

Original Article

Effect of Spinal Anesthesia on QT Interval: Comparative Study of Severe Pre-eclamptic and Normotensive Parturients Undergoing Cesarean Section

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ABSTRACT

Aim: This study aimed to compare the effect of spinal anesthesia on QT interval in severe pre-eclamptic and normotensive parturients who underwent cesarean section in a Nigerian tertiary hospital. **Patients and Methods:** Twelve-lead electrocardiogram (ECG) was obtained before, and at intervals after spinal anaesthesia on fifty severe pre-eclamptic (Group A) and fifty normotensive parturients (Group B) who underwent caesarean section. The effect of spinal anaesthesia on QT interval was compared. **Results:** The preoperative (baseline) mean QT interval was longer in group A than in group B; 453.10 ± 34.11 ms versus 399 ± 18.79 ms, $P < 0.001$. The prevalence of prolonged QT interval in the severe pre-eclamptic group before spinal anesthesia was 80% while in the normotensive group it was 0%, $P < 0.001$. At 5, 30, 60, and 120 min after the establishment of spinal anesthesia, the mean QT interval in the severe pre-eclamptic group was shortened and maintained within normal limits; 414.74 ± 28.05 , 418.28 ± 30.95 , 411.18 ± 19.21 and 401.36 ± 17.52 ms with $P < 0.001$ throughout. In the normotensive group, there was no significant change in the mean QT interval. **Conclusions:** This study demonstrated that the QT interval was more prolonged among the severe pre-eclamptic parturients. Spinal anesthesia using 0.5% hyperbaric bupivacaine normalized the QT interval and maintained it within normal limits during the study period.

KEYWORDS: Bupivacaine, pre-eclampsia, QT interval, spinal anesthesia

INTRODUCTION

Pregnancy triggers the development of cardiac arrhythmias or exacerbates the pre-existing ones.^[1,2] These developments are exaggerated in severe pre-eclamptic parturients.^[3] The principal cardiovascular changes in the pre-eclamptic patients are increased sympathetic activity, decreased intravascular volume, and elevated systemic vascular resistance.^[3] McDonald *et al.*^[4] reported an increased risk of adverse cardiovascular events like ventricular fibrillation, Torsade de Pointes, and death in the pre-eclampsia parturients. Severe pre-eclampsia/eclampsia accounts for 27.8% of maternal deaths in our environment.^[5] A common cardiac manifestation of pre-eclampsia is prolonged

QT interval,^[3,6] which is a marker of ventricular depolarization and prolonged QT syndrome and signifies a delay in the left ventricular depolarization phase.^[3,7] As the heart rate increases, the QT interval decreases. The effect of the heart rate (RR interval) on QT interval is often mitigated by Bazette's formula to yield the corrected QT (QT_c) interval: $QT_c = QT / \sqrt{RR}$.^[3,8] The QT interval is prolonged when QT_c is greater than 440 ms.^[9,10] Previous studies have implicated QT prolongation as a risk

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factor for developing potentially life-threatening ventricular tachyarrhythmias.^[11,12]

Anesthetic management of prolonged QT interval has not been well-studied in our environment. Therefore, this study aims at assessing the effect of spinal anesthesia on QT interval in severe pre-eclamptic parturients undergoing cesarean section in our tertiary health care facility.

MATERIALS AND METHODS

Following the Ethical Review Committee's approval, 100 American Society of Anesthesiology (ASA) II or III consenting parturients (50 severe pre-eclamptic parturients, Group A, and 50 normotensive parturients, Group B) scheduled for cesarean section under spinal anesthesia were enrolled into the study.

Written consent was obtained from all the participants. The patients with contraindications to spinal anesthesia, and those on medications that can affect the QT interval, like thiopental, succinylcholine, atropine, and glycopyrrolate, were excluded from the study.^[13]

