UDK: 616.379-008.64

DIFFERENTIAL IMPACT OF SUBARACHNOID BLOCKADE ON QTC INTERVAL PROLONGATION IN DIABETIC AND NON-DIABETIC PATIENTS


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ДИФФЕРЕНЦИАЛ ТАЪСИРГА ЭГА БЎЛГАН СУБАРАХНОИД БЛОКАДАЛАРНИНГ ДИАБЕТ ВА ДИАБЕТИ БЎЛМАГАН БЕМОРЛАРДА QTC ИНТЕРВАЛИНИНГ УЗАЙИШИГА ТАЪСИРИ

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ДИФФЕРЕНЦИАЛЬНОЕ ВОЗДЕЙСТВИЕ СУБАРАХНОИДАЛЬНОЙ БЛОКАДЫ НА ПРОДЛЕНИЕ ИНТЕРВАЛА QTC У ДИАБЕТИЧЕСКИХ И НЕДИАБЕТИЧЕСКИХ ПАЦИЕНТОВ

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Резюме. *Тадқиқот мақсади: Ушбу тадқиқот қандли диабетга чалинган ва чалинмаган беморларда субаракноид блокаданинг* QTc *интервалига таъсирини ўрганишга қаратилган бўлиб, спинал анестезия ва автоном невропатиянинг* QTc *узайишига таъсири ўрганилган. Диабет билан чалинган беморларда тез-тез учрайдиган спинал анестезия ва автоном невропатия,* QTc *интервалининг узайишига боғлиқ. Бироқ, субарахноид блокаданинг диабет билан касалланган беморларда* QTc *давомийлигига аниқ таъсири ҳали тўлиқ ўрганилмаган. Биз қандли диабетга чалинган беморлар субарахноид блокададан кейин қандли диабетга чалинмаган беморларга нисбатан* QTc *узайишини кўпроқ кўрсатиши гипотезасини қўйдик. Методлар: Учинчи даражали университет шифохонасида ўтказилган ва клиника тадқиқотлари маълумот хизмати билан рўйхатдан ўтказилган (идентификатор: KCT0004897) бу тадқиқотида 48 иштирокчи икки гуруҳга бўлиб ўрганилган: қандли диабетга чалинганлар (ДМ гуруҳи, n=24) ва чалинмаганлар (назорат гуруҳи, n=24). Барча беморларга спинал анестезияси ўтқазилган.* QTc *интервали, Т тишса чўққисидан охиригача бўлган интервал (*Tp-e *интервали), юрак уришининг ўзгарувчанлиги, қон босими ва юрак уриш тезлиги каби кўрсатгичлар бирламчи ҳолатда (T1) ва субарахноид блокададан кейин 1 (T2), 5 (T3) ва 10 дақиқаларда (T4) ўрганилган. Натижалар: Блокададан кейин 10 дақиқада қандли диабетга учраган беморлар гуруҳида* QTc *интервалининг сезиларли даражада узайиши кузатилди, бу эса уларнинг базавий қийматларига қараганда статистик жиҳатдан этиборга моликдир, назорат гуруҳи* QTc *интервалининг ўзгаришлари эса статистик жиҳатдан аниқ тастиқланмади. (ДМ гуруҳи учун p<0.0001 назорат гуруҳи учун p=0.06). Хулоса: Бизнинг натижаларимиз қандли диабетга учраган беморлар спинал анестезиясидан кейин қандли диабетга чалинмаган беморларга нисбатан* QTc *интервалининг кўпроқ узайиши кузатилишини аниқлади. Ушбу натижалар қандли диабетга чалинган беморларда субарахноид блокада ўтказилганда юрак электр фаолиятини кузатишнинг муҳимлигини таъкидлайди.*

Калит сўзлар: *Коррексия қилинган* QT *интервали, қандли диабет, узоқ* QT *синдроми, спинал анестезияси, субарахноид блокада.*

