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НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE

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ARTERIAL STIFFNESS, ECG REPOLARIZATION ABNORMALITIES AND ARRHYTHMIC RISK IN TYPE 2 DIABETIC CARDIOMYOPATHY: EFFECT OF SGLT2 INHIBITOR-FINERENONE-BASED COMBINATION THERAPY

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✓ ***Resume***

This study evaluated the dynamics of arterial stiffness, carotid atherosclerosis, ECG repolarization parameters and Holter-derived heart rate variability in 87 patients with type 2 diabetes and cardiomyopathy over a 6-month treatment period. The main group (n=41) received complex therapy (SGLT2 inhibitor, finerenone, metabolic support), the comparison group (n=46) received standard therapy. Pulse wave velocity decreased from 12.4±0.4 to 9.6±0.3 m/s in the main group versus 11.2±0.4 m/s in the comparison group (p=0.001). Corrected QTc (Bazett) shortened from 462.4±6.2 to 431.6±5.1 ms in the main group, returning to the normal range, while remaining borderline-pathological in the comparison group (452.8±5.9 ms; p=0.007). QT dispersion decreased by 28.0% in the main group versus 7.5% in the comparison group. These findings indicate that complex metabolic therapy provides a significant reduction in arterial stiffness and ventricular repolarization abnormalities, plausibly mediated through normalization of magnesium and potassium balance, supporting its antiarrhythmic potential in diabetic cardiomyopathy.

Keywords: diabetic cardiomyopathy, arterial stiffness, pulse wave velocity, QTc interval, QT dispersion, heart rate variability, SGLT2 inhibitors, finerenone.

СОСУДИСТАЯ РИГИДНОСТЬ, НАРУШЕНИЯ РЕПОЛЯРИЗАЦИИ ЭКГ И АРИТМОГЕННЫЙ РИСК ПРИ ДИАБЕТИЧЕСКОЙ КАРДИОМИОПАТИИ 2 ТИПА: ЭФФЕКТ КОМБИНИРОВАННОЙ ТЕРАПИИ НА ОСНОВЕ SGLT2-ИНГИБИТОРА И ФИНЕРЕНОНА

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✓ ***Резюме***

Изучена динамика артериальной жёсткости, каротидного атеросклероза, показателей реполяризации ЭКГ и вариабельности сердечного ритма по данным холтеровского мониторирования у 87 больных сахарным диабетом 2 типа с кардиомиопатией на фоне 6-месячной терапии. Основная группа (n=41) получала комплексную терапию, группа сравнения (n=46) — стандартную. Скорость пульсовой волны снизилась с 12,4±0,4 до 9,6±0,3 м/с в основной группе против 11,2±0,4 м/с в группе сравнения (p=0,001). Корригированный QTc (по Bazett) сократился с 462,4±6,2 до 431,6±5,1 мс в основной группе, вернувшись в нормальный диапазон, тогда как в группе сравнения оставался пограничным (452,8±5,9 мс; p=0,007). Дисперсия QT снизилась на 28,0% против 7,5%. Результаты подтверждают антиаритмический потенциал комплексной метаболической терапии при диабетической кардиомиопатии.

Ключевые слова: диабетическая кардиомиопатия, артериальная жёсткость, скорость пульсовой волны, интервал QTc, дисперсия QT, вариабельность сердечного ритма, SGLT2-ингибиторы, финеренон.

ИККИНЧИ ТУРДАГИ ҚАНДЛИ ДИАБЕТ ФОНИДАГИ КАРДИОМИОПАТИЯДА ТОМИР ҚАТТИҚЛИГИ, ЭКГ РЕПОЛЯРИЗАЦИЯ БУЗИЛИШЛАРИ ВА АРИТМОГЕН ХАВФ: SGLT2-ИНГИБИТОРИ ВА ФИНЕРЕНОН АСОСИДАГИ КОМПЛЕКС ТЕРАПИЯНИНГ ТАЪСИРИ

