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Effect of levocarnitine plus iron sucrose on nutritional status and life cycle in uremic patients with renal anemia

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Abstract: Research team believes that Levocarnitine (L-carnitine) combined with Iron sucrose (IS) has a more significant positive effect on the nutritional status and lifespan of uremic patients with renal anemia and has carried out research and demonstration based on this. First, research team selected 90 uremic patients with renal anemia admitted to our hospital from February 2019 to February 2022 and randomized them to an experimental group (n=45) and a control group (n=45) that were given L-carnitine+IS and L-carnitine, respectively. The clinical efficacy and adverse reactions of the two groups of patients were counted and fasting venous blood was collected before and after treatment to test nutrient proteins, calcium and phosphorus metabolism and renal function. In addition, 1-year prognostic follow-up was performed to count the prognostic survival of the patients. The results of the study showed that the clinical efficacy of the experimental group was better than that of the control group and the nutritional protein, calcium and phosphorus metabolism and renal function were better after treatment ($P<0.05$), but there was no difference in the incidence of adverse reactions between the two groups ($P>0.05$). Prognostic follow-up showed that there was no difference in the prognostic overall survival rate between the two groups ($P>0.05$), but the median survival of the experimental group was prolonged compared with the control group ($P<0.05$). In conclusion, L-carnitine combined with IS effectively ameliorated the anemia status of patients, improved their nutritional status and prolonged their median survival.

Keywords: Iron sucrose, levocarnitine, life cycle, nutritional status, Uremia

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INTRODUCTION

Uremia is an end-stage manifestation of renal failure. At this time, the patient's renal function has usually completely lost its normal function, resulting in serious disturbances of water-electrolyte balance and acid-base equilibrium as well as renal endocrine dysfunction, accompanied by a large number of urinary retention of metabolic end products and toxic substances in the body, carrying a high risk of mortality (Meijers *et al.*, 2024). Statistics show that the incidence of chronic renal failure among people over 50 years of age worldwide is about 1.7%, of which about 38% eventually develop into uremia, with a 5-year mortality rate exceeding 60% (Abdel-Kader, 2022; He & Xie, 2021). Hemodialysis remains the main way to save the lives of uremic patients at present and the mechanism is to replace the kidneys with machinery to complete the necessary metabolism of the human body (Kashani *et al.*, 2023). However, dialysis requires patients to maintain a long-term low-protein diet, which is easy to cause malnutrition and metabolic disorders (Boyer & Niaudet, 2022), affecting therapeutic efficacy while increasing the risk of other high-risk complications and infections, among which renal anemia is the most common (Michael *et al.*, 2022).

Levocarnitine (L-carnitine) is the main clinical drug to improve resilience and prolong the life cycle of erythrocytes, making it very common in the treatment of anemia (Abe *et al.*, 2021). However, recent studies have suggested that L-carnitine alone is difficult to completely improve renal anemia in uremic patients and there is a high possibility of recurrence (Calo *et al.*, 2012). Therefore, other combined medication schemes need to be found. Iron sucrose (IS) is an excellent iron supplement that has a positive impact on human hematopoietic function (Macdougall *et al.*, 2020). Meanwhile, iron, as one of the essential nutrients for the human body, is also one of the important links involved in immune and antioxidant functions (Yan *et al.*, 2023).

We hypothesize that L-carnitine combined with IS may have a better effect in the treatment of uremic patients with renal anemia. However, there is still little research to support our view. In this study, we will provide new reference and guidance for the future treatment of uremia by observing the effect of L-carnitine combined with IS on the nutritional status and life cycle of uremic patients with renal anemia.

MATERIALS AND METHODS

Study population

This study was conducted in Shaanxi Provincial Nuclear Industry 215 Hospital, Xianyang, Shaanxi, China. We selected 90 uremic patients with renal anemia admitted to Shaanxi Provincial Nuclear Industry 215 Hospital from February 2019 to February 2022 and randomized them to an experimental group (n=45) and a control group (n=45) that were given L-carnitine+IS and L-carnitine, respectively. In the control group, 34 males, 11 females;

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mean age (64.40±6.54) years; mean time on dialysis (10.44±3.73) months; mean body mass index (BMI) (21.03±1.67) kg/m^2; 21 diabetic nephropathies, 8 hypertensive nephropathies, 14 glomerulonephritis and 2 other cases. In the experimental group, 30 males, 15 females; mean age (66.22±5.68) years; mean time on dialysis (10.44±3.29) months; mean BMI (20.89±1.41) kg/m^2; diabetic nephropathy in 24 cases, hypertensive nephropathy in 5 cases, glomerulonephritis in 15 cases and other in 1 case. The Ethics Committee of Shaanxi Provincial Nuclear Industry 215 Hospital ratified the research (k2019205) and all the subjects signed informed consent. In addition, the research was conducted in strict accordance with *the Declaration of Helsinki*.

