RESEARCH ARTICLE

COMPARISON OF THE EFFECTS OF LEVOCARNITINE VERSUS NORMAL SALINE IN THE TREATMENT OF INTRADIALYTIC HYPOTENSION

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ABSTRACT

Objective: *To evaluate the outcome of levocarnitine versus normal saline in the treatment of intradialytic hypotension*

Study Design: *Pre-post quasi-experimental study*

Place and Duration of Study: *Oct 2024 to March, 2025 Armed Forces Institute of Urology (AFIU), Combined Military Hospital, Rawalpindi Pakistan .*

Patients and Methods: *Thirty five patients(experimental group:15 and control group:20) were included in the study over a period of 12 weeks. Outcomes, like Dialysis-related hypotension episodes, mean change in hemoglobin levels, fatigue, and cramps were measured. Data were analyzed using SPSS version 26.*

Results: *Both groups, had substantial decrease in Dialysis-related hypotension episodes, (p=0.05, for control: and experimental p=0.04). Experimental group found the elevation in Hb levels, (1.6g/dl, p=0.01). No changes were found in the serum creatinine and Echocardiographic outcomes.*

Conclusion: *L-carnitine supplementation reported to have significant changes in clinical outcomes, Dialysis-related hypotension, Hb levels, and quality of life in kidney Patients.*

Keywords: *Effects, Intradialytic hypotension, Levocarnitine, Normal Saline*

INTRODUCTION

In the 21st century, chronic kidney disease (CKD) has become one of the most significant and prevalent causes of mortality and morbidity.[1] CKD has been affecting an increasing number of patients, with an estimated 843.6 million individuals worldwide in 2017.[2] In order to sustain life, patients frequently necessitate renal replacement therapy, such as dialysis, as chronic kidney disease advance.[3] In South Asian countries that are rapidly urbanizing, such as Pakistan, the prevalence of chronic kidney disease (CKD) is likely to be exacerbated. A substantial portion of the 180 million population is predisposed to chronic diseases, including diabetes and hypertension, which are potentially associated with low birth weight and reduced renal reserve.[4] Hemodialysis is a frequently employed treatment for end-stage renal disease (ESRD), providing a critical intervention for numerous patients.[5]

Hemodialysis is capable of effectively eliminating contaminants and preserving fluid-electrolyte equilibrium; nevertheless, it poses specific obstacles.[6] Dialysis-related hypotension (DRH) is a prevalent and significant complication that impacts approximately 20-50% of dialysis sessions worldwide.[7] DRH is defined a substantial decrease in blood pressure that occurs during or immediately after dialysis, leading to symptoms such as vertigo, disorientation, and, in severe cases, cardiovascular instability.[8] This complication increases the likelihood of adverse cardiovascular events, elevates morbidity, and reduces dialysis efficiency.[7,9]

New evidence indicates that levocarnitine is advantageous in the treatment of DRH.[10] This naturally occurring compound is crucial for the metabolism of

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Received: 15 Mar 2025; revision received: 18 Apr 2025; accepted: 29 May 2025

fatty acids and the production of energy. However, patients with chronic kidney disease experience a substantial decrease in its levels as a result of impaired renal synthesis and dialytic losses.[11] Intradialytic hemodynamic stability has been enhanced by levocarnitine supplementation, which has also improved myocardial function and overall energy metabolism by addressing this deficiency.[10,12] The therapeutic efficacy of levocarnitine in reducing DRH remains a subject of ongoing research, despite its potential.

PATIENTS AND METHODS

Quasi experimental study was carried out in Nephrology department, AFIU, CMH Rawalpindi following Ethical Approval (vide letter no. Nephro-Trg-1/IRB/2024/017 dated 25/09/2024).

18-65 years of patients, clinically stable and with symptoms of intradialytic hypotension, muscle cramps, during or after session, muscle weakness.

Patients with previous history of levocarnitine therapy, blood transfusion, seizure disorder, or drugs senstitive to levocarnitine.

