The Correlation of Parathyroid Hormone and Heart Rate Variability in CAPD Patients

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Objective: *To investigate the correlation of parathyroid hormone (PTH) and cardiac autonomic nervous system (ANS) measured by heart rate variability (HRV) method in continuous ambulatory peritoneal dialysis (CAPD) patients.*
Material and Method: *Healthy subjects (HS) and two groups of CAPD patients classified by the PTH concentration: high PTH group (H-PTH; PTH = 150-300 pg/ml) and ultra-high PTH group (UH-PTH; PTH >300 pg/ml) were studied. Time and frequency domains of HRV were analyzed. For the frequency domain, the fast Fourier transform of the total power (TP), low frequency (LF), high frequency (HF), and LF/HF ratio were transformed by natural logarithm (ln). The Pearson's correlation was used to analyze the correlation between lnPTH and the parameters of HRV.*
Results: *Time and frequency domains of HS were at highest values whilst LF/HF ratio was the lowest. For UH-PTH CAPD patients, the values of standard deviation of R-R interval (SDNN), root mean square of the difference of R-R interval (RMSSD), lnTP and lnHF were significantly lower whereas lnLF was not significantly different compared to H-PTH. In addition, lnHF was found to have the highest negative correlation value with lnPTH concentration (r = -0.53).*
Conclusion: *PTH, a serious uremic toxin, influences the initiation of ANS dysfunction. According to decreased lnHF, a decrease in parasympathetic activity was demonstrated in UH-PTH. Consequently, the modality that can stimulate the parasympathetic activity should be considered in CAPD patients who were hyperparathyroidism.*

Keywords: *Heart rate variability, Parathyroid hormone, CAPD*

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End-stage renal disease (ESRD) is the stage of irreversible damage to the kidney leading to loss of its important function, which is the excretion of excess body water and waste products. ESRD is defined when the glomerular filtration rate (GFR) reduces less than 15 ml/min/1.73 m^2. The patients who are suffering from ESRD need a renal replacement therapy. CAPD is one of the most popular dialysis modalities because new CAPD patients have been supported with the cost of medical treatment by the national health security office (NHSO) of Thailand. Thus, this modality is the economic choice for the patients. As a result, a number of CAPD patients have been growing up and may become the biggest population of ESRD patients. Over 30% of ESRD patients, however, a number of studies presented that cardiovascular disease was the major cause of mortality[1].

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PTH is a polypeptide containing 84 amino acids produced and secreted by the chief cells of the parathyroid gland. The important function of PTH is the regulating in bone, calcium, and phosphate homeostasis. Because of detrimental kidney in ESRD, hypocalcaemia, hyperphosphatimia, and vitamin D deficiency can stimulate PTH secretion. This high plasma PTH has been called as secondary hyperparathyroidism (SPH). SPH plays a frequent complication and can be found approximately 50 to 62% in ESRD patients[2]. PTH is known as another potent uremic toxin, which has adverse effects not only to bone and kidney but also the other organs for instance, brain, smooth muscle, pancreas, adrenal gland, and particularly cardiovascular system[3]. Some authors proposed that long-term effect of PTH causes an irreversible change of the myocardial function and vascular calcification[4]. Cardiac autonomic neuropathy is another evidence for sudden cardiac death. The inhibition of an electroencephalogram (EEG) and nerve conduction velocity (NCV) in healthy dogs was induced by the administration of PTH. Furthermore,

the disturbance of EEG and NCV was diminished after parathyroidectomy[5]. Consequently, the normal cardiac function may be regulated by the ANS and it can be maintained by appropriate level of PTH.

