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A Pilot Study Aimed To Evaluate The Loss Of Carnitine During Intermittent (IHF) and Continuos Veno-Venous Hemofiltration (CVVH) In Acute Kidney Injury (AKI) Patients

[1]Alfonso Pacitti, [1]Paola Inguaggiato, [1]Tiziana Papalia, [2]Guido Martina, [3]Vincenzo Cantaluppi

[1]Nephrology and Dialysis Unit, Cuneo Hospital, Italy, [2]Nephrology and Dialysis Unit, Chivasso Hospital, Italy, [3]Nephrology, Dialysis and Kidney Transplantation Unit, University of Turin, Italy

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BACKGROUND

Several studies reported that Carnitine species (CA) are subjected to a substantial loss during hemodialysis (HD), thus requiring a scheduled replacement. However, no data are available on CA loss induced by intermittent (IHF) or continuous (CVVH) hemofiltartion in AKI patients.
Levo-carnitine (L-CA), a small molecular weight solute unbound to plasma proteins, is mainly eliminated by a renal clearance of 1-3 mL/min, indicating an extensive (98-99%) tubular reabsorption.
Basing on the rate of artificial clearance, during CVVH a loss of CA should be estimated >10 times greater than normal.
The loss of CA during IHF or CVVH may contribute to the neuro/miopathy typically observed in critically ill patients. In addition, recent studies sugegsted that CA exerts a protective effect on AKI induced by ischemia-reperfusion injury, different nephrotoxic agents and sepsis. On this basis, loss of CA during IHF and CVVH may slow the recovery from AKI.

AIM OF THE STUDY

The aim of the study was to evaluate the depurative kinetic of different CA species during post-dilutional (PD) IHF and CVVH in patients with AKI compared to chronic kidney disease (CKD) patients in stable hemodialytic treatment.

METHODS

CA species (Laevo-, Acetyl-L- and Propionyl-L-carnitine) were dosed by chromatographic methods in 5 CKD patients treated by a single PD IHF session [Tab I] and in 5 AKI patients submitted to PD CVVH [Tab II].
CA plasma values (CAs) were corrected for Plasma Water (PW) exclusion, to compute the Sieving Coefficient (SC) by the ratio of CA effluent (EF) (CAEF) to CA PW (CAPW) concentrations.
In CKD patients, CAEF were also measured on total EF collection. In another group of AKI patients (n=5), L-CA levels were measured daily during CVVH treatment [Tab III].

Pt Code	Gender	Age	Disease	Treatment type	Dialytic Age (yr)	L-Carnitine Therapy during	HD Duration Min
ANG	M	60	DM	HD	2.63	Yes	240
DIB	M	70	DM	HD	4 .83	No	266
FED	F	80	NAS	HD	1.6	No	232
GRA	M	49	GN	HD	2.88	NO	240
LAM	F	72	VAS	HD	3.12	NO	240

TAB I Patients with Chronic renal failure submitted to a HF session (DM = diabetes mellitus, NAS= nephroangiosclerosis, GN = Glomerulonephritis, VAS= Wegener M.)

NAME	Gender	Age	Days from ICU admittance	AKI cause	RIFLE	Outcome
BEGN.	M	69	9	neoplasia	F	
FIEC.	M	58	15	Sepsis	F	Death
CATT	M	78	10	CHF,	I	
GEN	F	76	0	ATN	F	
RON	M	62	13	Heart Tx	F	Death

Tab II Acute Renal Failure Patients performing CVVH (ATN= Acute Tubular Necrosis, CHF = Congestive Heart Failure, OHS, open heart surgery, Tx = transplantation)

Name	Diagnosis	Age (Yr)	Sex	RIFLE	OUTCOME	Dyalisis duration
SF	CHF/WL heart graft	43	M	F	FR	12
CL	CHF/ BPAoC/ECMO	52	M	F	Death	16
PA	Post-BPAoC/ septum recostruction	55	M	F	FR	15
TF	Septic shock post Heart tx	59	M	F	Death	16
RG	Septic shock post Heart tx	62	M	F	FR	13
MEAN		54.20				14.40
SD		7.33				1.82

