PRESS REVIEW

L-CARNITINE
A History of Quality

ALFASIGMA

October 2021

Additional L-carnitine Reduced the Risk of Hospitalization in Patients with Overt Hepatic Encephalopathy on Rifaximin

Publication date	Reference	Author/s	Study Type
June 2021	Dig Dis. 2021 Jun 28. doi: 10.1159/000518067	Kubota K., et al.	Open-label

KEY-WORDS

Hepatic encephalopathy, L-carnitine, Liver cirrhosis, Portosystemic shunt, Rifaximin

OBJECTIVES

This study aimed to assess the additional effects of L-carnitine in patients who were receiving rifaximin for hepatic encephalopathy (HE)

POPULATION INVOLVED/STUDY CHARACTERISTICS

83 patients were randomized to either:

- Group A (n = 42) Rifaximin alone 1200 mg/day
- Group B (n = 41) Rifaximin 1200 mg/day + L-carnitine 1500 mg/day

For 12 weeks treatment period

Inclusion: grade I or II HE according to the West Haven Criteria, one or more occurrences of overt HE after administration of non-absorbable disaccharides, and ≥ 20 years of age.

Exclusion: acute hepatitis and exacerbation of chronic hepatitis, poorly controlled hepatocellular carcinoma, history of malignancies other than hepatocellular carcinoma, and severe renal and/or heart failure.

OUTCOMES

The hospital admission rates in Groups A and B were 30.9% (13/42) and 9.8% (4/41), respectively. Additional L-carnitine significantly reduced the admission rate ($p = 0.028$)

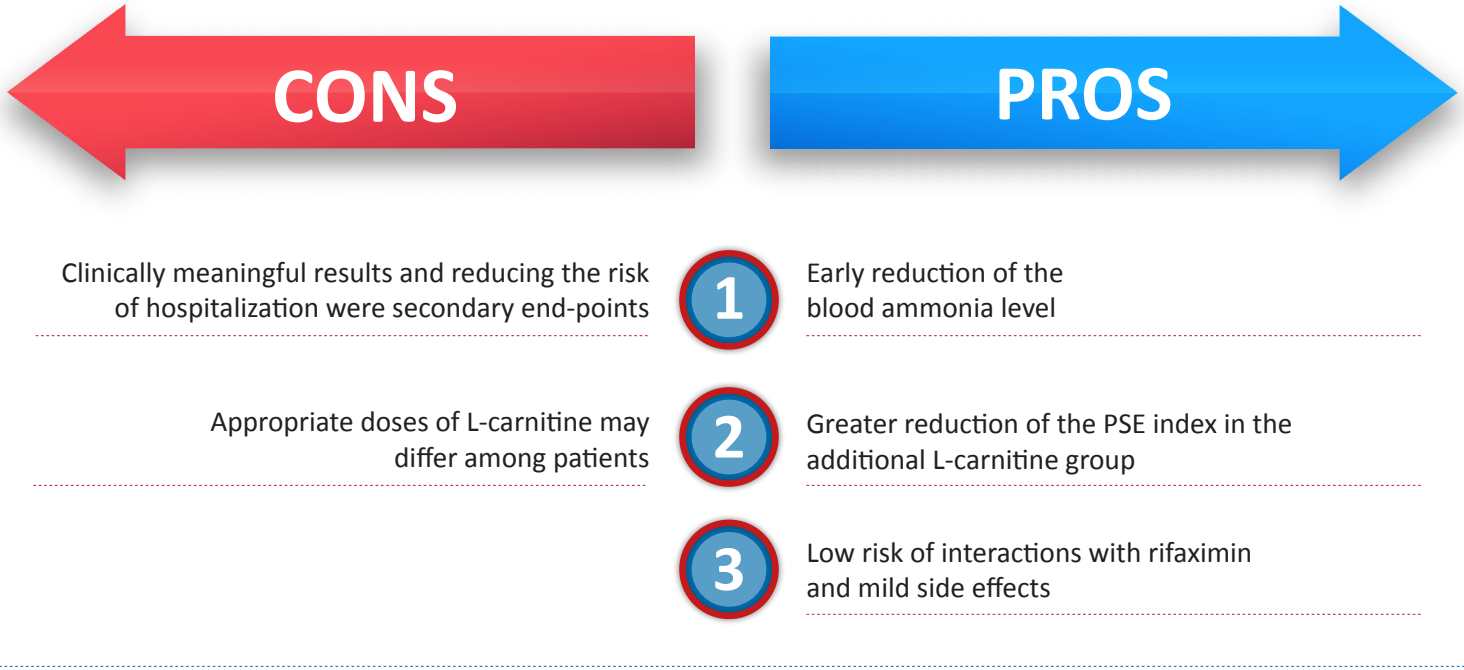
Additional L-carnitine Reduced the Risk of Hospitalization in Patients with Overt Hepatic Encephalopathy on Rifaximin

