Evidence for Self-Medication
International Review Journal

Real-world evidence for beneficial effects of essential phospholipids in patients with non-alcoholic fatty liver disease

Igor Maev, MD, PhD, Dr. Med. Sci., Chavdar Pavlov, MD, PhD, Dr. Med. Sci., Kirill M Starostin, MD, and Branko Popovic, MD

Essential phospholipids (EPLs) belong to the group of hepatoprotective agents and are recommended in the Russian guideline for the treatment of non-alcoholic fatty liver disease (NAFLD). A large-scale observational study now confirms this recommendation based on treatment satisfaction, improvement of ultrasound parameters and normalisation of liver enzyme levels.

Non-alcoholic fatty liver disease: a life-style disease

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in the world and affects roughly 37% of adults in Russia. NAFLD is regarded as the hepatic manifestation of metabolic syndrome, which includes obesity, dyslipidaemia, hypertension, and type 2 diabetes. Untreated, NAFLD may progress to non-alcoholic steatohepatitis (NASH), cirrhosis or hepatocellular carcinoma. The World Gastroenterology Organization recommends a resource-sensitive approach to NAFLD diagnosis that employs non-invasive methods such as ultrasound and measurement of liver enzymes. Presently EPL are recommended as one treatment option in several countries including Russia, Latvia, Poland, and China [1–4].

High treatment satisfaction with EPL treatment

The MANPOWER study, a Russian observational study, included 2843 NAFLD patients. These patients received EPL (1800 mg/day) for 24 weeks as an adjunct treatment to standard care and had at least one of four comorbidities: obesity, hypertension, type 2 diabetes and hypercholesterolaemia [5–7]. 80% of the patients had at least two other metabolic diseases in addition to NAFLD. The most frequent comorbidities were overweight/obesity (81%) and hypercholesterolaemia (75%). Many patients received medication to treat their comorbidities. It was alarming that 15% of patients with diabetes received no other medication apart from EPL, and 40% of the overweight/obese patients were not given appropriate treatment. In relation to the EPL therapy of these patients, the majority (82%) of physicians were either extremely satisfied (22%) or very satisfied (60%). Patient satisfaction with their EPL therapy was also very high (82%). The 6-month compliance rate of EPL treatment was estimated as 90.5% [5].

Significant improvements in ultrasound and in the blood parameters

The ultrasound results of NAFLD also improved significantly, especially in terms of the echogenicity and structure of the liver – and to a comparable extent in all comorbidity groups (see **Tab. 1**). At the start of the study, hyperechogenicity of the liver was present in 84.0% of the patients and a heterogeneous liver structure in 62.9%. After 24 weeks, a significant improvement in liver hyperechogenicity was found in 68.3% of the patients (95% confidence interval [CI] 66.6% to 70.1%) and in liver structure in 42.7% (95% CI 40.9% to 44.5%) ($p < 0.05$ compared to baseline). Considering only patients with ultrasound abnormalities detected at baseline, EPL therapy was accompanied with a significant and consistent ultrasound improvement with statistically significant ($p < 0.05$) improvement of liver echogenicity in 69.6% of patients at 12 weeks and maximal improvement of liver hyperechogenicity in 81.4% of patients at 24 weeks ($p < 0.05$) [6].

Levels of the liver enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) are useful parameters in the diagnosis of NAFLD; at the same time, liver enzyme levels do not

Evid Self Med 2022;2:220080 | https://doi.org/10.52778/efsm.22.0080
Affiliation/Correspondence: Igor Maev, MD, PhD, Dr. Med. Sci., A. I. Evdokimov, Moscow State University of Medicine and Dentistry, Ministry of Health of Russia, Moscow, Russia; Chavdar Pavlov, MD, PhD, Dr. Med. Sci., I. M. Sechenov First Moscow State Medical University, Ministry of Health of Russia, Moscow, Russian Federation; Kirill M Starostin, MD, Sanofi, Moscow, Russia; Branko Popovic, MD, Sanofi, Industriepark Hoechst, 65926 Frankfurt am Main, Germany (Branko.popovic@sanofi.com)

© 2022 Wissenschaftliche Verlagsgesellschaft Stuttgart

Tab. 1. Proportion (%) of patients with improved or unchanged ultrasonographic findings after 24 weeks of EPL treatment, according to comorbidity nature

Features [%]	Hypertension (n=1635)		Overweight/obesity (n=2285)		Type 2 diabetes mellitus (n=475)		High cholesterol (n=2119)	
	Improved	*No change*	*Improved*	*No change*	*Improved*	*No change*	*Improved*	*No change*
Diffuse liver hyperechogenicity	67.7	32.3	68.8	31.2	68.2	31.8	67.8	32.2
Heterogeneous structure of the liver*	43.6	56.4	43.3	56.6	40.6	59.3	43.7	56.2
Indistinctness and/or underlined vascular pattern	24.8	75.2	23.1	76.9	24.8	75.2	24.4	75.6
Distal echo signal attenuation	21.7	78.3	22.5	77.5	22.7	77.3	21.5	78.5