Abstract. *Objective: This study aimed to explore the effects of subarachnoid blockade on the QTc interval among diabetic and non-diabetic patients, considering the known impact of spinal anesthesia and autonomic neuropathy on QTc prolongation. Background: Both spinal anesthesia and autonomic neuropathy, commonly seen in diabetes, are associated with QTc interval prolongation. However, the specific influence of subarachnoid blockade on QTc duration in diabetic individuals has yet to be thoroughly examined. We hypothesized that diabetic patients would exhibit greater QTc prolongation following subarachnoid blockade compared to their non-diabetic counterparts. Methods: In this prospective observational study, conducted at a tertiary university hospital and registered with the Clinical Research Information Service (identifier: KCT0004897), 48 participants were divided into two groups: those with diabetes mellitus (DM group, n=24) and those without (control group, n=24). All subjects were undergoing spinal anesthesia. Measurements of the QTc interval, T wave peak-to-end interval (Tp-e interval), heart rate variability, blood pressure, and heart rate were recorded at baseline (T1) and at 1 (T2), 5 (T3), and 10 minutes (T4) post-subarachnoid blockade. Results: Significant prolongation of the QTc interval was observed in the DM group at 10 minutes post-blockade compared to their baseline values, whereas the QTc interval changes in the control group were not statistically significant (p<0.0001 for the DM group vs. p=0.06 for*

the control group). Conclusion: Our findings suggest that patients with diabetes experience a more pronounced prolongation of the QTc interval following spinal anesthesia compared to non-diabetic patients. These results underscore the importance of monitoring cardiac electrical activity in diabetic patients undergoing subarachnoid blockade.

***Keywords**: Corrected QT Interval, Diabetes Mellitus, Long QT Syndrome, Spinal Anesthesia, Subarachnoid Blockade.*

Introduction. Diabetes Mellitus (DM) is a chronic condition that precipitates severe complications including neuropathy, nephropathy, and retinopathy. Of particular concern is autonomic neuropathy related to the cardiovascular system, which may result in the prolongation of the corrected QT (QTc) interval. This prolongation is independently associated with an increased risk of mortality, ventricular arrhythmias, torsades de pointes, and sudden cardiac death, marking it as a critical predictor of mortality risk in DM patients. Cardiovascular complications are notably the leading cause of morbidity and mortality in this demographic [1, 5, 7].

Neuraxial anesthesia, favored for lower abdominal, pelvic, and lower limb surgeries due to its lower risk profile compared to general anesthesia, has been noted to cause significant QTc interval prolongation. Despite the absence of a clear mechanism for this effect, spinal anesthesia is preferred for certain surgeries in DM patients due to its benefits, including reduced oxidative stress during procedures like lower limb amputation [2,3,5].

Considering the exacerbation of QTc interval prolongation in DM patients with advancing neuropathy, it is imperative to assess the extent of QTc interval changes post-spinal anesthesia induction. This study hypothesizes that spinal anesthesia induces greater QTc interval prolongation in DM patients compared to those without DM, aiming to compare QTc interval, T wave peak-to-end (Tp-e) interval, blood pressure, heart rate, and heart rate variability before and after spinal anesthesia induction in both groups [10-13].

Methods. This prospective study received approval from the Institutional Review Board of Inha University Hospital, Incheon, Republic of Korea, and was conducted in adherence to the STROBE guidelines and the Declaration of Helsinki, 2013. Participants included were adults scheduled for elective lower abdominal or lower limb surgery under spinal anesthesia, divided into DM (n=24) and non-DM (n=24) groups based on their diabetic status and HbA1c levels. Exclusion criteria were extensive and included preoperative QTc >440 ms, ECG abnormalities, cardiovascular disorders, electrolyte imbalances, medication affecting the QTc interval, contraindications to spinal anesthesia, severe obesity, history of spinal surgery, or congenital spinal deformity [6-8].

All procedures were standardized, including monitoring, preload administration, and spinal anesthesia technique, to minimize external influences on QTc interval measurements. The study specifically measured QTc and Tp-e intervals, heart rate variability, and hemodynamic parameters at predefined intervals before and after spinal anesthesia was administered [9].

Statistical analyses aimed to compare changes in these measurements between the two groups over time, with sample size calculations based on previous studies to ensure sufficient power to detect significant differences. Data analysis was performed using IBM® SPSS® Statistics 19.0, employing appropriate statistical tests based on data distribution, with significance set at $p<0.05$.

Results. The study was successfully completed by 21 patients in the control group and 24 patients in the DM group. The control group experienced three dropouts: one patient withdrew consent during the ECG collection phase, another patient required general anesthesia due to difficulties in performing the subarachnoid blockade (SAB), and the third was excluded from the final analysis because their preanesthetic QTc interval exceeded 440 ms.

