

The Effect of Intravenous Lidocaine on QTc Changes During Spinal Anesthesia in Elderly Patients

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Background: Prolonged QT interval may lead to serious arrhythmias and ventricular fibrillation, hence prevention of the QT-interval prolongation is crucial for physicians. The aim of this study was to assess the influence of intravenous lidocaine on the QTc interval resulting from spinal anesthesia with bupivacaine.

Methods: In a randomized double blind trial, fifty male patients with mean age of 70.38 and ASA physical status II, who underwent spinal anesthesia for elective orthopedic lower limb surgical procedures, were assessed. Our subjects were divided into two groups, patients randomly received intravenously either 1.5 mg/kg lidocaine 2% as test group (n=25), or 0.05 ml/kg isotonic sodium chloride as control group (n=25), just before inducing of spinal anesthesia. Spinal anesthesia was performed in the sitting position with 3 ml of 0.5% hyperbaric bupivacaine. Values of the QTc interval, heart rate, and arterial blood pressure were measured before spinal anesthesia as well as 1, 5, 15, and 30 minutes after spinal anesthesia.

Results: With respect to the within-group values, statistically significant prolongation of the QTc interval as well as hemodynamic variability were detected in the measured times after blockade. There was no statistical difference between two groups according to hemodynamic parameters and the duration of the QTc interval before spinal anesthesia and times after spinal block with bupivacaine.

Conclusion: Administration of intravenous lidocaine may not prevent the prolongation of the QTc interval and hemodynamic changes resulting from spinal anesthesia with hyperbaric bupivacaine, in elderly subjects.

Keywords: spinal anesthesia; QT interval; bupivacaine

Prolonged QT interval may increase the risk of serious ventricular arrhythmia including polymorphic ventricular tachycardia (torsade de pointes), ventricular fibrillation and subsequently increasing morbidity and mortality [1]. Duration of QT interval is heart-rate dependent; lengthening with bradycardia and shortening with tachycardia and for this reason, it is recommended to drive a heart rate-corrected (QTc) interval which is most valuable during an intervention [2]. Considering the fact that its origin may be inborn or acquired, a QTc interval greater than 440 milliseconds is considered long [3], and most serious arrhythmia are associated with a QTc \geq 600 milliseconds [3-4].

Regional anesthesia is the most common method of anesthesia used in some procedures, particularly if the

patient is in the elderly group and orthopedic surgery [5-6]. Spinal anesthesia may have various influences on the QTc interval according to some studies [3-7]. Owczuk et al. documented the prolongation of the depolarization and repolarization time of the cardiac ventricles, as reflected by lengthening of the QTc interval in patients without cardiovascular disorders undergoing subarachnoid block with bupivacaine. They postulated that prolongation of the QTc interval was observed in the first minute after blockade and remained in subsequent measurements [3]. Deniz et al. examined the effects of bupivacaine and levobupivacaine on QT, QTc and p wave dispersion in pregnant women. The result of their study was in part similar to the mentioned study and there was a difference in calculated QTc interval, one minute after anesthesia and in later measurements [7].

Application for the local anesthetic agent; lidocaine, was found effective to inhibit the adverse hemodynamic phenomena and ECG rhythm accompanying tracheal intubation, both when it is administered intravenously and locally via transtracheal injection [8]. Owczuk et al. determined the effect of intravenous lidocaine on QT and QTc during laryngoscopy and tracheal intubation. They found lidocaine that was administered 1.5 mg/kg intravenously after induction of anesthesia, would have prevented the prolongation of the corrected QT interval induced by laryngoscopy and tracheal intubation [1]. To our knowledge, there is no data about the influence of intravenous lidocaine on QTc changes induced by spinal anesthesia with bupivacaine.

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In this study, we hypothesized that lidocaine would affect QTc changes after spinal anesthesia. To test the hypothesis, the effect of intravenous lidocaine was tested on corrected QT interval and hemodynamic responses to spinal anesthesia with bupivacaine.