Although normal heart has auto-regulatory function, it is also controlled by ANS consisting of sympathetic and parasympathetic nervous systems. Particularly, the ANS has an essential function in regulating cardiac contraction, heart rate (HR), and arterial blood pressure. The previous studies indicated that cardiac sudden death is due to the imbalance of ANS. The HRV method is a non-invasive clinical tool for evaluation of ANS functions. Furthermore, it is widely used as the prognostic indicators of cardiovascular disturbances as recommended by Oikawa et al[6] and it is generally defined as the quantification of R-R interval of an electrocardiogram (ECG). It normally consists of two standard measurements, which are time and frequency domains[7]. A number of studies have shown that the significant reduction of HRV is associated with cardiac mortality[8]. Cardiac autonomic dysfunction (CAD), one of the most important complications, is found in approximately 53% of ESRD patients[9,10]. In addition, the cardiac autonomic function directly correlates with the increase of HRV in time and frequency domains. Furthermore, it was found after one year treatment of the dialysis modalities[9]. However, there are a few studies about the effect of PTH on HRV in CAPD patients. Therefore, the aim of the present study was to investigate the effect of PTH on the cardiac ANS measured by the HRV method in CAPD patients.

Material and Method

Subjects

HS and CAPD patients were invited to participate in the present study. The study protocol approved by the Nopparat Rajathanee Hospital human subject committee was informed and written consent forms were obtained. HS (10 males and 10 females) were the volunteers recruited from the annual health check-up. For CAPD patients, they were screened from their medical history. The inclusion criteria for the patient group were as follows. 1) The patients received the double bag system containing 1.25% dextrose for removal of the excess volume or ultrafiltration and four cycles of 2-L dianeal solution (Baxter, USA) exchanges per day. 2) Kt/V, dialysis adequacy index, must be over 1.7 according to NKF-DOQI (National Kidney Foundation Dialysis Outcomes Quality Initiative) recommendation. 3) The patients had no sign of any inflammation and infection such as peritonitis. The exclusion criteria were patients with diabetes mellitus, severe hypertension, amyloidosis, myocardial infarction, heart failure, heart disease, cardiac arrhythmias (atrial and ventricular fibrillation), premature beat (frequent premature ventricular contraction), heart block as well as the patients prescribed drugs that were known to affect the ANS such as beta-blockers, antiarrhythmic drugs, and digitalis glycoside. The clinical data such as age, race, gender, and total months on dialysis before enrollment of CAPD patients were also documented. Causes of ESRD were chronic glomerulonephritis (n = 14), polycystic kidney disease (n = 5), hypertensive nephropathy (n = 5), obstructive uropathy (n = 1), nephrosclerosis (n = 1), and unknown (n = 4). Angiotensin-converting enzyme inhibitor and calcium channel blocker were antihypertensive drugs for fourteen and nine patients, respectively. All patients received phosphate binder such as aluminum hydroxide, calcium carbonate, calcium citrate, and lanthanum carbonate.

The screened subjects of both healthy and CAPD patients were recorded their vital signs; body temperature, HR, respiratory rate, and blood pressure, as well as the standard 12-lead ECG evaluated by cardiologist or nephrologists. Subjects who had ECG abnormalities and had a history of alcohol drinking and tobacco smoking were also excluded from the present study. In addition to vital sign recording, the venous blood of healthy subjects and CAPD patient was drawn for routine biochemical analysis and determination of PTH concentrations using electrochemiluminescence immunoassay from Roche Diagnostics. The obtained results were repeatedly analyzed for the final selection of the screened patients. The clinical and biochemical data of all patients did not significantly differ except the PTH. The patients whose PTH concentrations were from 150 to 300 pg/ml were classified as H-PTH group. Another group was classified as UH-PTH group when their PTH concentration was greater than 300 pg/ml. For the UH-PTH group, 0.25-0.5 μg of 1-α $(OH)_2D_3$ (active form of vitamin D) was prescribed daily by nephrologists. The present study therefore consisted of twenty healthy age-matched subjects who were assigned as the control group and thirty CAPD patients, which were assigned as the experimental group. The experimental group was divided into two groups according to the PTH concentration levels. There

were H-PTH (8 males and 7 females) and UH-PTH (7 males and 8 females) groups. Prior to the experimental day, all patient groups were asked to stop taking their routine drug, particularly antihypertensive drugs for 12 h (8.00 pm to 8.00 am) in order to avoid the effects of the patient heart rate. Unfortunately, a longer duration for drug stopping cannot be processed because the adverse treatment to the patients may be occurred.

