QT Intervals and Outcome of Pregnancy in Patients with Eclampsia

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Abstract
Background: Eclampsia is associated with considerable mortality and morbidity for the mother and the foetus. QT intervals and dispersions elongations are associated with dangerous arrhythmias and sudden death. Hypocalcaemia is related to both conditions.
Aim: To investigate the pattern of QT intervals and dispersions among eclamptic patients and determine outcomes in mother and foetus and also to find out if there is a relationship between the two conditions.
Method: Electrocardiograms of 32 patients with intra-partum eclampsia were compared with 30 normal matched for gestational age. Biochemical indices were also compared. Outcome in mother and foetus in the 2 groups were studied.
Results: The mean QT intervals and dispersions were comparable in subjects and controls. It was only in QTcmax that there was a significant prolongation in eclamptics (437.87$\pm$35.24 vs 420.36$\pm$ 32.07 msecs p< 0.05), though the mean QTcmax of the subjects was not absolutely prolonged. 59.4% of the patients had QTcmax prolonged compared to 13.3% of controls. The QTd and QTcd were prolonged in 18.8% and 15.6% of the patients respectively. No control had a prolongation of these intervals. There were 9(28.1%) foetal deaths in patients compared to none in controls. None of the QT intervals were related to either maternal or foetal outcome. There was significant difference in serum calcium between patient and control (9.03 $\pm$0.41 vs 10.4 $\pm$ 0.47mg/dl, p < 0.05). The higher the serum calcium, the tendency to better foetal outcome (r=0.83).
Conclusion: Many eclamptics had prolonged QT intervals and dispersions but were not associated with dangerous arrhythmias and sudden death.
Key Words: Eclampsia, QT Interval, QT Dispersions, Outcome

Introduction

Eclampsia is one of the four subgroups of hypertensive disorders of pregnancy [1]. It is characterized by generalized convulsion, elevated blood pressure and proteinuria with or without edema occurring after 20 weeks of gestation.[2] Eclampsia may complicate pregnancy ante partum, intrapartum and postpartum. It is a common complication of pregnancy occurring more in primigravidae than multiparrous women.

The incidence of eclampsia in Nigerian Patients in labour has been quoted variously from 0.42% in the North [3] to 2.76% in our Center [4]. Age, parity, weight and race have been noted to constitute important risk factors for developing eclampsia [5,6]. It is also associated with poor maternal and fetal outcomes [4].

QT interval is the total time taken for ventricular depolarization and

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repolarisation. QT dispersion (QTd) is the difference between maximum and minimum QT intervals across the 12 lead electrocardiogram (ECG); it is a reflection of regional variation in ventricular repolarisation[7]. It is a predictor of arrhythmia and sudden death in conditions like the long QT syndrome, cardiomyopathies and chronic heart failure and also in hypertensive patients [8]. Though QT prolongation has long been recognized as a predictor of mortality in various cardiovascular conditions; QTc dispersion (QTcd) which is a measure of myocardial repolarisation inhomogeneity is probably a better predictor [9].

Hypocalcaemia is an independent risk factor for QT interval prolongation [10] and also plays an important role in pathogenesis of eclampsia [11]. Sudden cardiac death and heart failure was reported to have occurred in 0.1% in patients with eclampsia in the MAGPIE trial [12].
QT intervals and dispersions are easy to obtain from surface ECG. If they predict dangerous arrhythmias and or sudden death in eclamptic patients, then they become useful tools in hands of obstetricians taking care of pregnant women in our environment and other developing economies .Studies investigating the relationship between QT intervals and eclampsia are few. We are not aware of studies in our environment investigating in particular the relationship between the QT dispersions and eclampsia. We thus decided to study the pattern of QT intervals and dispersions among our eclamptic patients and also characterize the maternal and fetal outcomes.

