MEDICAL SCIENCE

Assessment of QTc interval changes in patients undergoing spinal anesthesia for elective surgery

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ABSTRACT

Background and Aim: A prolonged QT interval is one of the causes of sudden death and the occurrence of arrhythmias. It is needed to revision more the increasing frequency of spinal anesthesia and unidentified causes of some of its complications, such as sudden and preventable death. This study aimed at examining the QTc interval changes in patients undergoing spinal anesthesia for elective surgery. *Materials and Methods:* This is an analytical study conducted from March 2020 till Feb 2022. We studied QTc interval changes before, during and after the spinal anesthesia. 177 patients aged 20-60 years selected for spinal anesthesia. The electrocardiogram (ECG) performed three periods before and 10 and 150 minutes after anesthesia. Data collected and analyzed via SPSS ver. 14.5. The significance level was P-value<0.05. *Results:* The average QT interval before operation, during operation and after operation was respectively (365.35 ± 30.32), (374.36 ± 28.99) (377.74 ± 30.52) and this difference is statistically significant. It was significant (P=0.01). The average QTc interval before operation, during operation and after operation was respectively (407.88±29.11) (408.13±26.22) (408.13±26.22) which was statistically significant (p = 0.03). *Conclusion:* Marcaine increased the QTc interval during spinal anesthesia, which was statistically significant. But spinal anesthesia had no significant effect on PR interval.

Keywords: Spinal Anesthesia, QTc interval, sudden death.

1. INTRODUCTION

One of the common complications of many drugs is long QT interval and can cause a dangerous and deadly torsade de pointes (TDP) arrhythmia, which is an independent risk factor for sudden cardiac death (Schächtele et al., 2016; Mohapatra et al., 2021; Khan et al., 2023). TDP can be appeared in the form of palpitations, syncope, pseudo-seizure movements, cardiac arrest and sudden death. The sudden consequences of this complication have eliminated the certain antibiotics, antihistamines, antipsychotics and probiotics. The prevalence of TDP has been estimated to be 4 cases per 100,000 people a year (Cubeddu, 2016). The spinal anesthesia is performed by injection of a local anesthetic in a subarachnoid space including cerebrospinal fluid, sing 22–25-gauge core needle. The common areas include the intervertebral space of L4-L5, L5-S1 and L3-L4 (Frank, 2008).

Spinal anesthesia is considered as a safe procedure. Each method, however good, will not be uncomplicated. However, this anesthetic technique can cause some complications. An overall estimate reported that the prevalence of regional anesthetic complications was 23% (Cunningham et al., 2014). These complications include such as hypotension, complete spinal cord blocks, post-dural-puncture headache (PDPH), seizure attacks, nausea and vomiting, back pain and neurological complications (Forkin and Nemergut, 2016). The most common anesthesiologist's concern is rare event of sudden cardiac arrest (Limongi and Lins, 2011). Although unexpected cardiac arrest is rare during this procedure, anesthesiologists should be informed about this possible complication while making decisions (Kopp et al., 2005; Dobson et al., 2013).

Cardiac arrest is described as rare and unexplained during spinal anesthesia (Bajwa et al., 2014; Porta et al., 2015). A total of three cardiac arrests in 10000 cases during non-cardiac surgery are considered a high rate (Irita et al., 2005; Kyokong et al., 2006). Although the mechanism of sudden cardiac arrest through spinal anesthesia is not totally realized, it can be because of a decrease in the activity of the sympathetic nervous system (Porta et al., 2015). Unexpected cardiac arrest and bradycardia may occur in patients who seem to be healthy and young during spinal anesthesia (Kopp et al., 2005).

The first case of cardiac arrest through spinal anesthesia, considered as unexplained complications, was reported in the 1940s. Since most reported cases occurred among young and healthy individuals, it was highly important, which itself explains the unpredictable incidence of sudden death and calls for a method to predict this and eliminate the concerns of patients and anesthesiologists in this regard as well as encouraging the patient to continue the treatment (Kopp et al., 2005; Bajwa et al., 2010).

