Assessment of Mean Arterial Blood Pressure Using Spectral and Chaotic Analyses in Different Antihypertensive Drug Treatments

BY Liau[1], CC Chiu[1], SJ Yeh[2]

[1]Graduate Institute of Electrical and Communications Engineering, Feng Chia University, Taiwan, R.O.C.
[2]Section of Neurology and Neurophysiology, Cheng-Ching General Hospital, Taiwan, R.O.C.

Abstract

Mean arterial blood pressure (MABP) was analyzed by spectral and chaotic analyses in hypertensive patients. Two antihypertensive drugs, Cozaar and Renitec, were adopted to investigate the effects on MABP. 17 subjects were separated randomly into two groups. MABP was acquired during both supine and tilt-up positions before and after treatment. Correlation dimension (CD) was applied to evaluate the complexity of MABP. In spectral analysis, the ratio of low- to high-frequency power was increased more in the group with Renitec. It may indicate that Cozaar has more manifest effect for suppressing the activity of sympathetic nervous system. In the two groups, CD values of MABP increased in the supine position. The nonlinear analysis results might reveal that patients will tend to be normal with the two drugs.

Keywords: mean arterial blood pressure (MABP), spectral analysis, chaos, correlation dimension (CD)

1. Introduction

In recent years, cerebrovascular diseases have been the top-ten leading causes of mortality in Taiwan [1]. Hypertensive diseases also threaten people's life all over the world [2]. Some studies have shown that in the acute phase of an ischemic stroke blood pressure is raised to help restoring cerebral perfusion, activates collateral arterial supply and enhances the treatment goal of minimizing infarct size so that antihypertensive drug should be taken when blood pressure is too high [3-5]. However, some other studies were opposed to this conclusion. Most patients with acute ischemic stroke do not need antihypertensive therapy because the rapid lowering of blood pressure may reduce cerebral blood flow owing to impaired cerebral autoregulation [6,7]. The blood pressure is mainly controlled by the balance between both parasympathetic and sympathetic nervous systems. Spectral analysis has been widely applied to evaluate the reflection of autonomic nerve system [8-10]. Mean arterial blood pressure (MABP) signals were acquired during both supine and tilt-up positions before and after 2 months treatment and bandpass-filtered in the low frequency range (0.07-0.15 Hz) and high frequency range (0.15-0.40 Hz) before applying spectral analysis. The chaotic natures can be quantified using mathematical theorems of chaos [11]. Chaotic analysis has been used to evaluate physiological phenomena, such as heart rate variability (HRV) [8], arterial pressure, renal blood flow [12,13] and cardiovascular system [14-16]. The correlation dimension (CD), one of the indexes of chaos, was applied to evaluate the complexity of MABP in this study. Melenovasky et al. [17] adopted 2 different hypolipidemic drugs to compare the effects in patients with hyperlipidemia. Their result shows that the difference between the effects of both drugs was found only for blood lipids. Kanaya et al. [18] compared differential effects on HRV of two drugs, Propofol and Sevoflurane. Results indicated that Sevoflurane has little or no effect on cardic parasympathetic tone. We adopted two antihypertensive drugs, Cozaar and Renitec, to investigate the effects on MABP after treatments by using two methods, spectral and chaotic analyses, to assess the physiological conditions in different antihypertensive drug treatment. The aim of this study is to investigate the effects of antihypertensive therapy and build up treatment guideline for hypertensive patients.

2. Methods

2.1. Subjects and measurements

Two antihypertensive drugs, Cozaar and Renitec, were adopted to investigate the effects on MABP after 2 months treatments. 17 hypertensive outpatients from the Section of Neurology of Cheng-Ching General Hospital were enrolled and separated randomly into two groups. One group with 9 subjects taking Cozaar treatment (mean age±SD=50.11±10.30 years), the other group with 8 subjects taking Renitec treatment (mean age±SD=50.75±14.37 years). Hypertension was defined as a clinic blood pressure ≧ 140/90 mmHg (WHO/ISH Guidelines 2000). Blood pressure was measured using a mercury sphygmomanometer BP monitor. Subjects were examined on a tilt-table that enabled a motor-driven change from a supine to an upright position within 10 seconds. Data acquisition was started after a 10-min relaxation period in the supine position. MABP signals were acquired during both supine and tilt-up positions before and after 2 months treatment. The personal computer combined with a general-purpose data acquisition board and LabVIEW environment for acquiring signals correctly was developed in our pervious study [19].

