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ORIGINAL ARTICLE

Effect of carnitine supplementation on inflammatory biomarker in hemodialysis patients.

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ABSTRACT... Objective: To determine the effect of carnitine supplementation on Inflammatory biomarker (C reactive protein) in hemodialysis patients. **Study Design:** Randomized Control Trial. **Setting:** JPMC Hospital, Karachi and PNS Shifa Hospital, Karachi. **Period:** 01-12-2022 to 30-04-2023. **Methods:** The hemodialysis patients were selected from the dialysis center and the controls were taken from nephrology wards. L- Carnitine supplementation was given to the hemodialysis patients. Hemodialysis patients were further subdivided into 2 groups, Intravenous group in which the subjects were given intravenous L-Carnitine supplementation and the Oral Group which constituted patients who received oral L-Carnitine supplementation. **Results:** In intravenous group the mean hemoglobin before supplementation was 9.9 (SD=±1.1) units and after treatment it was 10.5 (SD=±1.2) units. The change in hemoglobin was considered statistically significant with $p<0.01$. In oral group the mean hemoglobin before supplementation was 10.2 (SD=±1.1) units and after treatment it was 10.3 (SD=±1.1) units, the mean difference was not statistically significant with $p=0.05$. **Conclusion:** L-Carnitine supplementation demonstrated a significant reduction in CRP levels, with intravenous administration showing greater efficacy. These findings suggest the potential therapeutic value of L-Carnitine in mitigating inflammation and oxidative stress in CKD patients, offering a promising avenue for improving their overall health and reducing the risk of cardiovascular complications. Further research and clinical trials are warranted to explore the full extent of these benefits and optimize treatment strategies.

Key words: CRP, Hemodialysis, L-Carnitine.

INTRODUCTION

C-reactive protein (CRP) plays a role in modulating the inflammatory response. Proinflammatory cytokines cause the liver to generate this protein, which is then quickly elevated to high amounts.[1] The plasma half-life of this protein is 19 hours. Because of its quick ascent to high concentrations and brief half-life, CRP is a promising indicator of acute inflammation. However, C-reactive protein levels may persistently be high in chronic inflammation. Dialysis patients have a high frequency of chronic inflammation, which is demonstrated by elevated levels of inflammatory cytokines or C-reactive protein.[2] The prevalence of inflammation is reported to be between 35-65% of hemodialysis patients. In addition, greater inflammatory factor levels have been linked to a higher risk of morbidity and death.[3] The cause of inflammation in people with chronic renal failure is yet unknown. Given that both appear to be linked to the increased production of proinflammatory cytokines; it has been proposed that certain immunological and host-defense system changes brought on by dialysis may be pertinent.[4] Additionally, it has been proposed that the kind of dialysis membrane may be important. Several methods have been proposed, such as the back filtering of contaminated dialysate into the blood compartment, direct membrane contact with blood cells, and the production of complement fractions as a result of plasma protein-membrane interaction to be responsible for inducing cytokine production during hemodialysis.[5] CRP levels in malnourished hemodialysis patients are associated with low blood albumin levels. Excessive oxidative stress in conjunction with chronic inflammation may raise the risk of atherosclerosis in malnutrition.[6]

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To demonstrate the coexistence of these two disorders in these individuals Protein energy malnutrition may be the missing piece connecting morbidity and death in these people to chronic inflammation. CRP levels were found to be increased in 32% and 46%, respectively, of the cohorts studied in cross-sectional investigations of chronic renal failure and hemodialysis.[7] Because of this, CRP varies both within and between groups. However, there is a dearth of information detailing the variation in CRP readings within patients.[8] Researchers have recently looked into the hypothesis that the dialysis procedure may have contributed, at least in part, to the chronic inflammatory condition of the uremic patient.[9] They have offered information that suggests the elevation in CRP in stable dialysis patients may be brought on by back filtration of dialysate toxins stimulating monocyte/macrophage activity. The anti-inflammatory and antioxidant properties of carnitine help to reduce the buildup of lipid peroxidation end products. Carnitine has an important physiological role in the passage of fatty acids through the mitochondria and in the oxidative release of energy.[9] Additionally, it aids in mitochondrial removal of fatty acids. Any alteration to the homeostasis of carnitine may affect the lipid metabolism, red blood cell production, and heart muscle cell function. Numerous indicators of inflammation and oxidative stress have already been examined in relation to the effects of carnitine administration; however, the results were inconclusive.[10] Hence we investigated the effects of carnitine supplementation on CRP levels in hemodialysis patients. Prior reports have shown that carnitine therapy may lower CRP levels in dialysis patients, although there are few studies in this area.[10] We conducted a prospective, non-randomized, controlled experiment in the current investigation to examine the effect of carnitine supplementation on CRP levels in patients receiving hemodialysis.

METHODS

The described study was conducted as a randomized control trial, with the trial registered on ClinicalTrials.gov under the registration number NCT05817799. Ethical permissions were obtained from all participating institutions before the study commenced, ensuring that all ethical requirements were met, and informed consent was obtained from the participants. The trial took place at two public hospitals in Karachi over a period of five months from Dec 2022 to April 2023, a total of 83 participants were recruited after sample size calculation by using open epi website calculator using a reference study.[16] The patients were distributed into the Intravenous group (33 individuals) and the Oral Group (50 patients) by simple randomization method.

The Intravenous group received L-Carnitine supplementation intravenously at a dose of 20 mg/kg as an IV bolus delivered over two to three minutes after each hemodialysis session, which occurred three times a week for five months. On the other hand, the Oral group received 500 mg of L-carnitine supplements orally three times a day for the same five-month period. Vital signs were monitored daily throughout the supplementation period, and participants were closely observed for any signs of distress. Additionally, a maintenance dosage of 500 mg oral tablets was administered once a day for one month after the research period concluded. This rigorous methodology, with randomization and careful monitoring, allowed for a robust assessment of the impact of intravenous versus oral L-Carnitine supplementation on the study's outcomes.