Methods

After obtaining the approval of the Ethic's committee of Shahrekord University of Medical Sciences (Reference No. 88-3-2) and International Clinical Trials Registry Platform (IRCT registration number: IRCT201008272832N1), informed written consent was obtained from each patient. In a randomized double blind trial, fifty male patients aged more than 60 and less than 100 years with American Society of Anesthesiologist (ASA) physical status II were included in the study, and they were divided into two groups of 25 each; using a computer-base random allocation and double blind manner. Inclusion criteria were preoperative value of QTc interval ≤ 440 milliseconds and surgical procedures concerning lower extremities. Patients were excluded if they were receiving anti-arrhythmic drugs, or a history of symptomatic heart disease or circulatory insufficiency, or if they were receiving drugs known to prolong the QT interval. Exclusion criteria were also patients with symptomatic liver and kidney diseases, known hyperparathyroidism, cardiac arrhythmia, cardiomegaly, valvular heart disease and/or any abnormal echocardiographic changes and obesity. Standard spinal procedure was considered for all the participants. All patients were assigned for elective orthopedic lower limb surgical procedures (internal fixation of interthoracic fracture), considering the fact that we used no premedication before spinal anesthesia.

On arrival in the operating room, patients were put in supine position and standard monitoring such as electrocardiogram and pulse-oximetry. Noninvasive measurement of arterial blood pressure was initiated and preoxygenation was started using face mask at 5-6 lit/min. After intravenous catheterization, 10 ml/kg 0.9% saline solution was infused. Spinal anesthesia was done in the sitting position at the L4-L5 spinal level with a Whitacre 23 G spinal needle. After outflow of the cerebrospinal fluid, 3 ml of 0.5% hyperbaric bupivacaine solution (Bupivacaine Spinal 0.5% Heavy) was injected intrathecally. Immediately after spinal anesthesia, the patient was positioned supine and the level of anesthesia was assessed, and after 10 minutes of adequate blockade, surgical operation was permitted. Patients were randomly allocated to receive intravenously either 1.5 mg/kg lidocaine 2% as lidocaine group (test group) or 0.05 ml/kg isotonic sodium chloride as placebo group (control group), just before inducing of spinal anesthesia.

Standard derivation electrocardiogram (ECG) recording was obtained from patients participating in the study with a paper speed 25 mm/sec and a deflection of 1 mm/mv using paper-based ECG monitoring device. A 12-lead electrocardiogram as well as non invasive blood pressure measurement was performed in patients in supine position 5 minutes before spinal anesthesia as well as 1, 5, 15, 30 minutes of adequate blockade using pinprick stimulation test at T10-T12 dermatomes. Analysis data included assessment of mean values of the duration of QTc interval, mean values of systolic and diastolic blood pressure as well as heart rate, before and after spinal anesthesia, periodically. Correction of

QT interval was performed using Bazett's formula ($QTc = QT / \sqrt{RR}$) [3]. Statistical analysis was performed using SPSS 15.0 software, meanwhile intergroup comparisons were tested using Student's t-test for independent data considering Levene's test for homogeneity of variance. Interval data were analyzed using General Linear Model for repeated measurements, and Mauchly's Test of Sphericity was assumed for homogeneity of variance. Data were expressed as mean (95% confidence interval; 95% CI) and $p < 0.05$ was considered to be significant.

Results

Both groups were similar in terms of age, weight and height (Table 1). With respect to sensory block levels, the level of T10-T12 was detected in all patients participating in the study. Compared with respect to systolic and diastolic arterial blood pressure values measured at all time, lidocaine group and control group did not display significant differences, statistically ($p = 0.074$). Comparing times after spinal anesthesia there was a significant decrease in systolic and diastolic arterial blood pressure as well as heart rate in both groups ($p = 0.00$) (Figure 1-3). With regard to the mean of QTc interval values, a statistically significant difference was not found between the groups ($P = 0.645$), but prolongation of the corrected QT interval against the base value was detected during the times after spinal anesthesia in both groups ($p = 0.00$) (Figure 4). Prolongation of the QTc interval beyond the value of 500 milliseconds was observed in no patient of two groups of the study. However, neither grave arrhythmias nor complications were detected in the subjects participated in the study.

