Relationship between electrolytes and heart rate variability parameters in end-stage renal failure patients before and after hemodialysis

Tsai Lung Wen[1,4], Wang Chung-Kwe[2], Ing Fang Yang[3], Ten Fang Yang[4]

[1]EBM Center of Taipei Medical University Hospital, Taipei City,
[2]Department of Internal Medicine, Taipei Municipal Jen-Ai Hospital, Taipei City,
[3]Department of Internal Medicine, Jen Chi General Hospital, Taipei City,
[4]Graduate Institute of Medical Informatics, Taipei Medical University, Taipei City, Taiwan

ABSTRACT

Objective: One of the major causes of death in end-stage renal disease (ESRD) patients under maintenance hemodialysis (HD) is ventricular arrhythmias (VA). Heart rate variability (HRV) has been claimed to be related to disturbance of autonomic nervous system and therefore a predictor for VA occurrence. The purpose of this study is to evaluate the relationship between the HRV parameters and electrolytes before and after hemodialysis in ESRD patients.

Methods: There were 23 ESRD patients recruited for the study. Electrolytes for the analysis are Ca^{+2}, P^{+3}, Na^{+}, K^{+}, Cl^{-}. Single lead electrocardiographic signal was recorded for five minutes and the HRV parameters (time-domain) were then derived by a Taiwanese CheckMyHeart machine. Time-domain parameters used were SDNN, RMSSD, NN50. SAS version 8.2 was used for the statistical analysis and paired student t test was adapted to evaluate the statistical significance of their changes. Pearson's partial correlation coefficients were also derived from the same software.

Results: All electrolytes except chloride changes before and after hemodialysis were shown to be statistically significant analyzed by paired Student's test. Body weight changes significantly reduced from 57.57±6.78 kg to 55.26±9.92 kg (p<0.001) after the hemodialysis. Time-domain HRV parameters were shown to increase significantly after hemodialysis. There was no correlation between electrolytes changes and time- domain and frequency-domain HRV parameters after hemodialysis.

Conclusions: 1. All electrolyte changes before and after HD were statistically significant. 2. HRV parameters (SDNN, NN50 and rMSSD) significantly increased after HD. 3. QTc and QT intervals decreased after HD. 4. Partial correlation analysis revealed that there was no statistically significant correlation between electrolytes changes and the HRV parameters. *(Anadolu Kardiyol Derg 2007: 7 Suppl 1; 142-4)*

Key words: heart rate variability, electrolytes, hemodialysis, end-stage renal failure

Introduction

One of the major causes of death in end-stage renal disease (ESRD) patients under maintenance hemodialysis (HD) is ventricular arrhythmias (VA) (1-3). Heart rate variability (HRV) has been claimed to be related to disturbance of autonomic nervous system and therefore to be a predictor for VA occurrence. Alteration of electrolytes concentrations before and after hemodialysis has been documented to be closely related to VA in ESRD. The most important three factors for cardiac arrhythmias genesis are modulating factor, arrhythmia triggers, and substrate (4-6). The modulating factors can be detected by the HRV for the evaluation of autonomic function. Whereas, signal-averaged electrocardiogram (ECG) can be used for the detection of ventricular arrhythmias substrate (4-10). Electrolytes have been also attributed to the genesis of VA, especially the relationship of hyperkalemia and hypokalemia association with VA occurrence. Therefore, the purpose of this study is to evaluate the relationship between the HRV parameters and various electrolytes changes before and after hemodialysis in ESRD patients.

Methods

End-stage renal failure patients

There were 23 (12 men and 11 women) ESRD patients recruited for the study. They received regular hemodialysis three times per week at the hemodialysis units of a district general hospital and a university medical center during year 2006. All the patients have received a written informed consent approved by the Jen-Chi General Hospital ethic board, and they all agreed to participant the research.

Clinical indication for hemodialysis in the present study population is divided into two categories: (1) absolute indication with creatinine clearance rate (Ccr) <5 ml/min or serum creatinine (Cr) >8.0 mg/dl; (2) relative indication with Ccr<15 ml/min or serum Cr >6 mg/dl and with accompanying life-threatening complications as congestive heart failure, lung edema, hemorrhage diathesis, consciousness change, cachexia or uncontrollable hyperkalemia with drugs (11).