Reviewing the previous studies still shows the ECG changes and sudden death after spinal anesthesia (Pollard, 2002; Bajwa et al., 2010). The cardiac arrest is related to the spinal anesthesia and is reported in most sources (Bayesteh et al., 2022; Breivik and Norum, 2010). The essential cares in patients include controlling the vital signs and the proper functioning of the cardiovascular system and reducing the complications caused by such changes. Sudden death is mainly caused by dangerous cardiac arrhythmias, especially ventricular arrhythmias, which are controlled using ECG indices, especially QT interval changes. This method is not only available, but also inexpensive, less time-consuming and safe. It is easy to measure and its interpretation does not require much expertise.

Long QT can create dangerous ventricular arrhythmias and cardiac arrest (Straus et al., 2006). Measurement of QT interval changes is a non-invasive method that is measured by changes in heart rate and the cardiac repolarization. These changes are related to the long QT and increased risk of death and malignant ventricular arrhythmias (Ornek et al., 2010; Shinohara et al., 2016). The QTc interval is defined as proportionality between the QTI and RR variables in heart rates, which is used as an international fixed tool to measure the risk of sudden cardiac death not only in high-risk groups, but also in patients with low to moderate risks of arrhythmias (Ornek et al., 2010; Osadchii, 2017).

We decided to examine the effect of Marcaine-induced spinal anesthesia on the QTc interval considering the wide use of spinal anesthesia, the importance of cardiac arrest and its sudden death in spinal anesthesia and effect of long QTc on the development of dangerous and lethal arrhythmias.

2. MATERIAL AND METHODS

This study is an analytical investigation conducted on 177 patients during spinal anesthesia for elective surgery that had been referred to a tertiary institutional hospital in northeastern Iran from March 2020 to Feb 2022. Participants were recruited according to a set of inclusion criteria including: 1) Individuals aged between 20 to 60 years, 2) having ASA class I or II, 3) consent for undergoing spinal anesthesia, 4) the absence of abnormal heart rhythms, 5) negative history of treatment with cardiac medications, 6) negative history of mental disorders such as anxiety, 7) negative history of an underlying chronic disease, including diabetes, multiple sclerosis, thyroid disease, kidney disease and congenital heart disease, 8) normal pre-operative tests, including potassium, calcium and magnesium, 9) the absence of the following medications that can cause the long QTc: Antibiotics, including ciprofloxacin, clarithromycin, erythromycin, ketoconazole, itraconazole, as well as antiarrhythmic drugs, including pericinamide, amiodarone, sotalol, Ibothyllide, diphytanyl, quinidine, flecainide, propafenone and psychiatric drugs, including three-ring and four-ring antidepressants, droperidol, haloperidol, phenothiazine as well as methadone and bepridil (Fink, 2016).

An available sampling performed to select the patients. ECG was taken from the patient at three consecutive times; including before, 10 minutes and 150 minutes after anesthesia and changes in QTc and PR intervals were measured before operation, during and after the spinal anesthesia. The machine used included the SAN-IE ECG (E21, Taiwan); equivalence reliability was used to measure the reliability. Thus, its accuracy was examined with another electrocardiogram machine every day before using the machine.

Since the QTc value is more reliable than QT and also to calculate the heart rate, the QTc interval was calculated using the following formula: QTc = QT + 1.75 (heart rate - 60) and thus the heart rate did not affect the QT interval (Luo et al., 2004). Exclusion criteria included unwillingness to continue to participate in the research, discontinue the spinal anesthesia for any reason (addition or cancellation of general anesthesia).

Data Analysis

Sample size was calculated 161 individuals using G Power software ver. 3.1.9.2, F tests distribution family and repeated measures ANOVA at 95% confidence interval, 90% test power and effect size of 0.2 for the three comparisons; including before, during and after the intervention. 177 individuals were finally selected considering 10% drop-out rate with a probability. It should be mentioned that the effect size was considered according to the same study (Srivastava et al., 2022). Kolmogorov-Smirnov test was used to determine the normality of the data. The result of repeated measures ANOVA was used to compare the mean QT, QTc and PR intervals before, 10 and 150 minutes after anesthesia. Independent t-test was used to compare the QT and QTc intervals in both males and females. Pearson correlation coefficient test was also used to examine the relationship between QTc, QT and PR variables with weight, height and age variables. Data was then analyzed by SPSS ver. 14.5 at a significant level of $P< 0.05$.