DISCUSSION

Clinically, an important goal in treating patients with cirrhosis is preventing hospitalization-related complications, including HE, hepatic ascites, gastrointestinal bleeding, and sarcopenia. This clinical study has demonstrated that the additional L-carnitine therapy, compared with a standard rifaximin therapy, significantly reduced hospitalization risk in patients with overt HE. The early improvement of ammonia levels might help reduce the frequency of hospitalization

KEY POINTS

The addition of L-carnitine to standard Rifaximin treatment helps preventing hospitalization risk. However, the difference in the blood ammonia levels on the final dosing days in the two groups was not significant and differences between the two groups were not significant with respect to the PSE index although a trend was seen in the greater reduction of the PSE index in the additional L-carnitine group



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Quantitative efficacy of L-carnitine supplementation on glycemic control in type 2 diabetes mellitus patients

Publication date
April 2021

Reference
Expert Rev Clin Pharmacol. 2021 Apr 29;1-8.
doi: 10.1080/17512433.2021.1917381

Author/s
Dong-Dong Wang et al.

Study Type
Meta analisys

KEY-WORDS

L-carnitine; Quantitative efficacy; fasting plasma glucose; glycated hemoglobin; glycemic control; type 2 diabetes mellitus

OBJECTIVES

Efficacy of L-carnitine supplementation on glycemic control in type 2 diabetes mellitus patients

POPULATION INVOLVED/STUDY CHARACTERISTICS

Inclusion criteria:

- (a) randomized controlled trial (RCT),
- (b) type 2 diabetes mellitus,
- (c) reported literatures included fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c), and
- (d) exact dose and duration of L-carnitine

OUTCOMES

8 randomized controlled studies were eligible, including:

- 916 type 2 diabetes mellitus patients
- Mean age: 45.0 years to 57.8 years
- L-carnitine 2 g/day
- Study duration between 12 weeks to 12 months

Quantitative efficacy of L-carnitine supplementation on glycemic control in type 2 diabetes mellitus patients

DISCUSSION

L-carnitine was effective on Fasting Plasma Glucose (FPG), 2 g/day L-carnitine was required for at least 36.1 weeks. For the efficacy of L-carnitine on glycated hemoglobin (HbA1c), 2 g/day L-carnitine was required for at least 106 weeks

KEY POINTS

It was the first time to provide valuable quantitative information for efficacy of L-carnitine supplementation on glycemic control in type 2 diabetes mellitus patients

CONS

7 studies implemented in Italy. Therefore, more type 2 diabetes mellitus patients in other countries or regions are needed

PROS

1. First time proofing efficacy of L-carnitine in a Meta-analysis
2. Receiving the L-carnitine resulted in weight loss and improving blood sugar regulation
3.

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L-carnitine supplementation for muscle weakness and fatigue in children with neurofibromatosis type 1: A Phase 2a clinical trial

Publication date
March 2021

Reference
Ann Palliat Med. 2021 Mar; 10(3): 3286-3298
doi: 10.21037/apm-21-66

Author/s
Xiang-Geng Chi. et al.

