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Original Research Article

Effect of combined use of L-carnitine and hemodialysis on clinical efficacy and quality of life of uremic patients

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Abstract

Purpose: *To investigate the clinical efficacy of combined use of L-carnitine and hemodialysis in the treatment of uremic patients, and its effect on their quality of life.*
Methods: *A total of 160 uremic patients who were admitted to Lujiang County People's Hospital from November 2018 to August 2020 were selected and divided equally into dialysis group (hemodialysis), and combined group (L-carnitine + hemodialysis). Some clinical indices and parameters, including safety profile, National Institutes of Health Stroke Scale (NIHSS) score, CD4+ and CD4+/CD8+, and plasma protein levels were evaluated for both study groups.*
Results: *Patients treated with L-carnitine + hemodialysis in the combined group resulted in significantly higher clinical treatment effectiveness than those in the dialysis group ($p < 0.05$). However, safety profiles were comparable in the two groups ($p > 0.05$). No significant difference in NIHSS score between the two groups before treatment, but L-carnitine + hemodialysis led to a better NIHSS score than in the dialysis group after treatment ($p < 0.05$). However, there were better levels of CD4+ and CD4+/CD8+ in the combined group than in the dialysis group ($p < 0.05$). Similarly, although pre-treatment plasma protein levels in the two groups were comparable, there were significantly lower plasma protein levels in the combined group than in the dialysis group post-treatment ($p < 0.05$).*
Conclusion: *The combination of L-carnitine and hemodialysis in the treatment of uremia patients improves the clinical management of the patients, enhances their quality of life, and shows good safety profile. However, further clinical trials should be carried out prior to the application of the combined treatment in clinical practice.*

Keywords: *L-carnitine, Hemodialysis, Uremia, Quality of life, Clinical efficacy*

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INTRODUCTION

Uremia is a clinical syndrome consisting of various renal diseases that lead to progressive and irreversible decline in renal function, ultimately resulting in complete loss of renal function and metabolic disorders [1,2]. Uremia encompasses the signs and symptoms of advanced renal failure. Anorexia, edema, disturbance of consciousness, and vomiting are the main clinical manifestations of the disease. Uremia results in disturbance in water and electrolyte metabolism, leading to acid-base imbalance, and toxic consequences on the heart,

lung, muscle, blood, and nerves, all of which impose tremendous threats on the health of patients [3,4]. Hemodialysis is often used to manage the disease in the clinic. The mechanism involves the use a hemodialysis machine to remove the metabolic wastes from the blood so as to maintain normal levels of water, electrolytes and acid-base balance [5,6]. Hemodialysis is an artificial method of purifying the blood. However, in this process, water, electrolytes and nutrients in the blood would also be excreted from the body, making uremic patients prone to malnutrition. This underlines the need for conducting studies to produce decisive guide for the use of hemodialysis in the treatment of uremia [7,8]. L-Carnitine, a natural substance in the human body, improves myocardial function and immune function. It produces mild adverse reactions, and it can be excreted along with human urine [9]. Accumulating evidence show that the use of L-carnitine in combination with hemodialysis is beneficial to uremic patients with respect to mitigation of clinical symptoms, and it produces good effectiveness and safety profiles [10]. However, there is paucity of rigorous evidence-based trial to verify the overall efficacy of the combined treatment. To fill the gap, this study was undertaken to investigate the clinical efficacy of L-carnitine and hemodialysis in the treatment of uremic patients, and its impact on their quality of life.

METHODS

Participants

A total of 160 uremic patients hospitalized in Department of Renal Endocrinology, Lujiang County People's Hospital, from November 2018 to August 2020 were enrolled in this study and equally assigned to two groups: combined treatment group (L-carnitine in combination with hemodialysis) and hemodialysis group (hemodialysis). It is comprised of 49 males and 31 females in the dialysis group aged 25 to 76 years, with average age of 51.73 ± 9.78 years. The duration of uremia was 6 to 23 weeks (mean duration = 15.21 ± 4.77 weeks), and the duration of hemodialysis was 31 to 55 months (mean duration = 41.28 ± 7.62 months). The dialysis group is comprised of 50 males and 30 females in the dialysis group, in the age range of 25 - 76 years, (mean age, 51.88 ± 9.97 years), uremia duration of 6-23 weeks (mean duration, 15.28 ± 4.53 weeks, and hemodialysis duration of 31-55 months (mean duration = 41.56 ± 7.47 months). The baseline data were homogenous with respect to gender, age, duration of uremia and duration of hemodialysis between the two groups, as shown in Table 1.

