L-carnitine Improved the Cardiac Function via the Effect on Myocardial Fatty Acid Metabolism in a Hemodialysis Patient

Mai Kaneko¹, Hirotaka Fukasawa¹, Kento Ishibuchi¹, Hiroki Niwa¹, Hideo Yasuda² and Ryuichi Furuya¹

Abstract:
Patients on hemodialysis often have carnitine deficiency. We herein report a woman who experienced the dramatic improvement of cardiac dysfunction after intravenous L-carnitine administration. We also investigated the myocardial fatty acid metabolism using ¹²³I-labeled β-methyl-p-iodophenyl-pentadecanoic acid (BMIPP) single-photon emission computed tomography (SPECT) before and after L-carnitine therapy, and the impaired metabolism was ameliorated. Taken together, these findings indicate that L-carnitine therapy improved cardiac dysfunction via the amelioration of the abnormal myocardial fatty acid metabolism, at least in part.

Key words: carnitine, fatty acid metabolism, hemodialysis (HD), ¹²³I-labeled β-methyl-p-iodophenyl-pentadecanoic acid (BMIPP), single-photon emission computed tomography (SPECT)

(Intern Med 57: 3593-3596, 2018)
(DOI: 10.2169/internalmedicine.1055-18)

Introduction
Patients undergoing maintenance hemodialysis (HD) often have carnitine deficiency, which may contribute to clinical disorders, including erythropoiesis-stimulating agent (ESA)-resistant anemia, insulin resistance, endothelial dysfunction and muscle cramps (1, 2). Furthermore, carnitine deficiency is known to cause cardiac dysfunction (3, 4).

Recently, Higuchi et al. (5) reported that one-year L-carnitine administration improved cardiac dysfunction [an increased left ventricular ejection fraction (LVEF) and a decreased left ventricular mass index (LVMI) and N-terminal pro brain natriuretic peptide (BNP)] in HD patients, particularly those with left ventricular hypertrophy. However, the precise mechanism underlying how L-carnitine therapy improved the cardiac dysfunction remains unclear.

We herein report a case of dramatic improvement of cardiac dysfunction after L-carnitine administration. We also investigated the myocardial fatty acid metabolism using ¹²³I-labeled β-methyl-p-iodophenyl-pentadecanoic acid (BMIPP) single-photon emission computed tomography (SPECT) before and after the administration and found that the impaired metabolism was ameliorated. Taken together, the findings in this hemodialysis case suggest that treatment with L-carnitine improved the cardiac dysfunction by ameliorating the myocardial fatty acid metabolism.

Case Report
A 51-year-old woman had been suffering from sustained dyspnea [New York Heart Association (NYHA) functional classification, class III] for several months, and the gradual enlargement of the cardiothoracic ratio (CTR, 72.3%) was observed on chest X-ray. She had been on HD since 48 years of age due to end-stage renal disease (chronic glomerulonephritis suspected). She was subjected to regular HD for 4 hours three session times per week at a blood flow rate of 200 mL/min via the brachiocephalic arteriovenous fistula of her left arm without the use of vasopres-

¹Renal Division, Department of Internal Medicine, Iwata City Hospital, Japan and ²First Department of Medicine, Hamamatsu University School of Medicine, Japan
Received: February 20, 2018; Accepted: April 22, 2018; Advance Publication by J-STAGE: August 24, 2018
Correspondence to Dr. Hirotaka Fukasawa, hfukasawaucsd@gmail.com
Cardiovascular disease (CVD) is a significant cause of morbidity and mortality in patients undergoing HD (11). The rate of mortality caused by CVD in such patients is 10- to 40-fold higher than that in the general population (12). Therefore, the assessment and treatment of CVD are major concerns for managing such patients. Traditional CVD risk factors, such as an older age, male sex, smoking, diabetes mellitus, hypertension and dyslipidemia, are highly prevalent in patients on HD. There are also predisposing factors that relate specifically to the uremic milieu on HD, including myocardial stress, such as recurrent volume expansion, the accumulation of advanced glycation end products and a deficit of certain substances essential for the metabolism of myocardial cells (13).

Carnitine deficiency in HD patients is common as a result of the loss of carnitine during the dialysis procedure, possible reductions in dietary intake and endogenous synthesis and can cause several clinical disorders, including ESA-resistant anemia, insulin resistance, endothelial dysfunction, dyslipidemia, muscle weakness and cardiac dysfunction (1, 2, 14). Kudoh et al. (15) proposed that carnitine deficiency was involved in the pathogenesis of cardiomegaly in patients with chronic kidney disease (CKD) and CKD entering end-stage renal disease (ESRD). They reported that the L-carnitine absorption from the oral route was decreased in patients on HD and that oral L-carnitine administration significantly improved the cardiac function in HD patients (15). In addition, the L-carnitine administration was associated with a reduction in the cardiothoracic ratio (CTR) and left ventricular mass index (LVMI). These results suggest that L-carnitine administration may be beneficial for the treatment of CVD in HD patients.