Study Type
Observational

KEY-WORDS

Hepcidin; high-flux hemodialysis; low-flux hemodialysis; microinflammation; vascular calcification

OBJECTIVES

Investigate the effect of high-flux hemodialysis (HD) combined with levocarnitine on vascular calcification, microinflammation, hepcidin, and malnutrition in elderly patients on maintenance HD (MHD)

POPULATION INVOLVED/STUDY CHARACTERISTICS

75 elderly patients on MHD were randomly divided into three groups:

- (a) low-flux HD group (n = 25)
- (b) high flux HD group (n = 25)
- (c) joint group (n = 25)

OUTCOMES

Carnitine levels were normalized after carnitine supplementation (41.2-49.0 lmol/L). The patients not on carnitine supplementation exhibited no motor or intellectual disabilities, nor any feeding problem. The levels of serum FC levels after PCA administration remained within the normal range (48.0-68.2 lmol/L) in the patients on carnitine supplementation but fell below the normal range (18.7-30.8 lmol/L) in those who were not taking carnitine

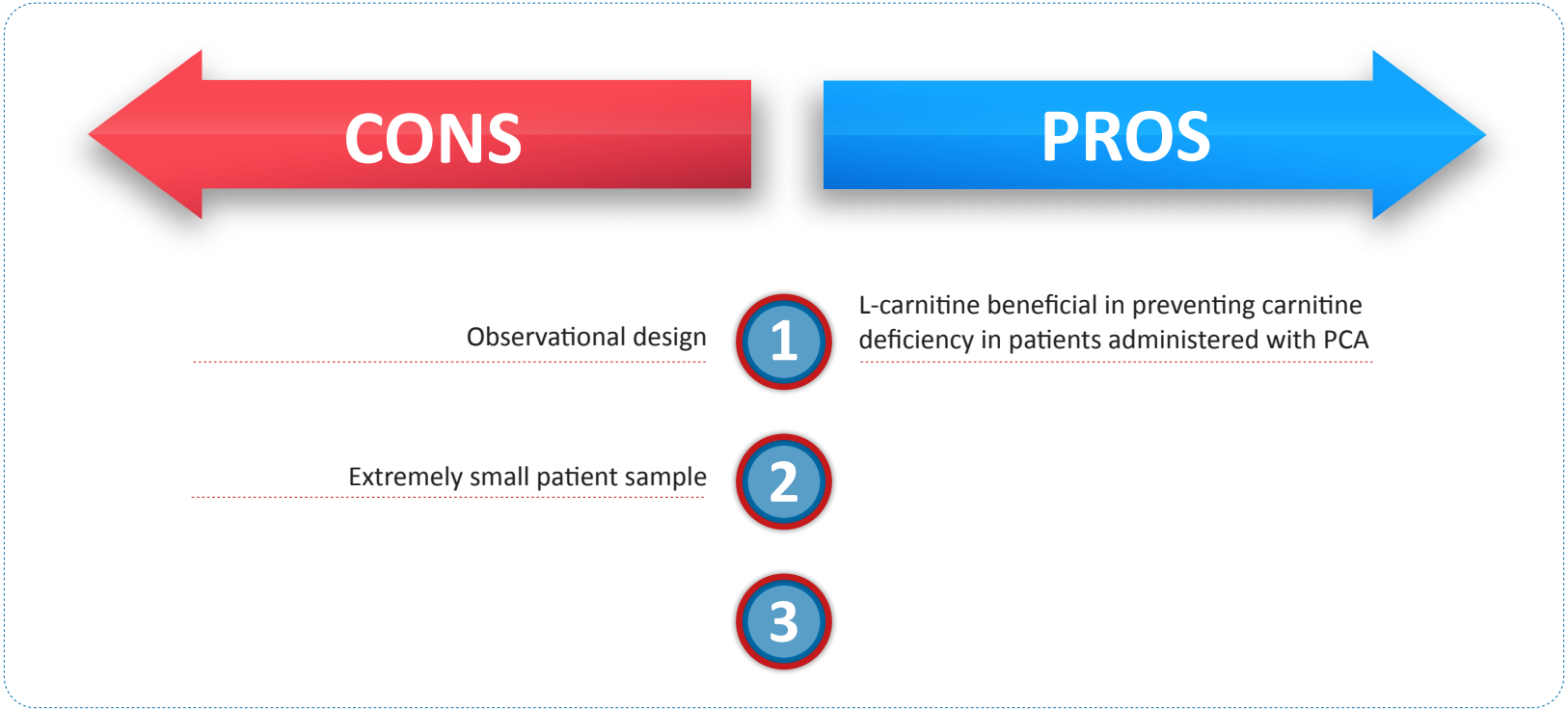
L-carnitine supplementation for muscle weakness and fatigue in children with neurofibromatosis type 1: A Phase 2a clinical trial

