Associations Between Acylcarnitine Moieties and Physical Domains of the Short Form 36 Quality of Life Questionnaire

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ABSTRACT

Background: Hemodialysis patients have a chronically low ratio of free to acylcarnitines. Also, hemodialysis patients have significantly lower scores on the Short Form-36 (SF-36) Quality of Life (QoL) physical domains.

Materials & Methods: The purpose of this paper is to assess trends between physical domains and acylcarnitine at baseline of a double-blind, placebo controlled intervention study performed at several dialysis clinics. Blood lab values, QoL questionnaire, physical assessments, and subjective global assessment (SGA) were recorded.

Results: Subjects' (n=65) mean age was 68.5 ±14 years. Total carnitine (TC), free carnitine (FC), and acylcarnitine (AC) concentrations were 35.67 ± 11.43 μmol/L, 19.91 ± 7.43 μmol/L, and 16.10 ± 6.18μmol/L, respectively. The mean PCS score was 30.68 ± 6.92 according to the QoL assessment. PCS was significantly associated with several medium chain (MC) and two MC dicarboxylic acid (DA) acylcarnitines. The bodily pain (BP) domain was significantly associated with many MC, the long chain (LC), and one MCDA acylcarnitines. The role physical (RP) domain was significantly associated with short chain (SC) and one MCDA acylcarnitines. The general health (GH) domain was significantly correlated with several LC acylcarnitines. The vitality (VT) domain was significantly correlated with the MCDA acylcarnitines. These results indicate that different domains of physical status are influenced by concentrations of specific carnitine moieties. PCS, GH, and BP scores are negatively associated with MC and LC acylcarnitines, indicating that when beta-oxidation is inhibited, BP increases. The RP is positively associated with MC and SC acylcarnitines, indicating that when partial beta-oxidation occurs, an individual is able to accomplish more physical tasks. Presence of all DA acylcarnitines positively correlated with PCS, BP, RP, GH, and VT domain scores. This data suggests that as mitochondrial fatty acid oxidation is reduced, increased peroxisomal oxidation increases physical status.

Introduction:

☐ In chronic kidney disease there is an altered carnitine homeostasis (Ricanati, Tserng, Hoppel, 1987)

☐ Carnitine is a small, water-soluble molecule
- ❖ Sources
  - ➢ 75% ingested
  - ➢ 25% synthesized internally
- ❖ Functions
  - ➢ Acyl shuttling into mitochondria
  - ➢ Free CoA balance
- ❖ In the urine of healthy subjects
  - ➢ 98-99% free carnitine reabsorbed & 5 μmol/kg/day of acyl + free lost in urine/day (Lombard et al, 1989)
- ❖ In the dialysate of patients on dialysis due to chronic kidney disease (Evans et al, 2000)
  - ➢ Approximately 1050 μmol/week lost (equal amounts of free & acyl)

Hypothesis:

☐ Carnitine is a vital molecule in the fatty acid oxidation pathway. Hemodialysis patients have a chronically low ratio of free to acylcarnitines (AC). In addition, hemodialysis patients have significantly lower scores on the Short Form-36 (SF-36) Quality of Life (QoL) physical domains. Reductions in energy production can have direct impacts on physical functioning capabilities. Therefore, we hypothesize that physical domains on the questionnaire are associated with plasma AC concentrationss.

Purpose:

☐ Since previous studies have concluded that quality of life measurements, especially those concerning physical functions, improve with L-carnitine supplementation, the purpose of this study is to find whether carnitine status correlates with quality of life (QoL) measurements in hemodialysis patients.

Materials & Methods:

☐ Baseline data from a 24 week L-carnitine intervention treatment in dialysis patients was used. This study was a randomized, double-blind clinical trial with a cohort of stage 5 CKD hemodialysis patients.

