Diurnal rhythm of blood pressure, heart rate and adrenergic activity in patients with normotension treated with continuous ambulatory peritoneal dialysis and haemodialysis

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Abstract

Purpose: People with normotension and with essential hypertension are subjected to the diurnal rhythm of blood pressure (BP) with higher values during the day than during the night. Among dialysed patients nocturnal reduction of BP is blunted. The aim of the study was to evaluate diurnal BP rhythm and adrenergic activity measured as values of catecholamines.

Material and methods: Study was performed among dialysed patients with normotension: 13 haemodialysed patients (HD), 8 patients treated by continuous ambulatory peritoneal dialysis (CAPD) and 10 controls (C). Ambulatory BP monitoring (ABPM) was done by using Micro SJ7400 AMP device. Catecholamines concentrations were measured by HPLC-ED method before and after cold pressure test.

Results: There was no significant difference between manual measurements of BP done by dialysis nurses and mean values of 24-hours ABPM in CAPD group and C group and 48-hours ABPM among HD patients. Diurnal BP was blunted in 80% of HD patients during the day of haemodialysis, 70% during the day without haemodialysis and in CAPD group in 50%. Heart rate (HR) variability was comparable in HD and CAPD groups and significant lower than in C group. Baseline noradrenaline (NA) as well as NA (ng/ml) post cold pressure test levels were significantly higher among HD patients (463±21, 546±31) and CAPD patients (452±76, 527±92) as compared with C (206±53*, 315±61*). (x±SD), *p<0.001

Conclusions: Despite increased adrenergic activity and altered diurnal rhythm of BP and HR exist in dialysed patients we didn't find directly relationship. Another or composed factors could affect diurnal rhythm of BP and HR.

Key words: noradrenaline, dialysis, ambulatory blood pressure monitoring, diurnal rhythm.

Introduction

Blood pressure (BP) among healthy people with normotension and with essential hypertension is commonly subjected to diurnal rhythm with higher values during the day and lower values during the night. Patients with secondary hypertension have the circadian rhythm of BP altered [1,2]. Among dialysed patients nocturnal BP reduction is significantly blunted [3-7]. Abnormal circadian rhythm of BP may be related to a high incidence of cardiovascular disease morbidity and mortality among patients with chronic kidney disease [3,4,8]. The pathogenetic mechanisms of the blunted nocturnal decrease of BP among those patients are still unclear.

Patients with chronic renal failure (CRF) showed increased neural sympathetic activity and elevated levels of catecholamines and it may influence on cardiovascular prognosis, [9-13]. It is not known whether these abnormalities are related to and if they are associated with chronic renal disease [3,14].

The aim of the study was to evaluate the correlation between diurnal rhythm of blood pressure and diurnal heart rate variability, and adrenergic activity measured by levels of catecholamines, among normotensive patients treated with continuous ambulatory peritoneal dialysis and haemodialysis.

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Received 10.12.2004 Accepted 09.05.2005

Material and methods

Patients

13 patients undergoing chronic haemodialysis (HD), 8 patients treated with continuous ambulatory peritoneal dialysis (CAPD) and 10 healthy persons (C) were selected to our study. The main selection criterion was normotension without antihypertensive drugs. Patients with a history or physical examination indicative of diabetes mellitus, coronary heart disease, congestive heart failure, cardiac arrhythmias, amyloidosis, infection or other systemic or malignant disease were excluded from the study.

The HD group consisted of 7 men and 6 women, aged between 23-59 years (average 42.2±3.4 years), time of haemodialyses from 7 to 204 months (average 56.1±18.1 months). The etiology of the renal failure included: chronic glomerulonephritis (7 patients), obstructive uropathy (3 patients), interstitial nephritis (2 patients), kidney tuberculosis (1 patient). In the CAPD group there were 3 men and 5 women, aged between 24-59 years (average 38.7±5.4 years), time of dialysotherapy from 4-82 months (average 38.3±17.0 months). The etiology of the renal failure included: glomerulonephritis (4 patients), obstructive uropathy (2 patients), interstitial nephritis (2 patients).

All patients received normal diet with free protein and salt intake and supplementation of calcium carbonate, vitamines, iron and recombinant epoetin in individual doses. The patients were anuric (diuresis <100 ml/day). Routine haemodialysis and peritoneal dialysis procedures were followed for each patient according to their individual orders. All procedures of haemodialysis were performed in the morning hours between 7.00 a.m. and 12.00 a.m. using low-flux, semi synthetic membranes with bicarbonate as the dialysate fluid.