Patients and Methods

This is a prospective study of 32 patients with intra-partum eclampsia admitted into the Labour ward service of Olabisi Onabanjo University Teaching Hospital, Sagamu Nigeria. They were recruited into the study after obtaining informed consent from the patient or accompanying relations. A structured questionnaire obtaining information about age, gestational age, parity and previous medical history was filled for each patient.
Clinical examination particularly to exclude any structural heart disease was performed by one of the authors. Blood pressure was taken 3 times at rest and the mean obtained. A patient was adjudged to be hypertensive if she was a known hypertensive patient on drugs or have systolic BP $\geq$ 140mm Hg and or diastolic BP $\geq$ 90mm Hg [13]. The patient was adjudged to be eclamptic if she had generalized convulsion, hypertension, and proteinuria of at least 2+ with or without edema [2,13].
Blood was taken for electrolytes and urea, creatinine and calcium. Hypocalcaemia was assumed if serum calcium was less than 9mg/dl.
A standard 12- lead Electrocardiogram (ECG) at 25mm/sec was performed on each patient. The tracings were coded and analyzed by one of the authors blinded to the clinical data of the patients.
QT interval was measured from the onset of the QRS complex to the end of the T wave; when T wave was inverted, the end of the measurement is taken as the point of return to the T-P baseline. When U wave was present, the end of the measurement was taken as the nadir between the T and the U waves. These measurements were manually done as the existing automated systems have not been found to be consistently superior to the manual method [9], and they are not available in our service. Three consecutive QT intervals were measured for each lead and the mean taken. Whenever the T wave was not clearly discernible, such lead was excluded from the analysis. The QT interval was corrected for heart rate using the Bazzett's formula[14] to obtain the corrected QT (QTc). The QT dispersion (QTd) was obtained by subtracting the minimum from maximum QT and the QTc dispersion

Table 1- Baseline characteristics of the patients and controls

Variable(mean±sd)	Subjects (n = 32)	Controls (n = 30)	p value
Age (years)	22.88±3.59	21.71±3.20	0.351
Gestational age(weeks)	35.18±3.70	34.21±4.26	0.506
Gravidity	1.59 ±0.80	1.50±0.65	0. 751
Serum Ca(mg/dl)	9.03 ± 0.41	10.41± 0.47	0.034

(QTcd) was obtained by subtracting the minimum QTc from maximum QTc. Presence of any arrhythmias was also noted.
The outcome of the labour was noted both in the mother (discharged or death) and in the fetus- normal delivery, elective caesarian section, emergency caesarian section or fetal death.
Exclusion criteria include patients on drugs likely to prolong the QT interval like halofantrine, chlorpromazine and quinolones.
Thirty patients matched for age and gestational age with normal BP and urinalysis were used as controls. They had blood chemistries and ECG as the subjects.

Statistical Analysis
Statistical analysis was carried out using SPSS version 10.0. Continuous data were reported as mean ± SD and categorical variables in proportion and frequencies. Student's t test was used to compare the significance of the continuous variables. Pearson's correlation coefficient was employed to test the relationship between relevant variables. Linear regression was also used to show the linear relationship and the proportion of variation in the relevant dependent variable as determined by the independent variable. The p-value < 0.05 was considered statistically significant.

Results
There were 32 patients who fulfilled the criteria for inclusion in the study. Their mean age at 22.80±3.59years was not different from that of the 30 controls at 21.71±3.20years.The other baseline characteristics of the subjects and controls are shown in Table 1. The mean gestational age and parity of the subjects and controls were also the same. The serum calcium of the subjects though not absolutely low at 9.03 ± 0.41 mg/dl was significantly lower than that of the controls at 10.4 ± 0.47 mg/dl. There were 12(37.5%) patients with hypocalcaemia. This was significantly more than 2(6.7%) of the controls (p<0.05). Nine (28.1%) fetal deaths were recorded in the subjects compared to none (0%) in the controls (p<0.05). Of the remaining 23 live births in the subject, 10(31.2%) was spontaneous delivery, 2(6.2%) delivered by elective caesarian section and 11(34.4%) by emergency caesarian section. There was no maternal death either in the subjects or controls.
There was a positive correlation between serum calcium and fetal outcome. The higher the serum calcium the more likely a favorable fetal outcome. The linear model (Y=0.29X) for the linear relationship between the dependent variable, foetal outcome and the predictor serum Ca was of a good fit (F= 70.99, r=0.83, P < 0.05). There were no maternal deaths in both subjects and controls.
When the repolarisation indices were considered (Table 2), there was no significant difference in the QTmax, QTmin, and QT dispersions of the patients and controls. Though the mean QTcmax of the subjects was not absolutely prolonged at 437.87±39.24, it was significantly longer than that of the controls at 420.36± 32.07 (p

< 0.05). Neither the QTcmin nor the QTcd showed any significant difference.
Nineteen (59.4%) patients had prolonged QTcmax (QTc max > 440 msecs), which was significantly more than 4 (13.3%) of the controls. Whereas none of the controls had QTd>50msecs, 6 (18.8%) of the subjects had their QTd longer than 50msecs. When QTcd was considered, 5(15.6%) of the patients' QTcd were longer than 80msecs compared to none in the controls. No arrhythmias except sinus tachycardia were observed in both subjects and controls. Twenty-eight (87.5%) of the subjects compared with 7 (23.3%) of the controls had sinus tachycardia. This was statistically significant.