The calculation was based on the following parameters:

$$n=(Z_{\alpha/2}+Z_{\beta}/\Delta/\sigma)^2\times 2\sigma^2$$

Where n is the required sample size per group, $Z_{\alpha/2}=1$ for 95% confidence, $Z_{\beta}=0.84$ for 80% power, $\Delta=10$ is the mean difference in DRH episodes, and $\sigma=15$ is the standard deviation of the outcome, based on previous study findings. [13] The formula yielded a required sample size of approximately 45 participants to achieve adequate statistical power. This was split into 20 participants in each group. The intervention protocol was designed to assess the effects of intravenous (IV) levocarnitine supplementation on dialysis-related outcomes. Xperimental groups patients were given, IV Levocarnitine 1gm 3 times a week. Where control group were given normal saline. And followed for 12 weeks.

All participants were advised to restrict salt intake to less than 4gm/day.

For control group A predetermined volume of 0.9% normal saline (generally 100–250 ml) was administered intravenously over a period of 5-15 minutes as soon as a drop in blood pressure indicative of IDH (e.g., systolic BP < 90 mmHg or a >20 mmHg drop from baseline) is detected during the hemodialysis session.[14] Routine follow-ups were scheduled for all patients to ensure adherence to prescribed protocols and monitor clinical outcomes. Control and experimental group both had 20 patients, there was lost to follow up for 5 in control group

Primary outcome was frequency of DRH for 12 weeks. Secondary outcomes were, Hb level, improvement in

Table I: Baseline characteristics of the study sample

Characteristic	Control Group (n = 15)	Experimental Group (n = 20)
Gender n%		
Male	10	12
Female	5	8
Age (years: Mean ± SD)	40.30 ± 13.58	47.30 ± 11.69
Duration of hemodialysis (Months: Mean ± SD)	9.20 ± 2.25	9.60 ± 2.50
BMI	23.5 ± 3.4	24.2 ± 3.6
Associated Conditions (Number of Patients)		
Diabetes mellitus with hypertension	02	03
Tuberous sclerosis	0	01
Chronic pyelonephritis	01	01
Chronic glomerulonephritis	02	-
Blood transfusion over study duration (units: Mean ± SD)	2.20 ± 2.13	3.30 ± 1.41
Time since last blood transfusion (Days: Mean ± SD)	36.50 ± 7.05	37.60 ± 8.18
Baseline Hemoglobin (g/dL: Mean ± SD)	9.5 ± 1.2	9.2 ± 1.4
Baseline Kidney Function (Mean ± SD)		
Serum Creatinine (mg/dL)	9.8 ± 2.0	10.2 ± 2.3
Blood Urea Nitrogen (mg/dL)	65 ± 15	67 ± 14
Baseline Dialysis Parameters (Mean ± SD)		
Pre-dialysis systolic BP (mmHg)	140 ± 12	138 ± 10
Post-dialysis systolic BP (mmHg)	125 ± 14	123 ± 12

kidney functions, echocardiographic outcomes, like LVEDV, LVEF, mitral inflow velocities.

Dialysis-related symptoms, including fatigue, muscle cramping, and myopathy, were assessed using a structured symptom checklist. The intervention's impact on clinical outcomes was quantified through the calculation of mean differences and percentage changes. SPSS (version 26) was employed to collect enter and conduct all analyses.

RESULTS

The final analysis comprised 35 patients: 15 in the control group and 20 in the experimental group, following the loss of 5 patients to follow-up in the control group. The control group exhibited a mean age of 40.30 years (± 13.58), whereas the experimental group demonstrated a mean age of 47.30 years (± 11.69). The duration of hemodialysis was comparable between the two groups (control: 9.20 ± 2.25 months; experimental: 9.60 ± 2.50 months). The baseline measurements of kidney function, and blood pressure were similar. The experimental group exhibited elevated blood transfusion rates (3.30 ± 1.41 units compared to 2.20 ± 2.13 units).

The analysis of dialysis-related hypotension (DRH) frequency outcomes are shown in Table II, Figures I. At baseline, the frequency of DRH episodes was comparable between the control group (3.6 ± 1.2 episodes/week) and the experimental group (3.2 ± 1.4 episodes/week), with no statistically significant difference ($p = 0.72$). After 12 weeks of intervention, the experimental group demonstrated a marginal increase in DRH episodes (2.9 ± 0.8 episodes/week), while the control group exhibited a reduction to 2.7 ± 1.0 episodes/week. The between-group comparison at 12 weeks approached statistical significance ($p = 0.05$).

