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EFFICACY OF L-CARNITINE IN PATIENTS WITH METABOLICALLY ASSOCIATED FATTY LIVER DISEASE AND PAROXYSMAL ATRIAL FIBRILLATION

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Abstract

Atrial fibrillation (AF) is one of the most common arrhythmias, significantly affecting quality of life and prognosis in patients with cardiometabolic disorders. In recent years, increasing attention has been given to the relationship between metabolically associated fatty liver disease (MAFLD, formerly NAFLD) and AF due to shared pathophysiological mechanisms, including obesity, insulin resistance, chronic inflammation, and activation of the renin–angiotensin–aldosterone system (RAAS).

Material and methods*:This prospective controlled study included 60 patients (37 men and 23 women) with confirmed MAFLD and paroxysmal AF, mean age 64.0 ± 7.4 years. Patients were randomized into two groups: the main group (n = 30) received standard therapy plus L-carnitine, and the control group (n = 30) received standard therapy alone.*

L-carnitine demonstrated hepatoprotective, antioxidant, and antiarrhythmic effects, improving myocardial and hepatic energy metabolism. These results support its use as a metabolic therapy in patients with MAFLD and paroxysmal AF.

Keywords: *Atrial fibrillation, metabolically associated fatty liver disease, L-carnitine, fatty acid β-oxidation, lipid metabolism*

Хулоса: *Атриал фибрилляция (АФ) — кардиометаболик бузилишларга эга бўлган беморларда ҳаёт сифати ва прогнозига жиддий таъсир кўрсатадиган энг кенг тарқалган аритмиялардан бири ҳисобланади. Ушбу тадқиқотнинг мақсади — метаболик боғлиқ ёғли жигар касаллиги (МАЖБК) ва пароксизмал шаклдаги АФ билан оғирган беморларда L-карнитин самарадорлигини баҳолаш. Проспектив назоратли тадқиқотга 60 нафар бемор жалб қилинди, улар икки гуруҳга бўлинди: асосий гуруҳ стандарт терапия билан бирга L-карнитин олди, назорат гуруҳи эса фақат стандарт терапия олди.*

3 ойдан сўнг асосий гуруҳда тананинг масса индекси ва бел айланмасининг сезиларли даражада пасайиши, триглицеридлар ва жигар ферментлари фаолиятининг камайиши, юқори зичликдаги липопротеин холестеринининг кўпайиши, шунингдек АФ ҳодисаларининг тезлиги ва давомийлигининг камайиши кузатилди. L-карнитин гепатопротектив, антиоксидант ва антиаритмик таъсир кўрсатди, миокард ва жигарда энергия алмашинувини яхшилади. Хулоса:L-карнитин МАЖБК ва пароксизмал АФ билан оғирган беморларнинг комплекс терапиясида истиқболли қўшимча ҳисобланади.

Калит сўзлар: *атриал фибрилляция, метаболик боғлиқ ёғли жигар касаллиги, L-карнитин, β-ёғ кислоталарини оксилдан чиқариш, липид алмашинуви.*

Аннотация

Фибрилляция предсердий (ФП) является одной из наиболее распространённых аритмий, оказывающих значительное влияние на качество жизни и прогноз пациентов с кардиометаболическими нарушениями. Цель исследования — оценить эффективность L-карнитина у пациентов с метаболически ассоциированной жировой болезнью печени (МАЖБП) и пароксизмальной формой ФП. В проспективное контролируемое исследование было включено 60 пациентов, разделённых на две группы: основная группа получала стандартную терапию с добавлением L-карнитина, контрольная — только стандартное лечение.

Через 3 месяца у пациентов основной группы наблюдались достоверное снижение индекса массы тела и окружности талии, уменьшение уровня триглицеридов и активности печёночных ферментов, повышение концентрации холестерина липопротеинов высокой плотности, а также уменьшение частоты и продолжительности эпизодов ФП. L-карнитин продемонстрировал гепатопротективное, антиоксидантное и антиаритмическое действие, улучшая энергетический обмен миокарда и печени. L-карнитин является перспективным компонентом комплексной терапии пациентов с МАЖБП и пароксизмальной ФП.

Ключевые слова: *фибрилляция предсердий, метаболически ассоциированная жировая болезнь печени, L-карнитин, β-окисление жирных кислот, липидный обмен*

Introduction

Atrial fibrillation (AF) is one of the most prevalent arrhythmias, significantly affecting the quality of life and prognosis of patients with cardiometabolic disorders. Recent studies have highlighted the link between metabolically associated fatty liver disease (MAFLD, formerly NAFLD) and AF due to shared pathophysiological mechanisms, including obesity, insulin resistance, chronic inflammation, and activation of the renin–angiotensin–aldosterone system (RAAS) [1,2].