Table 1- Demographic and anthropometric data of groups

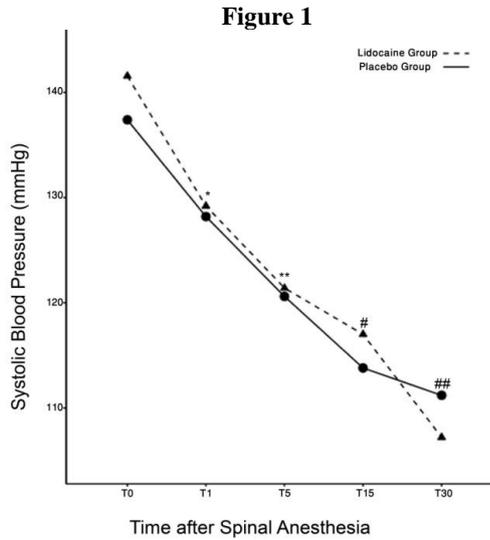
	Lidocaine group (n = 25)	Placebo group (n = 25)	P
Age (year)	71.44 \pm 6.53	69.32 \pm 6.31	0.249
Weight (kg)	77.00 \pm 5.91	74.92 \pm 6.91	0.259
Height (cm)	169.72 \pm 4.62	170.40 \pm 4.89	0.616

Data presented as Mean \pm SD

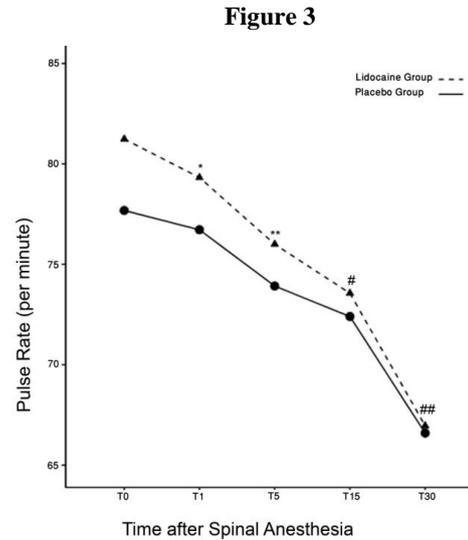
Discussion

Either inherited or acquired prolonged QT interval may lead to malignant arrhythmia and subsequent morbidity and mortality [9-13]. The current study revealed that prolongation of the depolarization and repolarization times of the cardiac ventricles, as reflected by prolongation of the QTc interval, occurs in elderly patients undergoing spinal anesthesia with hyperbaric bupivacaine considering the fact that both groups of the study were affected after adequate blockade, similarly. The study concluded that intravenous lidocaine has no protective effects on prolongation of QTc interval as well as hemodynamic parameters.

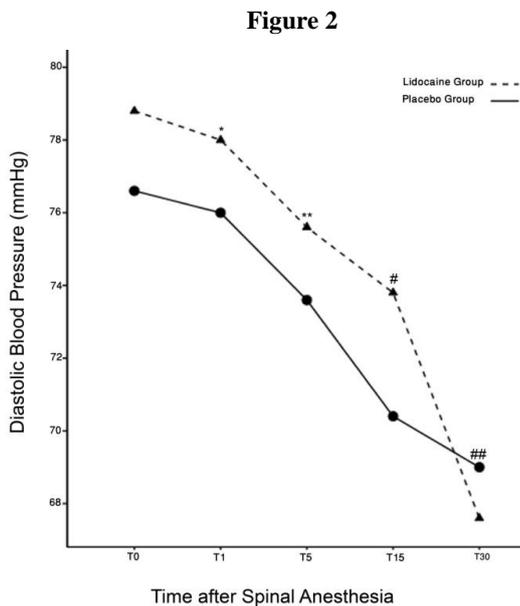
Deniz et al. detected no significant effects of levobupivacaine on QT interval in pregnant subjects undergone cesarean section. Moreover, they concluded that the QT interval of patients who received bupivacaine for spinal anesthesia was significantly shorter than control values at the minutes 5 and 10 after spinal anesthesia.



