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BRIEF ARTICLE

L-carnitine supplementation improves hematological pattern in patients affected by HCV treated with Peg interferon-α 2b plus ribavirin

Michele Malaguarnera, Marco Vacante, Maria Giordano, Massimo Motta, Gaetano Bertino, Manuela Pennisi, Sergio Neri, Mariano Malaguarnera, Giovanni Li Volti, Fabio Galvano

Michele Malaguarnera, Giovanni Li Volti, Fabio Galvano, Department of Biological Chemistry, Medical Chemistry and Molecular Biology, University of Catania, 95100 Catania, Italy
Marco Vacante, Maria Giordano, Gaetano Bertino, Sergio Neri, Mariano Malaguarnera, Department of Internal Medicine and Systemic Disease, University of Catania, 95125 Catania, Italy
Massimo Motta, Manuela Pennisi, Research Center "The Great Senescence", University of Catania, 95125 Catania, Italy
Author contributions: Malaguarnera M, Vacante M and Galvano F contributed to the study design, data analysis, and the drafting of the manuscript; Motta M, Bertino G and Neri S contributed to enrollment of patients and data interpretation; Giordano M helped with statistical analysis; Malaguarnera M, Pennisi M and Volti GL helped with data interpretation and data analysis.
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Correspondence to: Mariano Malaguarnera, AP, Department of Internal Medicine and Systemic Disease, Ospedale Cannizzaro, Viale Messina, 829-95125 Catania, Italy. malaguar@unict.it
Telephone: +39-95-7262008 Fax: +39-95-7262011
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Abstract

AIM: To evaluate the efficacy of L-carnitine on alleviating anemia, thrombocytopenia and leukopenia, and minimizing dose reductions in patients with chronic hepatitis C virus (HCV) in treatment with Interferon α (IFN-α) plus ribavirin.

METHODS: Sixty-nine patients with chronic hepatitis C were enrolled in the study and divided into two groups. group A (n = 35) received Peg-IFN-α 2b plus ribavirin plus L-carnitine, and group B (n = 34) received Peg-IFN-α and ribavirin for 12 mo. All patients underwent laboratory investigations including: red cell count, hemoglobin, white cell count, platelets, bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and viremia.

RESULTS: After 12 mo in group A compared to group B we observed significant differences in AST 108.8 *vs* 76.8 (IU/L; $P < 0.001$), ALT 137.9 *vs* 112.3 (IU/L; $P < 0.001$), viremia 4.04 *vs* 2.36 (× 10^6 copies/mL; $P < 0.001$), Hb 1 *vs* 3.5 (g/dL; $P < 0.05$), red blood cells 0.3 *vs* 1.1 (× 10^{12}/L; $P < 0.001$), white blood cells 1.5 *vs* 3 (× 10^9/L; $P < 0.001$) and platelets 86 *vs* 85 (× 10^9/L; $P < 0.001$). The end treatment responders were 18 *vs* 12 (60% *vs* 44%) and the non responders were 12 *vs* 15 (40% *vs* 50%) [odds ratio (OR) 1.65, 95% CI = 0.65-5.37, $P < 0.05$]. In group A compared to group B there was a significant improvement of sustained virological response in 15 *vs* 7 patients (50% *vs* 25%), while the relapsers were 3 *vs* 5 (10% *vs* 18%) (OR 3.57, 95% CI = 0.65-19.3, $P < 0.001$).

CONCLUSION: L-carnitine supplementations modulate erythropoiesis, leucopoiesis and thrombocytopoiesis, and may be useful in patients treated for HCV. L-carnitine treatment offers the possibility of achieving a sustained virological response while preventing overtreatment.