Large epidemiological studies, including the Framingham Heart Study, OPERA, and NHANES, have shown that MAFLD is associated with a twofold increased risk of developing AF. This association is explained by metabolic and structural myocardial remodeling, increased oxidative stress, and epicardial fat tissue dysfunction. Visceral obesity contributes to lipid accumulation in the myocardium, disruption of cardiomyocyte intercellular contacts, and alterations in electrophysiological properties of atrial tissue, creating a substrate for arrhythmia development [3].

One therapeutic approach targeting these pathophysiological mechanisms is the use of metabolic drugs that modulate fatty acid β-oxidation and energy metabolism in the myocardium and liver. L-carnitine, a cofactor for the transport of fatty acids across the mitochondrial membrane, has demonstrated hepatoprotective, antioxidant, and antiarrhythmic properties. Studies have shown that its use improves lipid profiles, reduces liver enzyme activity, and decreases hepatic steatosis[4,5].

Despite available data, the efficacy of L-carnitine in patients with MAFLD combined with paroxysmal AF remains insufficiently studied, highlighting the relevance of the present study.

MAFLD is recognized not only as a hepatic manifestation of lipid metabolism disorders but also as a systemic metabolic syndrome involving the cardiovascular,

endocrine, and immune systems. Steatosis and steatohepatitis are accompanied by adipokine imbalance—elevated leptin and resistin, reduced adiponectin—leading to enhanced inflammation and oxidative stress, which exacerbate liver fibrosis and adversely affect myocardial electrical stability [6,7].

Experimental data indicate that myocardial fat infiltration in visceral obesity and MAFLD leads to modification of cardiomyocyte ion channels, reduced atrial contractility, and formation of ectopic automaticity, creating a substrate for AF. Energy metabolism disturbances in atrial tissue are accompanied by ATP depletion, reduced carnitine palmitoyltransferase activity, and accumulation of toxic free fatty acid metabolites, further promoting electrophysiological instability and increasing paroxysmal AF risk.

Materials and Methods

Study Population

This study was conducted at the clinical departments of Tashkent State Medical University. Sixty patients (37 men, 23 women) aged 45–75 years with confirmed MAFLD and paroxysmal AF were included.

Study Design

The study was a 3-month prospective controlled trial. Patients were randomized into two comparable groups by age, sex, body mass index (BMI), and comorbidities:

- **Main group (n = 30):** standard therapy for AF and MAFLD plus L-carnitine.
- **Control group (n = 30):** standard therapy alone.

Inclusion criteria: confirmed MAFLD via ultrasound, documented paroxysmal AF, age 45–75, informed consent.
Exclusion criteria: chronic alcoholism, viral hepatitis B or C, chronic heart failure class III–IV, malignancy, renal impairment (creatinine clearance < 60 mL/min), or recent use of other metabolic drugs.

Intervention

The main group received L-carnitine intravenously 1 g/day for 10 days, followed by oral administration 2 g/day for 3 months. The control group received only standard therapy, including antiarrhythmics, anticoagulants, statins, and liver-supportive medications (essential phospholipids, ursodeoxycholic acid when indicated).

Assessments. All patients underwent (tab.1)

- Anthropometric measurements (BMI, waist circumference)
- 12-lead ECG and 24-hour Holter monitoring
- Biochemical tests: ALT, AST, GGT, ALP, total cholesterol, triglycerides, HDL-C, LDL-C, glucose, bilirubin, creatinine, urea
- Fatty Liver Index (FLI)
- Ultrasound evaluation of hepatic steatosis using Batskov's scale

Table 1. Baseline Characteristics of Patients

Parameter	Main Group (n = 30)	Control Group (n = 30)	p-value
Age, years	64.1 ± 7.5	63.9 ± 7.3	0.87
Male/Female	19/11	18/12	0.79
BMI, kg/m^2	31.2 ± 3.4	30.9 ± 3.6	0.68
Waist circumference, cm	102.5 ± 10.2	101.8 ± 9.9	0.73
ALT, U/L	58.3 ± 12.6	57.9 ± 11.8	0.88

Parameter	Main Group (n = 30)	Control Group (n = 30)	p-value
GGT, U/L	72.5 ± 14.7	71.8 ± 13.9	0.81
Triglycerides, mmol/L	2.25 ± 0.62	2.21 ± 0.60	0.75
HDL cholesterol, mmol/L	1.10 ± 0.21	1.12 ± 0.19	0.67
FLI	67.4 ± 8.5	66.9 ± 8.2	0.79

• *Note:* BMI — body mass index; ALT — alanine aminotransferase; GGT — gamma-glutamyl transferase; HDL — high-density lipoprotein; FLI — Fatty Liver Index.