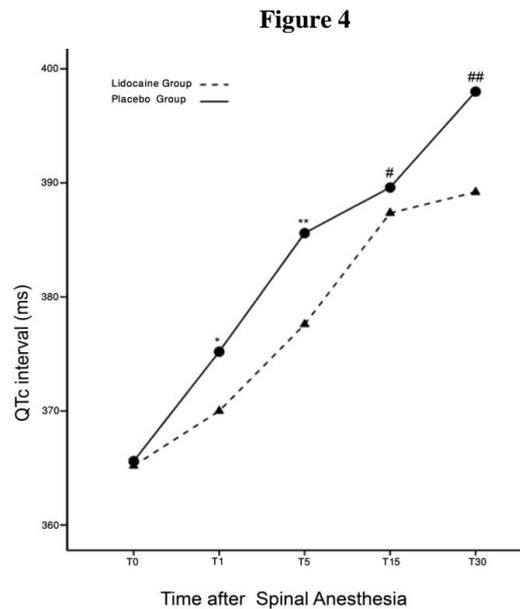
Mean systolic arterial blood pressure (SBP); *p < 0.005 compared with SBP value before spinal anesthesia (T0) and SBP value 1 minute after spinal anesthesia (T1) within groups; **p < 0.005 compared with SBP value before spinal anesthesia (T0) and SBP value 1, 5 minutes after spinal anesthesia (T1, T5) within groups; #p < 0.005 compared with SBP value before spinal anesthesia (T0) and SBP value 1,5,15 minutes after spinal anesthesia (T1, T5, T15) within groups; ; ###p < 0.005 compared with SBP value before spinal anesthesia (T0) and SBP value 1,5,15,30 minutes after spinal anesthesia (T1, T5, T15, T30) within groups.



Mean heart rate (HR); *p < 0.005 compared with HR value before spinal anesthesia (T0) and HR value 1 minute after spinal anesthesia (T1) within groups; **p < 0.005 compared with HR value before spinal anesthesia (T0) and HR value 1, 5 minutes after spinal anesthesia (T1, T5) within groups; #p < 0.005 compared with HR value before spinal (T0) and HR value 1,5,15 minutes after spinal anesthesia (T1, T5, T15) within groups; ###p < 0.005 compared with HR value before spinal (T0) and HR value 1,5,15,30 minutes after spinal anesthesia (T1, T5, T15, 30) within groups.



Mean diasystolic arterial blood pressure (DBP); *p < 0.005 compared with DBP value before spinal anesthesia (T0) and DBP value 1 minute after spinal anesthesia (T1) within groups; **p < 0.005 compared with DBP value before spinal anesthesia (T0) and DBP value 1, 5 minutes after spinal anesthesia (T1, T5) within groups; #p < 0.005 compared with DBP value before spinal anesthesia (T0) and DBP value 1,5,15 minutes after spinal anesthesia (T1, T5, T15) within groups; ###p < 0.005 compared with DBP value before spinal anesthesia (T0) and DBP value 1,5,15,30 minutes after spinal anesthesia (T1, T5, T15, 30) within groups.



Mean corrected QT interval using Bazett's formula (QTc); *p < 0.005 compared with QTc value before spinal anesthesia (T0) and QTc value 1 minute after spinal anesthesia (T1) within groups; **p < 0.005 compared with QTc value before spinal anesthesia (T0) and QTc value 1, 5 minutes after spinal (T1,T5) anesthesia within groups; #p < 0.005 compared with QTc value before spinal anesthesia (T0) and QTc value 1,5,15 minutes after spinal anesthesia (T1, T5, T15) within groups; ###p < 0.005 compared with QTc value before spinal anesthesia (T0) and QTc value 1,5,15,30 minutes after spinal anesthesia (T1, T5, T15,30) within groups.