Key words: L-carnitine; Chronic hepatitis C; Anemia; Interferon

Peer reviewers: Natalia A Osna, MD, PhD, Liver Study Unit, Research Service (151), VA Medical Center, 4101 Woolworth Avenue, Omaha NE 68105, United States; Sabine Mihm, Professor, Department of Gastroenterology, Georg-August-University, Robert-Koch-Str.40, Göttingen D-37099, Germany

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INTRODUCTION

Interferon α (IFN-α), in combination with ribavirin (RBV) treatment, represents the most efficacious therapeutic tool in the management of chronic hepatitis C[1,2]. The current standard of care results in successful outcomes in 70% of patients with hepatitis C virus (HCV) genotype 2 or 3 and in 48% of patients with HCV genotype 1. Systemic side effects such as fatigue, fever, chills, myalgia and nausea occur in most patients and normally disappear after a few weeks of treatment. Other side effects include hematologic, autoimmune, neurological and psychiatric disorders[3-7]. The frequency of hematologic adverse events including thrombocytopenia, anemia and neutropenia is higher. A recent study[5] reported anemia in 16%, thrombocytopenia in 20%, and leukopenia in 10% of Peg-IFN-α 2b plus RBV treated patients with HCV. These adverse events most frequently lead to drug discontinuation or to dose modifications. In our previous reports we have observed that L-carnitine improves responses and quality of life and reduces steatosis in patients with HCV treated with interferon[8-10]. L-carnitine (4-N-trimethyl ammonium 3-hydroxybutyric acid) is a conditionally synthesized nutrient from the amino acids lysine and methionine in the human liver, brain and kidney, but is largely obtained from meat and dairy products. Administration of L-carnitine is an accepted treatment for mitochondrial myopathy and encephalomyopathy, as well as other states of primary and secondary L-carnitine deficiency[11]. Recently, L-carnitine has been proposed as a potential adjuvant treatment to improve anemia, thrombocytopenia, leukopenia and immunological function[12-17]. The aim of our study was to evaluate the efficacy of L-carnitine in alleviating anemia, thrombocytopenia and leukopenia, and minimizing dose reductions in patients with chronic hepatitis C virus in treatment with IFN-α plus RBV.

MATERIALS AND METHODS

Patients

Between January 2004 and December 2007, a total of 69 patients with chronic hepatitis (27 women and 42 men, mean age 48 years) aged 32-63 years (median 46 years), were consecutively enrolled in the study (Figure 1).

The patients had to fulfill the following inclusion criteria: alanine aminotransferase (ALT) levels greater than 1.5-fold higher than the upper limit of normal, the presence of anti-HCV antibodies in the serum, HCV-RNA > 1000 copies/mL, and histological modifications in the liver biopsy. Exclusion criteria were: positive test for serum hepatitis B surface antigen, positive test for serum HIV antibodies, negative for HCV antibodies, alcoholic liver disease (daily alcohol consumptions < 20 g/d), and diabetes. The presence of other causes of hepatopathy, decompensated cirrhosis, pregnancy, and known contraindications for Peg-IFN-α or RBV therapy such as hemoglobinopathies, cardiopathy, hemochromatosis, diabetes mellitus, autoimmune diseases, major depression or other severe psychiatric pathological conditions were considered causes for ruling out.

Study design

The study was a prospective, randomized, open-label trial. Eligible patients were randomly assigned to one of the two study treatments in equal proportions by means of a computer-generated table of random numbers. They were divided into two groups (A and B) and they were stratified by HCV genotype (1 *vs* others) and the viremia. Group A received Peg-IFN-α 2b at a dose of 1.5 μg/kg per week for 12 mo intramuscularly, plus daily oral RBV, plus L-carnitine 2 g twice a day. The dose of ribavirin was adjusted to body weight: 800 mg for body weight below 60 kg, 1000 mg when it was between 65 kg and 75 kg, and 1200 mg when it was above 75 kg. Group B received Peg-IFN-α and RBV at the same dosage, way and duration. Patients were evaluated before treatment, 6 mo and 12 mo after the initiation of the therapy. A follow up evaluation was performed 6-mo after the end of the planned treatment. A medical interview and a physical examination were realized for all patients included in the study before starting therapy. Guidelines for discontinuing, interrupting or decreasing the dose of study medication because of adverse events and hematologic or biochemical abnormalities were prespecified in the protocol. Study drug was reduced and discontinued when: hemoglobin values of < 10 g/dL and 8.5 g/dL, absolute neutrophil counts of 0.75×10^9/L and 0.50×10^9/L, and platelet counts of $< 50 \times 10^9$/L and $< 25 \times 10^9$/L respectively. The study protocol was approved by the research ethics committee of Cannizzaro Hospital, Catania, Italy and was performed in accordance with the Declaration of Helsinki principles and the Good Clinical Practice Guidelines[18].

