getting cardiac conduction abnormalities, as these patients are exposed to numerous risk factors. Risk factors include advanced age, hypocalcemia, hypomagnesemia, hypokalemia, bradycardia, baseline prolonged QT interval, rapid infusion of pro arrhythmic drugs, genetics, family history, female sex and pre-existing cardiac disease. (Li EC et al, Indik JH et al, Zeltser D et al) [1-3].

QT interval is measured from the onset of QRS complex to end of T-wave. The blockade of potassium channels prolongs the period of ventricular repolarization and manifest as QT interval prolongation on ECG (Gupta A et al, Viskin S et al) [4,5]. this causes early afterdepolarisation (EADs) producing ventricular ectopics and later Tdp, ventricular fibrillation and sudden cardiac death.

Normal QT interval is < 440ms, QT interval from 440ms to 460ms and 440ms to 470ms are considered borderline for men and women respectively. Values > 460ms for men and > 470ms for women indicates prolonged QT interval. QTc interval > 510ms is considered clinically significant and associated with high incidence of torsade de pointes (Tdp) and cardiac arrest. (Letsay et al) [6]. In patients with other risk factors the Tdp can occur even with < 510ms. Bazett's formula has been used commonly to calculate corrected QT (QTc) interval.

QT prolongation can be classified as either inherited or acquired. Congenital long QT syndrome is an inherited disease caused due to genetic mutation that affects many ionic channels (Keating MT et al) [7]. Two or more risk factors are associated with high incidence of QT prolongation and Tdp (Shaffer D et al) [8]. Electrolytes abnormalities and exposure to pro arrhythmic drugs are the common causes of QT prolongation. Medications such as macrolides, fluroquinolones, azole antifungal agents, antiarrhythmic and antipsychotic drugs are known to cause QT prolongation (Guo D et al, Falagas ME et al, Poluzzi E et al, Roden D et al, Virgin S et al, Shah SA et al, Martell BA et al) [9-15]. QT prolongation due to drugs may be dose dependent or non dose dependent (Redfern WS et al) [16]. QT interval prolongation can manifest as Syncope, palpitation, dizziness, seizures and ventricular tachycardia or it can be asymptomatic (Owens RC et al) [17].

MATERIALS AND METHODS

Ours is a prospective observational study conducted in single tertiary hospital between March 2013 to December 2013. Written informed consent obtained from patient or his relatives and approval from scientic review board. Inclusion criteria being patients admitted during the study period (March-December 2013) in the medical ICU with sepsis [Patient having two or more components of systemic inflammatory response syndrome (SIRS) along with suspected or confirmed source of infection], minimum 48 hours stay in ICU and patients not requiring emergency surgery.

Exclusion criteria include age > 80 years, post CPR status, and patients with cardiac pacemakers. A 12 lead ECG was done in all these patients routinely. The incidence of QTc interval prolongation among these patients, and ICU duration of stay with associated mortality between normal and prolonged QTc patients was noted during their stay. The statistical analysis used was student t test and the software is Windostat Version 9.2.

RESULTS

In our study 155 patients with sepsis have been included. Among these patients 129 patients had normal QTc interval where as 26 patients had prolonged QTc interval. Older age group along with female sex had high incidence of QTc interval prolongation. The incidence of QTc prolongation was 16.7% (26/155). The APACHE (8.67 ± 5.53 Vs 13.46 ± 5.88), SOFA (2.35 ± 2.08 Vs 5.42 ± 3.26) and ICU duration of stay (92.92 ± 19.84 Vs 157.26 ± 52.53 hours) were statistically significant ($p<0.05$) in patients with prolonged QTc interval whereas the ICU mortality (14 deaths / 129 patients Vs 5 deaths / 26 patients) was not statistically significant.

The organism isolated were E-coli, Klebsiella, Pseudomonas, Acenetobacter, staphylococcus aureus and candida species. Thirty patients (blood -25, urine-1 and Mini BAL-4) without QT prolongation and 6 patients (blood-4, BAL-2) with QT prolongation cultures were sterile. Probably due to antibiotics administered at local hospital. The common organisms isolated in blood, urine and Mini BAL (Broncho alveolar lavage) were Pseudomonas, E-coli and Acenetobacter respectively in both groups. The maximum number of patients had respiratory tract infection followed by urinary tract infection.

