Effects of captopril on Specific Harmonic Indexes of the Peripheral Pressure Pulse Waveform

Sheng-Hung Wang, Wei-Kung Wang
Department of Electrical Engineering
National Taiwan University
Taipei, Taiwan
raxwang@yahoo.com.tw

Tse-Lin Hsu, Ming-Yie Jan,
Institute of Physics
Academia Sinica
Taipei, Taiwan

Yuh-Ying Lin Wang
Department of Physics
National Taiwan Normal University
Taipei, Taiwan

Abstract—There were evidences that the blood pressure measured on the radial artery under some vasodilators treatments will overestimate than which measured on the central artery. Our previous studies infer that the harmonic proportion of the 4th harmonic (C4) of the peripheral pressure pulse waveform could be an index related to the peripheral vascular tone. In this study, we used a vasodilator drug, captopril to verify the relationship between C4 and vasoactive drug. Thirteen male Wistar Kyoto rats weighing 270 to 350 grams were studied. The blood pressure waveforms measured on the tail artery were averaged every 10 minutes and Fourier transformed into frequency domain. The data measured 20 minutes before captopril (0.83mg/1kg) injection was used as control. Four 10 minutes after-drug data sets were compared with the control. The diastolic (DBP) and systolic (SBP) blood pressures decreased rapidly after captopril injection. The mean pulse pressure A0 has the same decreasing trend but less conspicuously. The harmonic proportion of the 4th harmonic decreases at the beginning but then increases dramatically. These results suggest that C4 could be an index related to the peripheral vascular tone. We present a harmonic based pulse waveform analysis method to provide a peripheral pressure waveform index which may be used to estimate the cardiovascular risk.

Keywords-captopril; harmonic analysis; pressure waveform analysis.

I. INTRODUCTION

Cardiovascular diseases and their treatments are important issues in modern days. The central aortic pressure is the main index to evaluate the cardiovascular risk [1] [2]. The radial or brachial pressure which has high correlation to the central aortic pressure [3] [4] is usually used as a noninvasive surrogate to estimate the cardiovascular risk for clinical measurement conveniences.

However, in some conditions such as pseudohypertension and some vasodilator treatments, the blood pressures measured on the peripheral radial artery are often overestimated than which measured on the central artery [5] [6]. Therefore, some pulse waveform analysis methods such as augmentation index [7] and harmonic index [8] are prompted to evaluate the cardiovascular risk.

Our previous studies on vasoconstrictors showed that both angiotensin and vasopressin increased the blood pressure and decreased the harmonic proportion of the fourth harmonic (C4) of the pressure pulse[9], defined as 100% × (A4/A0), where A4 and A0 are the amplitudes of the fourth harmonic and the DC component of the pulse waveform, respectively. In contrast, Fourier transformed some of the pressure waveforms on publishing reports for hypertension treatment studies on human subject, we observed that drugs that relax blood vessels (e.g., captopril, lasartan and NTG) and are effective hypertension treatments all increase C4 but exert inconsistent effects on other harmonics [10]. The C4 increasing effect was not seen in atenolol. These observations infer that a changed peripheral vascular resistance may exert a frequency-specific effect (the C4-related effect) on the pressure wave spectrum.

To provide a systematic investigation, in this study, we used a vasodilator drug, captopril, which is an Angiotensin-I converting enzyme inhibitor on the Wistar Kyoto (WKY) rats to verify the relationship between C4 and vasoactive drug. The decreased blood pressure by dilating peripheral arteries and increased C4 would be expected.