Clinical laboratory tests

A complete routine chemistry (including red cell count, hemoglobin, white cell count, platelets prothrombin time, fasting plasma glucose, blood urea nitrogen, serum creatinine, bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, γ-glutamyl transpeptidase and creatine phosphokinase levels) was performed at every medical visit. Anti-HCV antibodies were evaluated by using second generation enzyme-linked immunosorbent assay ELISA (Ortho-Diagnostic Systems, Raritan NJ, United States) and positive samples were confirmed by immunoblotting (RIBA; Chiron Corporation, Emeryville, CA, United States). Serum HCV

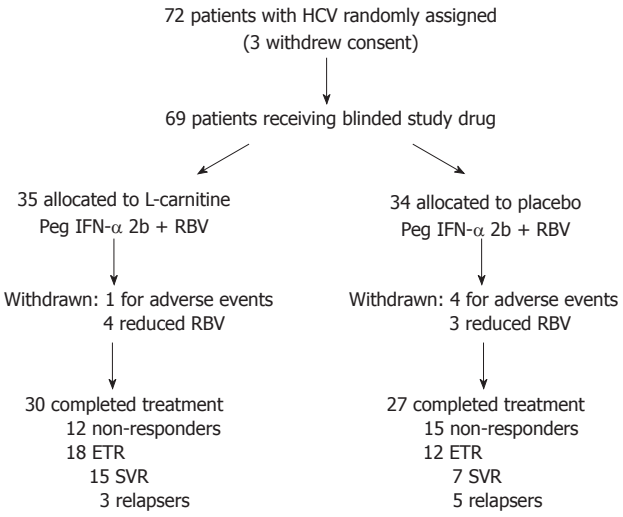

Figure 1 Trial profile of L-carnitine treatment. IFN-α: Interferon α; HCV: Hepatitis C virus; RBV: Ribavirin; SVR: Sustained virological responders; ETR: End-of-treatment responders.

Table 1 Characteristics of the subjects included in the study (mean ± SD)

	[1]Group A (n = 35)	[2]Group B (n = 34)
Mean age (yr)	47.6 ± 4.9	47.1 ± 5.4
Sex (M/F)	22/13	20/14
HCV exposure time (yr)	6.44 ± 4.2	7.08 ± 4.4
BMI (kg/m^2)	27.1 ± 3.1	27.4 ± 2.9
HCV genotype (n)		
1a	3	3
1b	24	25
2a	2	2
3a	6	4
Probable exposure (n)		
Blood transfusion	12	16
Intravenous drug abuse	7	6
Occupational	3	2
Unknown	13	10

There were not significant differences between groups. IFN-α: Interferon α; HCV: Hepatitis C virus; BMI: Body mass index. [1]Group A: Peg IFN-α + RBV + L-carnitine; [2]Group B: Peg IFN-α + RBV.

RNA levels were detected first time by standardized quantitative polymerase chain reaction (PCR) assay, with a lower limit of detection of 50 IU/mL. Then serum HCV RNA levels were measured by standardized quantitative PCR assay with a lower limit of detection of less than 1000 copies/mL, using the amplicor quantitative PCR system (Roche Diagnostic System Inc.-Branchburg, NJ, United States). HCV genotypes and subtypes were identified through a modification of the specific line probe assay (Inno-LiPA system; Innogenetics NV, Zwijnaarde, Belgium) as described by Stuyver *et al*[19]. The HCV genotypes were designated according to the nomenclature proposed by Simmonds *et al*[20].

Histology

Liver biopsy was realized in the 6 mo before the initiation of therapy and 6 mo after the end of treatment. It was obtained using a modified Menghini technique. The specimen was fixed in neutral formaldehyde 4% solution for routine histological processing and evaluation. The Knodell and Ishiak Histological activity index (HAI) score was used to assess the histological grading of the disease[21].