DISCUSSION

This observational study found that carnitine deficiency caused by PCA use was prevented by carnitine supplementation in patients with epilepsy on VPA. Carnitine supplementation will be beneficial in patients at risk of carnitine deficiency

KEY POINTS

Carnitine deficiency was not seen in patients with epilepsy on VPA when carnitine supplementation was provided. Carnitine supplementation may benefit patients at high risk of carnitine deficiency



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Levocarnitine supplementation for management of hypertriglyceridemia in patients receiving parenteral nutrition

Publication date	Reference	Author/s	Study Type
Sept 2021	Nutr Clin Pract. 2021 Sep 16. doi: 10.1002	Grucz TM., et al.	Retrospective, observational, single-center cohort study

KEY-WORDS

Carnitine; hypertriglyceridemia; intravenous lipid emulsions; parenteral nutrition

OBJECTIVES

The primary objective was to compare trends in triglyceride levels before and after the triglyceride-altering intervention. The triglyceride-altering intervention was defined as initiation of levocarnitine in PN for the levocarnitine group, and as reduction in lipid injectable emulsion for the control group intervention

POPULATION INVOLVED/STUDY CHARACTERISTICS

261 patients included in the analysis
Control: Reduction in lipid emulsion (164)
Levocarnitine: Reduction in lipid emulsion + Levocarnitine (97). Median dosage 5.7-9.9 mg/kg
Inclusion: Patients ≥ 18 years of age were included if they had a triglyceride level ≥ 175 mg/dl and a reduction in the dose or frequency of lipid injectable emulsion in PN while receiving PN during their index hospital admission
Exclusion: Patients with familial hypertriglyceridemia, inborn errors of metabolism managed by the genetics nutrition service, a gap in PN administration > 5 days, or administration of levocarnitine outside PN were excluded

OUTCOMES

The addition of levocarnitine to PN was associated with a significantly greater rate of reduction in triglyceride levels pre-intervention to post-intervention compared with a reduction in lipid injectable emulsion alone (-11 *vs* -3 mg/dl per day; 95% CI, -15 to -2; P = .012)

Levocarnitine supplementation for management of hypertriglyceridemia in patients receiving parenteral nutrition

DISCUSSION

Levocarnitine supplementation was associated with a significant reduction in preintervention to post-intervention triglyceride levels compared with the control group despite a lesser reduction in lipid provision in the levocarnitine group, and with its favorable adverse effect profile, it may be reasonable to consider supplementing levocarnitine in PN for hospitalized adult patients with elevated triglyceride levels

CONS

The retrospective, observational study design limits the ability to establish cause-and-effect relationships between the addition of levocarnitine in PN and triglyceride levels

Levocarnitine addition to PN without any changes in lipid injectable emulsion was not assessed

No standardized dosing protocol for levocarnitine supplementation in PN (at the time of the study)

PROS

1. Reduction in triglyceride levels pre-intervention to post-intervention

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Levocarnitine for pegaspargase-induced hepatotoxicity in older children and young adults with acute lymphoblastic leukemia

Publication date	Reference	Author/s	Study Type
August 2021	Cancer Med. 2021 Sep 16. doi: 10.1002	Schulte R., et al.	Multicenter Real World Data

KEY-WORDS

Adolescent, asparaginase, carnitine, chemical and drug-induced liver injury, precursor cell lymphoblastic leukemia-lymphoma, young adult

OBJECTIVES

Investigate real-world data on the safety and efficacy of levocarnitine supplementation during ALL induction therapy

POPULATION INVOLVED/STUDY CHARACTERISTICS

161 patients age ≥ 10 years who received levocarnitine during induction therapy for ALL, compared to a similar patient cohort who did not receive levocarnitine:

- Levocarnitine prophylaxis (n = 29)
- Levocarnitine rescue (n = 23)
- No Levocarnitine (n = 109)

Received between 1000 and 3000 mg levocarnitine oral daily for a median value of 29 days

OUTCOMES

Analysis of Average Marginal Effects (AME) showed incorporating levocarnitine prophylaxis into Children Oncology Group (COG)-style Acute Lymphoblastic Leukemia (ALL) induction therapy was predicted to significantly reduce the probability of developing c.bili > 3 mg/ dl (dy/dx -16.5%, 95% CI -0.27 to -0.06, p = 0.002) but not severe transaminitis (dy/dx -0.08%, 95% CI -0.19 to +0.03, p = 0.139)