TAB III : AKI patients followed along a CRRT period with pre-session L-CA

ANG	L-Carnitine (nmol/mL)			Acetyl-L-carnitine (nmol/ml)			Propionyl-L-carnitine (nmol/ml		
Time (min)	Plasm	Effluent	Sc	Plasma	Effluente	Sc	Plasma	Effluente	Sc
15	287	279	0,97	81	88	1,09	5,66	5,82	1,03
60	215	220	1,02	60	69	1,15	4,23	4,6	1,09
120	193	200	1,04	49	57	1,16	3,49	3,72	1,07
180	156	162	1,04	41	43	1,05	2,9	2,88	0,99
240	129	129	1	32	35	1,09	2,02	2,15	1,06
			1,01			1,108			1,048
DIB	Plasm	Effluent	Sc	Plasm	Effluent	Sc	Plasm	Effluent	Sc
15	22,26	19,13	0,86	3,82	4,12	1,08	0,29	0,26	0,9
60	20,29	16,85	0,83	3,38	3,44	1,02	0,21	0,22	1,05
120	14,17	14,8	1,04	2,64	2,93	1,11	0,19	0,19	1
180	12,09	13,77	1,14	2,67	3,42	1,28	0,17	0,2	1,18
240	10,73	10,76	1	3,45	3,78	1,1	0,15	0,15	1
			0,97			1,118			1,026
FED	Plasm	Effluent	Sc	Plasm	Effluent	Sc	Plasma	Effluente	Sc
15	17,45	17,41	1	3,46	3,87	1,12	0,18	0,16	0,89
60	13,83	14,29	1,03	2,62	3,21	1,23	0,13	0,12	0,92
120	11,48	11,46	1	2,22	2,56	1,15	0,08	0,09	1,13
180	10,45	9,91	0,95	2,54	2,68	1,06	0,07	0,08	1,14
240	9,21	9,16	0,99	2,28	2,74	1,2	0,06	0,06	1
			0,99			1,152			1,016
LAM	Plasm	Effluent	Sc	Plasma	Effluente	Sc	Plasma	Effluente	Sc
15	27,12	27,76	1,02	4,83	5,54	1,15	0,18	0,2	1,11
60	21	19,95	0,95	4,19	4,91	1,17	0,13	0,15	1,15
120	18,89	18,18	0,96	4,12	4,44	1,08	0,13	0,12	0,92
180	18,32	18,4	1	3,47	3,83	1,1	0,11	0,13	1,18
240	16,95	16,2	0,96	3,09	3,89	1,26	0,16	0,15	0,94
			0,97			1,152			1,06
GRA	Plasma	Effluente	Sc	Plasma	Effluente	Sc	Plasma	Effluente	Sc
15	28,9	27,96	0,97	6,86	7,69	1,12	0,36	0,41	1,14
60	23,7	24,22	1,02	5,66	6,42	1,13	0,31	0,33	1,06
120	20,57	21,13	1,03	4,68	5,38	1,15	0,27	0,3	1,11
180	17,5	17,4	0,99	3,74	4,36	1,17	0,2	0,23	1,15
240	16,87	16,99	1,01	3,32	3,75	1,13	0,19	0,19	1
			1,00			1,14			1,092
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Mean of Mean SC:			0,993			1,134			1,048
DS			0,016			0,020			0,031
Lower Confidence Int (p=0.01)			0,92			0,91			0,86

Tab IV CRF Patient: Plasma (C) / Effluent (UF) water concentrations SC are calculated . Plasma and effluent Area Under Curve (AUC) of individual patients are reported.

	L-Carnitine			Acetyl-L-carnitine			Propionyl-L-carnitine (nmol/ml)		
BEGN	(nmol/mL)			(nmol/ml)					
Time	PW	EF	SC_co	PW	EF	SC_c2	PW	EF	SC_c3
0	42.94			5.88			0.66		
30	43.36	43.84	1.01	5.95	6.12	1.02	0.66	0.67	1.00
180	39.16	30.94	0,78	4.61	4.06	0,88	0.56	0.48	0.84
FIECH									
Time	C0 (µM)	UF (C0)	SC_co	C2 (µM)	UF (C2)	SC	C3 (µM)	UF (C3)	SC
0	123.2			12.83			2.11		
30	110.4	95.88	0,86	12.15	11.57	0,95	1.88	1.66	0,88
180	88.25	88.06	0,99	10.54	11.17	1,05	1.56	1.55	0,99
CATT									
Time	C0 (µM)	UF (C0)	SC_co	C2 (µM)	UF (C2)	SC	C3 (µM)	UF (C3)	SC
0	34.88			4.65			0.6		
30	31.57	30.02	0,95	4.26	4.33	1,01	0.51	0.51	0,99
180	30.12	29.15	0,96	4.1	4.1	0,99	0.47	0.48	1,00
GEN									
Time	C0 (µM)	UF (C0)	SC_co	C2 (µM)	UF (C2)	SC	C3 (µM)	UF (C3)	SC
0	69.29			28.06			1.04		
30	63.36	63.64	1,00	25.54	27.6	1,08	0.9	0.97	1,07
180	56.7	53.68	0,94	20.46	21.98	1,07	0.77	0.83	1,07
RON									
Time	C0 (Mm)	UF (C0)	SC_co	C2 (µM)	UF (C2)	SC	C3 (µM)	UF (C3)	SC
0	7.23			1.08			0.08		
30	6.35	5.68	0.89	0.97	0.92	0.95	0.07	0.06	0.81
180	5.23	5.06	0,96	0.81	0.82	1,01	0.04	0.05	1.08