Efficacy and safety assessment

All enrolled patients were included in the intention-to-treat efficacy analysis and patients who received at least one dose of IFN-α plus ribavirin were included in the safety analysis. Data were analyzed by an "intention-to-treat" principle. We considered patients as "sustained virological responders" (SVR) when they showed an undetectable HCV RNA (< 50 IU/mL) in serum at the end of the follow up period. Relapse was defined as undetectable HCV-RNA levels at the end of treatment, but detectable levels during the follow up period. Adverse events were assessed by interviews, laboratory examinations and clinical examinations during treatment. They were graded as mild, moderate and severe on the basis of the WHO score. The treatment was definitively stopped in the case of severe events, such as hematological toxicity, hepatic failure or no compliance. In moderate and mild cases of adverse effects, a dose reduction of 50% was performed, until the resolution of the event, when a full dose was restarted.

Statistical analysis

Means and standard deviations have been used to describe the distribution of continuous variables. Differences in response rates in the two study groups and histological findings between the initial and follow-up liver biopsy specimens were evaluated by paired t test. A P value < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics

A total of 69 patients were included in the study (35 in the Peg-IFN-α plus RBV plus L-carnitine group and 34 in the Peg-IFN-α plus RBV group). Baseline demographic characteristics and histological findings in liver biopsy were similar between the two treatment groups.

The mean time since their chronic hepatitis C infection was comparable. The most frequent viral genotype in patients was 1b. Baseline viremia was parallel in the two groups (Table 1). No significant differences were assessed between the two groups for ALT, aspartate aminotransferase (AST) or fasting plasma glucose.

Effects of Peg-IFN-α plus RBV plus L-carnitine

Effects on biochemical pattern: After 6 and 12 mo and at follow up, we observed a significant decrease in AST (P < 0.001) and ALT (P < 0.001) levels.

Effects on viremia and histological grading of the disease: After 6 and 12 mo and at follow up viremia was significantly reduced (P < 0.001). HAI score was significantly reduced after 12 mo (P < 0.05).

Table 2 Laboratory parameters of subjects included in the study (mean ± SD)

	[1]Group A (n = 35)		[2]Group B (n = 34)	
	Before treatment	After 12 mo	Before treatment	After 12 mo
AST (IU/L)	145 ± 44.2	36.2 ± 12.8[a,d]	136 ± 41.4	59.2 ± 15.4[b,d]
ALT (IU/L)	182.1 ± 46.2	44.2 ± 13.8[b,d]	174.1 ± 42.2	61.8 ± 15.4[b,d]
Bilirubin (mmol/L)	10.7 ± 7.8	10.1 ± 5.6	10.2 ± 9.0	10.1 ± 7.8
Albumin (g/dL)	4.2 ± 0.8	4.2 ± 0.8	4.4 ± 0.8	4.0 ± 0.8[a]
Viremia (× 10^6 copies/mL)	5.44 ± 3.12	1.4 ± 1.1[b,d]	5.32 ± 3.21	2.96 ± 1.9[b,d]
HAI score	10.7 ± 3.1	8.4 ± 2.9[a]	10.5 ± 2.9	9.0 ± 3.0[a]
Hemoglobin (g/dL)	13.1 ± 1.8	12.1 ± 2.7[d]	13.4 ± 1.9	9.9 ± 2.7[b,d]
RBC (× 10^{12}/L)	4.7 ± 0.4	4.4 ± 0.7[a,d]	4.9 ± 0.6	3.8 ± 0.7[b,d]
WBC (× 10^9/L)	7.9 ± 1.8	6.4 ± 0.8[b,d]	7.8 ± 1.8	4.8 ± 0.8[b,d]
Platelets (× 10^9/L)	384 ± 22	298 ± 36[b,d]	412 ± 21	327 ± 24[b,d]

[a]$P < 0.05$, [b]$P < 0.001$, comparison within group A and within group B according to the values before the treatment; [d]$P < 0.001$, groups A *vs* B after treatment. RBV: Ribavirin; HAI: Histological activity index; RBC: Red blood cells; WBC: White blood cells; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; IFN-α: Interferon α. [1]Group A: Peg IFN-α + RBV + L-carnitine; [2]Group B: Peg IFN-α + RBV.

Effects on hematological pattern: After 6 mo red blood cells (RBCs), white blood cells (WBCs) and platelets were significantly reduced ($P < 0.001$); a significant decrease was also observed after 12 mo in RBCs ($P < 0.05$), WBCs ($P < 0.001$) and platelets ($P < 0.001$). At follow up, the decrease was observed only in platelets ($P < 0.001$).

