

Experience with Levocarnitine in Reducing Frequency of Intradialytic Hypotension in Patients on Maintenance

WAQAR AHMED, RIZWAN-UL-HAQ, MATEEN AKRAM, AHAD QUYYUM, ABAD-UR-REHMAN, SAQLAIN HAIDER

ABSTRACT

Aim: To assess the role of levocarnitine in reducing the frequency of intradialytic hypotension in maintenance haemodialysis patients.

Methods: 20 patients having 3 or more episodes of intradialytic hypotension/week on maintenance haemodialysis at Shaikh Zayed Hospital, Lahore were enrolled in the study. Each patient was dialyzed according to a standard protocol and dialysate. Each participant was infused with 20mg/kg body weight intravenous levocarnitine at the end of each dialysis session in the venous port while blood was being returned to the patient for 6 months. The number of intradialytic hypotensive episodes/week was noted during the 6 month period.

Results: At the start of the study 12 patients had 3 episodes of intradialytic hypotension/week, 3 patients had 4 episodes/week while 2 patients had 5 intradialytic hypotensive episodes/week. At end of 6 month study period, 12 patients had no intradialytic hypotensive episodes while 2 patients had 1 intradialytic hypotensive episode/week. There was 1 patient who had 2 episodes/week while 2 patients had 3 intradialytic hypotensive episode/week.

Conclusion: Intravenous levocarnitine at the end of each dialysis session helps in reducing frequency of intradialytic hypotension in maintenance haemodialysis patients.

Keywords: levocarnitine, intradialytic hypotension, maintenance haemodialysis.

INTRODUCTION

Levocarnitine is a non-essential amino acid. It plays a pivotal role in energy generation and metabolism. Levocarnitine helps transport long chain fatty acid across the mitochondrial membrane. Once the long chain fatty acids are inside the mitochondria they undergo beta oxidation, hence producing energy. The absence of levocarnitine can hamper this process¹.

Levocarnitine serum levels are found to be low in the maintenance hemodialysis population. The cause of this deficiency in this population is three-fold. The first cause is that since levocarnitine possesses a small molecular weight, it can be lost from the blood into the dialysate via the dialyzer. Secondly, patients on maintenance hemodialysis usually have a change in dietary habits which can be a result of uremia associated anorexia and change in taste preferences or it can be a result of dietary restriction as prescribed by the physician. A rich source of levocarnitine is red meat and dairy products. Lastly, levocarnitine is synthesized in the liver, kidney and brain. In the absence of adequate kidney function its synthesis is compromised to a certain extent².

Since deficiency of levocarnitine leads to a decreased availability of adenosine triphosphate

(ATP) it can potentially decrease myocardial contractility hence cause hypotension. Furthermore, there is sufficient evidence to suggest that levocarnitine has anti-inflammatory effects as a result its deficiency causes inflammation and vasodilatation hence hypotension³. Apart from hypotension levocarnitine deficiency is also known to a cause of erythropoietin resistant anemia, muscle cramps and fatigue⁴.

In our study we have studied the effect of intravenous levocarnitine supplementation in reducing the frequency of intradialytic hypotension in patients on maintenance hemodialysis.

METHODOLOGY

Our study was conducted at the Hemodialysis Unit of Shaikh Zayed Hospital, Lahore. The study protocol was pre-approved by the Institutional Ethical Committee. We enrolled 20 adult (>18 years of age) patients on maintenance hemodialysis who were having 3 or more episodes of intradialytic hypotension/week. Intradialytic hypotension was defined as per National Kidney Foundation recommendation as a drop in systolic blood pressure of at least 20mmHg or a mean arterial pressure drop of at least 10mmHg associated with hypotensive

Department of Nephrology, Shaikh Zayed Hospital, Lahore
Correspondence: Dr. Waqar Ahmad, Mobile: 03008484357, Email: waqar3013@gmail.com

symptoms like dizziness, nausea, vomiting, restlessness, muscle cramps etc.

Every attempt was made to minimize the effect of other factors that may cause intradialytic hypotension. All patients included in the study had an intradialytic weight gain of less than 2kg. Any modification in anti-hypertensive medication was made 1 month prior to the start of the trial. The dry weight of each participant was evaluated at every dialysis session. In the event of a hypotensive episode an electrocardiogram (ECG) was performed to rule out myocardial ischemia.