Inclusion and exclusion criteria

Eligible participants who met the criteria for clinical diagnosis of uremia, those who did not use iron supplements within one month before the study, and patients who provided written informed consent either directly or through family members, were included in the study.

Patients who were allergic to the drugs used in the study, those with mental illness, nausea and tumor, and patients who were uncooperative or had poor compliance, were excluded from the study.

Treatments

Following ethical approval, this study was conducted in strict accordance with Helsinki Declaration [11]. Patients in the dialysis group were treated with hemodialysis. A hemodialysis machine (Fresenius 4008S, Germany; product registration number: National Machinery Injection 20183451981) was used to perform hemodialysis on the patients at a dialysis rate of 300 mL/min and a dialysate flow rate of 500 mL/min.

Dialysis was performed once every 4 h, 3 times a week, for 6 months [11]. Patients in the combined group were treated with L-carnitine in combination with hemodialysis. L-Carnitine injection (Shandong Qidu Pharmaceutical Co. Ltd.; National Medicine Zhunzi H20113540;

Table 1: Baseline data for uremic patients [n) %)]

Variable	Dialysis group (n=80)	Combined group (n=80)	t/χ^2	*P*-value
Gender			0.026	0.871
Male	49	50		
Female	31	30		
Mean age (years)	51.73 ± 9.78	51.88 ± 9.97	-0.096	0.924
Duration of uremia (weeks)	15.21 ± 4.77	15.28 ± 4.53	-0.095	0.924
Duration of hemodialysis (months)	41.28 ± 7.62	41.56 ± 7.47	-0.235	0.815

specification: 1g/ampule) was mixed with 25 mL of physiological saline, and injected intravenously, 3 times a week for 6 months.

Before dialysis, the nurses educated the patients about their health. During the process, the nurses maximized the success of a one-time puncture. When pulling the needle, the nurse controlled the direction and strength of the needle to avoid excessive force and prevent the patient's internal fistula from a secondary injury.

Evaluation of parameters/indices

Clinical/treatment effectiveness

This was categorized into three: markedly effective, effective and ineffective. If the patient's condition was stable, and the patient did hemodialysis on time, and took medications properly, the treatment outcome was adjudged markedly effective. If the patient had occasional symptoms of uremia, but the patient performed hemodialysis on time and took prescribed drugs properly, the treatment outcome was deemed effective. However, if the patient's condition did not improve or even got worse, the treatment was regarded as ineffective.

Adverse reactions

Adverse reactions during treatment, comprising dizziness, nausea, dry mouth, and drowsiness, were recorded for the two groups.

National Institutes of Health Stroke Scale (NIHSS) score

The NIHSS score scale developed by the National Institutes of Health for assessment of the degree of neurological deficit in stroke was utilized in this study. The NIHSS score was based on the patient's level of consciousness, command coordination, eye movement, visual field defect, degree of paralysis of facial expression, degree of limb movement disorder, ataxia, and language expression, amongst other parameters. The lower the patient's NIHSS score, the better the patient's state.

Ability of daily living (ADL) score

The ADL scale was employed to assess the ability of daily living in each group. The scale has a full score of 100 points. The higher the patient's ADL score, the better the patient's state.

Immune function

The immune function indexes measured were T cell subsets CD4+, CD8+, and CD4+/CD8+ ratio. 2 mL of fasting venous blood was collected from each patient before and after treatment, and the levels of immune function indexes were determined using alkaline phosphatase staining method.

Plasma protein levels

(i) *Transferrin*: The immunoturbidimetric method was used to determine transferrin, and its concentration was measured based on rate of binding of the antigen to the antibody i.e., the kinetics of combination of the anti-human transferrin antibody and the transferrin in the sample. The ARRAY 360 and IMMAGE special protein analyzers and supporting reagents for the determination of transferrin were purchased from Beckman.

(ii) *Total protein*: Plasma total protein was determined using Biuret colorimetry

(iii) *Serum albumin*: Bromocresol green method was used for the determination of serum albumin. A complex was formed between albumin and bromocresol green at pH 4.2, and the solution changed from unbound yellow to blue-green. The absorbance of the complex at 628 nm was proportional to albumin concentration. The albumin concentration was extrapolated from an albumin standard calibration curve.