Heart rate variability

The measurements of HRV of HS and CAPD patients were performed on the morning of available days. All subjects were invited to rest in a quiet and comfortable room at temperature approximately 25°C for at least 20 minutes. Then, vital signs were determined using the vital sign monitor (Nihon Kohden, Japan). After the electrodes were applied on the patient's limb, the 30 minutes of raw signals from lead II of ECG were then recorded and stored for further analysis by the Biopac system MP 36 (Biopac System Inc., USA). The subjects were asked to relax their bodies and emotion during the whole recording period. Subsequently, each ECG was manually analyzed beat by beat for signal artifact rejection that may occur. The HRV was then calculated from R-R interval by Biopac Student Lab Pro software version 3.7.3. The HRV parameters were represented in time and frequency domains (see references 7 and 16 for more details). SDNN and RMSSD of the time domain parameters were computed by the statistic method following these equations: $SDNN = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(RR_i - m)^2}$ and $RMSSD = \sqrt{\frac{1}{n-1}\sum_{i=1}^{n-1}(RR_{i+1} - RR_i)^2}$ where m is the mean of R-R interval. In the frequency domain, the raw signals of ECG were calculated by the fast Fourier transform method. Their parameters were TP (total power <0.4 Hz), LF (low frequency = 0.04-0.15 Hz) and HF (high frequency = 0.15-0.4 Hz). The LF/HF ratio was also calculated. In order to get rid of the effects from the total power alteration, the absolute values had to be modified to normalized values (nu), which were calculated as the following formula: LF or HF (nu) = LF or HF (100)/(TP - VLF; very low frequency = 0.003-0.04 Hz) while TP = VLF + LF + HF). The natural logarithm was necessary for LF and HF transformation in order to avoid the skewness distribution. In the present study, the short-term measurement of HRV was used because this method has a number of advantages. Firstly, it can quickly perform and analyze, and its artifacts are easy to be manually edited. Secondly, because of the short-term recording, the subjects were asked to be under similar controlled condition. Finally, this method does not disturb the daily life of the subjects.

Statistical analysis

The data were analyzed statistically by the computer program. All data were presented as mean ± standard deviation (SD). The mean values were analyzed using analysis of variance (ANOVA). The correlation between each natural logarithm of HRV parameters and PTH concentration were made with Pearson's correlation test. The p-value <0.05 was accepted as statistically significant.

Results

Table 1 demonstrates demographic and clinical characteristics of the studied groups. Mean ages of HS, H-PTH and UH-PTH were not significant differences. Among three groups, systolic blood pressure (SBP) and the PTH concentration of HS were the lowest whereas the values of hematocrit (Hct) and albumin concentration of HS group were the highest. Additionally, the HR value of HS was significantly lower than that of UH-PTH (72±8.4 vs. 83±9.7; p = 0.037). For comparison between the H-PTH and UH-PTH, the levels of Hct and hemoglobin (Hb) in H-PTH were significantly higher than those levels in UH-PTH (37.6±2.72 vs. 33.67±3.27, p = 0.003 and 12.49±1.30 vs. 10.86±1.30, p = 0.029, respectively). In contrast, the PTH of UH-PTH was significantly higher than that of H-PTH (754.73±324.21 vs. 195.33±56.33; p<0.001). As shown in Table 2 and Fig. 1, all HRV parameters of HS were significantly

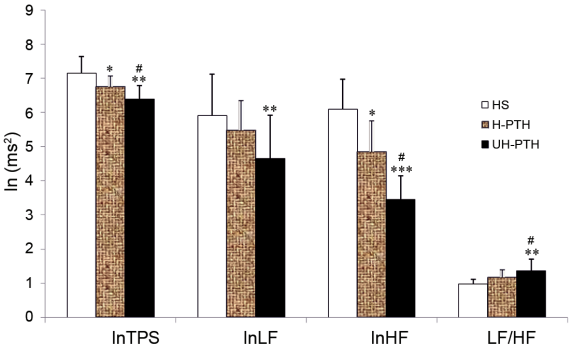

Fig. 1 The power of frequency domain parameters of each group was represented in natural logarithm. Data were shown as mean ± SD.
*p-value <0.05, **p-value <0.01 and ***p-value <0.001 were significant compared to HS.
#p-value <0.05 was significant compared between H-PTH and UH-PTH.