Ethical considerations

All research subjects presented an informed consent. The Ethics Committee of Gonabad University of Medical Sciences (IR.GMU.REC.1396.123)

3. RESULTS

The mean age, mean weight and mean height of the of the research subjects was respectively 35.21 ± 12.22 years, 68.11 ± 10.62 kg and 168.45 ± 9.12 cm. A total of 88 (49.7%) and 89 (50.3%) of the participants were males were females, respectively. A total of 22 (12.4%) were illiterate, 84 (47.5%) did not have the diploma, 50 (28.2%) had diploma degrees and 21 (11.9%) had university education, with the highest and lowest frequency being related to the individuals holding under education university education, respectively. The results on the participants' employment status were as follows: 17 permanent employees (9.16%), 80 self-employed individuals (45.2%), 1 retired individual (0.6%), 77 housewives (43.5%) and 2 unemployed individuals (1.1%). General, urological, gynecological, and orthopedic surgeries were performed on respectively 32 (18.1%), 36 (20.3%), 46 (26%) and 63 (35.6%) patients, with the highest and lowest frequency being related respectively to gynecological and general surgeries. The mean period of surgery and anesthesia was respectively 40.86 ± 16.12 and 58.24 ± 19.24 minutes. The mean intra and post-intervention QT interval was significantly higher than the pre-intervention one (Table 1).

Table 1 The comparison of QT and QTc intervals before, during and after intervention

Stage	QT interval		QTc interval	
	Number	Mean ± SD	Number	Mean ± SD
Before (MS)	177	365.35± 30.32	177	407.88± 29.11
During (MS)	177	374.36± 28.99	177	408.13± 26.22
After (MS)	177	377.74± 30.52	177	413.15± 25.63
The result of repeated measures ANOVA	F=9.3 df=2 p=0.01		F= 3.51 df=2 p=0.03	

LSD post hoc test explained that there was a significant difference between pre-intervention QT interval ($p = 0.01$) intra intervention QT interval ($p<0.01$). The mean post-intervention QTc interval was significantly higher than mean intra and post-intervention QTc interval (Table 1). The LSD post hoc test indicated that mean QTc interval between the post-intervention stage with pre-intervention ($P = 0.019$) and intra intervention stages ($P = 0.026$) was increased significantly. The intra and post-operative QTc interval was longer than the normal range in both patients, both of whom were in the orthopedic group. The mean pre, intra and post-intervention PR intervals were not statistically significant ($p = 0.27$) (Table 2) (Figure 1).

Table 2 The comparison of mean PR interval before, during and after intervention

Stage	The result of repeated measures ANOVA	Mean ± SD
Before (MS)	3.85±0.58	F=1.29
During (MS)	3.93± 0.61	Df=2
After (MS)	3.88 ± 0.61	P=0.27

