Effect of Carnitine Supplementation on Carnitine Levels and Left Ventricular Performance in Children on Chronic Hemodialysis

Kristen Sgambat MS RD, Ellini Ahmad MD, Lowell Frank MD, Craig Sable MD, Asha Moudgil MD , Children's National Medical Center, Washington DC, USA

ABSTRACT

Background: Carnitine is essential for transport of fatty acids into mitochondria and plays a key role in beta-oxidation and energy production in the myocardium. Carnitine deficiency can occur in patients on chronic HD due to its removal by dialysis and inadequate dietary intake. This may contribute to cardiomyopathy.

Methods: The carnitine levels and cardiac function of 8 children on chronic HD were compared before and after IV carnitine supplementation three times a week for 6 months. Standard echocardiographic (ECHO) measures of LV size and systolic and diastolic function as well as circumferential, radial, and longitudinal strain and strain rate analysis using speckle tracking were performed.

Results: Total (50 ± 36 vs. 267 ± 36 µmol/l) and free carnitine (29 ± 23 vs. 160 ± 23 µmol/l) levels increased significantly ($p < 0.001$), whereas acyl:free carnitine ratio remained unchanged after carnitine supplementation. There were no significant changes in standard ECHO measures of LV function including end diastolic dimension, mass index, ejection fraction, shortening fraction and mitral E/A and E/E' ratios after carnitine supplementation. However, there was a significant ($p = 0.02$) improvement in longitudinal strain rate (-1.46 ± 0.33 vs. -1.91 ± 0.37) after supplementation.

Conclusion: Carnitine supplementation improved total and free carnitine levels in children on chronic HD without impacting acyl:free carnitine ratio. LV performance improved after supplementation as assessed by strain rate analysis that was not obvious by standard ECHO measures.

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STUDY AIMS

•Evaluate effect of 6 months of IV carnitine supplementation on total and free carnitine levels and acyl:carnitine ratio in children on chronic HD

•Assess cardiac response to carnitine supplementation by standard ECHO as well as more sensitive parameters including LV strain and strain rate.

METHODS

Study Design: Prospective, longitudinal, open-labeled, controlled pilot study, with each participant serving as their own control.

Patients: Children age 2-21 years were recruited from the pediatric HD unit at Children's National Medical Center in Washington, D.C. Inclusion criteria: Children with ESRD on chronic HD > 3 months, on rhEPO therapy > 8 weeks, and iron replete (iron sat 20-50%,ferritin >100 umol/L). Exclusion criteria: iron deficiency, severe hyperparathyroidism (iPTH>1000 ng/ml), high hemoglobin >13 g/dL, taking myelosuppressive agents, recent GI bleed or severe infection.

Methods: Carnitine levels were assessed at baseline and monthly for a 3 mo observation phase. All patients were then given carnitine infusion (20 mg/kg) 3 times a week for 6 months and monthly carnitine levels obtained. Cardiac function was assessed at baseline and again after 6 months of carnitine therapy. Standard ECHO measures of LV size and systolic and diastolic function as well as circumferential, radial, and longitudinal strain and strain rate analysis using speckle tracking were performed. Interdialytic weight gain (IDWG) and blood pressures were monitored throughout the study.

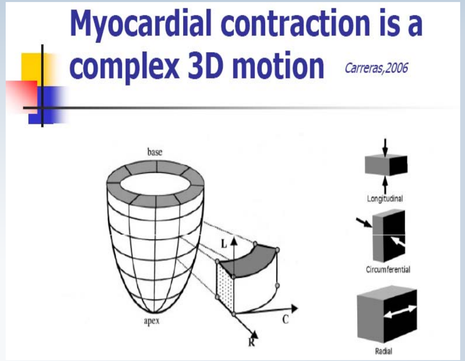
Statistical Analysis: Carnitine levels, interdialytic weight gain, predialysis BP and ECHO parameters before and after carnitine supplementation were analyzed. p value <0.05 was considered significant. Pre and post treatment ECHO parameters, mean BP, and IDWG were compared by student's t test. Comparison of carnitine levels between observation phase (5 values per patient) vs intervention phase (6 values per patient) were assessed longitudinally using random effects linear regression with STATA 11.0 Software.

SPECKLE TRACKING ECHO

•Myocardial function can be assessed by wall deformation (strain). Strain is change in length corrected for original length ("stretching" of the heart muscle fiber).

•Speckle Tracking ECHO assesses strain and strain rate in 3 planes: longitudinal, circumferential, and radial

•Strain rate closely relates to cardiac contractility and is not affected by volume changes or ventricular loading conditions



RESULTS

Table 1. Pre and post treatment plasma carnitine measurements

	Observation Phase Mean (95% CI)	Intervention Phase Mean (95% CI)	P
Total Carnitine (umol/L)	49.6 (13.2-85.9)	267.2 (231.4-302.9)	**0.00**
Free Carnitine (umol/L)	29.4 (5.9-52.9)	160.4 (137.3-183.5)	**0.00**
Acyl Carnitine (umol/L)	20.2 (3.6-36.9)	106.8 (90.6-123.1)	**0.00**
Acyl:Free Carntine Ratio	0.73 (0.58-0.87)	0.69 (0.55-0.83)	0.51

Table 2. Echocardiographic measures of left ventricular function

ECHO parameter	Pre-treatment ± SD	Post-treatment ± SD	P
End Diastolic Dimension	-.72 + 0.9	-.92 + .96	0.67
LV Mass/Ht $^{2.7}$	35.6 ± 14.4	35.3 ± 12.1	0.96
Ejection Fraction (%)	65.7 ± 8.5	65.9 ± 5.2	0.96
Shortening Fraction (%)	39.7 ± 5.6	38.0 ± 5.8	0.64
Longitudinal Strain Rate	**1.46 ± 0.33**	**1.92 ± 0.37**	**0.02**
Radial Strain Rate	2.72 ± 0.75	2.91 ± 1.05	0.69
Circumferential Strain Rate	2.65 ± 0.38	2.68 ± 0.50	0.91

RESULTS SUMMARY

•Patient demographics: 8 children on chronic HD with mean age 12.8 ± 1.9 years (range 9-16 years) completed the study (2 female, 6 male). Three participants were of Hispanic ethnicity, 3 African American, and 2 Caucasian. Mean dialysis vintage at initiation was 9.1 ± 6.9 months (range 3-23 months).

•Mean blood pressure and IDWG of patients did not change significantly between the observation and intervention phases of the study.

•Total, free, and acyl carnitine levels increased significantly ($p < 0.001$), but acyl:free carnitine ratio remained unchanged after carnitine therapy (Table 1).

• Longitudinal strain rate significantly improved ($p=0.02$) after supplementation (Table 2). The post carnitine longitudinal strain rate reflects a 35.3% improvement compared with pretreatment parameters.

CONCLUSIONS

•We were able to detect improvements in LV function by strain rate analysis that was not detected by standard ECHO. Speckle tracking analysis can detect early signs of LV dysfunction in children on chronic HD and supplementation with IV carnitine may improve LV performance in these children.

• Six months of IV carnitine supplementation improved total and free carnitine levels in children on chronic HD without impacting acyl:free carnitine ratio.

•Longer duration and/or higher dose of carnitine therapy may be needed to reduce the acyl to free carnitine ratio in this population. Further studies are needed.