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Consequences of Sympathetic Nervous System Stimulation on Aortic Pulse Wave Velocity and Pulse Pressure in Hemodialysis Patients

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Introduction

Arterial wall stiffness, assessed by measuring pulse wave velocity (PWV), predicts all cause mortality in patients with ESRD (1,2). Modification of pulse wave velocity in ESRD patients remains still unexplored (3,4,5). Furthermore, uraemic state is accompanied by disordered function of autonomous nervous system which in turn is considered responsible either for hypotensive episodes during dialysis sessions or for systematic hypertension due to altered function of Sympathetic Nervous System.

In particular, stimulation of SNS during a dialysis sessions is frequent with unexplored consequences. SNS signal targets vascular wall and transmission of the transmural pressure is achieved according to the mechanical properties of the vascular wall. Irregular SNS signal on the other hand, would result in disturbed vascular response. Adaptations of PWV to handgrip and thus to the stimulation of autonomous nervous system have not been reported previously and are subject of this study. We also attempt to correlate these modifications to the presence of vascular and particularly coronary calcification (CC) and to discuss its clinical implications.

Patients and Methods

We studied 54 stable dialysis patients with a mean age of 62.7±12.1 years and a mean duration on dialysis 55±42 months.

Pulse Wave Velocity evaluation

PWV was determined from carotid and femoral arterial pulses recorded simultaneously with ECG before and during handgrip. The SphygmoCor System appliance was used for the measurements which were performed the day between two dialysis sessions. Distance between two standard points in conjunction with the time consumed by the pulse wave to move from the first to the second defines PWV (distance-m/ time-sec)

Handgrip test

Sustained (isometric) muscle exercise causes a heart rate – dependent increase in cardiac output and systemic blood pressure. The test, which is based on this reflex, uses a handgrip dynamometer with handgrip maintained at 30% of the maximum voluntary contraction up to a maximum of 5 minutes, with blood pressure measured every minute with an ordinary sphygmomanometer. Responses were considered normal when: the increase in diastolic blood pressure, as a response to sustained handgrip, was ≥ 15 mmHg. Blood pressure was measured, with an ordinary sphygmomanometer. Patients were lying down throughout the study. Results were correlated to age, mean blood pressure, lipid profile, coronary disease and the presence of coronary calcification evidenced by spiral computed tomography. Results were also correlated to the total amount of phosphate binders containing CaCo3 and/ or Al(OH)3, which had been consumed by our patients since initiation of dialysis therapy. Epidemiological data of the patients are shown on table1.

Table 1. Epidemiological data of patients

N	54 (23M, 16F)
Age (years)	62.74±12.10
Time on dialysis (months)	55±42
Hypertension	19/54
Ischemic heart disease	15/54
Coronary calcification	24/54
Diabetes Mellitus	11/54

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Results

Laboratory data are shown on table 2.

Table 2. Biochemistry in the studied population (mv±sd)

Total cholesterol (mg/dl)	192±48
HDL (mg/dl)	46.7±9.7
LDL (mg/dl)	109±35
Triglycerides (mg/dl)	188±107
URR (%)	70±7.3
spKT/V	1.43±0.29
Calcification score (n=24)	302±77
	(Hounsfield units)

Elevated mean values of PWV and PP were found in our sample (mv11.7±3.6 m/sec and 53.2±18.7mmHg respectively). Significant increases in systolic, diastolic blood pressure, mean blood pressure and PWV were noted after the handgrip ($p<0.001$), whereas PP remained practically unchanged (Table 3). Raised PWV was positively correlated to coronary vascular calcification ($p<0.05$). When we compared the 24 patients who were positive for coronary calcification to the others, we observed that they were older (64 ± 8 vs 53 ± 24years, $p<0.005$), longer on dialysis (70 ± 42 vs 41 ± 24 months, $p<0.05$) and demonstrated significantly elevated PWV (12.8±4 vs 9.5±2.5m/sec, $p<0.01$).

Table 3. Response of the entity of patients to Handgrip (n=54)

	Before	After	P
Systolic BP(mmHg)	128±28	139±29	<0.001
Diastolic BP(mmHg)	75±16	82±18	<0.001
Mean BP(mmHg)	96.5±21	106±22	<0.001
Pulse Pressure (PP) (mmHg)	53±18	56±19	ns
PWV(m/sec)	11.7±3.6	12.53±4.6	ns

Furthermore, the elevated PWV remained unaffected after handgrip. No correlation with the type and the quantity of the phosphate binders or the rest parameters was found. Six of the patients who responded positively to handgrip (rise of diastolic pressure>15mmHg) did not behave differently than the remainder, who simply augmented PVW after handgrip.

Intragroup analysis revealed 18 individuals, in whom PWV was actually decreased ($p=0.001$). Triglyceride levels were lower in this group ($p<0.05$). No further difference was noted. In the remaining 36 individuals, PWV was raised significantly after handgrip ($p<0.01$), in spite the fact that they were not all positive responders (Table 4).