We had to exclude 3 patients from our study as 2 patients had an interdialytic weight gain of greater than 2 kg while 1 patient had a myocardial infarction during the study period.

All patients enrolled in the study were dialyzed through a native arterio-venous (AV) fistula using a standard protocol and uniform bicarbonate dialysate. The temperature of the dialysate was also kept constant at 37°C. All patients were dialyzed using a polysulphone dialyzer. At the end of each dialysis, levocarnitine injection at a dose of 20mg/kg body weight was infused into the venous line of the blood tubing while blood was being returned to the patient. The number of intradialytic hypotensive/week was noted for each patient.

RESULTS

Out of 20 adult participants we enrolled in our study 3 patients had to be excluded from the study for reasons explained above. Out of the 17 patients who completed the study protocol 10 were of male gender while 7 were females (Table 1)

The mean age of our participants was 46. The majority of the patients were in the 40-49 and 50-59 year age group with 6 participants in each group. There were 2 participants each in the 20-29 and 30-39 age group while there was only 1 participant in the 60-69 age group (Table 2).

When we stratified our patients according to their cause of renal failure, we found that the majority of the patients reached end stage renal disease secondary to diabetic kidney disease i.e. 12 participants out of a total of 17. There were 2 patients each who had reached end stage renal disease due to glomerulonephritis and lupus nephritis. There was only 1 participant who had end stage renal disease secondary to Alport's syndrome (Table 3).

At the start of the study there were 2 patients who were having 5 episodes of intradialytic hypotension/week, 3 patients were having 4 episodes of intradialytic hypotension per week while there were 12 patients who were having 3 such events on a weekly basis. After one month of intravenous

administration of levocarnitine at the end of each hemodialysis session, a reduction in intradialytic hypotensive episodes was seen with only 1 patient having 5 episodes of intradialytic hypotension/ week, 2 patients having 4 episodes/week, 13 patients 3 episodes/week while there was 1 patient who was having only 1 episode of intradialytic hypotension/ week.

After 2 months of levocarnitine administration, a further reduction in frequency of intradialytic hypotension episodes/week was seen with no patient having 5 such events on a weekly basis anymore. Furthermore, only 1 patient was having 4 episodes of intradialytic hypotension/week. There were 13 participants who were having 3 episodes of intradialytic hypotension/week, 2 participants having 2 episodes/week while only one patient having 1 episode/ week. At the mid-point of the study i.e., 3 months further improvement was seen as no patient was having 4 or more than 4 intradialytic hypotensive/ week while there were 6 participants who were still having 3 such events/week. 5 participants were having 2 episodes of intradialytic hypotension/week, 3 participants were having only 1 such episode on a weekly basis while there were 3 participants who became free of this problem at month 3. At month 4, there was no further improvement in frequency of intradialytic hypotension/week with the results being the same as month 3. Although further improvement was seen in the later months.

At month 5, there was no patient having 4 or more than 4 intradialytic hypotension episodes/ week. There were 3, 1 and 2 participants who were having 3, 2 and 1 intradialytic hypotensive/week respectively. There were 11 patients at month 5 who had become free of intradialytic hypotension.

At the end of the study i.e. month 6 a further improvement was seen when 12 patients had no intradialytic hypotension episode/ week while 2 patients had 1 episode/week and 1 patient had 2 episodes/week. 2 participants had 3 episodes of intradialytic hypotension/week while no patient had 4 or more episodes at the end of the study.

It was noteworthy that at the end of the study 5 out of 17 participants who were still having intradialytic hypotension were all diabetics. Furthermore, all patients who were having 4 or more episodes of intradialytic hypotension/week throughout the study were diabetic as well.