The C group consisted of 5 men and 5 women, aged 16-59 years (average 34.6±4.7 years). They received normal diet and were not treated with medications. Each patient was informed about the nature and purpose of the study and signed written consent.

Ambulatory blood pressure and heart rate measurements (AMBP)

Blood pressure (BP) and heart rate (HR) monitoring was done by Micro-SI 7400 AMP apparatus. In HD patients BP and HR were monitored for 48 hours: during the day of haemodialysis and on the following day without haemodialysis. Among CAPD patients and C group BP and HR were monitored for 24 hours. AMBP measured and recorded systolic (SBP), diastolic (DBP) and HR every 20 minutes during day-time (6.00 a.m. – 23.00 p.m.) and every 60 minutes during night-time (23.00 p.m. – 6.00 a.m.). Diurnal BP rhythm was considered to be lost when night BP was less than 10% of day BP. Diurnal HR profile was blunted, when the difference between day HR and night HR was not significant.

Manual blood pressure and heart rate measurements

The routine BP and HR measurements were performed by dialysis nurses before haemodialysis session (before HD), after haemodialysis session (after HD) and during the day without haemodialysis (day without HD) among HD patients and only once in CAPD and C groups. BP measurements were done using mercury sphingomanometer PRLTH 2.

Cold pressure test (CP)

After an adequate period of rest the hand of the subjects was plunged in icy water (O±C) up to the wrist for 1 minute. BP was measured traditionally before and after CP.

Catecholamines /CA/ (ng/l)

Noradrenaline, adrenaline and dopamine concentrations were determined by HPLC with electrochemical detection method. Blood samples for measurements of CA were obtained, before CP test and after CP test, from venous limb of forearm or arm arteriovenous fistula in HD patients and from forearm vein in CAPD and C groups. Blood collected for CA measurements was immediately transformed into ice-cold tubes with EDTA. Plasma was separated and stored at -70°C until the assay.

In HD patients all the experimental procedure were carried out three times: 1 hour before HD, 1 hour after HD and during the day without HD, in CAPD and healthy persons it was carried out only once.

Statistical analysis

The results are given as mean values ±SD. The statistical evaluation was done using Student's t-test for paired and unpaired data, regression analysis.

Results

We compared results of single manual measurements of BP done by dialysis nurses and average results of 24 hours ABPM in HD, CAPD, C groups. Mean values of ABPM showed a significant correlation with manual values among dialysed patients and healthy people. Among HD patients mean values of SBP in manual measurements were 131±7 mmHg before HD, 124±12 mmHg after HD, 127±10 mmHg during the day without HD and average results of SBP in ABPM were 126±6 mmHg during the day with HD and 122±9 mmHg during the day without HD. In this group mean values of DBP in manual measurements were 85±7 mmHg before HD, 77±10 mmHg after HD, 81±7 mmHg during the day without HD and average results of DBP in ABPM were 79±6 mmHg during the day with HD and 77±6 mmHg during the day without HD. There were no significant differences between manual measurements and ABPM measurements in HD groups. There was significant difference ($p<0.05$) between results of BP manual measurements before and after HD. The mean values of SBP and DBP were higher before HD procedures than after HD procedures. In CAPD group mean values of SBP in manual measurements was 130±20 mmHg and average result of SBP in ABPM was 124±26 mmHg. In this group mean values of DBP in manual measurements were 82±10 mmHg and average result of DBP in ABPM was 79±12 mmHg. There were no significant differences between manual measurements and ABPM measurements in CAPD group. In C group mean values of SBP in manual measurements was 125±11 mmHg and average result of SBP in ABPM was 121±11 mmHg. In this group mean values of DBP in manual measurements was 77±12 mmHg and average result of DBP in ABPM was 72±9 mmHg. There were no significant differences between manual measurements and ABPM measurements in C group (*Tab. 1*).

Table 1. **Single manual measurements and 24-hours ABPM in dialysed patients and control** (x±SD)

BP mmHg		HD group			CAPD group	Control group
		Before HD	After HD	Day without HD		
SBP	Manual measurements	131±7	124±12*	127±10	130±20	125±11
	Automatic measurements	126±6		122±9	124±26	121±11
DBP	Manual measurements	85±7	77±10*	8±7	82±10	77±12
	Automatic measurements	79±6		77±6	79±12	72±9

*p<0.05 compared to values before HD

Table 2. **Diurnal rhythm of BP and HR in dialysed patients and control** (x±SD)