Address for Correspondence: Ten-Fang YANG, MD, Associate Professor and Consultant Cardiologist Graduate Institute of Medical Informatics,
Taipei Medical University Address: 250 Wu-Xin Street, Taipei City, 110 Taiwan
Phone: +886-2-27361661 ext 2610 Fax: +886-2-27339049 E-mail: tfy@tmu.edu.tw or tfy@yahoo.com.tw

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HRV recordings

A Taiwanese machine DailyCare BioMedical's ReadMyHeart was used to record the HRV. One lead ECG (modified lead I) for 5 minutes was used for the analysis. The QRS complexes were detected and labeled automatically by the machine. The results of the automatic analysis were reviewed subsequently, and any errors in R-wave detection and QRS labeled were then edited manually. The patient`s ECGs were recorded 30 minutes before and after the hemodialysis therapy.

Analysis of HRV

Heart rate variability was assessed automatically by the machine from the calculation of the mean R-R interval and its standard deviation measured on short-term 5 minute electrocardiograms, normal-to-normal R-R interval data obtained from the edited time sequence of R-wave and QRS labeling were then transferred to a personal computer. For time-domain HRV measures, the mean normal-to-normal R-R intervals (NN) and the standard deviation of normal-to-normal R-R intervals during 5 minutes (SDNN) were calculated. For frequency-domain HRV parameters analysis, spectral power was quantified both by fast
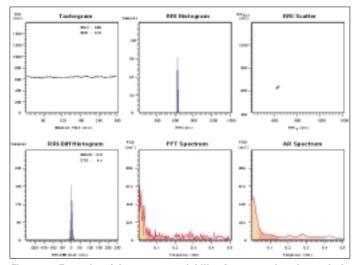

Figure 1. Example of heart rate variability frequency-domain analysis in ESRD patient pre-hemodialysis
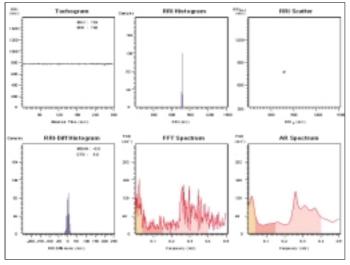

Figure 2. Example of heart rate variability frequency-domain in ESRD patient analysis post- hemodialysis

Fourier transformation and autoregressive method for the following frequency bands: 0.15–0.4 Hz (high frequency), 0.04–0.15 Hz (low frequency). The ECG signal used in the present study was derived from a "Modified Lead I-ECG" instead of traditional 12-lead ECGs. Time-domain parameters used were SDNN, RMSSD, NN50, and PNN50. Frequency-domain parameters selected were LF, HF, LF/HF. These parameters were defined in accordance with the 1996 ACC/AHA/ESC consensus (12):

Time-domain parameters

-SDNN (ms) - standard deviation of all the normal-to-normal (NN) intervals;

-RMSSD (ms) - the square root of the mean of the sum of the squares of differences between adjacent NN intervals;

-NN50 - number of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording; three variants are possible counting all such NN intervals pairs or only pairs in which the first or the second interval is longer

-PNN50 (%) - percentage of successive pairs of NN intervals differing by >50 ms

Frequency-domain parameters

-LF (ms^2) - the energy in power spectrum between 0.04 and 0.15 Hz;

-HF (ms^2) - the energy in power spectrum between 0.15 and 0.40 Hz;

-LF/HF - ratio between LF and HF powers.

Electrolytes measurements

All electrolytes including Ca^{+2}, P^{+3}, Na^+, K^+, Cl^- were measured before and after the hemodialysis. Body weight was also recorded before and after HD.

Statistical analysis

All statistical analyses were performed using SAS version 8.2. One-way analysis of variance was used to characterize changes in HRV variables before and after HD. Differences in quantitative parameters before and after HD were compared respectively, by the pair student t test and the Fisher exact probability test. Correlation between HRV parameters and electrolytes changes was assessed using Pearson partial analysis. All HRV variables were expressed as mean±SD. A "p" value<0.05 was determined as statistically significant.

Table 1. Age and sex distribution of ESRD patients

Gender	Number	Age, years
Male	12	62.73±1.40
Female	11	65.70±3.84

ESRD- end-stage renal disease

Table 2. Electrolytes changes before and after hemodialysis in ESRD patients

Electrolyte	Before hemodialysis	After hemodialysis	p
Ca^{+2}, mEq/L	9.04±0.57	10.75±0.99	<0.0001
P^{+3}, mEq/L	4.90±1.68	2.08±0.53	<0.0001
Na^+, mEq/L	136.09±4.01	140.30±2.12	<0.0001
K^+, mEq/L	4.22±0.63	2.91±0.48	<0.0001
Cl^-, mEq/L	97.04±3.96	99.96±1.87	0.0002