A comparison of demographic data and characteristics related to the blockade procedure revealed no significant differences between the two groups, ensuring comparability. Within the DM group, five patients were diagnosed with DM-related neuropathy, indicating a potential for heightened risk of QTc prolongation. The medication regimen varied among these patients, reflecting the diverse management strategies for DM and its complications.

This participant composition and the subsequent analysis provide a solid basis for assessing the impact of spinal anesthesia on the QTc interval among patients with and without DM, taking into account the heterogeneity in DM management and the presence of neuropathy in a subset of the DM group (Table 1).

The investigation into the relationship between diabetes mellitus (DM) medications and QTc prolongation did not yield any significant correlations. This study's primary endpoint was to examine the QTc interval alterations pre and post 10 minutes of spinal anesthesia (SAB) administration.

The findings revealed an average change in the QTc interval of 8.5 ± 19.9 ms in the control group and 30.8 ± 17.5 ms in the DM group, with a significant difference ($p = 0.001$) between them. Specifically, the QTc interval significantly increased in the DM group 10 minutes after SAB compared to their baseline, unlike the control group where the change was not deemed significant ($p < 0.0001$ vs $p = 0.06$), as depicted.

Table 1. Demographic and procedural data pertaining to both the control and diabetes mellitus (DM) groups are presented herein.

Characteristic	Control Group (n=21)	DM Group (n=24)	p-value
Age (years)	61.3 ± 12.4	61.1 ± 10.5	0.943
Sex (Male/Female)	15/6	19/5	0.801
Height (cm)	165.3 ± 9.2	166.7 ± 7.9	0.592
Weight (kg)	67.4 ± 12.5	67.7 ± 14.7	0.939
BMI (kg/m²)	24.5 ± 3.1	24.4 ± 4.9	0.919
Length of DM (years)	NC	10 [11]	-
HbA1c (%)	NC	8.5 [2.7]	-
DM Type (I/II)	NC	1/23	-
End Organ Damage (0/1/2)	NC	18/5/1	-
H-M Dosage (mg)	10.1 ± 0.8	10.2 ± 0.8	0.614
Onset Time (min)	7.8 ± 1.9	7.0 ± 1.3	0.14
Recovery Time (min)	116.2 ± 22.9	119.2 ± 19.5	0.644
Sensory Block Level	T11 [4]	T10 [2]	0.096

Additionally, the study categorized changes in the QTc interval before and after SAB in both DM and control groups, following international guidelines. Particularly, at 10 minutes post-SAB, 17% of patients in the DM group showed QTc intervals ranging from 450–480 ms and 8% had intervals between 481–500 ms.

Discussion. In this prospective analysis, we assessed the variations in the QTc interval at baseline, and at 1, 5, and 10 minutes following spinal anesthesia (SAB) in individuals with and without diabetes mellitus (DM). The study revealed a significant elongation of the QTc interval at 5 and 10 minutes post-SAB in the DM cohort compared to those without DM [2, 12, 13]. To our knowledge, this research is pioneering in contrasting QTc interval prolongation post-SAB between diabetic and non-diabetic patients. The principal finding was a more pronounced QTc interval extension in the DM patients compared to their non-diabetic counterparts. Specifically, significant QTc interval changes from baseline to 10 minutes post-SAB were observed in 29% and 8% of the DM group, in contrast to 14% and 0% respectively, in the control group. Additionally, a QTc interval exceeding 450 ms was documented in 25% of the DM participants, with a third experiencing an increase greater than 30 ms. This contrasts with previous research where a QTc interval alteration of 22 ms was noted post spinal anesthesia induction. The current study noted a differential increase of 31 ms for the DM group and 11 ms for the control group, suggesting that inclusion criteria variance may account for the observed discrepancies in QTc interval changes. Anesthesiologists often prefer regional blockade over general anesthesia for patients with long QT syndrome, attributing to lesser QTc interval prolongation post-induction. Despite the modest QTc interval extension post-SAB, especially in DM patients with baseline QTc intervals under 440 ms, the potential risk associated with a 30-ms increase in already prolonged QTc intervals warrants attention. Previous studies have linked QTc interval length with diabetic autonomic neuropathy progression, underscoring the importance of vigilant perioperative QTc interval monitoring in diabetic patients undergoing spinal anesthesia. The mechanism behind QTc interval prolongation post-SAB may relate to an imbalance in lumbar and thoracic sympathetic activity. The difficulty in directly affecting sympathetic fibers in the T1-T4 region and the resulting reflex sympathetic activation could explain the observed QTc interval extensions. Moreover, hemodynamic shifts, such as hypotension, may further stimulate sympathetic outflow, emphasizing the intricate relationship between autonomic nervous system changes and SAB.