Linear regression analysis did not show any correlation between the QT intervals and maternal or fetal outcomes. There was also no significant correlation between the QT intervals and serum calcium.

Discussion
This study of repolarisation intervals in eclamptic patients confirmed the previous observation that eclampsia is common in young primigravida in our environment [3, 15]
The QTcmax was the only variable of the QT intervals that was significantly prolonged than the controls. This finding is similar to that of Isezuo et al, though they considered QTmax alone [15]. However the mean QTcmax was not absolutely prolonged. It has been observed that a prolongation greater than 440msecs is associated with dangerous ventricular arrhythmias and increased mortality particularly after acute myocardial infarction [9, 16]. Almost sixty per cent of the patients had QTcmax > 440msecs, though none had ventricular arrhythmias or died. There had been doubts about the probability

Table 2a - Comparison of the QT intervals (continuous variables) in patients and controls

Variable(mean±sd)	Subjects (n= 32)	Controls (n= 30)	p-value
QTmax(msecs)	338.75±40.31	335. 71±21.02	0.082
QTmin(msecs)	298.75± 37.57	302.86±17.29	0.710
QTd(msecs)	40.00±12.65	32.86±12.67	0.134
QTcmax(msecs)	437.87±39.24	420.36±32.07	0.048
QTcmin(msecs)	391.56±32.96	379.64±35.01	0.407
QTcd(msecs)	52.56±17.15	40.93±13.85	0.053

Table 2b - Comparison of the QT intervals (categorical variables) in patients and controls

Variables (n %)	Subjects (n=22)	Controls (n=30)	p-value
QTcmax >440msec	19(59.4)	4(13.3)	< 0.05
QTc>50msec	6 (18.8)	0 (0.0)	< 0.05
QTcd>80msecs	5 (15.6)	0 (0.0)	<0.05
Sinus tachy	28 (87.5)	7 (23.3)	< 0.05
	df= 6	X2 = 28.65	

of prolonged QTc in causing sudden death in patients without underlying cardiac disease[17]. The study patients were particularly screened not to have any cardiac disorder and this might contribute to absence of arrhythmias and/or sudden death. Isezuo et al reported prolonged QTmax though they did not consider corrected QTcmax[15]. They did not also report sudden deaths.

Prolongation of QTd and QTcd which demonstrates ventricular myocardial inhomogenity may be more predictive of arrhythmias and sudden death[9,18]. Prolongations of QTd beyond 50msecs and QTcd beyond 80msecs have been observed in population studies to predispose to dangerous arrhythmias [19,20]. There were more patients than controls with prolongation of the dispersion intervals beyond 50msecs and 80msecs in this study though without accompanying ventricular arrhythmias and or sudden death.

Hypocalcaemia is known to influence eclampsia and QT interval prolongation. It however did not correlate with any of the QT intervals in this study, though higher serum calcium was associated with better fetal outcome.

The maternal outcome in which there was no maternal death showed significant improvement over the experience of earlier years of obstetric practice in our centre. In a review carried out between 1997-2002, the mortality rate in eclamptic patients was 6.1%.The fetal death at 28.1% in this present work was lower than the previous figure of 36.4% [4], though still unacceptably high. Failure of regular Ante Natal Care and delay in presenting to hospital when there are complaints are some of the factors that have been identified to contribute to adverse outcomes in our eclamptic patients[4].

The conclusion of this study is that there are many of our eclamptic patients with prolonged QT intervals and dispersions, these are however not associated with dangerous arrhythmias or sudden death. The mean intervals were not significantly longer than controls except in QTcmax. Hypocalcaemia was also common in our patients but did not correlate with the prolongation of the QT intervals. Fetal outcome is poorer in patients with eclampsia.

The limitation of this study includes the failure to measure serum magnesium which is also known to affect development of eclampsia and prolongation of QT intervals. It has however been shown in some studies that there is no significant difference in the serum magnesium of eclamptics and control subjects in our environment [15]. The number of subjects is small and therefore detracts from power to make far-reaching conclusions. A larger perhaps multi-centred study is advocated.

Regular and prompt ante natal clinic attendance is again emphasized in our pregnant women. Identification and special care for patients at risk for developing eclampsia is advocated.

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