*Worsening of "heterogeneous structure of the liver" occurred in 0.1% of patients in each comorbidity subgroup

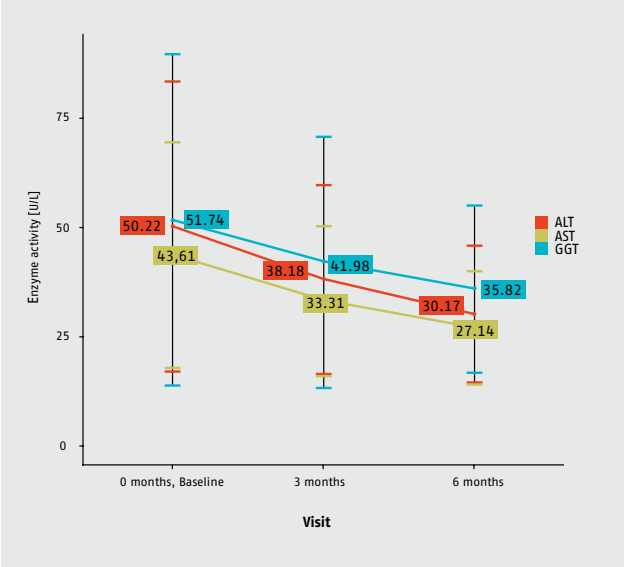

Fig. 1. Mean +/– SD liver function tests (U/L) at baseline and weeks 12 and 24 in the overall study population.
ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyl transferase

correlate with the histological severity of NAFLD. There was a consistent and significant reduction in serum levels of ALT, AST and GGT during the 24-week study period (see **Fig. 1**). Compared to the baseline levels, mean ALT decreased by 20.0 U/L, mean AST by 16.5 U/L and mean GGT by 15.9 U/L. The changes were already statistically significant after 12 weeks (all $p < 0.001$ in the paired t-test for the two timepoints). At the end of the study, the ALT, AST and GGT levels were normal in 75.8%, 89.2% and 62.5% of the patients respectively (all $p < 0.001$ compared to the baseline value) [7].

Summary

Based on the antifibrotic and antioxidative effects of EPL, the Russian Guidelines recommend EPL as an adjunct treatment for NAFLD. Real-world data confirm that EPL support the normalisation of pathological findings in NAFLD. Long-term intake of EPL can be particularly beneficial to patients with metabolic comorbidities and difficulties in maintaining changes to their lifestyle.

Literature

1. Lazebnik LB, Golovanova EV, et al. Non-alcoholic fatty liver disease in adults: clinic, diagnostics, treatment. Guidelines for therapists, third version. Experimental and Clinical Gastroenterology. 2021;185(1):4–52. (In Russ.) DOI: 10.31146/1682-8658-ecg-185-1-4-52
2. Derovs A, Pokrotnieks J, Derova J, Laivacuma S, Zeltiņa I, Vīksna L. Society of Digestive Diseases (Latvia). [Clinical practical guidelines for diagnostics, treatment and monitoring of non-alcoholic fatty liver disease]. Nealkohola taukainās aknu slimības diagnostikas, ārstēšanas un novērošanas klīniskās praktiskās rekomendācijas. Rīga: SIA Medicīna un Prese, 2020. 44 p.
3. Hartleb M, Wunsch E, Milkiewicz P, et al. Postępowanie z chorymi na niealkoholową stłuszczeniową chorobę wątroby: Zalecenia Polskiej Grupy Ekspertów NAFLD 2019. Med Prakt. 2019;10:47–74.
4. Fan JG, Wei L, Zhuang H, et al. Guidelines of prevention and treatment of nonalcoholic fatty liver disease (2018, China). J Dig Dis. 2019;20(4):163–73.
5. Maev IV, Samsonov AA, et al. Real-world comorbidities and treatment patterns among patients with non-alcoholic fatty liver disease receiving phosphatidylcholine as adjunctive therapy in Russia. BMJ Open Gastroenterol. 2019;6(1):e000307. https://doi: 10.1136/bmjgast-2019-000307. eCollection 2019.
6. Maev IV, Samsonov AA, et al. Effectiveness of phosphatidylcholine in alleviating steatosis in patients with non-alcoholic fatty liver disease and cardiometabolic comorbidities (MANPOWER study). BMJ Open Gastro 2020;7:e000341. doi:10.1136/bmjgast-2019-000341
7. Maev IV, Samsonov AA, et al. Effectiveness of phosphatidylcholine as adjunctive therapy in improving liver function tests in patients with non-alcoholic fatty liver disease and metabolic comorbidities: real-life observational study from Russia. BMJ Open Gastro 2020;7:e000368. doi:10.1136/bmjgast-2019-000368

Conflict of interest: K. Starostin and B. Popovic are employees of Sanofi. I. Maev and C. Pavlov declare no conflict of interest.

Disclosure: Medical writing and publication funded by Sanofi.

Information regarding manuscript

Submitted on: 19.11.2021
Accepted on: 01.04.2022
Published on: 10.04.2022

2022 Wissenschaftliche Verlagsgesellschaft Stuttgart