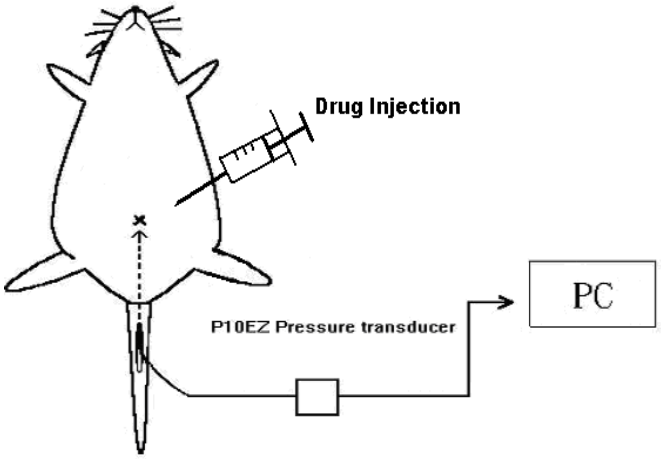

Figure 1. Eexperiment setup

978-1-4244-4713-8/10/$25.00 ©2010 IEEE

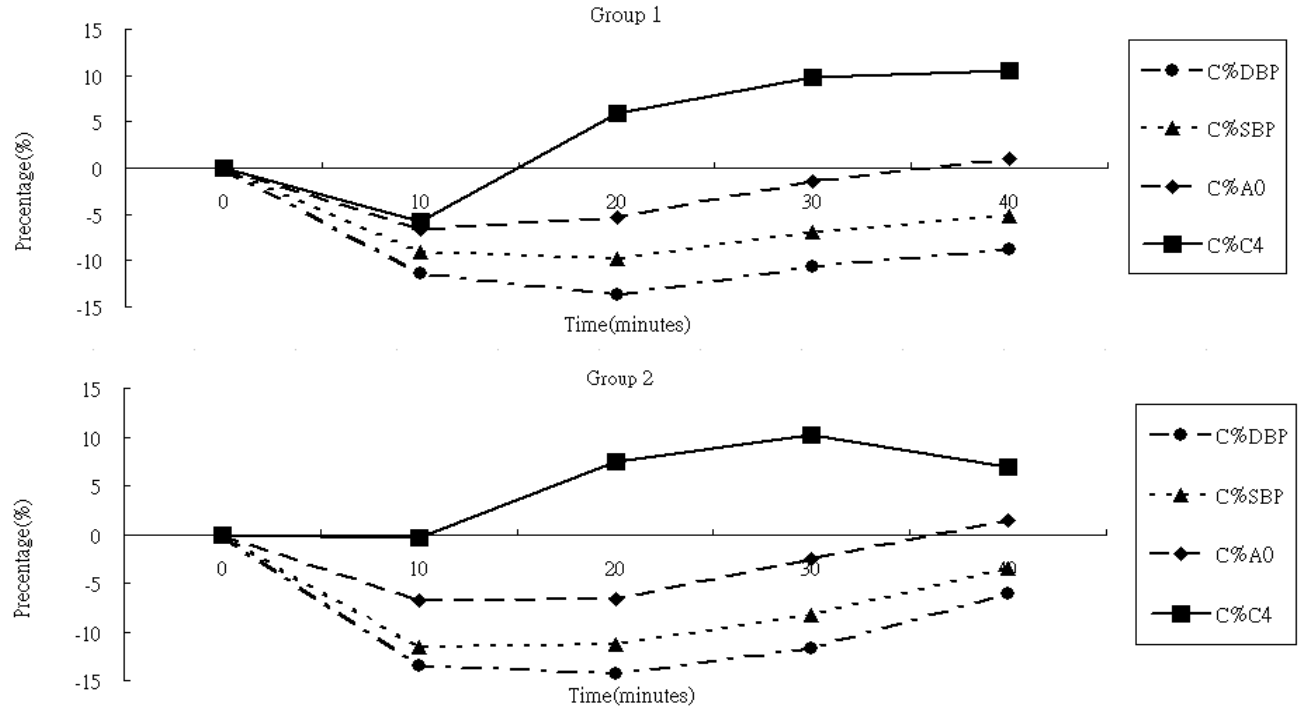

Figure 2. Percent changes of DBP, SBP, A0 and C4 with time

TABLE I. THE INDEXEX OF CONTROL

Group	Indexes			
	DBP (mm-Hg)	***SBP (mm-Hg)***	***A0*** (mm-Hg)	***C4***
1	71.79	109.73	15.82	7.20
2	58.82	93.65	14.19	8.14

II. METHOD

A. Experimen Preparations and Setup

Thirteen male Wistar Kyoto (WKY) rats weighing 270 to 350 grams were studied. The experiments were conformed to the "Guide for the Care and Use of Laboratory Animals" published by U.S. National Institutes of Health.