Inclusion criteria: Patients with uremia diagnosed clinically and renal anemia during hemodialysis treatment; patients who have contraindications to the treatment means and drugs used in this research; patients with complete clinical records who follow the doctor's advice. Exclusion criteria: Serious diseases of other vital organs; allergies to the drugs in this study; use of iron supplements before enrollment; hepatitis, hematological diseases and infectious diseases; mental or cognitive disorders.

METHODS

All patients underwent maintenance hemodialysis, 4 hours a time, 2-3 times a week. In addition, human erythropoietin for injection (Shenyang Sunshine Pharmaceuticals Co., Ltd., S19980074) was given subcutaneously, 120-150 U/kg/week; the dosage was adjusted according to the patient's hemoglobin (Hb), with a reduction of 25% when Hb reached 110 g/L. Furthermore, 1 g L-carnitine injection (Changzhou Pharmaceutical Factory Co., Ltd., H20000543) + 20 mL sodium chloride injection (0.9%) and administered intravenously and slowly after each hemodialysis session for more than 3 min. On this basis, patients in the experimental group were treated with IS. 100 mg IS injection (Nanjing Hencer Pharmaceutical Co., Ltd., H20046043) + 100 mL sodium chloride injection (0.9%) for intravenous administration 50 min before the end of hemodialysis, once a week for more than 30 min. Both groups of patients received continuous treatment for 3 months.

Clinical efficacy evaluation

The efficacy evaluation was based on the guidelines for the treatment of renal anemia in uremia (Avdonin *et al.*, 2023): An Hb increase of >30g/L and a hematocrit (Hct) increase of ≥ 10% after treatment are considered markedly effective; an Hb increase of ≥15g/L and an Hct rise of ≥5% are effective; Hb increase <15g/L and Hct increase <5% are ineffective.

Follow-up for prognosis

All patients were followed up for one year in the form of regular reviews. Their prognostic survival was recorded and the survival curves were drawn.

Endpoints

(1) The clinical efficacy and adverse reactions. (2) Fasting venous blood was collected from patients before and after treatment. Albumin (ALB), transferrin (TRF), total protein (TP), immunoreactive parathyroid hormone (iPTH), calcium (Ca), phosphate (P), serum creatinine (Scr) and blood urea nitrogen (BUN) were detected with an automatic biochemical analyzer, blood/urine creatinine were detected and the creatinine clearance rate (Ccr; Ccr= blood creatinine × urine volume per minute/blood creatinine) was calculated. Serum ferritin (SF) was detected by a hematology analyzer. Enzyme-linked immunosorbent assay was used to measure fibroblast growth factor-23 (FGF-23). (3) Prognostic survival was recorded and median survival was calculated.

STATISTICAL ANALYSIS

This study used SPSS 24.0 software for statistical analysis and GraphPad 9.0 software for graphic drawing. The comparison of counting data [n(%)] used chi-square tests. Measurement data ($\bar{\chi}$±s) were compared by independent sample t-tests and paired t-tests. The survival rate was calculated and compared with the Kaplan-Meier method and the Log-rank test, respectively. A significance level of $P<0.05$ was used.

RESULTS

Comparison of clinical efficacy

After treatment, the total effective rate (markedly effective+effective) was 82.22% in the experimental group and 62.22% in the control group, suggesting markedly higher efficacy in the experimental group treated by L-carnitine+IS ($P<0.05$) (fig. 1).

Comparison of anemia status

The two groups were not statistically different in pre-treatment ALB, TRF, TP and SF ($P>0.05$). A rise in ALB, TRF, TP and SF was observed in both groups after treatment, especially in the experimental group ($P<0.05$) (table 1).

Comparison of Ca-phosphorus metabolism

The two groups were also similar in Ca, P, iPTH and FGF-23 levels before treatment ($P>0.05$). After treatment, Ca levels increased in both groups and were higher in the experimental group ($P<0.05$); iPTH, P and FGF-23 all decreased and were even lower in the experimental group ($P<0.05$) (table 2).

