Serum hepcidin-25 level; is it related to cardiovascular mortality in hemodialysis patients

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Background

Cardiovascular disease (CVD) is an important cause of mortality and morbidity in haemodialysis (HD) patients. Iron accumulation in arterial wall is increased in atherosclerotic lesions. Hepcidin is a key hormone in iron balance. Studies showed an association between hepcidin and atherosclerotic disease. The aim of this study is to investigate the relation of serum hepcidin-25 (SH-25) and atherosclerosis measured by carotid intima-media thickness (CIMT) and mortality in HD patients.

Methods

Eighty-two HD patients enrolled in this study. DRG Hepcidin ELISA-GERMANY kit was used for the measurement of SH-25. CIMT was measured by high resolution real-time ultrasonography. After four years of first assessment relation of all cause and cardiovascular mortality with SH-25 and CIMT was investigated. Statistical analysis was performed by using statistical package SPSS version 20.0 (SPSS Inc., IL, USA).

Results

Two of the 82 patients were excluded because of renal transplantation. The patients living were younger(53.7±15.1 vs 65,2±15,5, P=0,001, CIMT was lower(0,83±0,2 vs 0,95±0,2, P=0,003.) but HS-25 was not different between groups(29,1±13 vs 32,4±22,4, P=0,767). The patients died of CVD were statistically significantly older (63.7±16.1 vs 53.7±15.1, P=0,008), had statistically significant higher CIMT (0,94±0,2 vs.83±0,2 , P=0,028.). SH-25 was statistically significantly higher in patients died of CVD (40,3±.25 vs, 29,1±.13 P=0,005). In the correlation analysis CIMT was positively correlated with age and SH-25 (R=0.505, P=0,021 and R=0.606 P=0,004; respectively). By linear regression analysis the correlation of CIMT with SH-25 persisted.

Conclusion

Our results implicate that hepcidin may be involved in pathophysiology of atherosclerosis and CV mortality in HD patients.

Table 1 general properties of patients

	Patients (N=82)
Male sex,%(no)	43.9%(36)
Age (years)	57.90±16.08
Dialysis vintage(months)	124.82±16.79
Diabetes mellitus, %(no)	26.8%(22)
History of CVD, %(no)	35.4%(29)
Current smoker, %(no)	-
Body weight(kg)	61.85±14.34
SBP	124.82±16.79
DBP	76.83±10.26
Kt/v	1.49±0.28
BMI(kg/m2)	25.63±14.44
Treatment characteristics	
Prescription of ESA, , %(no)	87.8%(72)
Use of iron replacement therapy, %(no)	67.1%(55)
Prescription of RAS inhibitors, %(no)	26.8%(22)
Prescription of calcium blocker, %(no)	24.4%(20)
Prescription of beta blocker, %(no)	29.3%(24)
Prescription of alpha blocker, %(no)	3.7%(3)
Prescription of statin, %(no)	3.7%(3)
Laboratory parameters	
Haemoglobin (g/dl)	10.69±1.35
Ferritin (ng/ml)	753.74±376.99
TSAT(%)	29,37±16,83
LDL Cholesterol(mg/dl)	91.45±35.18
HDL Cholesterol(mg/dl)	36.61±11.80
Albumin(g/dl)	3.62±.50
CRP(mg/L)	2.22±2.72
Hepcidin-25 (ng/ml)	30.17±17.06
CIMT(cm)	.8737±.1956

Abbreviations; BMI; body mass index, Ca;Calcium, CIMT; Carotid Intima-Media Thickness, CRP; C-Reactive Protein, DV; Dialysis vintage, HDL-C; high density lipoprotein cholesterol, LDL-C; low density lipoprotein cholesterol; LVM; Left Ventricular Mass, LVMI; Left Ventricular Mass Index, MAP; Mean arterial pressure, P; Phosphorus, PTH; parathyroid hormone.