Statistical analysis

All data analyses were performed with SPSS 20.0 software, while GraphPad Prism 8 was used for plotting graphs. Measurement data are expressed as mean ± standard deviation (SD), and paired comparison was done with independent sample *t*-test. Count data are presented as numbers, and the inter-group comparison was done by chi squared (χ^2) test. All statistical calculations were two-sided, with an α value of 0·05.

RESULTS

Treatment efficacy/effectiveness

There was significantly higher treatment effectiveness in the combined group than in the dialysis group ($p < 0.05$). These results are shown in Table 2.

Table 2: Comparison of clinical treatment effectiveness {n (%), N = 160}

Group	Markedly effective (n)	Effective (n)	Ineffective (n)	Total effectiveness [n (%)]
Dialysis	18	47	15	65（81%）
Combined	27	51	2	78（98%）
χ^2	-	-	-	11.123
P-value	-	-	-	0.001

Table 3: Adverse reactions {n (%)}

Group	Dizziness (n)	Nausea (n)	Dry mouth (n)	Lethargy (n)	Total {n (%)}
Dialysis	2	1	1	1	5（6%）
Combined	2	1	2	1	6（8%）
χ^2	-	-	-	-	0.098
P-value	-	-	-	-	0.755

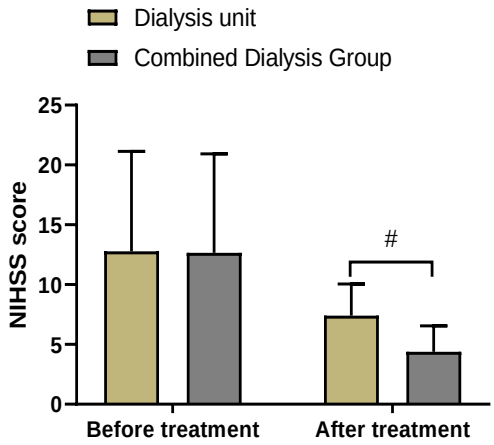

Figure 1: NIHSS scores in the two groups. Values are mean ± SD; #$p < 0.05$

Adverse reactions

The safety profiles of the two groups were comparable as shown in Table 3.

NIHSS scores

The NIHSS score did not differ between the two groups preoperatively ($p > 0.05$). However, post-treatment NIHSS score was significantly better in the combined group than in the dialysis group ($p < 0.05$; Figure 1).

ADL scores

Before treatment, the ADL score was similar in the two groups, but the ADL score in the combined group was superior to that in the dialysis group postoperatively ($p < 0.05$). These results are presented in Figure 2.

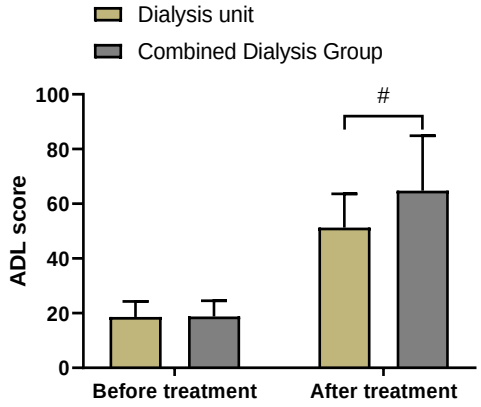

Figure 2: ADL scores in the two groups. Values are mean ± SD; #$p < 0.05$

Immune function indices

Preoperatively, the levels of T cell subsets, i.e., CD4+ and CD8+, and CD4+/CD8+ ratio did not differ significantly between the two groups ($p > 0.05$). However, treatment in the combined group resulted in better levels of CD4+ and CD4+ and CD4+/CD8+ ratio than in the dialysis group ($p < 0.05$; Table 4).

Plasma protein levels

Before treatment, the plasma protein levels in the two groups were similar ($p > 0.05$). However, post-treatment levels of plasma proteins were significantly higher in the combined group versus the dialysis group ($p < 0.05$; Table 5).