The study mentioned that shortening QTc interval may be related to the sympathetic suppression caused by spinal anesthesia [7]. Sen et al. concluded that QTc interval has been shortened during spinal anesthesia as compared with baseline value in the pre-eclamptic subjects [14]. The result of the present study is in part different, as we observed prolongation of QTc interval. We tested the hypothesis on male elderly patients, and revealed that spinal anesthesia with hyperbaric bupivacaine per se may prolong the duration of QTc interval when high level of spinal anesthesia is not considered, although there was no QTc interval more than 500 milliseconds in participants of the study.

Lidocaine has been widely used to prevent heart repolarization, and due to anti-arrhythmic feature, lidocaine is used in the treatment of the heart rate disturbances of ventricular origin [15-17]. However, studies regarding the effect of lidocaine on QTc interval during anesthesia are limited [1,15,18]. In the study of Owczuk et al., the effect of lidocaine on QTc interval prolongation associated with tracheal intubation was assessed. They speculated that lidocaine diminishes the prolongation of QTc interval, induced by tracheal intubation, and this effect of lidocaine could be associated with protective activation of the sympathetic system secondary to airway manipulation and reflected as inhibition of the prolonged repolarization [1]. The study of Hanci et al. disagrees with the previous study. They found that lidocaine was unable to suppress the laryngoscopy and intubation related sympathetic activity as well as to prevent QTc interval prolongation after tracheal intubation [15]. To some extent, our study agrees with Hanci et al., and we observed no prevention of the QTc interval prolongation in the lidocaine group. As we found either no study regarding to the effect of intravenous lidocaine on the QTc duration during spinal anesthesia or limited study related to its effect on the QTc duration during general anesthesia, we believe that the differences among the studies could be attributed to many factors including age, gender, adjuvant drug administration and presumably positioning after induction of anesthesia. More studies are needed to circumvent these problems in the future.

In this study, hemodynamic variability was observed in both groups after spinal block. After spinal anesthesia and administration of lidocaine or placebo, systolic and diastolic arterial blood pressure as well as pulse rate values underwent significant reduction in both groups, and there were similar decreases of the values within subsequent times after spinal blockade. The degree of hemodynamic variability accompanied with spinal anesthesia, mostly depends on the level of the block, due to the sympathetic conduction block. Studies noted that significant hypotension and bradycardia have been observed in cases of sympathetic blockade of T5 or higher [3,19]. With respect to the level of dermatom blockade in the study (T10-T12), there is no consensus that any hemodynamic variation would be related to the sympathetic block in the subjects, assuming that sympathetic block reaches 2 to 6 segments above the level of the sensory block [3,20-21]. Although we do not confirm the strict relationship between hemodynamic changes and fracture pain, we believe that these variations could be related in part to the pain relief after adequate blockade.

Several limitations related to this study have to be addressed. One of them is the manual calculation of QTc

interval on paper ECG. Unfortunately, we only searched QTc interval but not p wave dispersion or transmural dispersion of repolarization. Also we performed the study on male patients with relatively low population samples. It might be better to include these points in the future studies.

This study demonstrated that electrocardiographic effects of spinal anesthesia using hyperbaric bupivacaine in elderly male patients, scheduled for lower limb surgery, may lead to changes in periods of cardiac ventricular depolarization and repolarization; as reflected by the prolongation of QTc interval after spinal blockade and subsequent times measurements, and lidocaine as an anti-arrhythmic agent could not diminish this serious process. However, neither grave arrhythmias nor complications were detected in the subjects participated in the study. This may be related to the fact that the patients had a QTc interval lower than 500 milliseconds which is below the harmful threshold.

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