All consenting parturients were reviewed by the researcher once they were booked for cesarean section. On arrival into the operating suite, the patients were made to assume the supine position with a wedge under the right hip to displace the gravid uterus. The Electrocardiography (ECG) was done on all the parturients by the researcher using an ECG machine (CONTEC™ Electrocardiograph, Model ECG600G by CONTEC Medical Systems Co Ltd, No. 1112 Qinhua, West Street, China). After the application of ECG gel, chest electrodes were firmly attached to the respective positions from V1 to V6, and limb electrodes were attached to the appropriate locations. Twelve-lead ECG was obtained for all the patients. The standard ECG lead II was recorded and printed at a paper speed of 25 mm/s and amplification of 0.1 mV/mm about 5 min before, and at 5, 30, 60, and 120 min after the establishment of spinal anesthesia. Corrected QT (QT_c) interval was calculated using Bazett's formula: $QT_c = QT / \sqrt{RR}$.^[3,8]

The parturients were preloaded with 10 mL/kg of 0.9% saline for 15–20 min before spinal anesthesia. Using the standard aseptic technique with the patient in a sitting position, spinal anesthesia with 2.5 ml of 0.5% bupivacaine was administered via the L₃/L₄ intervertebral space. The parturients were returned to the supine position with the left uterine displacement in about 15° head-up position. A block dermatome level of T6 was ensured before spinal anesthesia was considered established, and other hospital peri-operative management protocols were strictly followed.

Sample size determination

The minimum sample size for this study was determined by using a validated formula^[14] to give a sample size of 50 for each arm and a total of 100 participants having used a 3.3% prevalence rate of severe pre-eclampsia in our local environment.^[15] The sampling method was purposive sampling with the recruitment of all consenting eligible patients until the sample size was completed.

The data were analyzed using the Statistical Package for Social Sciences (SPSS) software, version 21.0. The Chi-square test was used to compare the frequencies of two categorical variables. Paired sample t-test was used to compare the effect of spinal anesthesia on QT interval before and after spinal anesthesia in both the studied groups and an independent sample t-test was used to compare the QT parameters between the two groups. Pearson's correlation was used to determine the presence of a linear relationship between two or more continuous variables.^[16] A *P* value < 0.05 was considered to be statistically significant.

RESULTS

All the 100 enrolled participants (50 severe pre-eclamptic and 50 normotensive patients) completed the study.

Age and anthropometric parameters of the subjects

The mean ages of both groups were comparable; 29.28 ± 3.51 versus 30.64 ± 4.5 years, *P* = 0.095. The mean weight in the pre-eclamptic group was significantly more than the mean weight in the normotensive group; 83.02 ± 16.67 kg versus 73.52 ± 10.03 kg, *P* = 0.001. The mean height in the pre-eclamptic group was significantly more than the mean height in the normotensive group; 1.63 ± 0.08 m versus 1.60 ± 0.08 m, *P* = 0.024. Likewise, the mean Body Mass Index (BMI) in the pre-eclamptic group was significantly more than the mean BMI in the normotensive group; 30.93 ± 4.53 kg/m² versus 28.90 ± 3.57 kg/m², *P* = 0.015. The ages and anthropometric parameters are shown in Table 1.

The preoperative QT interval was significantly higher in the pre-eclamptic group than in the normotensive group; 453.10 ± 34.11 ms versus 399.00 ± 18.79 ms, *P* < 0.001 as shown in Table 2.

QT Interval before and after the establishment of the T6 height of the block in pre-eclamptic parturients.

The baseline mean QT interval before spinal anesthesia was prolonged; 453.10 ± 34.11 ms. It was significantly reduced to 414.74 ± 28.05 ms at 5 min following the attainment of T6 block, *P* < 0.001. At subsequent measurements, it remained significantly reduced,

Table 1: Age and anthropometric parameters of the subjects

Variable	Group A n (%)	Group B n (%)	Total n (%)	χ^2	T	P	Likelihood Ratio	CI Lower Upper
Age group (years)								
21-25	3 (6.0)	7 (14.0)	10 (10.0)	3.870 ^Y		0.037*	18.550	-2.961 0.241
26-30	31 (62.0)	19 (38.0)	50 (50.0)					
31-35	16 (32.0)	17 (34.0)	33 (33.0)					
36-40	0 (0.0)	7 (14.0)	7 (7.0)					
Mean±SD	29.28±3.51	30.64±4.50			-1.685 ^t	0.095		
Range	23-35	23-40						
Weight (kg)								
Mean±SD	83.02±16.67	73.52±10.03			3.453 ^t	0.001*	115.943	4.039 14.957
Range	54.00-108.00	53.00-91.50						
Height (m)								
Mean±SD	1.63±0.08	1.60±0.08			2.292 ^t	0.024*	67.411	0.004 0.668
Range	1.49-1.74	1.40-1.74						
BMI (kg/m ²)								
Mean±SD	30.93±4.53	28.90±3.57			2.487 ^t	0.015*	138.629	0.410 3.645
Range	24-42	20-35						