Table 1. Demographic and clinical characteristics of the studied groups

Parameter	HS (n = 20)	H-PTH (n = 15)	UH-PTH (n = 15)
Age (years)	50.30±12.75	51.13±10.05	52.00±9.21
Gender (M/F)	10/10	8/7	7/8
Duration of dialysis (months)	NA	39.93±20.44	44.40±19.51
SBP (mmHg)	112.50±10.05	124.70±9.10***	138.30±10.14***
DBP (mmHg)	78.60±6.96	73.33±6.17	78.90±9.41
HR (beats/min)	72.00±8.40	78.00±10.8	83.00±9.70*
Kt/V	NA	2.00±0.23	2.00±0.29
Hct (%)	43.80±3.19	37.60±2.72***	33.67±3.27***$^{\#\#}$
Hb (g/dl)	13.63±2.06	12.49±1.30	10.86±1.30***$^{\#}$
Albumin (g/dl)	4.59±0.26	4.25±0.30*	4.27±0.43*
Ca (mg/dl)	NA	9.42±0.76	9.19±1.12
P (mg/dl)	NA	5.97±1.17	6.11±1.11
PTH (pg/ml)	28.90±11.80	195.33±56.33**	754.73±324.21***$^{\#\#\#}$

The values were shown as mean ± SD.
p-value compared with HS were: *p<0.05, **p<0.01 and ***p<0.001.
p-value between H-PTH and UH-PTH were: $^{\#}$p<0.05, $^{\#\#}$p<0.01 and $^{\#\#\#}$p<0.001.
NA = not assessment

Table 2. Time and frequency domain parameters of HRV of the studied groups

Parameters	HS (n = 20)	H-PTH (n = 15)	UH-PTH (n = 15)
SDNN (ms)	85.30±14.12	67.73±17.01**	47.27±22.80***$^{\#\#}$
RMSSD (ms)	40.00±4.62	34.27±7.12**	25.33±10.42***$^{\#}$
lnTP (ms^2)	7.15±0.50	6.75±0.32*	6.39±0.41**$^{\#}$
lnLF (ms^2)	5.92±1.21	5.47±0.87	4.66±1.26**
lnHF (ms^2)	6.10±0.87	4.84±0.91*	3.45±0.69***$^{\#}$
LF/HF	0.97±0.15	1.16±0.23	1.37±0.24**$^{\#}$

The values were shown as mean ± SD. Frequency domain parameters were transformed by natural logarithm.
p-value compared with HS were: *p<0.05, **p<0.01 and ***p<0.001.
p-value between H-PTH and UH-PTH were: $^{\#}$p<0.05, $^{\#\#}$p<0.01 and $^{\#\#\#}$p<0.001.

highest whereas LF/HF ratio showed the lowest value. When HRV parameters were compared between H-PTH and UH-PTH, the values of parameters of H-PTH except for LF/HF ratio were significantly higher than those of UH-PTH. Those parameters were as follows: SDNN (67.73±17.01 vs. 47.27±22.80; p = 0.008), RMSSD (34.27±7.12 vs. 25.33±10.42; p = 0.033), lnTP (6.75±0.32 vs. 6.39±0.41; p = 0.048), and lnHF (4.84±0.91 vs. 3.45±0.69; p = 0.013), respectively. For lnLF, although the value was higher in H-PTH than that of UH-PTH, it cannot reach statistically significant difference (5.47±0.87 vs. 4.66±1.26; p = 0.08). For LF/HF ratio, this is the only parameter that the value was found lower in H-PTH compared to UH-PTH (1.16±0.23 vs. 1.37±0.24; p = 0.045).