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✓ ***Резюме***

Иккинчи турдаги қандли диабет фонида кардиомиопатияси бўлган 87 нафар беморда 6 ойлик даво давомида томир қаттиқлиги, каротид атеросклероз, ЭКГ реполяризация кўрсаткичлари ва Холтер мониторинги орқали юрак ритми вариабеллигининг динамикаси ўрганилган. Асосий гуруҳ (n=41) комплекс даво, таққослаш гуруҳи (n=46) эса стандарт даво олган. Пульс тўлқини тезлиги асосий гуруҳда 12,4±0,4 дан 9,6±0,3 м/с гача, таққослаш гуруҳида эса 11,2±0,4 м/с гача пасайган (p=0,001). Коррекцияланган QTc (Bazett бўйича) асосий гуруҳда 462,4±6,2 дан 431,6±5,1 мс гача қисқариб, нормал оралиққа қайтган, таққослаш гуруҳида эса чегаравий даражада қолган (452,8±5,9 мс; p=0,007). QT дисперсияси 28,0% ва 7,5% га камайган. Натижалар комплекс метаболик даволашнинг диабетик кардиомиопатияда антиаритмик салоҳиятини тасдиқлайди.

Калит сўзлар: диабетик кардиомиопатия, томир қаттиқлиги, пульс тўлқини тезлиги, QTc интервали, QT дисперсияси, юрак ритми вариабеллиги, SGLT2-ингибиторлари, финеренон.

Relevance

Increased arterial stiffness and ventricular repolarization abnormalities are recognized as important, though frequently underestimated, components of diabetic cardiomyopathy that contribute independently to cardiovascular mortalit [1,3]. Elevated pulse wave velocity (PWV) reflects structural changes of the arterial wall driven by chronic hyperglycemia, advanced glycation end-products and low-grade inflammation, while a prolonged and dispersed QT interval indicates heterogeneous myocardial repolarization and predisposes to malignant ventricular arrhythmias [2,5,8].

Electrolyte disturbances, particularly hypomagnesemia, are considered an important modifiable contributor to repolarization abnormalities in diabetic patients. Mineralocorticoid receptor antagonism with finerenone raises serum potassium and, in combination with SGLT2 inhibition, may favorably influence magnesium homeostasis, offering a plausible mechanistic link to improved ventricular repolarization. However, the combined vascular and electrophysiological effects of such therapy in diabetic cardiomyopathy remain insufficiently characterized [4,7].

The aim of this study was to evaluate the dynamics of arterial stiffness (pulse wave velocity, augmentation index, carotid intima-media thickness), ECG repolarization parameters (QTc, QT dispersion) and heart rate variability in patients with type 2 diabetic cardiomyopathy receiving complex metabolic therapy compared with standrd therapy.

Materials and methods

The study included 87 patients with type 2 diabetes mellitus and verified cardiomyopathy. The main group (Group I, n=41) received complex therapy (SGLT2 inhibitor, finerenone, and metabolic support including trimetazidine, alpha-lipoic acid and magnesium preparations); the comparison group (Group II, n=46) received standard therapy (metformin, ACEI/ARB, statins as indicated). A control group of 30 apparently healthy individuals was also examined. Arterial stiffness was assessed by carotid-femoral pulse wave velocity (PWV), augmentation index (AIx), ankle-brachial index (ABI) and carotid intima-media thickness (CIMT). Standard 12-lead ECG was used to measure corrected QT interval by both Bazett and Fridericia formulas, QT dispersion and absolute QT interval. Twenty-four-hour Holter monitoring provided heart rate variability parameters (SDNN, SDANN, RMSSD, pNN50, LF/HF ratio) and diurnal QTc variability. Serum magnesium and potassium were measured concomitantly. All

parameters were assessed at baseline and after 6 months of treatment. Statistical analysis was performed using Student's t-test and the chi-square test, with $p<0.05$ considered statistically significant.

Conflict of Interest: The authors declare no conflicts of interest.

Funding: The study was conducted without any specific funding from commercial or government entities.

Authors' Contributions: Study idea, concept, and design, statistical analysis.

Ethics Statement: The study was conducted in accordance with Good Clinical Practice standards and the principles of the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all patients for the study and permission for anonymous publication of the results.

Results and discussions

Arterial stiffness parameters improved significantly more in the main group than in the comparison group (Table 1).