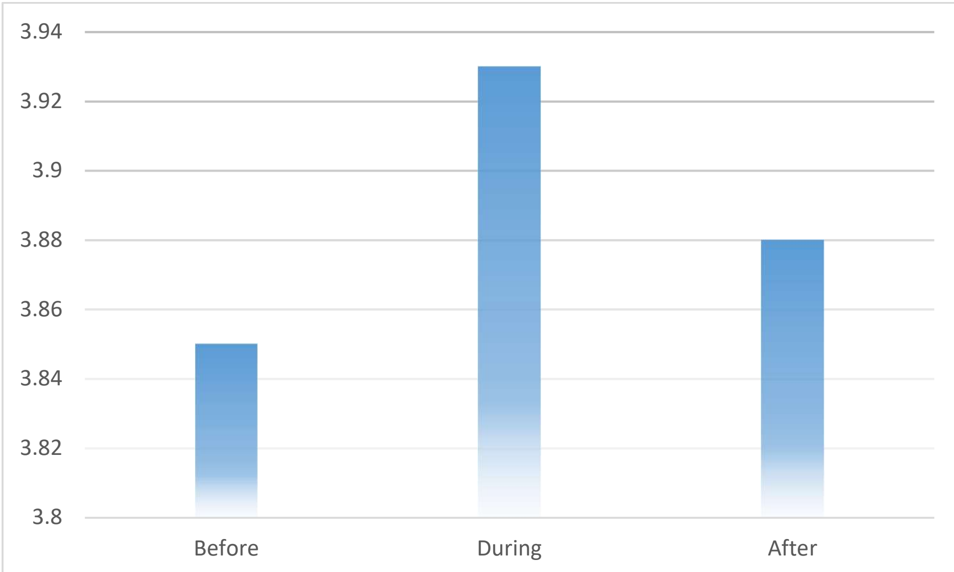

Figure 1 The comparison of mean PR interval before, during and after intervention

The mean pre, intra and post-intervention heart rates were respectively 83.01 ± 17.79, 79.92 ± 16.76 and 79. 69± 17.83 minutes, which these changes were significant (p = 0.01). The LSD post hoc test expressed that intra intervention (P = 0.01) and post-intervention heart rates (P = 0.01) were significantly lower that the pre-intervention heart rate. There was no significant relationship between patients' age with PR interval (P = 0.23, r = 0.09), QT interval (P = 0.07, r = 0.15) and QTc interval (P = 0.24, r = 0.09). Although QT interval increased with age, this relationship was not statistically significant. There was no significant difference between the patients' weight with PR interval (P = 0.11, r = 0.12), QT interval (P = 0.45, r = 0.06) and QTc interval (P = 0.51, r = 0.05). There was an inverse statistical relationship between QTc interval and the patients' height (p = 0.007, r = 0.20), it means that QTc interval was decreased by increasing the height. There was no statistically significant relationship between the patients' height and PR interval (P = 0.08, r = 0.13) and QT interval (r = 0.11, p = 0.13). Results of comparing the mean QT interval in males and females explained that the mean QT interval in females was significantly higher than males (p = 0.024) (Table 3). Results also indicated that the mean QTc interval is higher in males than females, which was statistically significant (p = 0.001) (Table 3) (Figure 2). The mean PR interval was higher in females (39.21 ± 5.88) than males (37.95 ± 5.70), which is not statistically significant (p = 0.15).

Table 3 The comparison of QT and QTc intervals between males and females

Stage	QT interval		QTc interval	
	Number	Mean ± SD	Number	Mean ± SD
Male	88	363.18± 29.22	88	414.37± 27.22
Female	89	373.47± 30.68	89	401.46± 23.31
The result of repeated measures ANOVA	T= 2.28 df=175 p=0.024		T=3.37 df=170 p=0.001	

