**Alexandra N. Demyanenko, Irina L. Alimova**

Smolensk State Medical University, Smolensk, Russian Federation

**Cardiac Autonomic Neuropathy and Hypoglycemia as Independent Predictors of *QTc* Elongation at Night in Adolescents With Type 1 Diabetes: Cohort Study**

**Corresponding author:**

*Demyanenko Alexandra N.*, postgraduate student of Pediatric Department with Neonatal Group in Smolensk State Medical University; pediatrician, functional diagnostics doctor in Smolensk Regional Children's Clinical Hospital RSFHF

**Address:** 214019, Smolensk, Krupskoy street, 28, **e-mail:** alex-glam@mail.ru

**Article received:** Mar 13, 2019, **submitted for publication:** Aug 26, 2019

***Background.*** *QTc elongation is the risk factor of sudden cardiac death. Patients with type 1 diabetes (T1D) can have QTc elongation due to hypoglycemia and cardiac autonomic neuropathy (CAN). The separate role of these two factors in QTc elongation development in T1D patients is still unknown.* ***Objective****. Our aim was to study the role of cardiac autonomic neuropathy and hypoglycemia as independent risk factors of QTc elongation* *at night in adolescents with T1D.* ***Methods.*** *Patients at the age of 10–17 years old with T1D were enrolled in the cohort study. All patients have undergone simultaneous 24-hour monitoring of electrocardiogram and glycemia. Results of nocturnal monitoring (23:00–07:00) were estimated. QTc elongation >450 ms was regarded pathological. CAN was diagnosed at decrease of ≥2 time domain parameters (SDNN <101 ms, SDNNi <48 ms, SDANN <85 ms, rMSSD <25 ms). Hypoglycemia was classified as 1st (≥ 3.0 and ≤3.9 mmol/L), 2nd (≥ 2.2 and <3.0 mmol/L) or 3rd (≤ 3.9 mmol/L along with cognitive defects and the need of acute hypoglycemia treatment) level. We also have distinguished prolonged (< 3.0 mmol/L and ≥120 min) and asymptomatic (≤ 3.9 mmol/L and no adrenergic symptoms) nocturnal hypoglycemia. We didn’t analyse hypoglycemia periods with >9.0 mmol/L.* ***Results.*** *QTc elongation >450 ms was revealed in 28 out of 100 patients. All patients with QTc>450 ms were similar on gender, age, HbA1C level with patients without any QTc elongation but they have longer history of T1D and higher frequency of 2nd level hypoglycemia and asymptomatic nocturnal hypoglycemia. According to the data from multivariate regression analysis independent predictors of QTc elongation were the following: CAN — odds ratio (OR) 9.0 (95% confidential interval [CI] 3.3–24.2), 2nd level hypoglycemia — OR 4.4 (95% CI 1.4–14.2), asymptomatic nocturnal hypoglycemia — OR 2.9 (95% CI 1.1–7.7) and T1D duration — OR 1.3 (95% CI 1.0–1.5).* ***Conclusion.*** *CAN and hypoglycemia (both clinically significant and asymptomatic nocturnal) are independent predictors of QTc elongation in adolescents with T1D.*

***Key words:*** *type 1 diabetes, children, hypoglycemia, asymptomatic nocturnal hypoglycemia, QT interval, Holter monitoring, 24-hour glycemia monitoring.*

*(****For citation:***Demyanenko Alexandra N., Alimova Irina L. Cardiac Autonomic Neuropathy and Hypoglycemia as Independent Predictors of *QTc* Elongation at Night in Adolescents With Type 1 Diabetes: Cohort Study*. Voprosy sovremennoi pediatrii — Current Pediatrics.* 2019; 18 (4): 0–00. doi: 10.15690/vsp.v18i4.2043*)*

