The correlation between cognitive impairment and ambulatory blood pressure in patients with cerebral small vessel disease

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Abstract. – OBJECTIVE: The present study was aimed to analyze the correlation between cognitive impairment and ambulatory blood pressure in patients with cerebral small vessel disease (CSVD).

PATIENTS AND METHODS: 108 patients with CSVD received in our hospital were selected. Assessment of cognitive impairment was by the Montreal Cognitive Assessment (MoCA). 39 cases were established as the impairment group and 69 cases were established as the normal group. 24 h ambulatory blood pressure was monitored, and changes in ambulatory blood pressure parameters between the two groups were compared. Also, the correlation between blood pressure parameters and MoCA score were analyzed.

RESULTS: Comparisons of ambulatory systolic blood pressure, ambulatory pulse pressure and the ratios of night blood pressure reduction of patients in both groups showed statistical differences ($p < 0.05$), while the changes in diastolic blood pressure showed no statistical differences ($p > 0.05$). The comparison of the blood pressure curves in both groups showed statistical differences ($p < 0.05$). The ambulatory systolic blood pressure, ambulatory pulse pressure and the ratio of night blood pressure reduction of patients with CSVD showed prominently negative correlations with MoCA score ($p < 0.05$).

CONCLUSIONS: Cognitive impairment and the ambulatory blood pressure of patients with CSVD are intimately correlated. The rise of ambulatory systolic blood pressure, pulse pressure, and the decline of blood pressure may represent risk factors for cognitive impairment in patients with CSVD. Improving blood pressure management will reduce the incidence of cognitive impairment caused by CSVD.

Key Words:
Cerebral small vessel disease, Cognitive function, Ambulatory blood pressure, Correlation.

Introduction

Cerebral small vessel disease (CSVD), a subtype of cerebrovascular disease, is an important factor that leads to senile dementia or senile vascular cognitive impairment[1]. A previous work showed[2] that almost half of vascular dementias are caused by CSVD. Cognitive function is intimately correlated with fluctuation of blood pressure[3]. Ambulatory blood pressure monitoring can display the circadian rhythm of blood pressure, the blood pressure level in certain periods and the control condition of blood pressure. The pathogenesis of CSVD is currently not well understood, but the incidences of hypoperfusion or ischemic injury, microembolization, structural changes of small blood vessels, changes around blood vessels and metabolic encephalopathy are generally considered correlative factors, which can ultimately lead to neurologic deficits[4]. Hypertension is an important risk factor for the incidence of cognitive impairment, which can lead to encephalanalosis or neurofibrillary denaturation and worsen atherosclerosis to different degrees[5]. Also, hypertension is a key factor causing hyaline degeneration of arteriole walls[6]. In the present study, we analyzed the correlation between cognitive impairment and ambulatory blood pressure in patients with CSVD, to provide a reference for clinical control of blood pressure and prevention of cognitive impairment in CSVD.

Patients and Methods

Patients

108 patients with CSVD received in our hospital from January 2014 to January 2016 were selected. Diagnostic criteria of CSVD included: cerebral micro bleeds or lacunar infarction,

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without obvious carotid artery stenosis (>50%); watershed infarction; subcutaneous lesions of diameter over 15 mm. The inclusion criteria included: 1- aged from 45-80 years old; 2- met the diagnostic criteria of CSVD, confirmed by head MRI; 3- no record of cerebral trauma, tumor, surgery or radiation; 4- no neurological disorders, psychonosema or disorders such as anxiety and depression; 5- were able to complete the MoCA score, and with complete data on ambulatory blood pressure. The exclusion criteria included: 1- complicated with refractory hypertension; 2- recent record of myocardial infarction or atrial fibrillation; 3- complicated with severe liver or kidney disease; 4- complicated with active bleeding disease or impairment of blood coagulation. After receiving consent and approval by the patients and their families, 39 cases were established as the impairment group and 69 cases as the normal group, according to whether the patients had cognitive impairment or not. The impairment group included patients with MoCA score under 23 points, 21 males and 18 females, aged 46-74 years old, with an average age of 66.8 ± 12.4. 14 cases had a history of drinking, 16 had a history of smoking, 10 had hypertension and 8 had diabetes mellitus. The duration of education was 13-35 years, with average duration of 25.6 ± 8.2 years. The normal group included 36 males and 33 females, aged 45-78 years old, with an average age of 68.2 ± 15.2 years. 25 cases had a history of drinking, 23 had a history of smoking, 19 had hypertension and 17 had diabetes. The duration of education was 12-34 years, with average duration of 25.0 ± 7.6 years. The general parameters between the two groups had no statistical difference ($p > 0.05$). We obtained approval from the Ethics Committee of Yishui Central Hospital and informed consent of patients or their families.