Effects of Peg-IFN-α plus RBV

Effects on biochemical pattern: After 6 mo there was a significant decrease in albumin ($P < 0.05$). After 6 and 12 mo and at follow up we observed a significant decrease in AST ($P < 0.001$) and ALT ($P < 0.001$) levels.

Effects on viremia and histological grading of the disease: Viremia was significantly reduced after 6 mo ($P < 0.05$), after 12 mo ($P < 0.001$) and at the follow up ($P < 0.001$). The HAI score was significantly reduced after 12 mo ($P < 0.05$).

Effects on hematological pattern: After 6 and 12 mo and at follow up RBCs, WBCs and platelets were significantly reduced ($P < 0.001$).

Comparison between treatments

The comparison between the Peg-IFN-α plus RBV plus L-carnitine group and the Peg-IFN-α plus RBV group showed a significantly greater decrease after 6 mo in Hb 0.7 *vs* 2.8 (g/dL; $P < 0.05$), RBCs 0.5 *vs* 1 (× 10^{12}/L; $P < 0.001$), WBCs 0.9 *vs* 3.7 (× 10^9/L; $P < 0.001$) and platelets 82 *vs* 100 (× 10^9/L; $P < 0.001$). After 12 mo there were significant improvements in AST 108.8 *vs* 76.8 (IU/L; $P < 0.001$), ALT 137.9 *vs* 112.3 (IU/L; $P < 0.001$), viremia 4.04 *vs* 2.36 (× 10^6 copies/mL; $P < 0.001$), Hb 1 *vs* 3.5 (g/dL; $P < 0.05$), RBCs 0.3 *vs* 1.1 (× 10^{12}/L; $P < 0.001$), WBCs 1.5 *vs* 3 (× 10^9/L; $P < 0.001$) and platelets 86 *vs* 85 (× 10^9/L; $P < 0.001$). At the end of the follow up, the results confirmed the improvements in AST 90.9 *vs* 69.6 (IU/L; $P < 0.001$), ALT 125.3 *vs* 101.9 (IU/L; $P < 0.001$), viremia 3.64 *vs* 2.34 (× 10^6 copies/mL; $P < 0.001$), Hb 0.3 *vs* 2 (g/dL; $P < 0.05$), RBCs 0.1 *vs* 0.8 (× 10^{12}/L; $P < 0.001$), WBCs 0.3 *vs* 2.3 (× 10^9/L; $P < 0.001$) and platelets 68 *vs* 56 (× 10^9/L; $P < 0.001$) (Table 2). The end treatment responders were 18 *vs* 12 (60% *vs* 44%) and the non responders were 12 *vs* 15 (40% *vs* 50%) (OR 1.65; 95% CI = 0.65-5.37; $P < 0.05$). When comparing the Peg-IFN-α plus RBV plus L-carnitine group and the Peg-IFN-α plus RBV group we observed a significant improvement of SVR in 15 *vs* 7 patients (50% *vs* 25%), while the relapsers were 3 *vs* 5 (10% *vs* 18%) (OR 3.57; 95% CI = 0.65-19.3; $P < 0.001$).

Adverse events

No serious adverse events (WHO grade 3 or 4) have been reported in the two groups. Five patients of the Peg-IFN-α 2b plus RBV treated group and 2 of the other group showed mild psychological disorders such as anxiety, irritability and depression. Furthermore, other side effects registered in both groups were anorexia (12% in Peg-IFN-α 2b plus RBV patients *vs* 18% in Peg-IFN-α 2b plus RBV plus L-carnitine), nausea (20% *vs* 21% respectively), weight loss (14% *vs* 5%), headaches (44% *vs* 40%), fatigue (44% *vs* 25%), myalgia (30% *vs* 20%), musculoskeletal pain (30% *vs* 22%), irritability (18% *vs* 16%), hypertriglyceridemia (34% *vs* 18%), hypercholesterolemia (24% *vs* 8%), and hyperglycemia (12% *vs* 4%). Median Hb concentration significantly fells during the first 3 mo of treatment in the Peg-IFN-α 2b plus RBV group, but remained stable in the Peg-IFN-α 2b plus RBV plus L-carnitine group. The patients treated with Peg-IFN-α 2b plus RBV plus L-carnitine experienced a fall in median hemoglobin concentration from 13.1 g/dL (range 11.8-14.0 g/dL) to 12.1 (range 11.2-14.0 g/dL) at the end of therapy. The patients treated with Peg-IFN-α 2b plus RBV experienced a fall in median hemoglobin concentration from 13.4 g/dL (range 11.4-15.1) to 9.9 g/dL (range 9.1-12.4 g/dL) at the end of therapy. In the Peg-IFN-α 2b plus RBV plus L-carnitine group, 30 patients showed good adherence to their medication and duration of therapy, 2 reduced RBV dose to 1000 mg; 2 reduced RBV dose to 800 mg; and 1 dropped out from the treatment due to headaches. In the Peg-IFN-α 2b plus RBV group, 23 patients showed good adherence to their medication