RESULTS

The descriptive demographic data of the samples is reported in Table-I.

Variables	Intravenous Group (n=33)	Oral Group (n=50)	P-Value
	Mean± SD	Mean± SD	
Age (years)£	45.27 ± 8.50	44.10 ± 8.92	0.47
weight (kg)£	67.09 ± 9.27	69.06 ± 9.01	0.36
Female n(%)	17 (51.5)	25 (50.0)	0.89¥
Male n(%)	16 (48.5)	25 (50.0)	

Table-I. Descriptive statistics on demographic data of samples (n= 83)

£P-value was obtained using independent sample t-test

¥ P-value was obtained using Pearson Chi Square test

Figure-1 reports the effect of carnitine supplementation on CRP levels in Hemodialysis patients at pre and post stages. In intravenous group the mean CRP before supplementation was 5.6 (SD±2.6) units and after treatment it was 3.4 (SD±1.9) units. The change in CRP was considered statistically significant with $p<0.01$. In oral Hemodialysis patients the mean CRP before supplementation was 5.5 (SD±2.0) units and after treatment it was 4.6 (SD±1.9) units, the mean difference was also statistically significant with $p<0.01$.

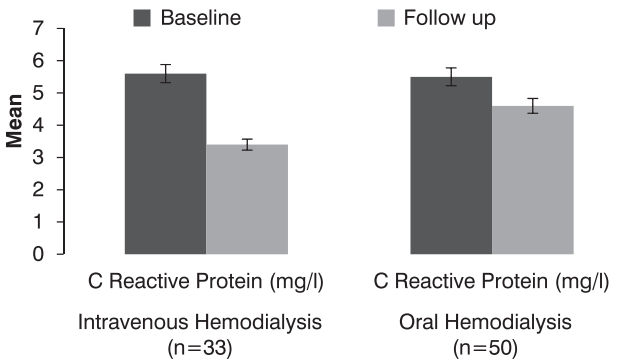

Figure-1. Effect of carnitine supplementation on CRP levels in hemodialysis patients.

DISCUSSION

C-reactive protein levels have risen in more than 50% of CKD patients, and this prevalence is considerably greater among dialysis patients, according to earlier research. Vascular calcification can be accelerated by chronic inflammation, which raises the risk of CVD. Some of the reasons for chronic inflammation in CKD include the buildup of fluid overload and uremic toxins, reduced renal clearance, infection of fistula in dialysis patients, and interaction of dialyzer with the patient's blood.[11]

In our study results we found that both CKD group and hemodialysis group had raised CRP levels as compared to the control group. This result is consistent with the published literature which states that uremic state is associated with chronic inflammation and raised CRP levels.[12] The highest levels of CRP among the study groups were seen in hemodialysis patients. This is caused by dialysate toxins that were filtered back into the system activating monocyte and macrophage activation. Our results are consistent with the results published earlier.[13,14]

Supplementation with L-Carnitine lead to a significant reduction in CRP levels in hemodialysis group and this decrease was more significant in the intravenous group. This is probably due to better availability of dose via the intravenous route. Our results are consistent with published literature.[15] Duranay and co authors showed in their study that supplementation of hemodialysis patients with L-Carnitine reduced the levels of CRP along with other inflammatory cytokines.[16]

L-carnitine's impact might be attributed to its ability to decrease protein kinase C activity. According to İzgüt-Uysal et al., treatment of L-carnitine reduced the activity of protein kinase C-mediated reaction in neutrophils.[17] Additionally, it has been discovered that carnitine and its derivatives have an antiperoxidative impact on a number of tissues. On the other hand, these chemicals have a scavenging effect on reactive oxygen species and decrease the formation of hydroxyl radicals.[17]

Our findings imply that L-carnitine, because of its antiperoxidative activity, may be helpful in minimizing tissue damage that is caused by superoxide radicals in disseminated inflammatory disorders, in addition to the stabilizing impact of L-carnitine on damaged cell membranes. The significance of this study lies in its contribution to understanding the connection between CKD, chronic inflammation, and elevated CRP levels, particularly in hemodialysis patients. Moreover, the research highlights the potential therapeutic value of L-Carnitine in reducing inflammation and protecting against oxidative stress in individuals with CKD, which could have implications for improving the overall health and well-being of these patients and potentially reducing their risk of cardiovascular disease. These findings may guide further investigations and the development of targeted interventions for CKD patients, ultimately improving their quality of life and health outcomes.

CONCLUSION

In conclusion, our study reaffirmed the high

prevalence of elevated C-reactive protein (CRP) levels in both chronic kidney disease (CKD) and hemodialysis patients, underscoring the association between uremia and chronic inflammation. Importantly, L-Carnitine supplementation demonstrated a significant reduction in CRP levels, with intravenous administration showing greater efficacy. These findings suggest the potential therapeutic value of L-Carnitine in mitigating inflammation and oxidative stress in CKD patients, offering a promising avenue for improving their overall health and reducing the risk of cardiovascular complications. Further research and clinical trials are warranted to explore the full extent of these benefits and optimize treatment strategies.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Sadia Rehman:** Principal investigator.
2	**Muhammad Farhan:** Supervision.
3	**Santosh Kumar:** Clinical supervision of clinical trial in JPMC, data collection.
4	**Saira Bano:** Statistical analysis, literature review.
5	**Asma Naveed:** Clinical supervision of clinical trial at PNS shifa, data collection.
6	**Neha Niaz Ahmad:** Data collection, write up, analysis of results.