Methods

Montreal Cognitive Assessment (MoCA) was adopted to evaluate the cognitive function of patients, including eight aspects: executive capability, attention and concentration, language, memory, abstract thinking, visual space structural skill, calculation capacity and orientation capacity in cognition territory. Patients with less than 12 years of education were given 1 additional point and the total score was 30 points. A Welch Allyn CardioPerfect software system (Welch Allyn, New York, NY, USA) was adopted to apply 24 h monitoring of ambulatory blood pressure. 8:00-23:00 was set as day-time and 23:00-8:00 was set as night-time. Blood pressure was measured every half hour during day-time and every hour during night-time. Patients were allowed to take part in daily activities during blood pressure monitoring. The criteria of effective blood pressure were: 70-260 mmHg for systolic blood pressure (SBP), 40-150 mmHg for diastolic blood pressure (DBP), 20-150 mmHg for pulse pressure (PP). Patients with atrial fibrillation were excluded.

Observational Indices

1. Levels of blood glucose and blood fat of the two groups were compared, including fasting blood glucose (FBG), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC). 2. Differences in ambulatory blood pressure parameters in the two groups were compared, including 24 h mean SBP, mean day-time systolic blood pressure (DSBP), mean night-time blood pressure (NSBP), 24 h mean DBP, day-time mean diastolic blood pressure (DDBP), night mean diastolic blood pressure (NDBP), 24 h mean PP, day mean pulse pressure (DPP) and night mean pulse pressure (NPP). The ratios of night blood pressure reduction were calculated. (ΔMBP) = (DMBP-NMBP) ÷ DMBP×100%, ΔMBP between 0-10% indicated non-dipper blood pressure, 10-20% indicated dipper blood pressure, over 20% indicated super dipper blood pressure and less than 0% indicated reverse dipper blood pressure. 3. The correlations between the parameters of ambulatory blood pressure and MoCA score were analyzed.

Statistical Analysis

SPSS 20.0 software (Version X; IBM, Armonk, NY, USA) was used for analysis. Measurement data are presented as mean ± standard deviation ($\bar{x} \pm s$) and comparisons between groups were by independent sample *t*-test. Enumeration data are presented as case or percentage (%), and comparisons between groups were by χ^2-test. Pearson testing was adopted for correlation analyses. $p < 0.05$ was taken as statistically significant.

Results

Comparison of the Levels of Blood Glucose and Blood Fat

Comparison of the levels of blood glucose and blood fat in the two groups showed no statistically significant differences ($p > 0.05$) (Table I).

Table I. Comparisons of the levels of blood glucose and blood fat (mmol/L).

Group	FBG	TG	LDL-C	TC
Impairment group	5.33 ± 0.78	1.87 ± 0.60	3.25 ± 0.77	4.76 ± 1.02
Normal group	5.24 ± 0.83	1.79 ± 0.57	3.38 ± 0.91	4.98 ± 1.13
t	0.563	0.678	0.789	1.035
p	0.432	0.324	0.219	0.120

FBG: fasting blood glucose; TG: triglyceride; LDL-C: low density lipoprotein cholesterol; TC: total cholesterol.

Comparisons of Ambulatory Blood Pressure Parameters

The comparisons of the ambulatory SBP, ambulatory PP and the ratios of night blood pressure reduction of patients in both groups showed statistically significant differences ($p < 0.05$), while changes in DBP were not significant ($p > 0.05$) (Table II).

Comparison of Fluctuations of Blood Pressure Curves

Dipper blood pressures in the impairment group were lower than in the normal group, and the differences were statistically significant ($p < 0.05$) (Table III).

Correlation Analysis of Ambulatory Blood Pressure Parameters and MoCA Score

The ambulatory SBP and the ratios of night blood pressure reduction of patients with CSVD showed prominently negative correlations with the MoCA score ($p < 0.05$) (Table IV).

Discussion

CSVD is a form of arteriole lesion. The pathological vessels are mostly perforating arterioles of diameters between 30-300 μm, which are the major supply to gray matter nuclei, white matter nuclei and brainstem in the deep brain. These arterioles barely have blood vessel walls. Their outer layers are composed of corneal endothelial cells and a few smooth muscle cells, and have direct contact with the foot processes of astrocytes. This form of arteriole, stemming from large cerebral arteries such as the middle cerebral artery and basilar artery, are terminal branches without collateral anastomosis. CSVD leads to permanent brain parenchyma injury through multiple mechanisms and the main symptoms include leukoaraiosis and lacunar infarction[7]. Multiple studies have demonstrated[8,9] the intimate correlation between CSVD and the occurrences of cognitive decline and dementia. Cognitive im-

Table II. Comparisons of the parameters of ambulatory blood pressure (mmHg).