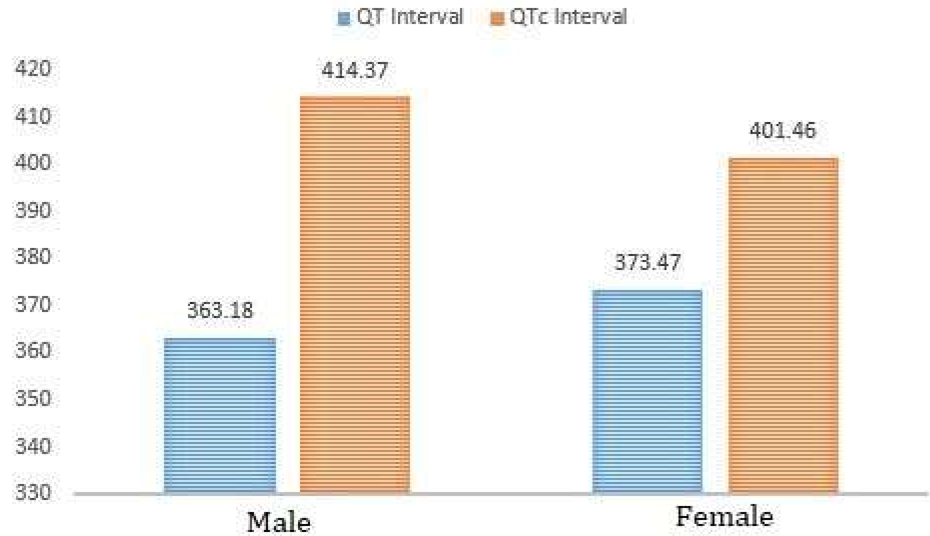

Figure 2 The comparison of QT and QTc intervals between males and females

4. DISCUSSION

Comparing the QTc interval changes in spinal anesthesia explained that spinal anesthesia in patients undergoing elective surgery can affect the QTc interval and increase it; it indicates that the mean post-intervention interval is higher than intra intervention interval and intra intervention interval is higher than pre-intervention interval. The QTc interval increased surrounded by the normal range, except for the two cases. Consistent with this study, Owczuk et al., (2005) observed long QTc interval in the first minute spinal anesthesia and QTc prolongation had not negative effect on the of the cardiovascular function (Owczuk et al., 2005). In this study, none of the subjects suffered from cardiac problems during anesthesia although the QTc interval was extended beyond the normal range in two cases (orthopedic surgery). Extended QTc interval in orthopedic patients can be caused by the longer duration of surgery in these patients.

Owczuk et al., (2005) explained in a study that 8 patients had abnormally prolonged QTc interval among 20 patients undergoing elective orthopedic surgery. It is recommended to examine such topic in future studies. In a study conducted on QTc interval during cesarean within spinal anesthesia among 40 patients, Guillon et al., (2010) explained that there is no change in the QTc interval; they, however, observed significant changes in QTc interval after oxytocin injection. In this study, the QTc interval indicated a higher increase in 150 minutes compared to 10 minutes after the spinal anesthesia. Oxytocin injection may also play a role in such increase, which demands further studies. It should be noted that this study examined all surgical procedures including patients undergoing cesarean section, but the study of Guillon et al., (2010) was conducted only on patients undergoing cesarean section and did not include other surgical procedures.

One of the advantages of this study is the large sample size compared to the study conducted by Guillon et al., (2010) the results of this study explained that there was no significant difference in PR intervals before, during and after intervention ($p = 0.27$). Twardowski et al., (2014) also explained that epidural anesthesia did not affect the PR interval of patients undergoing elective surgery, which is consistent with this study. This study indicated that there is a significant difference in mean heart rate before, during, and after intervention ($p = 0.01$). Pre-intervention heart rate was greater intra and post-intervention heart rate, which decreased during the intervention. Owczuk et al., (2005) also realized that there are no essential changes in heart rate of patients under spinal anesthesia, which is inconstant with the results of this study.

The heart rate was not reduced during spinal anesthesia in the study conducted by Owczuk et al., (2005) which may be caused by the low sample size. Consistent with this study, a case-report study referred to a heart rate reduction during spinal anesthesia as a phenomenon (Dyamann et al., 2013). Also, the results of a review study explained that spinal anesthesia decreases the heart rate in patients (Limongi and Lins, 2011). A reduction in heart rate during spinal anesthesia has been proved in scientific references. A reduction in the activity of the sympathetic nervous system and an increase in the activity of the parasympathetic system can be considered as a risk factor for these changes.

The cardio toxic effects of Marcaine are among other risk factors (Forkin and Nemergut, 2016). The discrepancy between the results of the above study and this study can be allocated to the fact that samples were selected only from one gender (male) in the study conducted by Owczuk et al., (2005) whereas this study includes both genders.

The most important limitation of this study was post-anesthesia genetic tendency to an extended QT interval that was not controlled. Other limitations of the present study included non-random selection of samples and low sample size for comparing mean QTc intervals in various surgical procedures and especially in orthopedic patients undergoing other surgical procedures.

5. CONCLUSION

Marcaine during spinal anesthesia made longer the QTc interval, which was statistically significant. However, this increase was normal in other patients, except for patients undergoing orthopedic surgery. Moreover, the spinal anesthesia reduced heart rate, but had no significant changes on the PR interval.