To evaluate the correlation between HRV parameters and the PTH concentration, data were analyzed using the Pearson's correlation test, which was shown in Fig. 2. The results show that there were negative correlation between lnPTH with lnTP (r = -0.39; p = 0.045) and lnHF (r = -0.53; p = 0.002), respectively.

Discussion

The present study was conducted in ESRD patients, thus, it was not surprising that Hct and Hb values were lower when compared to the control group

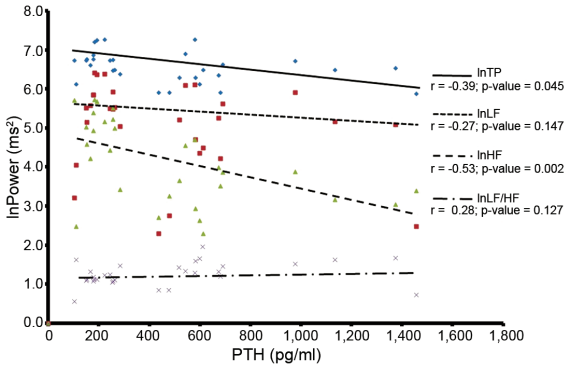

Fig. 2 The correlation coefficients between PTH concentrations and HRV parameters.

(HS). PTH can reduce the erythropoietin synthesis and induce the bone marrow fibrosis. Subsequently, the synthesis of red blood cell from bone marrow was then inhibited[11]. As the highest value of PTH level was found in UH-PTH, it may cause the lowest Hct value in this group. A study using the HRV method in 383 hemodialysis patients found that both SDNN and RMSSD were negatively correlated with the increasing of autonomic dysfunction mortality[6]. The present study shows the defection of the ANS in CAPD patients determined by the drop off of HRV parameters (SDNN and RMSSD) as compared to HS. This result confirmed the previous studies that CAD was an important complication of ESRD patients[10]. The decline of HRV parameters in dialysis patients may arise from dialysis inadequacy. Because of a lot of uremic toxin, for example, urea, creatinine, and PTH may not be completely eliminated. A comparative study between before and after twelve months of dialysis treatment on autonomic dysfunction in seven CAPD patients demonstrated a significant improvement of time domain parameters of HRV suggesting an effective elimination of uremic toxin[9]. A prospective study compared HRV parameters in dialysis patients during dialysis and after renal transplantation at one and six months. The levels of HRV parameters at six months after renal transplantation were extensively returned from low to nearly normal healthy values. This may result from partially removal of uremic toxin by transplanted kidney[12]. Both studies indicated that urea was a dominant uremic toxin. The current study found that the CAPD patients had lower HRV values than HS. As the CAPD patients were selected from sufficient dialysis adequacy evaluated by Kt/V and nPCR (normalized protein catabolic rate). Therefore, urea may not be involved but the high level of PTH may account for low HRV parameters in the present study.

PTH has been known as a very potent uremic toxin. The previous studies indicated that PTH affects not only the pathogenesis of bone but also the other essential organs, especially the cardiovascular system and nervous system[13-15]. For the nervous system, PTH results in the reduction of its function and propagation. The pathological effects of the nervous and cardiovascular system induced by hyper-parathyroidism are still uncertain. The proposed mechanism is the accumulation of intracellular calcium occurred by two ways. The PTH stimulates the opening of L-type calcium channel and inversely activates Ca^{+2}-Na^{+} exchanger. Calcium ions then move finally into the cells. The deterioration effect of the intracellular accumulation of calcium ion is the inhibition of ATP synthesis by mitochrondria oxidation[15].