Comparison of renal function

The two groups were not statistically different in pre- and post-treatment renal function indexes ($P>0.05$). In both groups, Scr and BUN decreased after treatment, while Ccr increased ($P<0.05$) (table 3).

Table 1: Comparison of nutritional proteins before and after treatment

Indicators	Timing	Control group (n=45)	Experimental group (n=45)	t	P
ALB (g/L)	Before treatment	34.50±7.69	35.75±5.67	0.878	0.382
	After treatment	38.63±4.89	43.33±6.53	3.865	<0.001
TRF (mg/L)	Before treatment	1.29±0.30	1.26±0.28	0.535	0.594
	After treatment	1.45±0.34	1.61±0.30	2.357	0.021
TP (g/L)	Before treatment	48.55±5.41	48.23±4.63	0.300	0.765
	After treatment	56.16±4.98	60.31±5.15	3.882	<0.001
SF (ng/mL)	Before treatment	112.05±30.79	113.08±34.37	0.150	0.881
	After treatment	274.38±47.29	327.36±44.23	5.488	<0.001

Table 2: Comparison of Ca-phosphorus metabolism before and after treatment

Indicators	Timing	Control group (n=45)	Experimental group (n=45)	t	P
Ca (mmol/L)	Before treatment	2.14±0.15	2.10±0.09	1.710	0.091
	After treatment	2.32±0.18	2.77±0.13	13.700	<0.001
P (mmol/L)	Before treatment	2.02±0.30	1.96±0.16	1.179	0.242
	After treatment	1.63±0.16	1.43±0.08	7.319	<0.001
iPTH (ng/L)	Before treatment	431.15±66.21	427.79±65.22	0.243	0.809
	After treatment	316.29±47.40	284.14±47.18	3.225	0.002
FGF-23 (pg/mL)	Before treatment	767.14±149.78	788.32±167.76	0.632	0.529
	After treatment	596.94±126.33	543.39±105.03	2.187	0.031

Table 3: Comparison of renal function before and after treatment

Indicators	Timing	Control group (n=45)	Experimental group (n=45)	t	P
Scr (μmol/L)	Before treatment	530.20±63.90	547.49±65.25	1.270	0.208
	After treatment	468.62±53.73	477.64±49.04	0.832	0.408
BUN (mmol/L)	Before treatment	18.54±4.11	18.22±2.72	0.438	0.663
	After treatment	13.51±2.58	13.82±2.88	0.545	0.587
Ccr (mL/min)	Before treatment	10.52±2.42	9.82±2.95	1.236	0.220
	After treatment	14.64±3.01	14.66±2.54	0.042	0.967

Table 4: Comparison of adverse reactions

Types of adverse reactions	Control group (n=45)	Experimental group (n=45)	t	P
Constipation	3 (6.67%)	2 (6.67%)		
Vomiting	5 (11.11%)	1 (2.22%)		
Elevated blood pressure	4 (8.89%)	2 (6.67%)		
Arrhythmia	3 (6.67%)	3 (6.67%)		
Gastrointestinal reactions	2 (6.67%)	2 (6.67%)		
Infection	1 (2.22%)	0 (0.00%)		
Overall incidence	40.00%	22.22%	3.318	0.069

Comparison of adverse reactions

According to statistics, the incidence of adverse reactions during treatment was 22.22% in the experimental group and 40.00% in the control group, with no significant difference (P>0.05) (table 4).

Comparison of prognosis

88 cases were successfully followed up, including 44 cases in the experimental group and 44 cases in the control group. There was no difference in overall survival between the two groups (P>0.05). However, the median survival of the experimental group was (11.30±1.86) months, longer compared to the control group (P<0.05) (fig. 2).

DISCUSSION

In this study, we explored the effect of L-carnitine combined with IS on uremic patients with renal anemia and found that the anemia status was obviously improved and the treatment effect was remarkable under the combination therapy, with important application potential.

We found that the experimental group had superior clinical outcomes and nutrient protein levels, suggesting that L-carnitine combined with IS can ameliorate renal anemia in uremic patients more effectively.