and duration of therapy; 3 reduced RBV dose to 800 mg; 4 dropped out from the treatment for anemia; 2 reduced RBV dose to 1000 mg; and 2 dropped out from the treatment due to leukopenia.

DISCUSSION

The primary goal of treatment for chronic HCV infection is a sustained virological response. However, a substantial proportion of patients do not have an optimum response to current treatment regimens[22]. In our study, when comparing the Peg-IFN-α plus RBV plus L-carnitine group versus the Peg-IFN-α plus RBV group we observed a significant improvement of sustained virological response in 50% *vs* 25% of patients. L-carnitine is a necessary nutrient factor in energy production and its deficiency is known to decrease energy availability in vital organs. The carnitine content decreases when endogenous synthesis becomes insufficient, and under such conditions carnitine has been beneficial in restoring the level to normalcy[23]. L-carnitine is a natural constituent of higher organisms, in particular cells of animal origin, and its deficiency is usually associated with a failure to thrive or due to recurrent infections[24]. L-carnitine is also reported to inhibit apoptosis and improve the function of the bone marrow progenitors by increasing the number of colony forming units[25]. In patients treated with a placebo, we observed a significant decrease in Hb, in RBCs, in WBCs and in platelets after 6 and 12 mo and at the end of follow up. Decreased Hb levels represent a common side effect of the IFN-α and RBV combination, or the pegylated IFN-α (Peg IFN-α) and RBV combination used to treat HCV infection, with 29% to 36% of treated patients developing anemia. In a recent study, 54% of patients on this regimen experienced Hb decreases of 3g/dL or more from pre-treatment levels[26,27]. In a large clinical trial[28] anemia (defined as Hb < 12 g/dL) resulted in a RBV dose reduction in 22% of patients and, in a community-based setting, anemia resulted in the discontinuation of therapy in 36% of patients. In 3070 patients with HCV genotype 1 treated with RBV plus IFN 2a or 2b the RBV dose was reduced owing to an adverse event in 30.2%[29]. Between 2.1% and 3.8% of patients met the discontinuation criterion[29]. Anemia might become evident in the first several weeks of RBV therapy and might continue for the duration of combination therapy[30,31]. Anemia is a common complication associated with RBV, by both a decrease in erythrocyte precursor production and reduced survival of red blood cells[32]. In our study we observed a significantly greater decrease in hemoglobin and red blood cells in the Peg-IFN-α plus RBV group than the Peg-IFN-α plus RBV plus L-carnitine group[33]. In thalassemic patients, El-Beshlawy *et al*[34] observed a significant increase in blood transfusion interval after L-carnitine therapy. This was previously reported and can be explained by the protective effect of L-carnitine on the red blood cells from oxidative stress and the stabilization to their membranes where latent peroxidative damage has occurred[35,36]. The autoxidation of globin chains and iron overload were the suggested mechanisms for the increased oxidative stress. The counteracting effect of antioxidants on lipid peroxidation and their protective effect against oxidative damage of erythrocytes in β-thalassemia were demonstrated[37]. It has been suggested that L-carnitine may act via stabilization of the red blood cell membrane, thereby increasing the erythrocyte[38]. Relationships between L-carnitine and erythrocyte osmotic fragility, deformability and membrane fluidity have been demonstrated[39,40]. Alternatively, the beneficial effects on anemia may be a result of a reduction in lipid peroxidation[41]. The results of our study showed a greater decrease in white blood cells in the Peg-IFN-α plus RBV group compared to the Peg-IFN-α plus RBV plus L-carnitine group. In 3070 patients with HCV genotype 1, the proportion of patients with neutropenia who met the criterion for Peg IFN dose reduction were: 21.1% receiving Peg IFN-α 2a, 19.4% receiving standard dose Peg IFN-α 2b, and 12.5% receiving low dose Peg IFN-α 2b. Between 2.1 and 5.9% of patients met the discontinuation criterion based on neutropenia[29]. L-carnitine is known to improve neutrophil and macrophage functions, such as chemotaxis and phagocytosis in aged rats, at lower concentrations[16]. Sener *et al*[42] suggested that this compound inhibited leukocyte apoptosis possibly through its free radical scavenging and antioxidant properties. The increase in neutrophil functions, observed after L-carnitine treatment may be attributed to the ability of L-carnitine to increase the activities of glucose-6-phosphate dehydrogenase and myeloperoxidase by L-carnitine[23]. Moreover, preservation of membrane integrity is a vital phenomenon for efficient phagocytosis as well as chemotaxis. The increase in neutrophil functions and organ cell counts observed in aged animals after L-carnitine treatment may also be related to the property of L-carnitine to preserve membrane integrity. L-carnitine is well known to exhibit membrane modulatory effects and thereby preserve cellular membrane integrity[43]. In a recent study, Poynard *et al*[6] reported thrombocytopenia in 20% of HCV patients treated with Peg-IFN-α plus RBV. The results of our study showed a significantly greater decrease in platelet count in the Peg-IFN-α plus RBV group compared to the Peg-IFN-α plus RBV plus L-carnitine group. Some studies indicate that L-carnitine modulates platelet functions and production[44-46]. L-carnitine acts by reacting with fatty acids and this mechanism may affect the biological function of cells. Pignatelli *et al*[47] showed that carnitine affects arachidonic acid metabolism and, in turn, blood platelet functions. *In vitro* studies by Saluk-Juszczak *et al*[17] demonstrated that L-carnitine may modulate platelet activation through antioxidant mechanisms and the inhibition of the arachidonic acid cascade. Arachidonic acid has a key role in the activation of blood platelets and in the formation of free radicals via the stimulation of NADPH oxidase in these cells. L-carnitine interfering with arachidonic acid metabolism has a direct effect on platelet activation and oxidative stress. L-carnitine inhibits platelet superoxide anion formation elicited