For the healthy population, HRV is alternatively controlled by sympathetic and parasympathetic nervous systems. The predominating regulation is the function of the parasympathetic nervous system responding to inhibit the norepinephrine (NE) secretion from sympathetic nerve terminal. Sympathetic activity therefore is reduced. SDNN, RMSSD, and TP are the HRV parameters that can be the representation of sympathetic, parasympathetic, and total ANS, respectively. The SDNN inversely correlates to sympathetic nervous system whereas RMSSD has direct correlation to the parasympathetic nervous system[16]. In the present study, the highest value of SDNN, RMSSD and TP were found in HS while the values of these parameters of H-PTH were higher than those of UH-PTH. The results indicated that the PTH influenced an increase in sympathetic activity and decrease in parasympathetic activity. The present result was consistent with the study by Curione M et al in which the 28-patients with primary hyperparathyroidism (PHPT) were designedly compared with 29-healthy subjects. Their results from short-term HRV analysis showed that the elevation of LF/HF ratio and the reduction of SDNN had been found in the patient group indicating that PHPT was the cause of the increasing of sympathetic activity. It has been documented that HF is the indicator of parasympathetic activity whilst LF is the indicator of both parasympathetic and sympathetic activity. HF has direct relationship to parasympathetic activity but LF has inverse relationship to sympathetic activity[17,18]. The HF and LF levels were significantly lowest in

the UH-PTH group. The results again confirm the reduction of parasympathetic activity and the rise in sympathetic activity.

In order to determine which HRV parameters was correlated with the concentration of PTH. The Pearson's correlation was used in the present study. The results revealed that there was an inverse correlation between the level of lnPTH concentration and lnHF and lnTP. The lnHF had the highest correlation coefficient ($r = -0.53$, p-value <0.01). The study by Vlachojannis, et al found the higher level of NE secreted from synaptic terminal in both serum and dialysate fluid in CAPD patients with hyper-parathyroidism when compared to healthy subject serum[19]. The possible hypothesis may be that the high level of PTH in CAPD patients activates the synthesis and secretion of NE into the blood circulation. The large amount of NE can initiate the toxic effects to the heart. It induces the elevation of cardiac work by the increasing of heart rate and contractility. Subsequently, the cardiac oxygen demand is needed. Moreover, NE is directly toxic to beta-receptor[20,21]. Accordingly, the alteration of HRV in CAPD patients with hyperparathyroidism may the result from these phenomenon. The beneficial suggestion of this study is to stimulate the parasympathetic activity in the CAPD patients who are hyperparathyroidism. The modality that enhances parasympathetic activity should be considered for HRV improvement. Alternatively, LF/HF ratio, which is an indicator of sympatovagal balance, was increased in both patient groups. It can be confirmed that hyperparathyroidism is the important factor for decreased HRV. However, there have been a few studies concerning the influence of PTH on HRV in dialysis patients. Consequently, the obtained results from the present study can be used as basic information for the further study.

Conclusion

PTH, uremic toxin, produced by parathyroid glands can partly induce cardiac autonomic dysfunction as detected by the lowest values of time and frequency domains in UH-PTH and highest in HS using HRV, which was a non-invasive method. In particular, a decrease in parasympathetic activity was demonstrated by having the highest inverse correlation between lnHF and lnPTH. The benefit from the present study is that the parasympathetic activating modality should be introduced to the CAPD patients with hyperparathyroidism. Further interesting study will follow of the effect of PTH on HRV in CAPD patients compared as before, during dialysis, and after kidney transplantation.

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Potential conflicts of interest

None.