The experiment setup is showed as figure 1. The rats were anesthetized with urethane (1.32 gram per kilogram). The environment temperature was kept in 32 ± 2 ℃. The tail artery was cannulated with an intravenous catheter (Angiocath Plus, 22 gauge needle size, 1.00 in. needle length, $0.9 \times 25 mm^2$, Becton- Dickinson, Seoul, Korea) with physiological saline and heparin (3 gram per litre), which was connected to a pressure transducer (P10EZ Ohmeda, Singapore). The cannulation opening in the tail was about 1 cm from anus. The blood pressure pulse was then passed through the catheter tip to the pressure transducer.

B. Data Acquisition and Signal processing

After the operations ware completed, the rats were placed quietly for 120 to 180 minutes for stabilization. Then the signal which was received from pressure transducer was send to an A/D card (PCI-9111, ADLink, Taiwan) at sampling rate of 4096 Hz. A 2-second pulses sequence was acquired every minute and 20 data sequences were recorded and averaged as control data before giving an injection to the abdomen of rats with captopril (0.83 melligram per kilogram). The data sequences would be sampled until the end of the experiment.

The pulse waveform was averaged for every 10 minutes and slightly adjusted with the slope to make the start and the end point at the same height. The adjusted data are Fourier transformed into frequency domain. In this study, we only focused on the change in the fourth harmonic and computed the harmonic proportion (*C4)* instead of the amplitude (*A4)*. *C4* was defined as C4 = A4/A0, where A0 is the mean value of pulse pressure.

The pulse waveform of the 20-minute data before injection was used as control. The captopril affects the pressure wave index, systolic blood pressure, diastolic blood pressure, A0 and C4 were presented as the percentage changes $\%C^{index}$ in the experiment between drug and control,

$$(\%C^{Index}) = 100 \times \frac{Index,test - Index,cont}{Index,cont} \quad (1)$$

, where Index,cont is the index of pulse waveform of the control, Index,test is the index of pulse waveform of the testing pulse waveform.

Identify applicable sponsor/s here. *(sponsors)*

III. RESULTS

The data were separated as two groups according to the initial SBP that were above 100 mm-Hg as group 1 (n = 7) and others as group 2 (n = 6). The controlled data are showed on table 1. The testing data are based on the control.

Figure 2 shows the effects of captopril on pressure indexes (DBP, SBP, A0 and C4). Both groups give similar effect on all the four indexes despite that group 1 shows a decreasing effect at 10 minutes and group 2 shows recovering effect at 40 minutes. The diastolic blood pressure decreased rapidly and reached the lowest point at 20 minutes (13.74% in group 1 and 14.31% in group 2) then increased gradually in both groups. The systolic blood pressure and the mean pulse pressure A0 have the same decreasing trend with the diastolic blood pressure but the changes of the A0 were less conspicuous.

The harmonic index C4 decreases at the beginning but then increases dramatically. In group 1, the C4 increase 9.86% at 30 minutes and 10.49% at 40 minutes. In group 2, the C4 increase 10.22% at 30 minutes and 6.88% at 40 minutes.

The rapidly decrease of systolic and diastolic blood pressure at in 20 minutes makes the A0 decrease significantly ($p < 0.05$) but the changes of A0 unobvious after 20 minutes. In the other hand, the 4th harmonic proportion C4 is increasing significantly ($p < 0.05$) after 20 minutes. The reduced increasing of C4 at 40 minutes in group 2 may be caused by the recovering of blood pressure.

IV. DISCUSSION

Captopril is an angiotensin-I converting enzyme inhibitor which may dilate the peripheral arteries and treats the hypertension. The decrease of systolic blood pressure is the immediate index. However, the great drop of peripheral systolic blood pressure could lead to overestimation of the effect of vasodilator drugs [11].