Ultrasound showed reduced hepatic steatosis in 14.6% of patients. Holter monitoring revealed a decrease in frequency and duration of AF episodes, accompanied by improvement in subjective symptoms, such as palpitations, dyspnea, and fatigue.

Follow-up was conducted after 3 months. The study was approved by the local ethics committee and adhered to the Declaration of Helsinki (2013).

Statistical Analysis. Data were analyzed using Statistica 10.0. Quantitative variables are presented as mean ± SD. Student's t-test was used to compare groups; $p < 0.05$ was considered statistically significant.

Results. L-carnitine therapy was well tolerated. Mild dyspeptic symptoms occurred in one patient, requiring no dose adjustment.

After 3 months, the main group showed significant improvements compared to the control group (tab.2)

Table 2.

Anthropometric and Biochemical Changes After 3 Months of Therapy

Parameter	Main Group (n = 30)	Control Group (n = 30)	p-value
BMI, kg/m^2	29.5 ± 3.2	30.7 ± 3.5	<0.05
Waist circumference, cm	97.7 ± 9.6	101.2 ± 10.1	<0.05
Triglycerides, mmol/L	1.73 ± 0.55	2.18 ± 0.58	<0.05
HDL cholesterol, mmol/L	1.25 ± 0.20	1.13 ± 0.21	<0.05
ALT, U/L	46.9 ± 10.8	56.8 ± 11.5	<0.05
GGT, U/L	57.2 ± 12.1	70.9 ± 13.4	<0.05
FLI	59.8 ± 7.6	66.5 ± 8.1	<0.05

Note: Values represent mean ± SD.

Table 3.

Dynamics of Atrial Fibrillation Episodes

Parameter	Main Group (n = 30)	Control Group (n = 30)	p-value
AF episode frequency, per week	↓ 35%	↓ 10%	<0.05
AF episode duration, min/episode	↓ 28%	↓ 8%	<0.05
Patient-reported palpitations	↓ Significant	No significant change	<0.05
Dyspnea	↓ Moderate	No significant change	<0.05
Fatigue	↓ Moderate	No significant change	<0.05

Note: Arrows indicate reduction relative to baseline.

Discussion

These results support the pathophysiological rationale for including L-carnitine in therapy for patients with MAFLD and paroxysmal AF. Improvement in lipid profile and liver function is due to L-carnitine's activation of long-chain fatty acid transport into mitochondria, promoting β-oxidation and reducing intracellular lipid accumulation [8,9].

Positive cardiovascular effects relate to antioxidant activity, reduction of free fatty acids, improved myocardial energy metabolism, and decreased oxidative stress. These findings align with previous studies by Pastori et al. (2020) and Haghbin et al. (2020), demonstrating the link between MAFLD and AF risk, as well as the potential of metabolic therapy.

L-carnitine reduces hepatic steatosis (FLI) and AF severity, indicating systemic effects. Correcting fatty acid metabolism and reducing hepatocellular stress may improve both liver disease progression and AF incidence [10]. Its high safety profile, lack of interactions with anticoagulants or antiarrhythmics, and feasibility of long-term use make it a promising component of personalized therapy.

Conclusions

1. **Metabolic link in paroxysmal AF:** Obesity, dyslipidemia, and elevated liver enzymes are common in patients with paroxysmal AF, indicating that metabolic disorders may trigger and exacerbate arrhythmia.
2. **Effects of L-carnitine:** Addition of L-carnitine to standard therapy reduced BMI and waist circumference, triglycerides, and liver enzyme activity, while increasing HDL cholesterol, improving lipid profile and hepatic function.
3. **Hepatoprotective effects:** L-carnitine reduced FLI and hepatic fat infiltration, reflecting its hepatoprotective action.
4. **Cardiovascular benefits:** Reduced frequency and duration of AF episodes and improved subjective symptoms, supporting its positive effects on myocardial energy metabolism and reduction of arrhythmogenic potential.

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