References

1. Cnossen N, Kooman JP, Konings CJ, van Dantzig JM, van der Sande FM, Leunissen K. Peritoneal dialysis in patients with congestive heart failure. Nephrol Dial Transplant 2006; 21 (Suppl 2): ii63-6.
2. Drueke TB. Cell biology of parathyroid gland hyperplasia in chronic renal failure. J Am Soc Nephrol 2000; 11: 1141-52.
3. London GM, De Vernejoul MC, Fabiani F, Marchais SJ, Guerin AP, Metivier F, et al. Secondary hyperparathyroidism and cardiac hypertrophy in hemodialysis patients. Kidney Int 1987; 32: 900-7.
4. Amann K, Ritz E, Wiest G, Klaus G, Mall G. A role of parathyroid hormone for the activation of cardiac fibroblasts in uremia. J Am Soc Nephrol 1994; 4: 1814-9.
5. Guisado R, Arieff AI, Massry SG, Lazarowitz V, Kerian A. Changes in the electroencephalogram in acute uremia. Effects of parathyroid hormone and brain electrolytes. J Clin Invest 1975; 55: 738-45.
6. Oikawa K, Ishihara R, Maeda T, Yamaguchi K, Koike A, Kawaguchi H, et al. Prognostic value of heart rate variability in patients with renal failure on hemodialysis. Int J Cardiol 2009; 131: 370-7.
7. Sztajzel J. Heart rate variability: a noninvasive electrocardiographic method to measure the autonomic nervous system. Swiss Med Wkly 2004; 134: 514-22.
8. Rubinger D, Revis N, Pollak A, Luria MH, Sapoznikov D. Predictors of haemodynamic instability and heart rate variability during haemodialysis. Nephrol Dial Transplant 2004; 19: 2053-60.
9. Dursun B, Demircioglu F, Varan HI, Basarici I, Kabukcu M, Ersoy F, et al. Effects of different dialysis modalities on cardiac autonomic dysfunctions in end-stage renal disease patients: one year prospective study. Ren Fail 2004; 26:

35-8.
10. Ranpuria R, Hall M, Chan CT, Unruh M. Heart rate variability (HRV) in kidney failure: measurement and consequences of reduced HRV. Nephrol Dial Transplant 2008; 23: 444-9.
11. Al Hilali N, Al Humoud H, Ninan VT, Nampoory MR, Puliyclil MA, Johny KV. Does parathyroid hormone affect erythropoietin therapy in dialysis patients? Med Princ Pract 2007; 16: 63-7.
12. Yang YW, Wu CH, Tsai MK, Kuo TB, Yang CC, Lee PH. Heart rate variability during hemodialysis and following renal transplantation. Transplant Proc 2010; 42: 1637-40.
13. Ogard CG, Sondergaard SB, Vestergaard H, Jakobsen H, Nielsen SL. Myocardial perfusion defects and the left ventricular ejection fraction disclosed by scintigraphy in patients with primary hyperparathyroidism. World J Surg 2005; 29: 914-6.
14. Wang AY, Wang M, Woo J, Lam CW, Li PK, Lui SF, et al. Cardiac valve calcification as an important predictor for all-cause mortality and cardiovascular mortality in long-term peritoneal dialysis patients: a prospective study. J Am Soc Nephrol 2003; 14: 159-68.
15. Ritz E, Stefanski A, Rambausek M. The role of the parathyroid glands in the uremic syndrome. Am J Kidney Dis 1995; 26: 808-13.
16. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Eur Heart J 1996; 17: 354-81.
17. Curione M, Letizia C, Amato S, Di Bona S, Di Fazio F, Minisola S, et al. Increased risk of cardiac death in primary hyperparathyroidism: what is a role of electrical instability? Int J Cardiol 2007; 121: 200-2.
18. Tory K, Suveges Z, Horvath E, Bokor E, Sallay P, Berta K, et al. Autonomic dysfunction in uremia assessed by heart rate variability. Pediatr Nephrol 2003; 18: 1167-71.
19. Vlachojannis JG, Tsakas S, Alexandri S, Petropoulou C, Goumenos DS. Continuous ambulatory peritoneal dialysis is responsible for an increase in plasma norepinephrine. Perit Dial int 2000; 20: 322-7.
20. Laaksonen S, Voipio-Pulkki L, Erkinjuntti M, Asola M, Falck B. Does dialysis therapy improve autonomic and peripheral nervous system abnormalities in chronic uraemia? J Intern Med 2000; 248: 21-6.
21. Mylonopoulou M, Tentolouris N, Antonopoulos S, Mikros S, Katsaros K, Melidonis A, et al. Heart rate variability in advanced chronic kidney disease with or without diabetes: midterm effects of the initiation of chronic haemodialysis therapy. Nephrol Dial Transplant 2010; 25: 3749-54.