Data are represented as mean+standard deviation
* - paired t-test

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Results

The mean age of the 23 patients was 65.71±1.98 years and the time on maintenance HD therapy was about 3 years. Of the 23 patients, 12 (52%) were men and 11 (48%) were women, mean age of male was 62.73±1.40 years and female was 65.73±3.84 years. Electrolytes changes before and after hemodialysis are shown in Table 2. It shows that Ca^{+2}, P^{+3}, Na^+, K^+, Cl^- increased significantly after HD. Body weight, ECG QT interval parameters and HRV (in time- and frequency-domain) data before and after hemodialysis are presented in Table 3. It shows that body weight, QT, SDNN, RMSSD and NN50, except QTc interval also increased significantly after HD. Pearson partial correlation coefficients between HRV parameters and electrolytes changes are shown in Table 4. There was no statistically significant correlation between electrolytes changes and HRV parameters.

Table 3. Body weight, ECG QT interval parameters and HRV data of ESRD patients before and after hemodialysis

Variables	Before hemodialysis	After hemodialysis	p
Body weight, kg	57.57±6.78	55.26±9.92	<0.0001
QT, ms	373.39±51.72	350.52±53.69	0.0186
QTc, ms	428.04±56	408.91±63.38	0.1748
SDNN, ms	24.46±18.86	26.2±20.61	0.0414
RMSSD, ms	26.68±26.3	46.74±51	0.0486
NN50	2.04±3.26	22.29±50.3	0.0424
HF(FFT), ms²	33.6±1.21	44.4±1.42	0.0234
LF(FFT) , ms²	57.4±11.2	60.22±12.1	0.0215
HF(AR), ms²	34.7±1.41	44.5±2.15	0.0231
LF(AR) , ms²	57.21±1.04	63.2±1.15	0.0331

Data are represented as mean+standard deviation
* - paired t-test
AR- autoregressive model, ECG- electrocardiogram, FFT- fast Fourier transformation, HF- high frequency power, HRV- heart rate variability, LF- low frequency power, NN50- number of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording, QTc– QT corrected interval, RMSSD - the square root of the mean of the sum of the squares of differences between adjacent NN intervals, SDNN - standard deviation of all the normal-to-normal (NN) intervals

Table 4. Pearson partial correlation between HRV parameters and electrolytes changes

	Ca^{+2}	P^{+3}	Na^+	K^+	Cl^-
Weight	0.1340	0.2341	0.1345	0.2321	0.2223
QT	0.1590	0.1246	0.1456	0.2345	0.4561
QTc	0.8247	0.1345	0.2156	0.2134	0.1345
SDNN	0.8256	0.1567	0.1112	0.1112	0.1534
RMSSD	0.2325	0.2215	0.3332	0.2223	0.2211
NN50	0.1890	0.3326	0.2221	0.1151	0.1145
HF(FFT)	0.1321	0.1211	0.1312	0.1221	0.1211
LF(FFT)	0.3247	0.1245	0.2156	0.2534	0.5345
HF(AR)	0.7256	0.6567	0.3112	0.2112	0.5534
LF(AR)	0.7256	0.5567	0.4112	0.2111	0.5534

*- All parameters have not statistically significant relationship with electrolytes changes.
Frequency-domain parameters are represented in normalized units
AR- autoregressive model, FFT- fast Fourier transformation, HF- high frequency power, HRV- heart rate variability, LF- low frequency power, NN50- number of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording, QTc- QT corrected interval, RMSSD- the square root of the mean of the sum of the squares of differences between adjacent NN intervals, SDNN - standard deviation of all the normal-to-normal (NN) intervals

Limitations

Several limitations have to be considered in the present study:

1. The present study was performed in a district general hospital and a university Hospital Hemolysis units and they may not represent the general ESRD populations.

2. Heart rate variability derived from the short term five minutes ECG recording although has been claimed to be highly correlated to the 24-hour ECG recording, their clinical value needs to be clarified in the future study.

3. For this ESRD hemodialysis population, 24-hour ECG monitoring is not feasible due to inconvenience and unable to study the immediate changes of the electrolytes and their relationships to the HRV parameters.

Conclusions

1. All electrolyte changes before and after HD are statistically significant.

2. Heart rate variability parameters (SDNN, NN50 and rMSSD) significantly increased after HD.

3. QTc and QT interval decreased after HD.

4. Partial correlation analysis revealed that there was no statistically significant correlation between electrolytes changes and all the HRV parameters.

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