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Effects of Atorvastatin on Aortic Pulse Wave Velocity (PWV) in Hemodialysis Patients: A Preliminary Study

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Introduction

Arterial wall stiffness, assessed by measuring pulse wave velocity (PWV), may predict all cause mortality in patients with ESRD (1,2). Hypolipidemic drugs are known to prevent development of arterial stiffness in hemodialysis patients with hypercholesterolemia and/or type 2 diabetes mellitus (3,4). Recently reduced baroreflex sensitivity has been associated with increased arterial stiffness (5). Moreover, adaptations of PWV to "handgrip" and thus to the stimulation of autonomous nervous system have been reported by our team in a previous study, where ESRD patients were found either to keep the ability to respond to handgrip augmenting PWV or to decrease PWV after handgrip because of loss of aortic distensibility (6). Our initial hypothesis was that the latter group could get some benefit from hypolipidemic treatment.

Methods –Patients

In the present study we selected 20 stable dialysis patients who did not respond to the stimulation of SNS in the basal study. Ten pts were scheduled to receive 10 mg per day of atorvastatin for 6 months, while the other 10 were used as controls.

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). PWV was determined in two occasions, at the beginning and at the end of the 6 month period before and during handgrip.

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, and coronary disease. KT/V was kept >1.2 and dialysis conditions were kept stable.

Results

Characteristics of the study cohort are shown on tables 1 and 2.

Table 1. Characteristics of the study cohort

Gender (male/female)	**13/7**
Age (years)	**63.8±9.6**
Duration of dialysis (months)	**57.4±45.7**
Hypertension, n	**9**
Diabetes mellitus, *n*	**0**
Smoking history, *n*	**4**
Ischaemic heart disease, *n*	**8**

Table 2: Biochemistry in the study cohort (mv±sd)

BMI	**24.7±3.5**
Total cholesterol (mg/dl)	**189±49**
HDL (mg/dl)	**46.7±9.7**
LDL (mg/dl)	**104±34**
Triglycerides (mg/dl)	**199±115**
spKT/V	**1.46±0.29**

Elevated mean values of PWV were found in our sample (mv11.7±3.8 m/sec). Significant increases in systolic, diastolic blood pressure, mean blood pressure were noted after the handgrip ($p<0.001$). PWV remained unchanged at the basal study in the entity of the patients.(Table 3)

Table3: Response of the study cohort to Handgrip at the basal study (n=20)

	Before	**After**	**p**
Systolic BP(mmHg)	127±26	137±37	<0.001
Diastolic BP(mmHg)	71±13	80±16	<0.001
PWV(m/sec)	11.7±3.8	12.7±3.8	ns

Two patients of the intervention group had to stop atorvastatin because of elevation of liver enzymes. Six months later PWV still remained unchanged

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(11.45±3m/sec). However, patients in atorvastatin group responded positively to handgrip, augmenting substantially PWV (12.94±3.1, p<0.05). This was not observed in the control group (table 4).

Table 4: PWV response to handgrip after 6 months of atorvastatin
Administration in the study group and in controls (C)

	Before	After	p
Systolic BP(mmHg)	129±19	138±15	<0.001
Diastolic BP(mmHg)	74±10	80±1	<0.001
PWV(m/sec)	11.45±3	12.97±3.1	<0.05
(C)Systolic BP(mmHg)	132±40	137±15	<ns
(C)Diastolic BP(mmHg)	67±18	70±18	<ns
(C)PWV(m/sec)	12.88±3.4	12.5±3.4	<ns

Results did not correlate to age, initial blood pressure or lipid profile.

Discussion

Efforts to modify aortic stiffness have been reported to show an impact on patients' morbidity indexes. (7) In the present study, we have selected patients with previously identified unresponsiveness of the SNS. We presumed that those patients, who handle inadequately dialysis stress by not being able to demonstrate arteries' contraction, might get benefit from statin treatment. Autonomic function, a key component of cardiovascular control, is often impaired in chronic kidney disease (CKD) and is important in the development of intra-dialytic hypotension (IDH), which recently has been demonstrated to be associated with increased mortality in HD patients [8]. Indeed, we have shown that these patients restored the ability of their vessels to react to SNS stimulants after 6 months of atorvastatin treatment. This could not be shown in the otherwise similar control group. In spite the limited number of patients in this preliminary study, our results imply that atorvastatin could be beneficial for restoration of aortic stiffness. Long term follow up in appropriately designed studies, would reveal the propable clinical benefit in survival. As mentioned earlier, 6-month fluvastatin administration in dialysis patients with type 2 Diabetes Mellitus resulted in reduction of PWV, not related to blood pressure changes(4). Accordingly, in our study cohort, blood pressure was not correlated to the observed PWV modifications, which are attributed to the statin antioxidant /anti-inflammatory action. However, present results need confirmation by studies with larger number of patients and longer observation periods.

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