χ^2 : Chi-square test, *: $P < 0.05$ (statistically significant), n: Total no. of people in the group, %: percentage of the total, ^Y: Yates corrected

^t: Independent sample *t*-test. Baseline QT parameters of the subjects

Table 2: Baseline QT parameters of the subjects

Variable	Group A n (%)	Group B n (%)	Total n (%)	χ^2	T	P	Likelihood ratio	CI Lower Upper
Pre-op QT interval								
Mean±SD (ms)	453±34.11	399±18.79			9.824 ^t	<0.001*		
Pre-op QT interval								
Low	4 (8.0)	8 (16.0)	12 (12.0)	68.333		<0.001*	87.183	<0.001 0.030
Normal	6 (12.0)	42 (84.0)	48 (48.0)			<0.001*		
Prolonged	40 (80.0)	-	40 (40.0)			<0.001*		

χ^2 =Chi-square test, *: $P < 0.05$ (statistically significant) n: Total no. of people in the group, %: percentage of the total, ^t: Independent sample *t*-test

Table 3: QT Interval before SA and after the establishment of T6 height of the block in pre-eclamptic parturients (Group A)

QT interval before SA	QT interval after SA	t	T	P	LR	CI 95% Lower Upper
453.10±34.11	5	414.74±28.05	8.494	<0.001*	174.671	25.855 46.505
453.10±34.11	30	414.28±30.95	7.431	<0.001*	146.037	-15.136 -0.304
453.10±34.11	60	411.18±19.21	7.798	<0.001*	202.053	-15.019 -3.621
453.10±34.11	120	401.36±17.52	9.722	<0.001*	186.187	-13.631 -0.489

SA=Spinal anesthesia, *t*=Paired sample test, LR=likelihood ratio, CI=Confidence interval

Table 4: QT Interval before SA and after the establishment of T6 height of the block in normotensive parturients (Group B)

QT interval before SA	QT interval after SA	t	T	P	LR	CI 95% Lower Upper
399.00±18.79	5	396.94±20.80	0.750	0.457	174.671	-15.136 -0.304
399.00±18.79	30	398.80±16.85	0.093	0.926	146.037	-15.019 -3.621
399.00±18.79	60	400.62±18.45	-0.611	0.544	202.053	-13.631 -0.489
399.00±18.79	120	399.62±20.48	-0.188	0.852	186.187	-13.932 2.372

SA=Spinal anesthesia, *t*=Paired sample test LR=likelihood ratio, CI=Confidence interval

$P < 0.001$, and maintained within normal limits as shown in Table 3.

QT Interval before and after the establishment of spinal anesthesia using hyperbaric bupivacaine in normotensive patients scheduled for cesarean section.

The baseline mean QT interval before the administration of spinal anesthesia was 399.00 ± 18.79 ms. There was no significant change at various measurements after spinal anesthesia as shown in Table 4.

DISCUSSION

Prolonged QT interval signifies a delay in the left ventricular depolarization phase. The QT interval was commonly prolonged among the severe pre-eclamptic parturients.^[3,6] The normal acceptable range of QT interval is 380–440 ms in healthy individuals.^[8]

In this study, the mean QT interval 5 min before spinal anesthesia was 453.10 ± 34.11 ms. It was normalized within 5 min following the attainment of T6 height of the block and was maintained within normal limits throughout the study period with a mean value of 414.74 ± 28.05 ms. The mean QT interval among the normotensive parturients before spinal anesthesia was 399.00 ± 18.79 ms. The mean value 5 min after the attainment of T6 height of the block in this group was 396.94 ± 20.80 ms. The spinal anesthesia had no significant effect on the QT interval among the normotensive parturients. The QT interval was higher among the severe pre-eclamptic parturients compared to the normotensive parturients before the administration of spinal anesthesia until 120 min after spinal anesthesia. This study demonstrated an 80% prevalence of prolonged QT interval among the severe pre-eclamptic parturients while no pregnant normotensive parturients had prolonged QT interval. This study found that prolonged QT interval commonly occurs in severe pre-eclamptic parturients. This may be one of the causes of increased perinatal mortality in them.