ความสัมพันธ์ระหว่างพาราไทรอยด์ฮอร์โมนและความแปรปรวนของอัตราการเต้นของหัวใจในผู้ป่วยที่ได้รับการล้างไตทางช่องท้อง

วีระศักดิ์ อัศววงศ์อารยะ, นันทนา ชปิลเลส, สิรินันท์ นิลวรางกูร, อัมพร จาริยพงศ์สกุล

วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ระหว่างพาราไทรอยด์ฮอร์โมนกับระบบประสาทอัตโนมัติของหัวใจด้วยวิธีวิเคราะห์ความแปรปรวนของอัตราการเต้นของหัวใจในผู้ป่วยที่ได้รับการบำบัดด้วยการล้างไตทางช่องท้อง

วัสดุและวิธีการ: ทำการศึกษาในกลุ่มผู้ที่มีสุขภาพสมบูรณ์ และกลุ่มที่ได้รับการบำบัดด้วยการล้างไตทางช่องท้องซึ่งจะถูกแบ่งเป็นอีกสองกลุ่มตามระดับความเข้มข้นของพาราไทรอยด์ฮอร์โมนได้เป็นกลุ่มพาราไทรอยด์ฮอร์โมนสูง (H-PTH) โดยพาราไทรอยด์ฮอร์โมนอยู่ระหว่าง 150 ถึง 300 พิโครกรัมต่อมิลลิลิตร และกลุ่มพาราไทรอยด์ฮอร์โมนสูงมาก (UH-PTH) เมื่อพาราไทรอยด์ฮอร์โมนมากกว่า 300 พิโครกรัมต่อมิลลิลิตร โดเมนเวลาและโดเมนความถี่ของความแปรปรวนของอัตราการเต้นของหัวใจจะถูกวิเคราะห์ในแต่ละกลุ่ม ในแต่ละพารามิเตอร์ของโดเมนความถี่ที่ถูกแปลงด้วย fast fourier transform ได้แก่ total power (TP), low frequency (LF), high frequency (HF) และ LF/HF ratio จะถูกคำนวณด้วย natural logarithm (ln) ความสัมพันธ์ระหว่าง lnPTH และแต่ละพารามิเตอร์ของ HRV จะถูกวิเคราะห์ด้วย Pearson's correlation

ผลการศึกษา: กลุ่มผู้ที่มีสุขภาพสมบูรณ์จะมีระดับของพารามิเตอร์สูงที่สุดทั้งของโดเมนเวลาและโดเมนความถี่ ขณะที่มี LF/HF ratio ต่ำสุด สำหรับกลุ่มที่ได้รับการบำบัดด้วยการล้างไตทางช่องท้องพบว่า standard deviation of R-R interval (SDNN), root mean square of the difference of R-R interval (RMSSD), lnTP และ lnHF ของกลุ่ม UH-PTH จะมีค่าต่ำกว่ากลุ่ม H-PTH อย่างมีนัยสำคัญนอกจากนี้ยังพบว่า lnHF มีความสัมพันธ์แบบผกผันกับระดับความเข้มข้นของพาราไทรอยด์ฮอร์โมนสูงที่สุด ($r = -0.53$)

สรุป: พาราไทรอยด์ฮอร์โมนเป็น uremic toxin ที่รุนแรงชนิดหนึ่งโดยมีผลรบกวนการทำงานของระบบประสาทอัตโนมัติที่ควบคุมการทำงานของหัวใจ จากผลของการวิเคราะห์ที่พบว่ามีการลดลงของ lnHF แสดงว่ามีการลดลงของการทำงานของระบบประสาท parasympathetic ดังนั้นข้อเสนอแนะจากการศึกษาครั้งนี้สำหรับผู้ป่วยที่มีภาวะ hyperparathyroidism คือ วิธีการรักษาใดที่มีผลเพิ่มการทำงานของระบบประสาท parasympathetic ควรได้รับการพิจารณานำมาใช้ในผู้ป่วยกลุ่มนี้