2.2. Data analysis

In this study, the MABP value was calculated for each heart beat as follows:

$$\text{MABP}_i = \frac{1}{V_i - V_{i-1}} \sum_{k=V_i}^{V_{i-1}} x(k)$$

where $x(\cdot)$ is the arterial blood pressure pulse signal continuously acquired from the analog output. V_{i-1} is the wave-through time index in the (i-1)th pulse beat, and V_i is the time index of the wave-through in the ith pulse beat. Therefore, MABP_i is the calculated MABP value for the ith pulse beat.

2.2.1. Power spectral density analysis

We use spectral analysis of blood pressure to explore the specific autonomic nervous system activity. MABP signals are bandpass filtered in the low frequency range (0.07-0.15 Hz) and high frequency range (0.15-0.40 Hz) before applying spectral analysis. The ratio of low- to high-frequency power (L/H) was calculated as an index of sympathetic activity.

Power spectral density is calculated as follows: A discrete-time signal $x(n)$, the DFT analysis relationship is:

$$X(k) = \sum_{n=0}^{N-1} x(n) \exp\{-j \frac{2\pi}{N} kn\} \qquad k=0,1,2\ldots,N-1$$

Then power spectral density is given by:

$$S_{xx}(k) = \frac{1}{N}|X(k)|^2 = \frac{1}{N} X(k) X^*(k)$$

Where k is the frequency sample index and N is the number of samples. $S_{xx}(k)$ is the power spectral density function.

2.2.2. Chaotic analysis

The nonlinear parameter, correlation dimension (CD), was calculated to evaluate the complexity of MABP. The signal was reconstructed from time series before measuring the chaos properties to determinate the complexity and regularity. A new coordinate system, phase space, was used to reconstruct an attractor. Phase space is an abstract mathematical space that can expresses the behavior of a dynamic system. In the phase space, the behavior of a dynamic system (trajectory or orbit) finally converges to the stationary state, called attractor. Due to the number of phase space coordinates cannot be calculated immediately from the time data, it is necessary to reconstruct the n-dimensional phase space from a signal record of time series measurement. The n-dimensional attractor can be reconstructed from one-dimensional projected data of time series using embedding method. The n-dimensional vector is constructed as follows:

$$X(t) = \{x(t), x(t+\tau), \ldots\ldots, x(t+(m-1)\tau)\}$$

Where $X(t)$ is the newly reconstructed n-dimensional vector; τ is delay time; m is an embedding dimension of the reconstructed phase space.

The correlation function is calculated as follows:

$$C_d(R) = \lim_{N\to\infty} \left[\frac{1}{N^2} \sum_{i,j=1, i\neq j} H_E(R - |X_i - X_j|) \right]$$

Where $C_d(R)$ is correlation function; N is the total number of time series; H_E : Heaviside step function; $H_E=1$, if $R - |X_i - X_j| \geqq 0$, $H_E=0$, otherwise; R is radius.

The CD value is obtained from the slope of the curve that $C_d(R)$ is plotted against R because CD is unknown in the beginning, a series of calculations with gradually increasing an embedding dimension has to be performed until the slope tends not to increase.

3. Results

Results revealed that the values of MABP in the group with Cozaar were reduced significantly after 2 months treatment in both supine and tilt-up positions. However, there was no significant reduction in the group with Renitec after 2 months treatment (Table 1). It may showed that Cozzar has more manifest effect in lowering blood pressure than that of Renitec.

Table 1. Mean arterial blood pressure values of group with Cozaar (9 subjects) and group with Renitec (8 subjects).

	Group with Cozaar (Mean±SD mmHg)	
Supine	PRE	2M
	104.67±20.21*	85.70±11.19*
Tilting	PRE	2M
	104.83±18.97**	83.87±8.83**

	Group with Renitec (Mean±SD mmHg)	
Supine	PRE	2M
	98.90±15.40	92.68±14.54
Tilting	PRE	2M
	98.75±20.82	92.47±19.41

* $p < 0.03$, ** $p < 0.02$, PRE indicates before treatment and 2M means treatment after 2 months.

In spectral analysis, the ratio of low- to high-frequency power (L/H, an index of sympathetic activity) was increased more in the group with Renitec comparing to that with Cozaar in MABP after 2 months treatment (Table 2, 3). It may indicate that Cozaar has more manifest effect for suppressing the activity of sympathetic nervous system than that of Renitec.

Table 2. The ratio of low- to high-frequency power (L/H) in the group with Cozaar.