DISCUSSION

The non-specific symptoms of early uremia, such as fatigue and back pain lead to difficulty in diagnosing the disease at the early stage [12]. At present, there are clinical methods to slow down

Table 4: Comparison of levels of immune function indexes (mean ± SD, N = 80)

Group	CD4+ (%)		CD8+ (%)		CD4+/CD8+	
	Before treatment	***After treatment***	***Before treatment***	***After treatment***	***Before treatment***	***After treatment***
Dialysis	29.34 ± 1.28	35.42 ± 1.12	29.77 ± 1.38	27.47 ± 1.31	1.03 ± 0.42	1.32 ± 0.27
Combined	29.27 ± 1.25	39.52 ± 1.09	29.69 ± 1.34	27.61 ± 1.22	1.01 ± 0.45	1.48 ± 0.26
t	0.35	-23.465	0.372	-0.7	0.291	-3.818
P-value	0.727	＜0.001	0.71	0.485	0.771	＜0.001

Table 5: Comparison of plasma protein levels (mean ± SD, N = 80))

Group	Transferrin (mg/L)		Total protein (g/L)		Albumin (g/L)	
	Before treatment	***After treatment***	***Before treatment***	***After treatment***	***Before treatment***	***After treatment***
Dialysis	1166.28±78.72	1682.34 ± 85.56	65.17 ± 7.04	68.47 ± 6.77	34.29 ± 3.22	37.28 ± 3.11
Combined	1166.35±78.69	2279.78 ± 99.63	65.12 ± 7.00	78.54 ± 13.26	34.31 ± 3.17	45.31 ± 5.29
t	-0.006	-40.69	0.045	-6.05	-0.04	-11.704
P-value	0.995	<0.001	0.964	<0.001	0.968	<0.001

the progression of kidney failure, but complete treatment can only be achieved by replacing the kidney. The clinical treatment of uremia involves mainly hemodialysis which is largely due to the shortage of donor kidneys [13]. Due to multiple side effects and impairments of quality of life, the efficacy of hemodialysis remains far from satisfactory [14]. Therefore, there is need for newer treatment options for uremia so as to alleviate the suffering of patients and improve their quality of life.

Several studies have described the total clinical treatment effectiveness and adverse reactions of L-carnitine when used in combination with hemodialysis in the treatment of uremic patients. These studies have certain repeatability and limitations. On the basis of previous research, the present study used combination of hemodialysis and L-carnitine to treat uremia, and expanded the research scope by focusing on its impact on patients' immune function, quality of life, and plasma protein levels [15].

According to our results, the clinical treatment effectiveness in patients in the combined group was significantly better than that of the patients in the dialysis group, but the incidence of adverse reactions was similar in the two groups. These results indicate that L-carnitine in combination with hemodialysis was superior to the use of only hemodialysis in treatment of uremia, and it had good safety profile. L-carnitine used in combination with hemodialysis had higher clinical safety. After receiving hemodialysis, the quality of life of patients with uremia is compromised. Not only does this drawback counter the treatment effect, it also causes psychological problems for the patient, and an unacceptably high burden on the patient's family members.

Comparison of NIHSS scores, ADL scores and levels of immune function indices between the two groups of patients revealed better NIHSS score, ADL score and CD4+ and CD4+/CD8+ ratio in the combined group than in the dialysis group. These results indicate that L-carnitine effectively enhanced immune function of the patients, and improved their quality of life. These outcomes might be attributed to the fact that L-carnitine enhanced the immune function of patients, thereby reducing the side effects of hemodialysis, and improving the quality of life of patients [16].

L-Carnitine is an important endogenous compound which is synthesized *in vivo*. Its basic function is to carry long-chain fatty acids during beta-oxidation for energy generation. It has been suggested that the combination of hemodialysis treatment with application of L-carnitine treatment enhances cellular energy metabolism, improves cellular function, and reduces the occurrence of various adverse reactions in uremic patients [17]. In addition, it has been reported that, compared with sole hemodialysis treatment, the combined application of L-carnitine and hemodialysis helped patients improve their nutritional indicators such as transferrin, total protein and albumin [18].

The present study compared the plasma protein levels of the two groups of patients, and showed that L-carnitine and hemodialysis was associated with better plasma protein levels. These results suggest that L-carnitine may help uremic patients increase their body plasma protein levels, thereby promoting recovery.

The findings of this study suggest that the use of L-carnitine and hemodialysis may improves clinical treatment effectiveness and enhances

quality of life of uremic patients. Moreover, the combined treatment shows acceptable safety profile. Therefore, further clinical trials are required prior to use in clinical practice.

DECLARATIONS

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Ethical approval

The study was reviewed and approved by the ethics committee of Lujiang County People's Hospital, China.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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