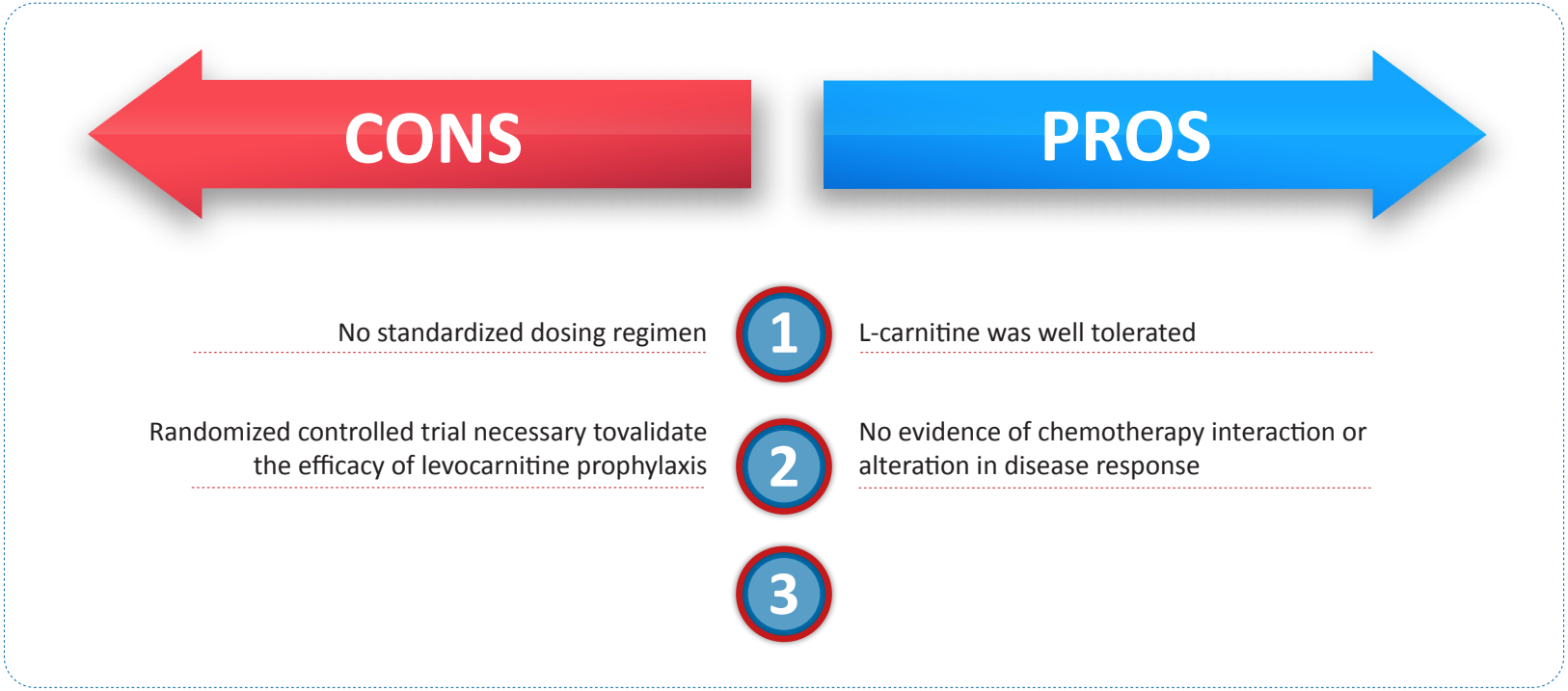
Levocarnitine for pegaspargase-induced hepatotoxicity in older children and young adults with acute lymphoblastic leukemia

DISCUSSION

A clear efficacy signal from levocarnitine **prophylaxis** was evident in patients at high risk for hepatotoxicity who received levocarnitine prophylaxis prior to PEG-ASP. No clear benefit was found for levocarnitine **rescue** following severe hepatotoxicity

KEY POINTS

Levocarnitine supplementation might be useful in preventing hepatotoxicity of pegaspargase in children with ALL



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