Table 1. Showing clinical characteristics in sepsis patients with or without QT prolongation

Clinical Characteristics	Sepsis Patients Without QT Prolongation (N=129) (Mean ± SD)	Sepsis Patients With QT Prolongation (N=26)(Mean ± SD)	P value
Age (In Years)	55.15 ± 14.34	65.69 ± 14.38	<0.05
Sex	Males- 70 Females- 59	Males- 9 Females- 17	
QTc Interval (Mean)	433.50 ± 15.81	494.42 ± 28.81	<0.05
APACHE - II	8.67 ± 5.53	13.46 ± 5.88	<0.05
SOFA	2.35 ± 2.08	5.42 ± 3.26	<0.05
ICU Length of Stay (In Hours):	92.92 ± 19.84	157.26 ± 52.53	<0.05
Outcome(Death) :	14	5	0.23

Table 2. Focus of sepsis in our study population

Focus of Sepsis	Patients Without QT Prolongation. (N=129)	Patients with QT Prolongation (N=26)
Central Nervous System	11	1
Respiratory System	42	8
Cardio Vascular System	2	0
Gastro Intestinal Tract	23	3
Genito – Urinary Tract	35	6
Invasive Lines	8	6
Unknown	8	2

Among 26 patients with QTc prolongation, drug related QT prolongation was seen in maximum patients (10 patients), these drugs were fluroquinolones, macrolides, quinine, amiodarone, and fluconazole. Cardiac cause for prolonged QTc interval was seen in 4 patients (previous myocardial infarction, Congestive heart failure, and Systemic hypertension with left ventricular hypertrophy). Eight patients had electrolytes abnormalities related QT prolongation (hypokalemia. hypocalcemia, and hypomagnesemia). Two patients had family history of QT prolongation and one patient had bradycardia related and in one patient the cause was not known.

Table 3. Showing organisms isolated in culture

Organisms	Sepsis Patient Without QT Prolongation (N=129)			Sepsis Patient With QT Prolongation (N=26)		
	Blood	Urine	BAL	Blood	Urine	BAL
E.Coli	5	14	0	0	3	0
Klebsiella	9	7	8	1	0	1
Pseudomonas	11	4	1	4	2	1
Acenetobacter	8	1	12	1	0	4
Staphylococcus aureus	2	0	3	1	0	0
Candida species	8	2	4	1	1	0
Sterile	25	1	4	4	0	2

Table 4. Showing probable causes of QT interval prolongation.

Causes of QT Interval Prolongation	Patients with QT Prolongation (N=26)
Cardiac cause	4
Drugs	10
Bradycardia related	1
Electrolytes abnormality	8
Family history	2
Unknown cause	1

DISCUSSION

The clinical characteristic between two groups has two groups. Probably QTc prolongation can be considered as one of the severity and morbidity indicator in critically ill patients. In both group groups the cause of mortality was due to MODS. There was no difference in mortality between two groups. The severity of organ involvement was more in QTc prolonged group. Qtc prolongation had effect on severity of organ involvement and morbidity but not on mortality.

Table – 2 shows the foci of sepsis in our study population. Maximum patients had respiratory tract infection and genitor-urinary tract infection. In 8 patients the focus of infection was not identified. The micro-organisms isolated in blood, urine and broncho-alveolar lavage (BAL) are shown in Table-3. The organism isolated were E-coli, Klebsiella, Pseudomonas, Acenetobacter, staphylococcus aureus and candida species. Thirty patients (blood -25, urine-1 and BAL-4) without QT prolongation and 6 patients (blood-4, BAL-2) with QT prolongation cultures were sterile. In blood Pseudomonas, in urine E-coli and in BAL Acenetobacter were the common organism isolated in both groups. The high incidence of acenetobacter in BAL was due to VAP/HCAP found in maximum patients shifted from other hospitals. The probable cause of QT interval prolongation has been shown in Table – 4. Among 26 patients with QTc prolongation, cardiac cause was seen in 4 patients (previous myocardial infarction, Congestive heart failure, and systemic hypertension with left ventricular hypertrophy). Drug related QT prolongation was seen in 10 patients (fluroquinolones, macrolides, quinine, amiodarone, and fluconazole).

Eight patients had electrolytes abnormalities related QT prolongation (hypokalemia. Hypocalcemia, and hypomagnesemia). Two patients had family history of QT prolongation and one patient had bradycardia related and in one patient the cause was not known.

CONCLUSION

Prolonged QTc interval can be considered as one of the severity and morbidity indicator in critically ill septic patients with other established scores like APACHE-II and SOFA. Older age and female sex has been associated with high incidence of QTc interval prolongation.

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DECLARATION OF INTEREST

None declared.

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