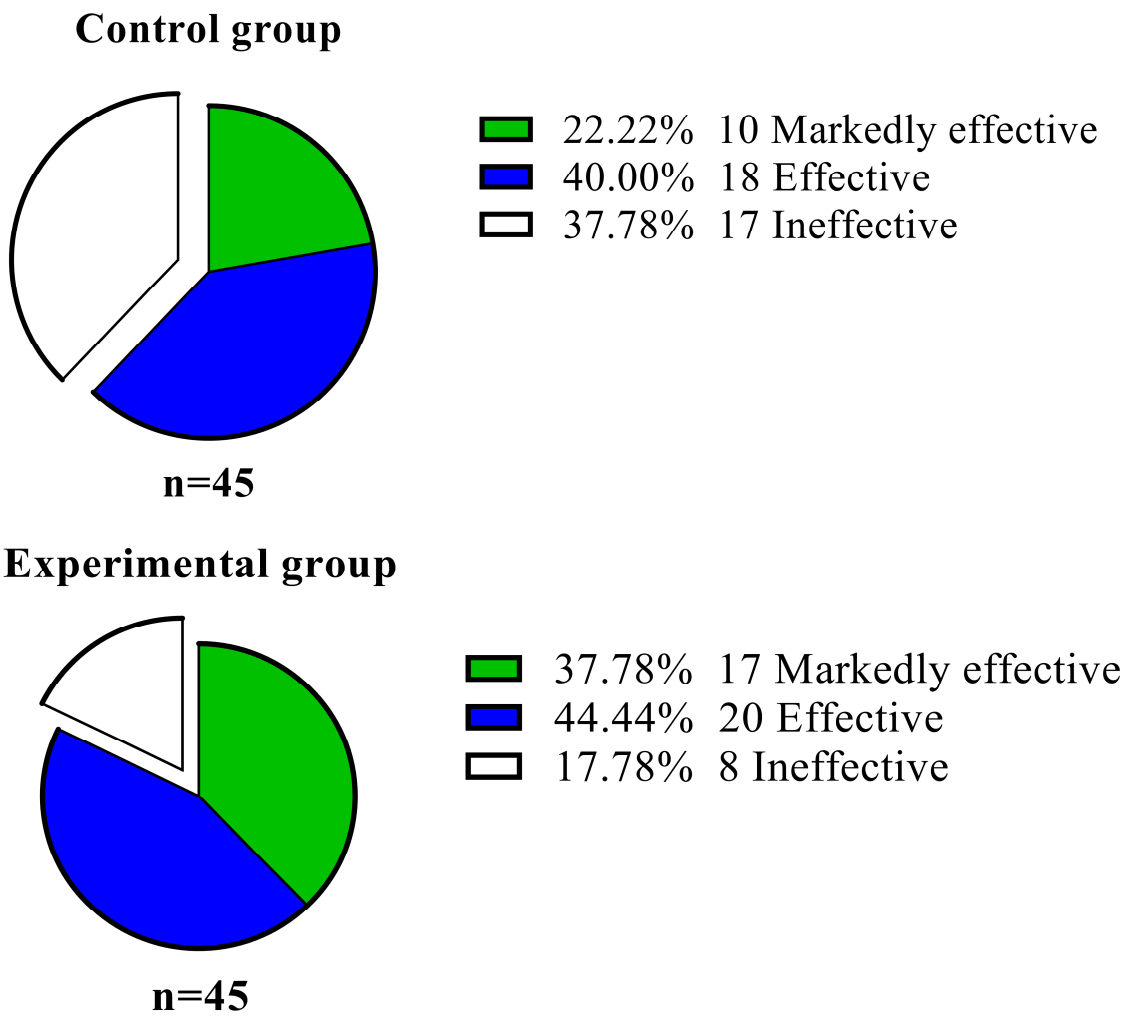

Fig. 1: Comparison of clinical efficacy, total effective rate of the experimental group was more than the control group.