	Group with Cozaar MABP	
Supine	PRE	2M
	L/H=4.71±2.61	L/H=6.21±3.73
Tilting	PRE	2M
	L/H=7.70±9.24	L/H=7.0±7.29

PRE indicates before treatment and 2M means treatment after 2 months.

Table 3. The ratio of low- to high-frequency power (L/H) in the group with Renitec.

	Group with Renitec MABP	
Supine	PRE	2M
	L/H=6.05±2.65	L/H=10.18±7.31
Tilting	PRE	2M
	L/H=9.72±11.09	L/H=13.98±13.17

PRE indicates before treatment and 2M means treatment after 2 months.

One sample subject's power spectrum density result in the group with Cozaar is shown in Figure 1. We can observe that the power in LF decreases both in supine and tilting positions after treatment 2 months.

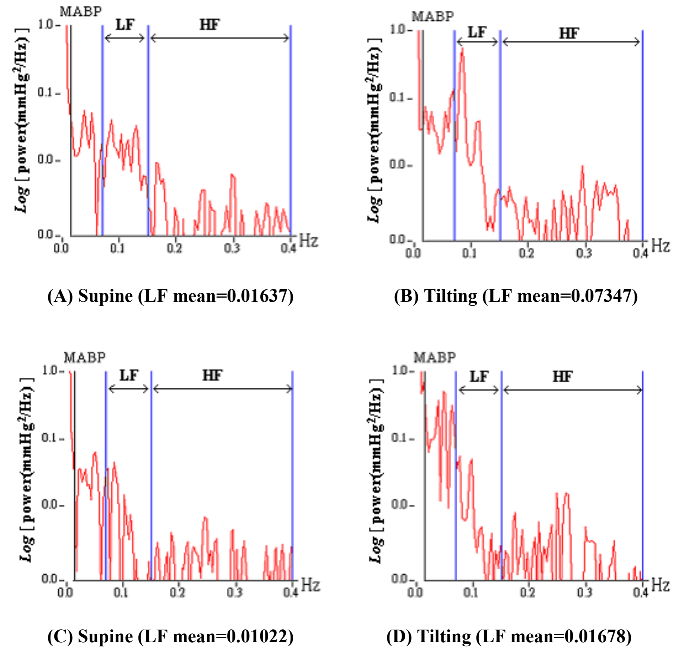

Figure 1. Spectral analysis results of one sample subject in the group with Cozaar. (A) Before treatment in supine position. (B) Before treatment in tilting position. (C) After treatment 2 months in supine position. (D) After treatment 2 months in tilting position.

In the group with Cozaar, CD values of MABP increased in the supine position and decreased in tilt-up position after 2 months treatments. In the other group with Renitec, CD values of MABP also increased in both supine and tilt-up positions after 2 months treatments. The results are depicted in Table 4. The CD values were significant different between supine and tilting in the group with Renitec. However, there was no significant difference exist in two groups before and after treatment.

Table 4. The result of chaotic analysis: CD values of MABP in two groups.

	Group with Cozaar		Group with Renitec	
Supine	PRE	2M	PRE	2M
	2.64±0.87	3.12±1.62	2.86±0.77*	3.19±1.04#
Tilting	PRE	2M	PRE	2M
	2.01±1.20	1.78±1.44	1.31±0.65*	1.89±0.76#

$p < 0.02$, # $p < 0.05$, PRE indicates before treatment and 2M means treatment after 2 months.

4. Discussion and conclusions

In the result of spectral analysis, the L/H, which reflects sympathetic tone, was increased more in the group with Renitec comparing to that with Cozaar. It may indicate that Cozaar has more manifest effect for suppressing the activity of sympathetic nervous system than that of Renitec. According to the physiological response, people will have higher blood pressure when their sympathetic nerves are more active. Thus, we speculate the reason that Cozaar could lower blood pressure more is the effect for suppressing the activity of sympathetic nervous system.

At the same time, based on the findings that the CD at rest was increased in two groups after 2 months treatment, we hypothesize that the regulation of the MABP is more complex in the two groups because the CD is considered to be an index of complexity in the dynamic system. Due to normative physiology has greater CD values (higher complexity) [20], the nonlinear analysis results might reveal that patients will tend to be normal with both Cozaar and Renitec treatments in supine position after 2 months treatment. The chaotic analysis is applicable to the complexity of blood pressure since the blood pressure is reported to have a chaotic nature [12].

In conclusion, the two antihypertensive drugs seem to be good to patients' physiology according to the analytic results. The difference between the two drugs is the effect to decrease blood pressure. For this reason, which drug should be adopted to lower blood pressure depend on the patient's condition at the first few days. Further studies are needed to assess the clinical significance of cardiovascular regulation in patients with hypertensive diseases.