Parameter	Baseline (n=87)	Main (n=41)	Comparison (n=46)	p (between-group)
CIMT, mm	1.02±0.03	0.88±0.02	0.97±0.03	0.238
Augmentation index (AIx), %	31.8±1.6	23.4±1.1	28.6±1.4	0.134
Pulse wave velocity (PWV), m/s	12.4±0.4	9.6±0.3	11.2±0.4	0.001
Magnesium, mmol/L	0.71±0.02	0.86±0.02	0.76±0.02	<0.001

Table 1. Dynamics of arterial stiffness and magnesium levels (M±m)

PWV decreased from 12.4±0.4 to 9.6±0.3 m/s (22.6%) in the main group, compared with a reduction to 11.2±0.4 m/s (9.7%) in the comparison group; the between-group difference remained significant (p=0.001). CIMT and AIx also showed a stronger improvement in the main group, although the between-group difference for these parameters did not reach statistical significance, suggesting that structural arterial changes regress more slowly than functional (stiffness) parameters over a 6-month period. Serum magnesium rose significantly more in the main group (0.71→0.86 mmol/L), consistent with the known effect of combined SGLT2 inhibitor and finerenone therapy on electrolyte homeostasis.

Parameter	Baseline (n=87)	Main (n=41)	Comparison (n=46)	p (between-group)
QTc Bazett, ms	462.4±6.2	431.6±5.1	452.8±5.9	0.007
QT dispersion, ms	61.4±3.2	44.2±2.4	56.8±3.0	0.001
SDNN, ms	86.2±3.8	108.6±4.1	92.4±3.9	0.004
LF/HF ratio	3.28±0.19	2.26±0.14	3.02±0.18	<0.001

Table 2. Dynamics of ECG repolarization and heart rate variability parameters (M±m)

QTc (Bazett) shortened from 462.4±6.2 to 431.6±5.1 ms in the main group ($p<0.001$), moving out of the pathological range into the normal interval, whereas in the comparison group it remained borderline-pathological at 452.8±5.9 ms (between-group p=0.007). QT dispersion decreased by 28.0% in the main group versus only 7.5% in the comparison group. Qualitative repolarization abnormalities decreased from 59.8% to 34.1% in the main group, while the reduction in the comparison group did not reach statistical significance (p=0.235). These changes were consistent with the restoration of magnesium and normalization of potassium balance, supporting a plausible antiarrhythmic mechanism of the combination therapy.

SDNN increased by 26.0% in the main group, exceeding the prognostically unfavorable threshold, while the comparison group remained below it (7.2% increase). The LF/HF ratio decreased by 31.1% in the main group, indicating a significant reduction in sympathetic predominance, while sympathetic hyperactivation persisted in the comparison group. Nevertheless, all six HRV parameters in the main group remained significantly different from control-group values, indicating that cardiovascular

autonomic neuropathy retains a partially irreversible, structural component that cannot be fully reversed within 6 months of therapy.

These findings are consistent with recent evidence linking elevated pulse wave velocity to increased cardiovascular mortality risk in type 2 diabetes, and with reports associating atherosclerosis indicators with QT interval prolongation in this population. The observed improvement in arterial stiffness and repolarization parameters with SGLT2 inhibitor-finerenone-based therapy suggests a combined hemodynamic, electrolyte and anti-fibrotic mechanism, extending the established cardiorenal benefits of this therapeutic combination to vascular and electrophysiological domains.

Conclusion

1. Complex metabolic therapy (SGLT2 inhibitor, finerenone, metabolic support) provides a significantly greater reduction in pulse wave velocity compared with standard therapy (22.6% versus 9.7%), while structural carotid changes regress more slowly.
2. QTc interval and QT dispersion improve substantially more with complex therapy, with QTc returning to the normal range only in the main group, supporting an antiarrhythmic effect linked to electrolyte normalization.
3. Heart rate variability parameters improve significantly with complex therapy but do not reach control-group values, confirming the partially irreversible structural nature of diabetic cardiovascular autonomic neuropathy.
4. Serum magnesium and potassium normalization on complex therapy is temporally and pathophysiologically linked to the observed shortening of QTc and QT dispersion, supporting their monitoring as adjunctive markers of arrhythmic risk in diabetic cardiomyopathy.

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