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Author contributions

All authors contributed equally in the writing of the manuscript.

Ethical approval

All research subjects presented an informed consent. The Ethics Committee of Gonabad University of Medical Sciences (IR.GMU.REC.1396.123)

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES AND NOTES

1. Bajwa S, Bajwa SS, Sood A. Cardiac arrest in a case of undiagnosed dilated cardiomyopathy patient presenting for emergency cesarean section. Anesth Essays Res 2010; 4(2):11 5. doi: 10.4103/0259-1162.73520
2. Bajwa SJ, Singh A, Kumari A, Gupta R. Unanticipated cardiac arrest under spinal anesthesia: An unavoidable mystery with review of current literature. Anesth Essays Res 2014; 8(1):99. doi: 10.4103/0259-1162.128923
3. Bayesteh H, Mohammadpour A, Sahebanmaleki M, Moavensaidi M, Shayan SK. Effect of intravenous injection of aminophylline on rapid reduction of headache caused by spinal anesthesia. J Pharm Negat Results 2022; 22:680-3. doi: 10.47750/pnr.2022.13.S03.104
4. Breivik H, Norum H. Regionalanalgesi–fordeler og ulemper (Regional analgesia--risks and benefits). Tidsskr Nor Laegeforen 2010; 130(4):392-7. doi: 10.4045/tidsskr.08.0220
5. Cubeddu L. Drug-induced inhibition and trafficking disruption of ion channels: Pathogenesis of QT abnormalities and drug-induced fatal arrhythmias. Curr Cardiol Rev 2016; 12(2):141-54. doi: 10.2174/1573403X126616 0301120217
6. Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Sheffield JS. Cardiovascular Disorders. In: Williams Obstetrics. McGraw-Hill New York, NY, USA 201 4; 24:973-1000.
7. Dobson CP, Kim A, Haigney M. QT variability index. Prog Cardiovasc Dis 2013; 56(2):186-94. doi: 10.1016/j.pcad.2013.0 7.004
8. Dyamann D, Kumar BSS, Zacharia BT. Unexpected bradycardia and cardiac arrest under spinal anesthesia: Case reports and review of literature. Middle East J Anesthesiol 2013; 22(1):121-5.
9. Fink MP. Tachycardia and Bradycardia. In: Textbook of Critical Care 2016; 7:76-87.
10. Forkin KT, Nemergut EC. Miller's anesthesia. Anesthe siology 2016; 124(4):977-8.
11. Frank RL. Lumbar puncture and post-dural puncture headaches: Implications for the emergency physician. J