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Discussion

PWV was found to be substantially increased in renal patients compared to a similar group of healthy individuals, where values don't exceed 6m/sec. This reflects decreased vessel contractibility and thus renders these patients prone to morbid situations (6). It has been shown that increased PWV is an independent risk factor for increased morbidity and mortality (1,2). Therefore attempts towards modifying arteries' response by control of blood pressure and administration of hypolipidemic agents, aim to improve life span of renal patients and limit morbidity. However, not all patients respond to these agents for reasons not well described in the literature. It has been shown that *patients who were unable to establish a decrease of PWV after BP reduction* were more susceptible to all-cause and cardiovascular mortality compared to those who responded positively (7). We examined the ability of dialysis patients with elevated PWV to respond to SNS stimulants augmenting PWV, checking thus the extent of preservation of aortic distensibility. *Renal patients who preserve the ability to respond to SNS stimulants*, should increase PWV. Actually, two thirds of our patients increased PWV after handgrip test. This fact means that those patients maintain the ability to contract their vessels and they would behave similarly in response to BP reduction. However, we observed a substantial number (33%) of patients who in fact decreased PWV, exhibiting disturbed large-artery compliance. We suggest that those might be the patients who would not get benefit from BP regulation but they could respond to other ways of PWV modification.

In the present study, we demonstrated that presence of coronary calcification was positively correlated to increased PWV. It seems that coronary calcification reflects vascular calcification which renders vascular wall stiff and less compliant. This finding was recently reported also by Haydar et al (8). CC detected by electron beam tomography correlates with plaque burden, vessel stenosis and is predictive of future cardiac events in general population. (9) Patients in our study were older, longer on dialysis and were incapable to respond to handgrip. Also, they comprise a group of dialysis patients who are candidates for *intradialytic hypotension.* Likewise, Chesterton et al describe that reduced baroreflex sensitivity is associated with increased vascular limb calcification and arterial stiffness in a group of 34 HD patients (9). On the other hand, *more than half of patients in the present study maintain their ability to further augment PWV*. If, this represents an additional risk when SNS is stimulated during dialysis, remains to be clarified. Morbidity related to dialysis hypotension could be explained by these frequent elevations of PWV after hypotensive events during dialysis and we could expect improvement if we could achieve PWV reduction. Follow-up of these patients after the appropriate interventions, will validate *our hypothesis that basal response to handgrip would differentiate the group of patients who would benefit from diverse interventions.*

In conclusion, dialysis patients exhibit elevated values of PWV. Coronary calcification seems to be a major determinant of the augmented PWV. Older patients and those who are longer on dialysis, cannot respond to SNS stimulation. Handgrip test reveals two groups of patients:

1.Those, who *keep the ability to respond to handgrip augmenting PWV and would respond to BP lowering agents.*

2.Those who actually *decrease PWV after handgrip and who are candidates for hypolipidemic factors, that are also known to ameliorate PWV.*

References

1. Blacher J, Guerrin AP, Pannier B, et al. Arterial calcifications, arterial stiffness and cardiovascular risk in end-stage renal disease.Circulation 1999 May11;99(18):2434-9
2. Safar ME, Blacher J, et al. Central pulse pressure and mortality in end-stage renal disease.Hypertension 2002 Mar1;39(3):735-8
3. Vurmans JLT, Boer WH. Contibution of Volume overload and Angiotensin II to the Increased Pulse Wave Velocity of Hemodialysis Patients.J. Am Soc Nephrol 13:177-183, 2002
4. Raison J, Rudnichi A, Safar ME. Effects of atorvastatin on aortic pulse wave velocity in patients with hypertension and hypercholesterolaemia: a preliminary study. J Hum Hypertens 2002 oct;16(10):705-10
5. Ichihara A, Hayashi M, et al. Fluvastatin prevents development of arterial stiffness in hemodialysis patients with type 2 diabetes mellitus.Nephrolol, Dial, Transplant.(2002) 17: 1513-151
6. Benetos A, Henry OF, Rudinichi A, Safar ME. Aortic Pulse Wave Velocity predicts cardiovascular Mortality in Subjects>70 years of age Arteriosclerosis, Thrombosis, and Vascular Biology 2001;21:2046
7. Guerin AP, Blachair J, Pannier B , Marchais S, Safar M, Gerard M. Impact of aortic stiffness attenuation on survival of patients in End Stage Renal Failure.Circulation2001;103:987
8. Haydar AA, Covic A, Colhoun H, Rubens M, Goldsmith DJ: Coronary artery calcification and aortic pulse wave velocity in chronic kidney disease patients. Kidney Int 2004:65(5)1790-1794
9. Raggi P, Callister TQ, Cooil B et al: Identification of patients at increased risk of first unheralded myocardial infarction by electron beam computed tomography. Circulation 2000;101:85-855
10. Chesterton L, Sigrist M, Bennett T, McIntyre C. Reduced baroreflex sensitivity is associated with increased vascular calcification and arterial stiffness. ERA-XLI Congress Abstract book:2004;227