Table 2 Comparision of the patients living and all deaths

Parameter	Living (n=49)	Died (n=31)	P
Age (years)	53.7±15.1	65,2±15,5	0,001
Gender (male, n, %)	18(36,7%)	18(58,1%)	0,062
BMI (kg/m^2)	26.9±18,2	23,9±4,9	0,296
Diabetes (n, %)	12 (24%)	10(32,3%)	0,448
Hypertension (n, %)	25(51%)	17(54,8%)	0,739
ESA treatment(n, %)	43(87.8%)	27(87.1%)	0.741
Iron treatment(n, %)	33(67.3%)	20(64.5 %)	0.635
DV (months)	84,2±68,4	74.2±57.8	0,882
MAP(mmHg)	92,9±12,4	93.1±10,3	0,956
Kt/V	1,5±0,3	1.45±0,3	0,405
Hemoglobin (g/dl)	10,8±1,4	10.6±1,3	0,836
Ferritin (ng/ml)	786,9±387,8	707.1±349,3	0,148
Glucose (mg/dl)	96,1±29,6	113±48,1	0,168
Albumin (g/dl)	3,7±0,5	3,6±0,4	0,253
CaxP (mg^2/dl^2)	47,7±11,8	45,3±11,1	0,293
PTH(pg/ml)	659,7±589,4	723,4±853,4	0,550
HDL-C (mg/dl)	38,0±12,2	34,4±11,3	0,132
LDL-C (mg/dl)	97,3±37,2	84,4±29,6	0,226
CRP (mg/l)	2,1±2,9	2,32±2,59	0,398
Hepsidin (ng/ml)	29,1±13	32,4±22,4	0,767
LVMI(gr/m²)	136,2±36,6	147,4±40,3	0,258
LVH (n, %)	33(67,3%)	24(77,4%)	0,332
CIMT (cm)	0,83±0,2	0,95±0,2	0,003

Table 3 Comparision of the patients living and deaths from cardiovascular disease

Parameter	Living (n=49)	Deaths from CVD(n=21)	P
Age (years)	53.7±15.1	63.7±16.1	0,008
Gender (male, n, %)	18(36,7%)	13(61,9%)	0,052
BMI (kg/m^2)	26.9±18,2	23,2±4,5	0,168
Diabetes (n, %)	12 (24%)	7(33,3%)	0,448
Hypertension (n, %)	25(51%)	13(61,9%)	0,402
ESA treatment(n, %)	43(87.8%)	17(81%)	0,612
Iron treatment(n, %)	33(67.3%)	14(66.7%)	0.690
DV (months)	84,2±68,4	84,4±63,3	0,681
MAP(mmHg)	92,9±12,4	94,9±11	0,601
Kt/V	1,5±0,3	1,44±0,31	0,305
Hemoglobin (g/dl)	10,8±1,4	10,6±1,5	0,758
Ferritin (ng/ml)	786,9±387,8	715,3±343,7	0,189
Glucose (mg/dl)	96,1±29,6	106,5±31,7	0,214
Albumin (g/dl)	3,7±0,5	3,6±0,43	0,301
CaxP (mg^2/dl^2)	47,7±11,8	44.2±10.3	0,135
PTH(pg/ml)	659,7±589,4	824,9±1001,9	0,613
HDL-C (mg/dl)	38,0±12,2	36.6±11.3	0,551
LDL-C (mg/dl)	97,3±37,2	86±31	0,365
CRP (mg/l)	2,1±2,9	2,4±2,5	0,324
Hepsidin (ng/ml)	29,1±13	40,3±25,4	0,005
LVMI(gr/m²)	136,2±36,6	145,7±36,7	0,284
LVH (n, %)	33(67,3%)	16(76,2%)	0,459
CIMT (cm)	0,83±0,2	0,94±0,2	0,028

Table 4 The correlation between CIMT with demographic and biochemical parameters in deaths from cardiovascular disease

Variables	CIMT r	CIMT P
Age (years)	0,501	0,021
BMI (kg/m^2)	0,091	0,696
DV (month)	0,196	0,396
Kt/V	0,05	0,828
MAP(mmHg)	0,042	0,856
Glucose(mg/dl)	0,125	0,620
Hemoglobin(g/dl)	-0,22	0,926
Albumin(g/dl)	-0,76	0,742
CRP (mg/l)	0,178	0,441
CaXP(mg^2/dl^2)	0,338	0,134
Ferritin (ng/ml)	0,167	0,469
PTH(pg/ml)	0,255	0,264
Hepsidine (ng/ml)	0,606	0,004

Table 5 Linear regression analysis

Model		Unstandardized coefficients B	Unstandardized coefficients Standard error	Standardized coefficients Beta	t	Sig.
1	(Constant)	,666	,129	,476	5,174	,000
	Hepcidin-25	,003	,001	,282	2,372	,029
	Age	,003	,002		1,405	,177

DOI: 10.3252/pso.eu.54ERA.2017