Emerg Med 2008; 35(2):149-57. doi: 10.1016/j.jemermed.2007.03.024
12. Guillon A, Leyre S, Remérand F, Taihlan B, Perrotin F, Fusciardi J, Laffon M. Modification of Tp-e and QTc intervals during caesarean section under spinal anaesthesia. Anaesthesia 2010; 65(4):337-42. doi: 10.1111/j.1365-2044.2010.06246.x
13. Irita K, Kawashima Y, Morita K, Seo N, Iwao Y, Tsuzaki K, Makita K, Kobayashi Y, Sanuki M, Sawa T, Obara H, Oomura A. Critical incidents during regional anesthesia in Japanese Society of Anesthesiologists-Certified Training Hospitals: An analysis of responses to the annual survey conducted between 1999 and 2002 by the Japanese Society of Anesthesiologists. Masui 2005; 54(4):440-9.
14. Khan J, Parihar AS, Umalkar G, Gadkari C. An unusual case of organophosphate poisoning presenting Wellens or Pseudo-Wellens pattern: A diagnostic dilemma. Medical Science 2023; 27: e96ms2726. doi: 10.54905/disssi/v27i132/e96ms2726
15. Kopp SL, Horlocker TT, Warner ME, Hebl JR, Vachon CA, Schroeder DR, Gould AB, Sprung J. Cardiac arrest during neuraxial anesthesia: Frequency and predisposing factors associated with survival. Anesth Analg 2005; 100(3):855-65. doi: 10.1213/01.ANE.0000144066.72932.B1
16. Kyokong O, Charuluxananan S, Sriprajittichai P, Poomseetong T, Naksin P. The incidence and risk factors of hypotension and bradycardia associated with spinal anesthesia. J Med Assoc Thai 2006; 89 Suppl 3:S58-64.
17. Limongi JAG, Lins RSDM. Cardiopulmonary arrest in spinal anesthesia. Rev Bras Anesthesiol 2011; 61(1):110-20. doi: 10.1016/S0034-7094(11)70012-5
18. Luo S, Michler K, Johnston P, Macfarlane PW. A comparison of commonly used QT correction formulae: The effect of heart rate on the QTc of normal ECGs. J Electrocardiol 2004; 37:81-90. doi: 10.1016/j.jelectrocard.2004.08.030
19. Mohapatra TK, Nayak RR, Mondal A, Nanda SS. A novel and Emerging Coronavirus Infection: Repurposing and Scale of Advances of Therapeutics, Immunotherapeutics and Vaccine Development. Drug Discovery 2021;15(35), 06-33
20. Ornek E, Ornek D, Alkent ZP, Ekin A, Basaran M, Dikmen B. The effects of volatile induction and maintenance of anesthesia and selective spinal anesthesia on QT interval, QT dispersion and arrhythmia incidence. Clinics 2010; 65(8):763-7. doi: 10.1590/S1807-59322010000800005
21. Osadchii OE. Role of abnormal repolarization in the mechanism of cardiac arrhythmia. Acta Physiol (Oxf) 2017; 220:1-71. doi: 10.1111/apha.12902
22. Owczuk R, Sawicka W, Wujtewicz MA, Kawecka A, Lasek J, Wujtewicz M. Influence of spinal anesthesia on corrected QT interval. Reg Anesth Pain Med 2005; 30(6):548-52. doi: 10.1016/j.rapm.2005.06.005
23. Pollard JB. Common mechanisms and strategies for prevention and treatment of cardiac arrest during epidural anesthesia. J Clin Anesth 2002; 14(1):52-6. doi: 10.1016/S0952-8180(01)00355-5
24. Porta A, Girardengo G, Bari V, George A, Brink P, Goosen A, Crotti L, Schwartz P. Autonomic control of heart rate and QT interval variability influences arrhythmic risk in long QT syndrome type 1. J Am Coll Cardiol 2015; 65:367-74. doi: 10.1016/j.jacc.2014.11.015
25. Schächtele S, Tümena T, Gaßmann KG, Fromm MF, Maas R. Co-prescription of QT-interval prolonging drugs: An analysis in a large cohort of geriatric patients. PLoS One 2016; 11(5):e0155649. doi: 10.1371/journal.pone.0155649
26. Shinohara S, Sakamoto I, Numata M, Ikegami A, Teramoto K, Hirata S. Cardiac arrest during spinal anesthesia for cervical conization: A case report. Clin Case Rep 2016; 4(5):466-8. doi: 10.1002/ccr3.545
27. Srivastava R, Pradhan D, Sharma L, Jyoti B, Mehrotra V. Efficacy of 0.1% topical tacrolimus in the management of symptomatic geographic tongue: A placebo-controlled study. J Dent Res Rev 2022; 9:73-7. doi: 10.4103/jdrr.jdrr_1 27_20
28. Straus SMJM, Kors JA, De-Bruin ML, Hooft CSV, Hofman A, Heeringa J, Deckers JW, Kingma JH, Sturkenboom MCJM, Stricker B, Witteman JCM. Prolonged QTc interval and risk of sudden cardiac death in a population of older adults. J Am Coll Cardiol 2006; 47(2):362-7. doi: 10.1016/j.jacc.2005.08.067
29. Twardowski P, Owczuk R, Wujtewicz MA, Wojciechowski J, Marjanski T, Marciniak A, Wujtewicz M. Anaesthesiology and intensive care the influence of epidural anesthesia on the electrical activity of heart atria. Polish J Thorac Cardiovasc Surg 2014; 2:156-61. doi: 10.5114/kitp.2014.43843