In this study, we conduct a systemized investigation to verify our previous observations from the published reports of other research groups [10] which analyzes the effects of vasodilator on C4. We used a harmonic analysis method to analyze the effects of vasodilator drugs on rats systematically. Under the affection of captopril, the decreasing of blood pressure and the increasing of C4 is significant. It infers that a changed peripheral vascular resistance may exert a frequency-specific effect (the C4-related effect) on the pressure wave spectrum.

In additional, in traditional chinese medicine, the lung meridians correlates with peripheral circulation (肺主皮毛). Captopril treats the hypertension by dilating the peripheral arteries. The increasing of C4 in the experimental result might infer that C4 is an index of lung meridians in traditional chinese medicine [12].

This study is just a beginning. In the future, more hypertension drugs would be test. The changes in A0 and C4 would be observed, especially the difference between the affection form β-adrenoceptor blocker (heart-related) and vasodilator (peripheral vascular-related) drugs. The C4 could be an index related to the peripheral vascular tone as well as lung meridian, therefore could be useful in estimating cardiovascular risk.

ACKNOWLEDGMENT

This study was supported in part by the National Science Council, Taiwan, under grant no. 97-2112-M-003-006-MY3

REFERENCES

[1] Agabiti-Rosei E, Mancia G, O'Rourke MF, Roman MJ, Safar ME, Smulyan H, et al. Central blood pressure measurements and antihypertensive therapy: a consensus document. Hypertension 2007; 50(1):154–160.

[2] O'Rourke MF. Ascending aortic pressure wave indices in cardiovascular disease. Am J Hypertens 2004; 17: 721–723.

[3] Kikuya M, Ohkubo T, Asayama K, Metoki H, Obara T, Saito S, Hashimoto J, et al. Ambulatory blood pressure and 10-year risk of cardiovascular and noncardiovascular mortality: the Ohasama study. Hypertension 2005; 45(2): 240–245.

[4] Domanski MJ, Davis BR, Pfeffer MA, Kastantin M, Mitchell GF. Isolated systolic hypertension: prognostic information provided by pulse pressure. Hypertension 1999; 34: 375–380.

[5] O'Rourke MF, Vlachopoulos C, Graham R. Spurious systolic hypertension in youth. Vasc Med 2000; 5: 141–145.

[6] Williams B, Lacy PS, Thom SM, Cruickshank K, Stanton A, Collier D, et al.; CAFE Investigators; Anglo-Scandinavian Cardiac Outcomes Trial Investigators; CAFE Steering Committee and Writing Committee. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study. Circulation 2006; 113(9):1213–1225.

[7] Weber T, Auer J, O'Rourke MF, Kvas E, Lassnig E, Berent R, Eber B. Arterial stiffness, wave reflections, and the risk of coronary artery disease. Circulation 2004; 109: 184–189.

[8] Wang SH, Hsu TL, Jan MY, Wang Lin YY, Wang WK. Age-related changes in specific harmonic indices of pressure pulse waveform. Chwee Teck Lim, James C.H. Goh (Eds.): The 13th international conference on Biomedical Engineering, Singapore: 2008, Proceedings 23, pp. 183–185, 2009.

[9] Hsu TL, Chao PT, Hsiu H, Wang WK, Li SP, and Lin Wang YY. Organ-specific ligation-induced changes in harmonic components of the pulse spectrum and regional vasoconstrictor selectivity in Wistar rats. Exp. Physiol. 2006;91(1):163–170.

[10] Hsu TL, Wang SH, Wang WK, Li SP, Lin Wang YY. Analysis of the augmentation index in the frequency domain using vasoactive drugs data. Paper in review.

[11] Hirata K, Vlachopoulos C, Adji A, O'Rourke MF. Benefits from angiotensin-converting enzyme inhibitor 'beyond blood pressure lowering': beyond blood pressure or beyond the brachial artery? J Hypertens 2005; 23(3):551–556. Erratum in: J Hypertens. 2005; 23(4):903-904.

[12] Wang WK, Chen HL, Hsu TL, Lin Wang YY. Alteration of pulse in human subjects by three chinese herbs. Am. J. Chinese Med. 1994 Vol.12 2: 197-203.