☐ Cohort
- ❖ The patients for the study are treated at the Dialysis Center of Lincoln, NE and its constituent satellite sites as well as Davita Clinics in Cleveland.
- ❖ The criterion for patient selection include:
  - ➢ Inclusion criteria:
    - ✓ Age ≥ 19 years
    - ✓ At least three hours of low acetate hemodialysis treatments three times per week
    - ✓ Received dialysis ≥ 6 months
    - ✓ MOS SF36 PCS <35
    - ✓ Plasma free carnitine < 40 mol/L
  - ➢ Exclusion:
    - ✓ Previous treatment with L-carnitine within 6 months of study
    - ✓ Excessive blood loss within two months of study
    - ✓ skeletal muscle function diseases
    - ✓ liver disease
    - ✓ pregnancy

Randomization
- Pharmacist

Baseline data Collection
- ➢ Subjective Global Assessment (SGA),
- ➢ Tricep skinfold (TSF)
- ➢ Mid-arm circumference (MAC)
- ➢ Sit-to-Stand & Gait Speed (STS & GS)
- ➢ Medical charts reviewed for descriptive variables
- ➢ Lab values assessed particularly for AC and TC concentrations

100 ml IV Saline Placebo ← **Treatment 10 minutes post HD** → **100 ml IV w/ 20mg/kg L-Carnitine**

12 week data collection point (same as baseline)

24 week data collection point (same as baseline)

Figure 1: Flow of subjects from screening to end of trial

☐ Utilized data from:
- ❖ Data collected from pt interview, medical records, nursing flow sheets, laboratory reports
- ❖ Acylcarnitine
  - ✓ Analyzed by HPLC/ESI/MS/MS following derivatization with pentafluorophenacyl trifluoromethanesulfonate (Minkler et al, Analytic Chem, 2005)

Baseline Sample Characteristics:

Age	68.49±14yr
Gender	55.4% male
Ethnicity	75.4% Caucasian 20.0% African American 4.6% Hispanic
Etiology	41.9% TII DM 33.9% HTN 24.3% Other
Weight	81.54±20kg
BMI	27.90±6.4
Months on Dialysis	39.70±36
Albumin	3.8+0.4
Hgb	12+1.5
Hct	38+5
BUN	49+2
Session length	222.63±27 min
EPO Dosage	6390.67±7694 units
Tricep Skin Fold	13.99±6.7 mm
Mid-arm Circumference	29.93±5.8 cm
C-reactive Protein	16.08±20 mg/dL
Sit-to-stand Test	5.19±4.2 completions
Gait Speed	13.15±35 sec
Protein intake/day	64.06±27 g
Kilocalorie intake/day	1649.52±587
SGA	5.20±1.0
Physical Composite Score	30.1+6.9
Mental Composite Score	47.89±12

Table 1: Descriptive data defining cohort population at baseline

Acyl-carnitine Moieties Categories and QoL:

Acyl Moiety (mmoles/L)	Acyl Chain Size	PCS	Bodily Pain	Physical Fx	General Health	Vitality
tigoyl	Short			0.26		
3-hyroxy-isovaleryl	Short			0.31		
isobutyryl	Short			0.29		
myristoyl	Medium		-0.27	0.28		
lauroyl	Medium	-0.35	-0.49			
decanoyl	Medium	-0.26	-0.48			
octanoyl	Medium	-0.30	-0.53			
hexanoyl	Medium		-0.40			
linoleoyl	Long		-0.38			
oleoyl	Long		-0.66		-0.27	
stearoyl	Long		-0.30			
palmitoyl eoyl	Long		-0.44		-0.29	
palmitoyl	Long		-0.47		-0.29	
sebacoyl*	Medium			0.29		
3-methyl-glutaroyl*	Medium	0.27				0.26
adipoyl*	Medium	0.32	0.28			

Table 2 : A comparison of specific AC moieties and the correlations to specific categories of the quality of life (QoL) questionnaire . * These moieties are dicarboxilic acid AC

RESULTS SUMMARY

☐ It is most interesting to note:
- ❖ The positive correlations between short-chain AC and physical functioning
- ❖ The negative correlations between bodily pain and medium and long chain AC
- ❖ The negative correlations between physical composite score and medium chain AC
- ❖ The positive correlations between medium chain dicarboxylic AC and several different categories