by arachidonic acid and collagen, but it has no effect on thrombin-induced platelet aggregation[47,48]. The well established beneficial effects of L-carnitine (including modulation of cell energy production, fat metabolism, erythropoiesis, leucopoiesis and thrombocytopoiesis) strongly suggests that supplementation of these nutrients may be useful in patients treated for HCV even if our study was conducted on a relatively small sample size. L-carnitine treatment offers the possibility of tailoring treatment to patients and selecting the treatment duration that ensures the best chance of achieving a SVR while preventing overtreatment.

COMMENTS

Background

Interferon α (IFN-α), in combination with ribavirin (RBV), represents the most efficacious therapeutic tool in the management of chronic hepatitis C, but the frequency of hematologic adverse events including thrombocytopenia, anemia and neutropenia during treatment is high. These adverse events most frequently lead to drug discontinuation or to dose modifications.

Research frontiers

Recently L-carnitine has been proposed as a potential adjuvant treatment to improve anemia, thrombocytopenia, leukopenia and immunological function. L-carnitine is also reported to inhibit apoptosis and improve the function of the bone marrow progenitors by increasing the number of colony forming units.

Innovations and breakthroughs

The study showed a significantly greater decrease in platelets, and red and white cells in the Peg-IFN-α plus RBV group compared to the Peg-IFN-α plus RBV plus L-carnitine group. L-carnitine treatment may offer the possibility of tailoring treatment to patients and selecting the treatment duration that ensures the best chance of achieving a sustained virological response while preventing overtreatment.

Applications

The well established beneficial effects of L-carnitine, including modulation of cell energy production, fat metabolism, erythropoiesis, leucopoiesis and thrombocytopoiesis strongly suggested that supplementation of these nutrients may be useful in patients treated for HCV.

Peer review

Although being small in sample number, this is a sound clinical trial with promising results. This is a straight and well conducted investigation. The manuscript is well written.

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