Interdialytic weight gain significantly decreased in the experimental group (1.8 ± 0.4 kg, $p = 0.04$) compared to the control group (2.4 ± 0.6 kg, $p = 0.58$). Hemoglobin levels improved more in the experimental group (10.8 ± 1.1 g/dL, $p = 0.01$) than in the control group (9.8 ± 1.0 g/dL, $p = 0.62$). Serum creatinine and dialysis adequacy remained stable in both groups. Additionally, the experimental group reported significant improvements in fatigue (4.5 ± 1.1, $p = 0.01$) and muscle cramping (1.0 ± 0.4, $p < 0.01$) compared to the control group.

The comparison of echocardiographic parameters between the experimental and control groups revealed no significant differences across all measured variables. Left ventricular ejection fraction (LVEF) were also similar, with mean values of 56.00 ± 7.50% in the experimental group versus 55.50 ± 8.00% in the control group $p = 0.811$.

Table II: Comparison of clinical and laboratory outcomes between control and experimental groups at baseline and after 12 weeks of intervention

Outcome	Time Point	Control Group (Mean ± SD)	Experimental Group (Mean ± SD)	*p* value
Frequency of DRH episodes/week				
	Baseline	3.6 ± 1.2	3.2 ± 1.4	0.72
	12 weeks	2.7 ± 1.0	2.9 ± 0.8	0.05
***p* value**		0.05	**0.04***	