	Diurnal rhythm	HD group		CAPD Group	Control
		Day with HD	Day without HD		
SBP (mmHg)	Day-time	129±12	123±14	127±24	125±11
	Night-time	122±12	118±20	121±30	110±11
	Difference Day/night (%)	6±11	4±12	7±12	12±2^ ^
DBP (mmHg)	Day-time	80±9	78±9	82±12	75±5
	Night-time	76±12	74±6	78±5	62± 9
	Difference Day/night (%)	4±6	6±5	5±9	18±6^ ^
HR (beats/min)	Day-time	80±20	80±18	82±12	79±5
	Night-time	74±24	69±6*	74±12	61±4**
	Difference Day/night	6±18	11±9^	8±8	18±5^ ^

^ p<0.05 compared to day with HD; * p<0.05 compared to day-time; **p<0.001 compared to day-time; ^ ^p<0.01 compared to dialysed patients

We evaluated diurnal rhythm of BP and HR in dialysed patients and control. Diurnal rhythm of BP and HR were blunted in dialysed patients especially in HD patients. In C group all people had normal diurnal rhythm of SBP and DBP and average differences day/night were 14±2% and 13±6% respectively. Among HD group diurnal rhythm of SBP and DBP were blunted in 80% during the day with HD and during the day without HD in 75% and 67% respectively. Average differences of SBP day/night were 6±11% and of DBP 4±10% during the day with HD. Average differences of SBP day/night were 7±12% and of DBP 6±5% during the day without HD. In CAPD group diurnal rhythm of BP (so SBP and DPB) was blunted in 67% Average differences of SBP day/night were 7±12% and of DBP 6±9%.

Heart rate variability was the highest in C group. The significant difference day/night was 18±5 beats/min (p<0.01). In HD group diurnal HR was blunted during the day with HD, difference day/night was 6±18 beats/min. In the same group there was significant difference day/night 11±9 beats/min (p<0.05) during the day without HD. In CAPD group diurnal HR was blunted, difference day/night was 8±8 beats/min (*Tab. 2*).

Noradrenaline (NA) plasma concentration in dialysed patients was higher than in control, both in HD patients before HD, after HD, during the day without HD and CAPD patients (p<0.001). Increase in NA concentration during cold pressor test was smaller in dialysed patients compared with C group. Mean values of NA were similar in HD and CAPD groups. In HD group mean value of NA before CP were 465±38 ng/ml before HD, 463±36 ng/ml after HD, 473±35 ng/ml during the day without HD and 546±54 ng/ml, 557±48 ng/ml, 549±47 ng/ml after CP, respectively (p<0.001). In CAPD group mean value of NA before CP was 452±76 ng/ml and after CP was 527±92 ng/ml (p<0.01). In C group mean value of NA before CP was 206±53 ng/ml and after CP was 315±61 ng/ml (p<0.01) (*Tab. 3*).

The values of plasma adrenaline and plasma dopamine were similar in each group (*Tab. 3*).

There was no correlation between diurnal rhythm of SBP, DBP, HR and the serum levels of NA at the rest and stimulated after the CP test in each study groups.

Discussion

The problem of sympathetic and parasympathetic activity in chronic kidney disease is known in literature for 50 years. In 1968 Hennesey and all reported about autonomic neuropathy in chronic renal failure [15]. Since many authors informed that sympathetic hyperactivity may be associated with mortality and cardiovascular events in patients with CRF. Increased sympa-

Table 3. **Mean values of noradrenaline, dopamine, adrenaline concentration in the blood at the rest and after cold pressure test (CP) of dialysed patients and control group** (x±SD)

Catecholamines		HD group			CAPD group	Control group
		Before HD	After HD	Day without HD		
Noradrenaline (ng/ml)	Before CP test	465±38^	463±36^	473±35^	452±76^	206±53^
	After CP test	546±54*^	557±48*^	549±47*^	527±92*^	315±61*
Dopamine (ng/ml)	Before CP test	84±24	85±22	8822	93±8	90±17
	After CP test	86±24	86±23	90±22	95±5	93±18
Adrenaline (ng/ml)	Before CP test	92±12	89±10	89±9	93±5	84±14
	After CP test	94±6	92±11	90±9	96±5	87±15

* $p<0.001$ compared to „Before CP test"; ^ $p<0.001$ compared to Control group

thetic activity may play a role in raise of the blood pressure and organ damage, heart and vessels, especially [9,12,13,16].

Accepted biochemical marker of sympathetic activity is catecholamines concentration in the blood. Investigators consider that plasma noradrenaline concentration is the best index of adrenergic function [12,13].