Our analysis of heart rate variability (HRV) post-SAB did not reveal significant differences between diabetic and non-diabetic groups or before and after SAB, suggesting that SAB's impact on autonomic nervous system modulation may be limited. This contrasts with previous findings indicating a reduction in HRV components correlating with the cephalad spread of blockade. The study limitations include the potential underestimation of QTc interval prolongation impacts due to the exclusion of patients with severe neuropathy and the relatively short post-SAB monitoring duration. Future research should extend QTc interval monitoring to capture the full scope of SAB effects and consider the variability in local anesthetic types, dosages, and blockade levels. Despite these limitations, our findings highlight the need for careful QTc interval monitoring in diabetic patients undergoing spinal anesthesia, with particular caution for those with pre-existing QTc interval prolongations.

Conclusion. In summary, our study demonstrated that the prolongation of the QTc interval following spinal anesthesia is significantly more pronounced in patients with diabetes mellitus (DM) than in those without DM. This finding underscores the importance of close monitoring of the QTc interval in diabetic patients undergoing procedures involving

spinal anesthesia to mitigate potential cardiac risks associated with QTc interval prolongation.

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ДИФФЕРЕНЦИАЛЬНОЕ ВОЗДЕЙСТВИЕ СУБАРАХНОИДАЛЬНОЙ БЛОКАДЫ НА ПРОДЛЕНИЕ ИНТЕРВАЛА QTC У ДИАБЕТИЧЕСКИХ И НЕДИАБЕТИЧЕСКИХ ПАЦИЕНТОВ

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Резюме. *Цель: Целью данного исследования было изучение влияния субарахноидальной блокады на интервал QTc среди пациентов с диабетом и без него, учитывая известное воздействие спинальной анестезии и аутономной нейропатии на удлинение QTc. Введение: И спинальная анестезия, и аутономная нейропатия, часто встречающиеся при диабете, ассоциированы с удлинением интервала QTc. Однако конкретное влияние субарахноидальной блокады на продолжительность QTc у лиц с диабетом до сих пор не было тщательно изучено. Мы предполагали, что у пациентов с диабетом будет наблюдаться более значительное удлинение QTc после субарахноидальной блокады по сравнению с недиабетическими пациентами. Методы: В этом проспективном наблюдательном исследовании, проведенном в университетской клинике третьего уровня и зарегистрированном в Сервисе Информации о Клинических Исследованиях (идентификатор: KCT0004897), 48 участников были разделены на две группы: с сахарным диабетом (группа СД, n=24) и без него (контрольная группа, n=24). Все субъекты проходили спинальную анестезию. Измерения интервала QTc, интервала от пика до конца волны T (интервал Tp-e), вариабельности сердечного ритма, артериального давления и частоты сердечных сокращений регистрировались на исходном уровне (T1) и через 1 (T2), 5 (T3) и 10 минут (T4) после субарахноидальной блокады. Результаты: У группы с диабетом было отмечено значительное удлинение интервала QTc через 10 минут после блокады по сравнению с исходными значениями, тогда как изменения интервала QTc в контрольной группе не были статистически значимыми ($p<0.0001$ для группы СД против $p=0.06$ для контрольной группы). Заключение: Наши результаты предполагают, что пациенты с диабетом испытывают более выраженное удлинение интервала QTc после спинальной анестезии по сравнению с недиабетическими пациентами. Эти результаты подчеркивают важность мониторинга электрической активности сердца у пациентов с диабетом, проходящих субарахноидальную блокаду.*

Ключевые слова: *Исправленный интервал QT, Сахарный диабет, Синдром удлиненного интервала QT, Спинальная анестезия, Субарахноидальная блокада.*