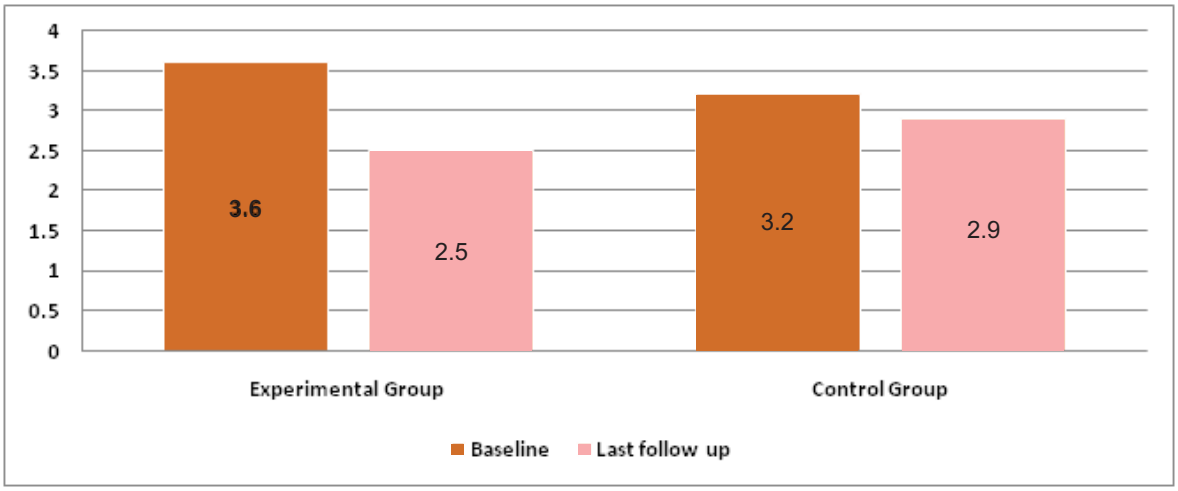

Figure I. Mean frequency of DRH episodes/week among study groups

Table III: Comparison of outcomes at baseline and after 12 weeks

Outcome	Time Point	Control Group (Mean ± SD)	Experimental Group (Mean ± SD)	*p*-value
Interdialytic weight gain (kg)				
	Baseline	2.5 ± 0.7	2.3 ± 0.6	0.58
	12 weeks	2.4 ± 0.6	1.8 ± 0.4	**0.04***
Hemoglobin (g/dL)				
	Baseline	9.5 ± 1.2	9.2 ± 1.4	0.62
	12 weeks	9.8 ± 1.0	10.8 ± 1.1	**0.01***
Serum creatinine (mg/dL)				
	Baseline	9.8 ± 2.0	10.2 ± 2.3	0.55
	12 weeks	9.9 ± 1.8	9.5 ± 2.0	0.44
Dialysis adequacy (Kt/V)				
	Baseline	1.2 ± 0.2	1.3 ± 0.3	0.45
	12 weeks	1.2 ± 0.2	1.4 ± 0.2	**0.01***
Fatigue (1–10)				
	Baseline	7.5 ± 1.0	7.4 ± 0.8	0.81
	12 weeks	6.8 ± 1.2	4.5 ± 1.1	**0.01***
Muscle cramping frequency/week				
	Baseline	2.2 ± 0.8	2.4 ± 1.0	0.65
	12 weeks	2.0 ± 0.6	1.0 ± 0.4	**0.00****

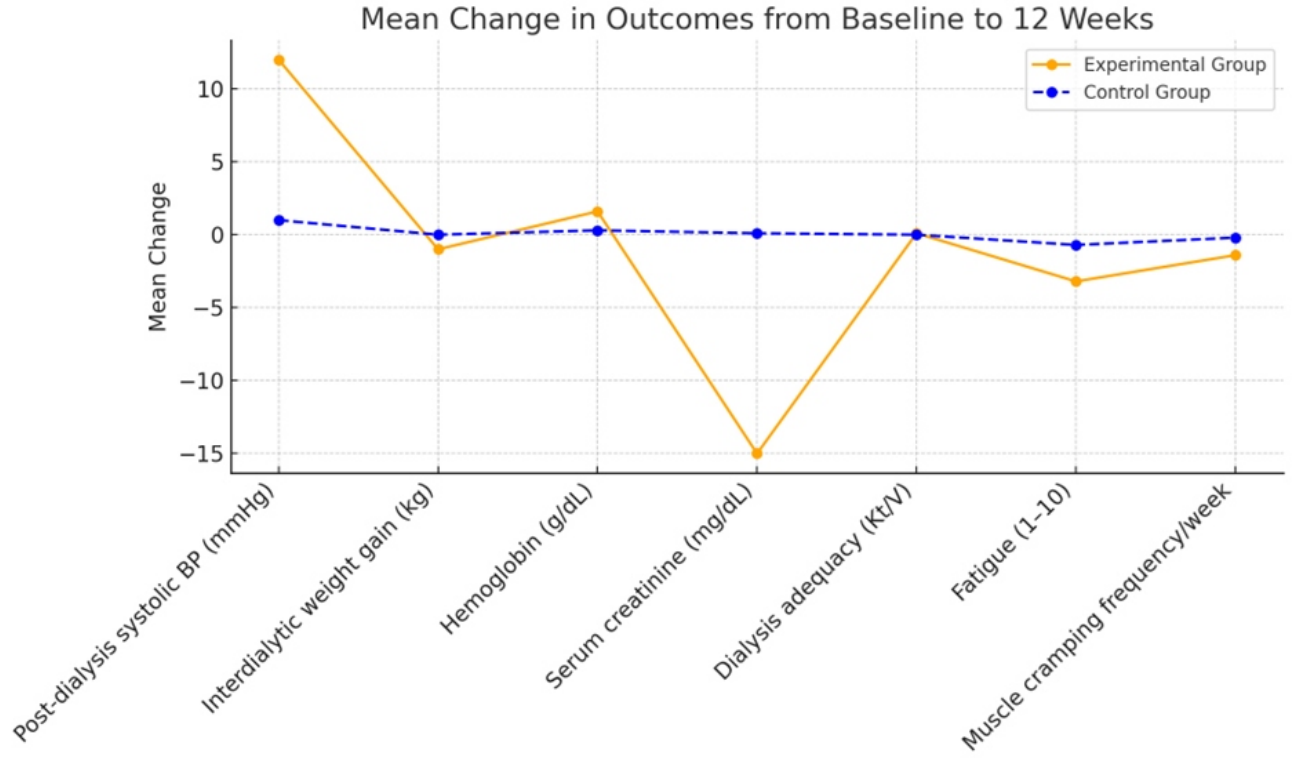

Figure II. Mean change in clinical and laboratory outcomes between control and experimental groups at baseline and after 12 weeks of intervention