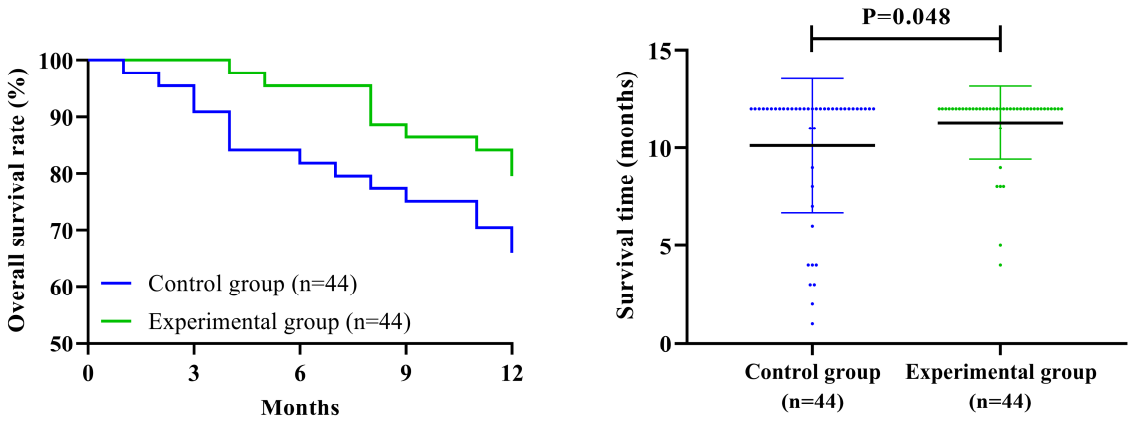

Fig. 2: Comparison of prognostic survival and survival time, there was no difference in prognostic 1-year overall survival between the two groups, but the median survival was prolonged in the experimental group compared to the control group.

This is because iron is one of the essential nutrients for the human body and an important part of Hb in erythrocytes, with its level directly determining the body's hematopoietic capacity (Koekkoek & Berger, 2023). IS is composed of sucrose and iron hydroxide colloid, which can quickly bind to TRF after entering the human body, with a good iron supplementation effect (Arastu *et al.*, 2022). On the basis of changing the lipid composition of the erythrocyte membrane, alleviating oxidative stress and stabilizing the erythrocyte membrane by L-carnitine, the use of IS further increases the iron ion content in Hb and enhances the erythrocyte activity (Sindone *et al.*, 2023). The combination of the two can better exert drug effects, resulting in more significant improvements in anemia and nutritional status for patients (Aghebat-Bekheir & Abdollahi, 2024). This can be confirmed by the inter-group comparison of Ca-phosphorus metabolism, where the experimental group had higher Ca and lower iPTH, P and FGF-23 levels, indicating a more stable Ca-phosphorus metabolism in the experimental group. Studies by Koekkoek KWA *et al*. have also confirmed that iron and carnitine aspects are essential nutrients in critical illnesses (Koekkoek & Berger, 2023).

In the comparison of renal function, both groups showed a significant improvement in renal function after treatment, with no statistical inter-group difference. It can be seen that IS has no obvious effect on improving the renal function of patients. L-carnitine can provide energy for cells, promote lipid oxidation and decomposition, increase the activities of cytochrome C reductase and oxidase and alleviate renal ischemia and hypoxia, thus improving renal function (Pagano *et al.*, 2020).

We also found that L-carnitine combined with IS has high clinical safety and great application value. Previous clinical studies have shown that IS supplementation has the advantages of low toxicity, intravenous application, 100% bioavailability, fast onset, low frequency of medication, no gastrointestinal irritation, strong patient tolerance and wide clinical application (Dave *et al.*, 2022). However, excessive use may still cause an excess of iron in the human body, exacerbating oxidative stress reactions in the blood and ultimately affecting the health of patients (Wang *et al.*, 2021). In a study by Song *et al*., the use of L-carnitine has also been indicated to alleviate IS-induced oxidative stress (Song *et al.*, 2023).

Finally, the longer median survival in the experimental group also suggesting that L-carnitine combined with IS can also improve the prognosis of patients. We believe that this is also due to the fact that L-carnitine combined with IS not only has excellent renal function improvement effects, but can comprehensively enhance the nutritional status of patients, thus providing a more reliable guarantee for their prognosis (Rehman *et al.*, 2025). However, the overall survival rate did not show a significant inter-group difference, possibly due to the short follow-up time, so further extension of the follow-up period is needed for confirmation.

The limitation of this study is that due to the possibility of contingency caused by the small number of cases, more cases need to be included for validation. Moreover, more observational indicators need to be analyzed to more comprehensively evaluate the impact of L-carnitine combined with IS on uremic patients with renal anemia, so as to provide a more reliable reference for clinical practice.

CONCLUSION

L-carnitine combined with IS can improve the nutritional status of uremic patients with renal anemia, regulate Ca-phosphorus metabolism and provide a more reliable safety guarantee for the prognosis of patients.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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There is no acknowledgement statement in this paper.

Conflict of interest

There is no conflict of interest.

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