In our study we noticed that, the rest levels of NA and levels of NA after stimulation by cold pressure test were higher in dialysed patients with normotension, in CAPD group and HD group as compared with controls. Most authors reported about increased NA level among patients with CRF and dialysed patients treated by HD and CAPD, both with normotension and with hypertension [17-19]. Another authors reported that NA levels remain in normal range [20]. Vlachojanis and all [21] found that highest NA concentration occurred in long-time treated CAPD patients. In our analysis NA plasma levels were unchanged during standard HD procedures similarly to other reports [22,23]. Only some authors informed about decrease NA plasma concentration after HD procedure [16,19]. Long-term nocturnal haemodialyses could reduce plasma NA concentration [24]. In our study dopamine and adrenaline plasma levels remained in normal range among dialysed patients as in another studies [25]. Some authors reported about elevated plasma dopamine concentration in CRF patients compared with control [17,19].

Many studies were performed in order to evaluate the effect of sympathetic activity on BP regulation in dialysed patients. Manual classic measurements of BP were basis in the early studies. Since several years ambulatory blood pressure monitoring is available in medical study and practice. ABPM is a known method which is applied to diagnosis and control of treatment arterial hypertension. ABPM allowed to diagnose "white coach" hypertension. ABPM is used by nephrologists in Dialysis Centre, too [26,27]. It is very important to estimate true values of BP in HD patients. Dialysis nurses exam BP in HD patients several times: before HD, during HD procedure and after HD but there is no control during the day without HD. BP is examined in CAPD patient by dialysis nurse only during control visit in Dialysis Unit once a month. We performed ABPM for 48 hours in HD patients inclusive the day with HD therein HD procedure and the day without HD. In CAPD group and in controls ABPM was performed for 24 hours. We compared mean value of ABPM with single manual measurements done by dialysis nurses. The differences were not significant. According to our results, we suggest that manual measurements performed by dialysis nurses are sufficient to estimate blood pressure in normotensive CAPD and HD patients. Some authors inform that office measurements of BP performed carefully by nurses is sufficient to control BP [28,29].

We estimated diurnal BP rhythm in dialysis patients with normotension. We found altered diurnal rhythm of BP among 80% patients during the day with HD and among 70% patients during the day without HD. In CAPD group 50% of patients were non-dipper. Most of authors examined diurnal BP rhythm in dialysed patients both HD and CAPD and found blunted or even reverted rhythm in hypertensive patients [5,6,30]. Only few authors estimated diurnal rhythm of BP in HD patients during the day with HD and during the day without HD, separately. Some authors noticed significant difference between first and second day [31]. Another didn't find significant difference [32]. Abnormal diurnal rhythm of BP was to be related with organs damage and poor cardiovascular prognosis in patients with secondary hypertension and in patients with CRF [33].

The physiological mechanisms mediating the variability and diurnal rhythm of BP are unclear. Some authors suggest that sympathetic neural function may contribute importantly to the regulation of BP during the day and the night in patients without CRF [34-36].

Some authors reported that altered circadian rhythm of BP is associated with autonomic dysfunction among patients with CRF [3]. Another authors suggest that autonomic dysfunction is not a major contributor to non-dipping in CRF. An altered diurnal rhythm of BP is common after renal transplant but is not related to degree of autonomic dysfunction [14]. Cattone and all present that hypertensive patients with CRF are characterized by higher values of NA, but there are no differences in sympathetic activity between dipper and nondipper subjects [25]. We received the same results among HD and CAPD patients with normotension as Cattone and all.

We estimated diurnal heart rate variability in patients treated by HD and CAPD and compared with controls. We evaluated diurnal rhythm of HR during the day with HD and during the day without HD, separately. There were not significant differences between average values of HR in day-time and night-time in CAPD group and among HD patients during the day with HD.

There was normal diurnal rhythm of HR in HD patients during the day without HD but the difference day-time and night-time was smaller then in control group. We noticed that average values of HR from day-time were no differed in each studies group, but there were no decrease HR during night-time in CAPD group and HD group during the day with HD. Our results were according to the literature [7]. We suppose there is a pseudonormal rhythm of HR during the day without HD, because in the night before next haemodialysis plasma potassium level in HD patients may go high and so decrease HR.

Autonomic dysfunction in most CRF patients, hypertensive or normotensive, treated by HD or CAPD independently, is the fact and abnormal diurnal rhythm of BP and HR in most of them seems to be truth, but there was not strongly correlation.

We didn't find directly relationship between sympathetic hyperactivity and altered diurnal rhythm of BP and HR among HD and CAPD patients with normotension. A small quantity of patients participated in our study. Many dialysed patients have arterial hypertension or hypotension, concomitant diseases and these patients were excluded from the study.

Another studies are need to evaluate what factors play a main role influencing diurnal BP rhythm among dialysed patients.

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