			Conf Interval	
	MEAN	SD	up. Limit	lo. Limit
C0	0,99	0,02	1,04	0,95
C2	1,15	0,06	1,13	0,86
C3	0,97	0,05	1,11	0,88

Tab V AKI Patient: Plasma water (C) / Effluent (UF) concentrations . Sieving Coefficients (SC) are calculated by plasma / effluent water concentrations ratios

Name	L-Carnitine (Start CVVH)	L-Carnitine (during CVVH)	Days of Treatment
SF	23,98	10,56	12
CL	30,12	7,19	16
PA	26,67	6,94	15
TF	28,34	3,15	16
RG	25,31	6,91	13
Mean	26,88	6,95	14,40
SD	2.43	2,62	1,82
P =	0,00058907		

TAB VI: AKI patients followed along a CRRT period

	CO	C2	C3	Urea
	11,46	9,48	10,31	5,43
	12,85	5,05	0,28	3,08
	28,14	10,18	15,32	8,00
	13,10	17,01	16,28	6,76
Mean	16,39	10,43	10,55	5,82
SD	7,87	4,94	7,33	2,11

TAB VII Ca species plasma rebound measured 30' min after the end of the HF session (% of the end session levels)

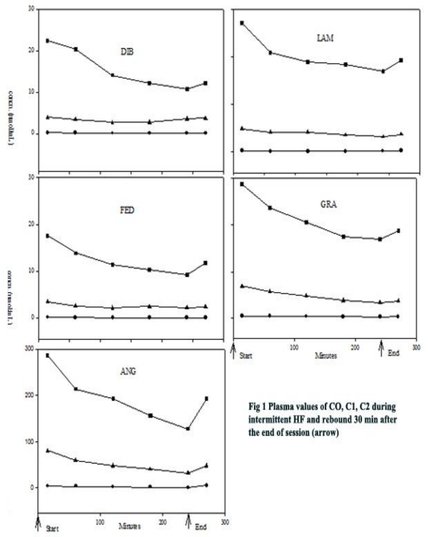

Fig 1 Plasma values of C0, C1, C2 during intermittent HF and rebound 30 min after the end of session (arrow)

RESULTS

In CKD [Tab IV] as well as AKI [Tab V] patients, the mean SC values of every CA species were into the lower limit of confidence of 1.0 (p< 0.01), indicating the identity among CAPW and CAEF and a complete passage through the membrane .

In the AKI group on CRRT, the plasma CAs significantly decreased from 26,88 ± 2,4 to 6,95 ± 2,6 µM/L in a period of 14,4 ± 1,8 days. [Tab VI]

In CKD patients on IHF, a decrease of CA during the session was observed with a rebound at 30' after the end (slower equilibration of inner body compartments) [Tab VII]. CA kinetic in all CKD patients is reported in Fig. 1

The total loss of CA species measured on EF collection was proportional to CA income and CAs: the only CKD patient in treatment with L-CA (1g i.v. 3 times/week) had a loss of 583±29 mg compared to the average value of 52.6±14 of the other cases.

CONCLUSIONS

Prolonged intense CVVH treatment was associated with a daily loss of hundred of milligrams of L-CA.

The SC observed in PD CVVH and confirmed in PD IHF suggested that CA was efficiently removed by convection-based techniques.

CA loss could be hardly compensated by endogenous synthesis for the slow subtraction and the substantial equilibration of the body compartments.

The depletion of CA body pool during CVVH may be a co-factor for critical illness neuro/miopathy and organ dysfunction. The lack of CA may contribute to mitochondrial dysfunction and delayed tissue regeneratio in spesis-associated AKI (Fig. 2).