CONCLUSIONS

☐ The results from this small sample indicate that specific AC moieties, primarily defined by chain length, have a direct correlation with perceived QoL.
- ❖ Short chain AC indicate that β-oxidation occurred to some extent. The positive correlations between these moieties and physical functioning indicate that these metabolized acyl chains are supporting activity.
- ❖ The negative correlations between medium and long chain AC indicates that these moieties have incomplete β-oxidation.
- ❖ Lastly, the positive benefits seen in the dicarboxylic acids indicate that acyl chain oxidation in the peroxisomes benefiting the QoL of the subjects.
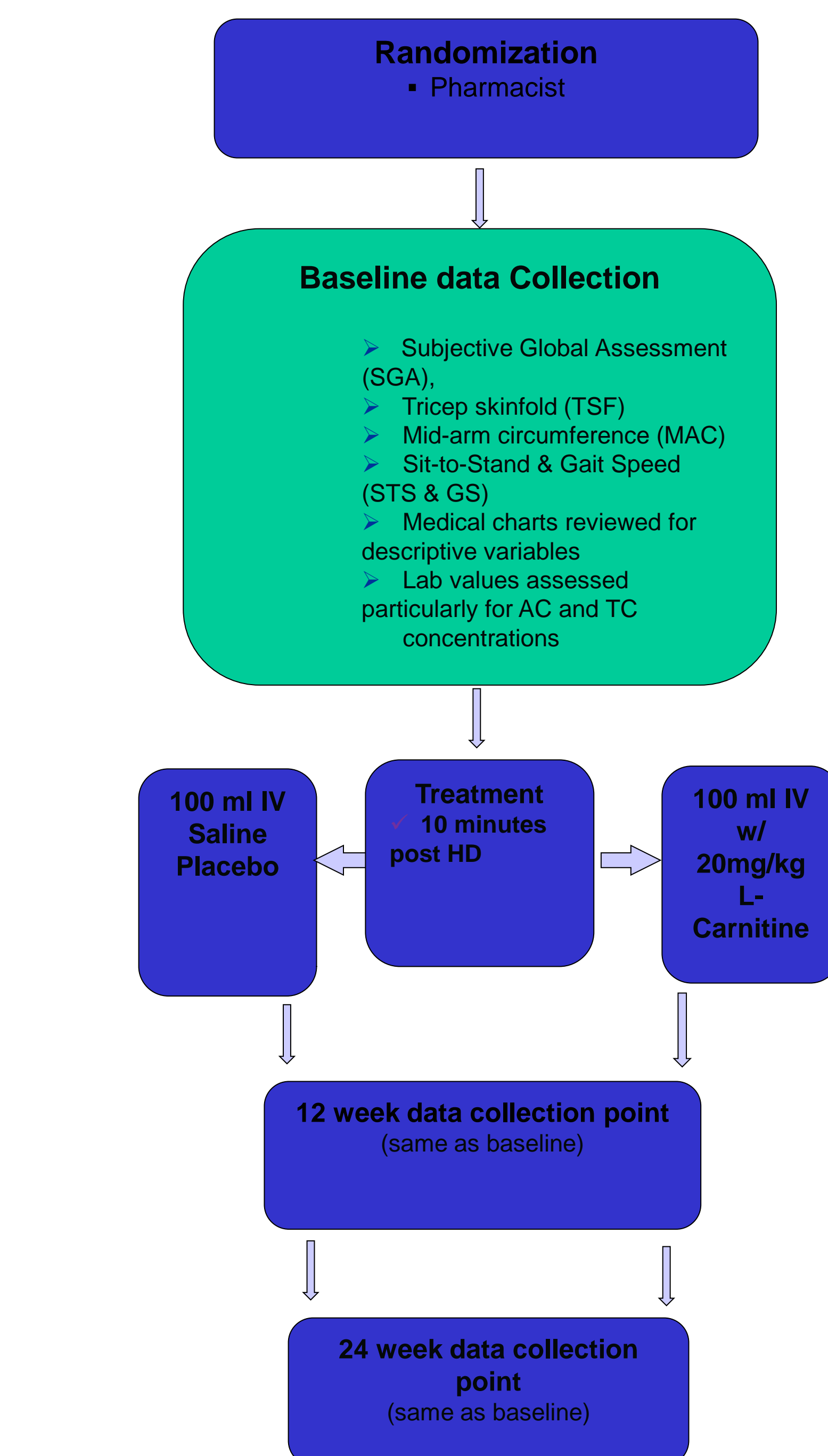 - ✓ Future research on the effect of peroxisomes on hemodialysis QoL is necessary.