Table 1: Gender distribution of patients

Gender	n	%age
Male	10	59
Female	7	41
Total	17	100

Table 2: Age distribution of patients

Age (Year)	n	%age
20-29	2	12
30-39	2	12
40-49	6	35
50-59	6	35
60-69	1	6

Table 3: Etiology of end stage renal disease

	n	%age
Diabetes Mellitus	12	70
Glomerulonephritis	2	12
Lupus nephritis	2	12
Alport's Syndrome	1	6

Table 4: Intradialytic hypotensive episodes

Intradialytic hypotensive episodes/week	0	1	2	3	4	5
Baseline	-	-	-	12	3	2
Month 1	-	1	-	13	2	1
Month 2	-	1	2	13	1	-
Month 3	3	3	5	6	-	-
Month 4	3	3	5	6	-	-
Month 5	11	2	1	3	-	-
Month 6	12	2	1	2	-	-

DISCUSSION

Levocarnitine levels are usually low in patients on maintenance hemodialysis secondary to loss during dialysis, decreased intake and reduced synthesis by the kidney. It has been proposed that supplementation with levocarnitine in the hemodialysis population can improve hypotension, fatigue, muscle cramps and erythropoietin resistant anemia⁵.

In our study, we found a significant improvement in reduction of number of intradialytic hypotension episodes/week as described above. We also noticed that patients being supplemented with levocarnitine were reporting improved energy and physical strength levels. They admitted a relief from fatigue. Since fatigue is a subjective complaint we were unable to quantify this improvement. We believe that the possible explanation for this improvement in physical strength is the same as that given for the decrease in intradialytic hypotension episodes. The supplemented levocarnitine shuttles the long chain fatty acids from the cytoplasm into the mitochondria where the fatty acids undergo beta oxidation resulting in an enhanced level of energy generation which can lead to better cardiac and smooth muscle contractility⁶. Furthermore, studies have shown levocarnitine to have anti-inflammatory effects which can improve muscular strength as well. Although, we did not find any significant improvement in haemoglobin levels with levocarnitine

supplementation. The bioavailability of orally supplemented levocarnitine is low (<15%) in healthy adults, specially in end stage renal disease patients⁷. Hence, it is generally recommended to supplement levocarnitine intravenously in the dialysis population. It is prudent to supplement it post-dialysis in the venous port as it can be lost through the dialyzer into the dialysate.

Even though all patients had a reduction in the number of intradialytic hypotensive episodes/ week, there were 5 patients who were still experiencing these events during dialysis at the end of the study period. It was interesting to note that all of these 5 patients were diabetics. These patients did experience a reduction in the number of intradialytic hypotensive episodes/ week but they never got free of the problem during the study period. Furthermore, we noted that patients who had end stage renal disease secondary to a non-diabetic cause responded rapidly to levocarnitine supplementation. All diabetics enrolled in our study had a history of diabetic retinopathy treatment and peripheral neuropathy. We believe that the involvement of diabetic autonomic neuropathy in causing intradialytic hypotensive episodes cannot be underplayed in these patients. Interestingly, these patients did experience a certain degree of improvement with levocarnitine supplementation. More studies with larger sample sizes and prolonged study periods are required to assess if such patients can become free of intradialytic hypotension.

REFERENCES

- Hoppel, C. The physiological role of carnitine. In: L-Carnitine and Its Role in Medicine: From Function to Therapy, Ferrari, R, DiMauro, S, Sherwood, G (eds), Academic Press, London, 1992, p. 5-19
- Ahmad, S. Carnitine, kidney and renal dialysis. In: L-Carnitine and Its Role in Medicine: From Function to Therapy, Ferrari, R, DiMauro, S, Sherwood, G (eds), Academic Press, London, 1992, p. 381.
- Savica V, Santoro D, Mazzaglia G. L-carnitine infusions may suppress serum C-reactive protein and improve nutritional status in maintenance hemodialysis patients. J Ren Nutr 2005; 15:225.
- Hurot JM, Cucherat M, Haugh M, Fouque D. Effects of L-carnitine supplementation in maintenance hemodialysis patients: a systematic review. J Am Soc Nephrol 2002; 13:708.
- Semeniuk J, Shalansky KF. Evaluation of the effect of intravenous l-carnitine on quality of life in chronic hemodialysis patients. Clin Nephrol 2000; 54:470.
- Consensus Group Statement. Role of L-carnitine in treating renal dialysis patients. Dial Transplant 1994; 23:177.
- Fornasini G, Upton RN, Evans AM. A pharmacokinetic model for L-carnitine in patients receiving haemodialysis. Br J Clin Pharmacol 2007; 64:335.