**RESULTS**

**Table 1.** Characteristics of patients with T1D due to the length of *QTc* interval

|  |  |  |  |
| --- | --- | --- | --- |
| **Indexes** | **Patients with *QTc* >450 *n* =28** | **Patients with *QTc* ≤450 *n* =72** | ***р*** |
| Age, years | 12,5 (12,0; 13,8) | 13,5 (12,0; 15,0) | 0,229 |
| Gender (female), abs (%) | 16 (58) | 28 (39) | 0,099 |
| HbА1C (%) | 10,4 (9,7; 12,6) | 10,4 (8,6; 11,5) | 0,221 |
| Duration of a disease, years | 7,5 (4,0; 9,0) | 4,0 (2,5; 6,0) | 0,045 |
| Nocturnal hypoglycemia, abs (%) | 12 (42) | 28 (38) | 0,717 |
| Hypoglycemia (1st level), abs (%) | 2 (16) | 22 (78) | 0,001 |
| Hypoglycemia (2nd level), abs (%) | 8 (67) | 6 (21) | 0,020 |
| Hypoglycemia (3rd level), abs (%) | 0 | 0 | - |
| Prolonged hypoglycemia | 2 (17) | 0 | - |
| Asymptomatic nocturnal hypoglycemia, abs (%) | 11 (90) | 13 (46) | 0,012 |

***Note.*** *1st level (≥ 3.0 and ≤3.9 mmol/L), 2nd level (≥ 2.2 and <3.0 mmol/L) or 3rd level (≤ 3.9 mmol/L along with cognitive defects and the need of acute hypoglycemia treatment), prolonged hypoglycemia (< 3.0 mmol/L and ≥120 min), asymptomatic nocturnal hypoglycemia (≤ 3.9 mmol/L and no adrenergic symptoms of hypoglycemia).*

**Table 2.** The indexes of heart rate variability according to the data from Holter monitoring of patients with T1D

|  |  |  |  |
| --- | --- | --- | --- |
| **Indexes** | **Patients with *QTc* >450 *n* =28** | **Patients with *QTc* ≤450 *n* =72** | ***р*** |
| SDNN, ms<101 ms, abs (%) | 97,4 (85,0; 138,0)14 (50) | 148,2 (125,5; 177,1)0 | 0,024- |
| SDNNi, ms<48 ms, abs (%) | 84,7 (78,8; 89,2)16 (57) | 87,8 (70,1; 101,4)10 (14) | 0,6810,001 |
| SDANN, ms<85 ms, abs (%) | 47,6 (41,6; 115,7)18 (64) | 124,7 (109,2; 145,3)24 (33) | 0,0040,005 |
| rMSSD, ms<25 ms, abs (%) | 28,1 (22,0; 64,6)14 (50) | 52,6 (42,3; 79,8)6 (8) | 0,0040,001 |

**Table 3.** The results of multivariate logistic regression of risk factors associated with *QTc* elongation >450 ms

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Indexes** | **OR** | **95% CI** | **χ2** | ***р*** |
| Duration of a disease, years | 1,25 | 1,04–1,50 | 4,02 | 0,029 |
| Hypoglycemia (1st level) | 0,18 | 0,04–0,80 | 3,41 | 0,007 |
| Hypoglycemia (2nd level) | 4,40 | 1,37–14,19 | 5,24 | 0,017 |
| Asymptomatic hypoglycemia | 2,94 | 1,12–7,73 | 1,51 | 0,003 |
| CAN | 9,00 | 3,34–24,24 | 9,16 | 0,021 |
| SDNN | 0,94 | 0,89–0,99 | 2,94 | 0,037 |
| SDANN | 0,99 | 0,96–1,02 | 2,30 | 0,435 |
| rMSSD | 1,05 | 0,99–1,10 | 2,92 | 0,090 |

***Note.*** *OR — odds ratio, CI — confidential interval. Model characteristics: R2 =0,71.*

**FINANCING SOURCE**

Not specified.

**CONFLICT OF INTERESTS**

Not declared.