Table III: Comparison of outcomes at baseline and after 12 weeks

Parameters	Control Group (Mean ± SD)	Experimental Group(Mean ± SD)	*p*-value
LVEDV index, mL/m²	62.80 ± 15.50	62.50 ± 16.00	0.870
LVEF (%)	55.50 ± 8.00	56.00 ± 7.50	0.811
Mid RV (cm)	2.96 ± 0.35	2.95 ± 0.30	0.932
Early diastolic mitral inflow velocity (E), cm/s	81.00 ± 24.50	80.00 ± 25.00	0.876
Late diastolic mitral inflow velocity (A), cm/s	85.00 ± 21.00	84.50 ± 20.00	0.910
Early diastolic mitral annulus velocity (e'), cm/s	6.10 ± 1.60	6.00 ± 1.50	0.822
Mitral E/e'	13.70 ± 4.20	13.80 ± 4.00	0.889
PAP, mm Hg	32.50 ± 8.50	32.00 ± 9.00	0.865

DISCUSSION

Our findings indicate that L-carnitine supplementation resulted in significant improvements in several clinical markers, suggesting its potential benefits for this patient population.

Both the experimental and control groups had a decrease in dialysis-related hypotension (DRH) occurrences during the course of the 12-week trial. Groups did not differ in the baseline frequency of DRH incidents (p = 0.72). The experimental group had a little increase in DRH episodes (2.9 ± 0.8 per week) after 12 weeks, in contrast to the control group, which demonstrated a decrease (2.7 ± 1.0 per week). While the between-group comparison at 12 weeks was almost statistically significant (p = 0.05), the within-group analysis revealed significant decreases in DRH episodes in both the control and experimental groups (p = 0.05 and p = 0.04, respectively). Previous research has shown that L-carnitine supplementation alleviated DRH episodes in certain trials but not others. This finding lends credence to that finding. Lynch et al. [15] found 145 people in 4 randomized controlled trials (RCTs) studying hypotension due to dialysis and 149 people in 6 RCTs studying muscle cramps. Efforts to alleviate hypotension and muscle cramps caused by hemodialysis were not beneficial. Recently, Chewcharat et al. [12] evaluated dialysis-related hypotension in a meta-analysis of 8 RCTs including 224 participants. Based on the evidence, it seems that L-carnitine may ward against this condition. The meta-analysis gained a better understanding of the effectiveness of L-carnitine supplementation using subgroup analyses that were based on technique, dosage, and duration of supplementation. Although our results provide credence to the better trend shown in previous meta-analyses, we did not find a statistically significant reduction in DRH episodes in the experimental group. Demographics, sample size, and analytical methods (such as the subgroup analyses used by Chewcharat et al.) all have a role in the results. Longer supplementation periods and more accurate doses may give higher benefits due to the complex effects of L-carnitine on dialysis-related hypotension, according to our meta-analyses. The improvement in hemoglobin levels (+1.6 g/dL, p = 0.01) observed in the experimental group is consistent with earlier studies highlighting L-carnitine's role in ameliorating renal anemia. Mechanisms such as enhanced red blood cell function and reduced erythropoietin requirements have been proposed to explain this effect. These findings align with the literature where L-carnitine supplementation has been linked to improved erythropoiesis and anemia management in hemodialysis patients. [16,17] Additionally, significant reductions in fatigue and muscle cramps observed in this study are in agreement with findings by Kuwasawa et al. and Ulinski et al. who reported that L-carnitine alleviates dialysis-related symptoms and improves quality of life. [17,18]

CONCLUSION

L-carnitine supplementation reported to have significant changes in clinical outcomes, DRH, Hb levels, and QoL in kidney Patients.

CONFLICT OF INTEREST: None.

SOURCE OF FUNDING: None.

Authors' Contribution

Aqsa Saleem: Conception of study/Designing/Planning

Nouman Kashif: Analysis/Interpretation/Discussion

Faisal Basharat: Experimentation/Study Conduction

Maryam Sibghat: Manuscript Writing

Misbah Farooq: Critical Review

Farrukh Islam: Critical Review

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