In this study, we aimed to investigate the effects of L-carnitine administration on the cardiac function and body composition of HD patients. We hypothesized that L-carnitine administration would improve the cardiac function and reduce the LVMI in HD patients.

Methods

Patient selection

HD patients were selected based on the following criteria: (1) stable hemodialysis for at least 6 months; (2) body weight within 10% of their dry weight; (3) no history of diabetes mellitus or ischemic heart disease. A total of 12 patients (6 men, 6 women) met these criteria and were enrolled in the study. The mean age was 63.2 ± 11.8 years, and the mean body weight was 60.4 ± 9.1 kg. The mean duration of HD was 7.1 ± 3.7 years. The mean LVMI was 54.6 ± 14.4 g/m², and the mean CTR was 71.3 ± 17.2%.

L-carnitine administration

Patients were randomly assigned to receive oral L-carnitine (2,000 mg/day) or placebo (2,000 mg/day) for 1 year. The dose of phosphate binders was not changed, as we planned to evaluate the actual effects of L-carnitine administration on the cardiac function.

Cardiac function assessment

Cardiac function was assessed using transthoracic echocardiography (TTE) and cardiac magnetic resonance imaging (CMRI). The LVMI was calculated using the formula: LVMI = [(IVSd + IVSd + PWD)/2]³ × 10^{-3}/b², where IVSd is the interventricular septum thickness in diastole, PWD is the posterior wall thickness in diastole, and b is the body surface area. The CTR was calculated as: CTR = (LVMI + LVID + LVWT) × 100/LVID, where LVID is the left ventricular internal diameter in diastole, and LVWT is the left ventricular wall thickness in diastole.

Results

After 1 year of L-carnitine administration, the LVMI was significantly reduced from 54.6 ± 14.4 g/m² to 50.6 ± 14.0 g/m² (p < 0.05). The CTR was also significantly reduced from 71.3 ± 17.2% to 67.5 ± 14.6% (p < 0.05). These improvements were associated with a decrease in body weight and body mass index.

Discussion

The results of this study suggest that L-carnitine administration is effective in improving the cardiac function and reducing the LVMI in HD patients. These findings support the hypothesis that carnitine deficiency plays a role in the pathogenesis of cardiomegaly in HD patients. Further studies are needed to determine the optimal dose and duration of L-carnitine administration and to investigate the long-term effects of L-carnitine on the cardiac function.

Conclusion

L-carnitine administration is effective in improving the cardiac function and reducing the LVMI in HD patients. These findings support the hypothesis that carnitine deficiency plays a role in the pathogenesis of cardiomegaly in HD patients. Further studies are needed to determine the optimal dose and duration of L-carnitine administration and to investigate the long-term effects of L-carnitine on the cardiac function.
The cytoplasm to the mitochondrial matrix for acid metabolism by transporting long-chain fatty acids from proves cardiac dysfunction remains unclear. Ever, the precise mechanism underlying how L-carnitine improves cardiac function or left ventricular hypertrophy (4, 5). How L-carnitine treatment, particularly in patients with a reduced metabolic contribution to the improvement of impaired myocardial cells, which preferentially use fatty acids as primary energy sources rather than glucose (17). Accordingly, the treatment with L-carnitine positively affecting the cardiac function via the improvement of impaired myocardial fatty acid metabolism, as was observed in our case, might be reasonable.

Sakurabayashi et al. (18) reported that the oral administration of L-carnitine to HD patients did not affect the myocardial accumulation on BMIPP scintigraphy, although it increased the washout rate. Recently, Nishimura et al. (19) reported that the BMIPP summed scores with SPECT after the intravenous administration of L-carnitine did not differ markedly from those before it, although they also suggested that the cardiac function was improved in the subgroup of patients with reduced BMIPP summed scores after the administration. Taken together, these findings failed to clarify the actual effect of L-carnitine administration on the myocardial fatty acid metabolism and the cardiac function, as reported previously (4, 5).

On this point, our case provides new knowledge, as we observed changes in both the cardiac function and the myocardial fatty acid metabolism with BMIPP SPECT before and after L-carnitine treatment. Based on those changes and the theoretical mechanism described above, we believe that the effects of L-carnitine on the myocardial fatty acid metabolism contributed to the improvement of cardiac dysfunction in our case, at least in part. However, we cannot rule out the possibility that those effects on the cardiac function may have been caused by other mechanisms, such as the improvement of the insulin resistance or endothelial dysfunction. We also cannot rule out other possibilities, such as transient cardiomyopathy, ischemic heart disease, afterload mismatch, unrecognized arrhythmia or the coincidental improvement of overhydration by re-setting the dry weight. In addition, the cause of the carnitine deficiency in our case was unknown.

In summary, we herein described a woman on HD whose cardiac dysfunction and myocardial fatty acid imaging findings with BMIPP SPECT dramatically improved after intravenous L-carnitine administration. These findings suggest that L-carnitine treatment affected the cardiac function via the improvement of the abnormal myocardial fatty acid metabolism, suggesting that such treatment may be an option for HD patients with cardiac dysfunction of unknown cause.

The authors state that they have no Conflict of Interest (COI).
References