Acknowledgement

The authors would like to thank the National Science Council, Taiwan, R.O.C., for supporting this research under Contract No. NSC92-2218-E035-001.

References

[1] Department of Health, Taiwan, R.O.C. (network address: http://www.doh.gov.tw/)

[2] World Health Organization (network address: http://www.who.int/en /)

[3] T. Knoll, R. Haberl, When lowering blood pressure is risky. Cerebral infarct-the paradox of prevention and acute therapy, MMW Fortschritte der Medizin 2000;142:25-27.

[4] J. O'Connel, C. Gray, Treatment of post-stroke hypertension. A practical guide, Drugs & Aging 1996;8:408-415.

[5] M. Brainin, Antihypertensive therapy in stroke: acute therapy, primary and secondary prevention, Acta Medica Austriaca 1995;22:54-57.

[6] K. Kanemaru, A. Kanemaru, I. Kuwajima, Antihypertensive therapy in patients with stroke, Nippon Rinsho- Japanese Journal of Clinical Medicine 2001;59: 945-948.

[7] J. Tovar, J. Alvarez-Sabin, P. Armario, Treatment of the rise in arterial pressure during the acyte phase of stroke. Recommendation of catalan societies of arterial hypertension and neurology, Revista de Neurologia 1999; 29:1271-1276.

[8] S. Kagiyama, A. Tsukashima, I. Abe, S. Fujishima, S. Ohmori, U. Onaka, Y. Ohya, K. Fujii, T. Tsuchihashi, M. Fujishima, Chaos and spectral analyses of heart rate variability during head-up tilting in essential hypertension, Journal of the Autonomic Nervous System 1999;76:153-158.

[9] M. Pagani, F. Lombardi, S. Guzzetti, O. Rimoldi, R. Furlan, P. Pizzinelli, G. Sandrone, G. Malfatto, S. Dell'Orto, E. Piccaluga, M. Turiel, G. Baselli, S. Cerutti, A. Malliani, Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog, Circulation Research 1986;59: 178-193.

[10] P.B. Persson, Spectrum analysis of cardiovascular time series, American Journal of Physiology 1997;273:1201-1210.

[11] P. Grassberger, I. Procaccia, Measuring the strangeness of strange attractors, Physica 9D 1983;189-208.

[12] C.D. Wagner, P.B. Persson, Chaos in blood pressure control, Cardiovascular Research 1996;31:380-387.

[13] C.D. Wagner, P.B. Persson, Nonlinear Chaotic dynamics of arterial blood pressure and renal blood flow, American Journal of Physiology 1995;268:621-627.

[14] T.M. Griffith, N. Holstein-Rathlou, P.B. Persson, Chaos: introduction to the spotlight issue, Cardiovascular Research 1996;31:331.

[15] C.D. Wagner, P.B. Persson, Chaos in cardiovascular system: an update, Cardiovascular Research 1998;40:257-264.

[16] A. Trzebski, M. Smietanowski, Non-linear dynamics of cardiovascular system in humans exposed to repetitive apneas modeling obstructive sleep apnea: aggregated time series data analysis, Autonomic Neuroscience: Basic and Clinical 2001;90:106-115.

[17] V. Melenovsky, D. Wichterle, J. Simek, J. Malik, T. Haas, R. Ceska, M. Malik, Effect of atorvastatin and fenofibrate on autonomic tone in subjects with combined hyperlipidemia, American Journal of Cardiology 2003;92:337-341.

[18] N. Kanaya, N. Hirata, S. Kurosawa, M. Nakayama, A. Namiki, Differential effects of propofol and sevoflurane on heart rate variability, Anesthesiology 2003;98:34-40.

[19] C.C. Chiu, S.J. Yeh, Assessment of cerebral autoregulation using time-domain cross-correlation analysis, Computers in Biology and Medicine 2001;31:471-480.

[20] D.T. Kaplan, M.I. Furman, S.M. Pincus, S.M. Ryan, L.A. Lipsitz, A.L. Goldberger, Aging and complexity of cardiovascular dynamics, Biophysical Journal 1991;59:945-949.

Address for correspondence
Name: Ben-Yi Liau
Full postal address: Graduate Institute of Electrical and Communications Engineering, Feng Chia University, No. 100 Wenhwa Rd., Seatwen, Taichung, Taiwan 40724, R.O.C.
E-mail address: p9218027@knight.fcu.edu.tw