In congruence with these findings, Gupta *et al.*^[9] in a study on QT_c, revealed that 98% of the severe pre-eclamptic patients had prolonged QT interval.

Similarly, Sen. *et al.*^[3] in their study on severe pre-eclamptic patients found the prevalence of prolonged QT interval to be 72% and none was found among the normotensive parturients. The increased incidence of prolonged QT interval among the severe pre-eclamptic parturients may be a result of exaggerated sympathetic influence with vagal withdrawal in them, thus, modulating the autonomic nervous system. In addition, it may also be a result of hypocalcemia following the treatment with intravenous magnesium sulfate.^[13] This

study demonstrated that the baseline mean QT interval in the pre-eclamptic group was 453.10 ± 34.11 ms which is considered prolonged.

Unlike general anesthesia that further prolongs the QT interval,^[13] the QT interval was significantly reduced after the attainment of T6 height of the block and was maintained within normal limits throughout the study period. In agreement with the findings of this study, Sen *et al.*^[3] in a study on pre-eclamptic parturients reported that the mean baseline QT before the administration of spinal anesthesia in the severe pre-eclamptic group was prolonged with a mean QT_c of 452 ± 17.5 ms. It was significantly shortened by 5 min following the attainment of T6 height of the block to normal range.

The similarity in the findings could be because similar volume of local anesthetic agent, similar intervertebral space for spinal anesthesia, and similar height of block were used. The spinal anesthesia normalizes the QT interval when it is prolonged probably because of its associated sympathectomy. At 5 min before the initiation of spinal anesthesia, the baseline mean corrected QT_c interval in the severe pre-eclamptic parturients was above the normal limit. It was significantly higher than the mean value in the normotensive group. It was demonstrated that the QT_c interval was reduced to the normal limit within 5 min following the attainment of the T6 height of the block. Both groups were maintained within normal limits throughout the study period.

This finding is similar to that of Sen *et al.*'s^[3], where the mean QT_c was prolonged and significantly higher in the severe pre-eclamptic group than the normotensive group before the initiation of spinal anesthesia and was normalized from 5 min after the attainment of T6 height of the block until the end of the study period.

From this study, it was demonstrable that there was no relationship between the QT interval and the development of arrhythmias in both study populations. This is in keeping with the findings of Owczuk *et al.*^[17] This observation could be because none of the parturients had a QT_c interval that exceeded 660 ms which Khan *et al.*^[18] reported as the threshold for dysrhythmias. In addition, maybe because severe pre-eclamptic parturients were on magnesium sulfate treatment as part of the hospital's treatment protocol for prevention of disease progression to eclampsia. This prevents the development of Torsade de Pointes, common arrhythmias secondary to prolonged QT interval.^[13]

CONCLUSION

This study demonstrated that at baseline, the most severe pre-eclamptic parturients had prolonged QT

interval while none of the normotensive parturients had prolonged QT interval and that spinal anesthesia with 0.5% hyperbaric bupivacaine shortened the QT interval when it was prolonged. The prolonged QT interval was normalized within 5 min following the establishment of spinal anesthesia and was maintained within normal limits during the perioperative period.

This study strengthens the role of spinal anesthesia for cesarean section as a safe technique of anesthesia for cesarean deliveries on parturients with severe pre-eclampsia. This is important in our subregion where maternal morbidity and mortality are still high and strategies to reduce it is a top national priority. It, therefore, recommends an increase in the availability of spinal anesthesia services across all strata of the health system in our country for obstetric patients.

Strengths and limitations

The strength of this study includes a higher sample size of 50 subjects per group. The previous study recruited 25 subjects per group.

This study had some limitations. There was a paucity of studies on the research topic worldwide, and to the extent of my literature search, none was found in our subregion. Hence, the comparison was more with foreign studies.

It was non-randomized, and therefore, was subject to selection bias.

Several confounders that could influence the QT interval were not factored into this study, for example, body mass index and electrolyte derangement.

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Declaration of patient consent

The Author certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given her/their consent for her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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