Parameter of blood pressure	Impairment group	Normal group	*t*	*p*
24 h systolic blood pressure (SBP)	136.45 ± 15.42	127.47 ± 16.50	5.834	0.022
Day mean systolic blood pressure (DSBP)	141.03 ± 14.85	133.28 ± 13.86	5.667	0.026
Night mean blood pressure (NSBP)	130.86 ± 16.73	122.97 ± 18.20	4.280	0.038
24 h mean diastolic blood pressure (DBP)	89.35 ± 9.28	86.56 ± 8.36	1.554	0.127
Day mean diastolic blood pressure (DDBP)	95.36 ± 10.33	92.74 ± 10.85	1.243	0.203
Night mean diastolic blood pressure (NDBP)	85.62 ± 7.33	83.94 ± 8.02	0.958	0.362
24 h mean pulse pressure (PP)	48.68 ± 5.89	40.33 ± 6.22	5.935	0.020
Day mean pulse pressure (DPP)	53.42 ± 4.49	44.68 ± 7.21	6.765	0.013
Night mean pulse pressure (NPP)	43.85 ± 8.39	36.79 ± 6.84	6.478	0.016
Ratio of night blood pressure reduction (ΔMBP)	10.46 ± 3.10	16.27 ± 5.33	6.173	0.021

Table III. Comparison of the fluctuations of blood pressure curves [n (%)].

Group	Cases	Dipper	Non-dipper	Supper-dipper	Reverse-dipper
Impairment group	39	10 (25.64)	12 (30.77)	10 (25.64)	7 (17.95)
Normal group	69	37 (53.62)	13 (18.84)	7 (10.14)	12 (17.39)
χ^2			9.820		
p			0.020		

Table IV. Correlation analysis of ambulatory blood pressure parameters and MoCA score.

Parameter of blood pressure	*r*	*p*
24 h systolic blood pressure (SBP)	-0.374	0.036
Day mean systolic blood pressure (DSBP)	-0.394	0.033
Night mean blood pressure (NSBP)	-0.310	0.040
24 h mean pulse pressure (PP)	-0.367	0.031
Day mean pulse pressure (DPP)	-0.418	0.035
Night mean pulse pressure (NPP)	-0.395	0.042
Ratio of night blood pressure reduction (ΔMBP)	-0.443	0.028

pairment includes persistent decline of concentration, decreased rate of information processing and decline of speech fluency. MoCA makes quick assessment of mild cognitive impairment, and compared to the Mini-Mental State Examination (MMSE), is superior and more reliable[10]. A previous study[11] confirmed that decline of cognitive function has a prominent correlation with the fluctuation of blood pressure. Each 10 mmHg rise of systolic pressure is companied by a 7% increase in the risk of cognitive decline, which supports the correlation between blood pressure and cognitive impairment. Through this study, the ambulatory SBP, ambulatory PP and the ratios of night blood pressure reduction of patients in both groups showed statistical differences, while the DBP showed no statistical differences. Correlation analysis showed that the ambulatory SBP, ambulatory PP and the ratio of night blood pressure reduction prominently were correlated negatively with MoCA score[12]. In addition, from the fluctuations of the blood pressure curves of both groups, the ratio of dipper blood pressure in the impairment group was significantly lower, which suggested weaker circadian rhythm of blood pressure in CSVD patients with cognitive impairment[13]. A possible reason included that the high load condition of SBP led to higher PP and weaker circadian rhythm of blood pressure. Persistent high blood pressure worsened the damage to endothelial function of small vessels, which led to brain white matter damage, and sequentially enhanced the cognitive impairment in CSVD[14].

Conclusions

Cognitive impairment in patients with CSVD is intimately correlated with fluctuations of ambulatory blood pressure. The rise of ambulatory SBP, PP and the decline of blood pressure might be risk factors for cognitive impairment of patients with CSVD. Improving blood pressure management of patients will reduce the prevalence of the cognitive impairment in patients with CSVD.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Hollocks MJ, Brookes R, Morris RG, Markus HS. Associations between the brief memory and executive test (BMET), activities of daily living, and quality of life in patients with cerebral small vessel disease. J Int Neuropsychol Soc 2016; 22: 561-569.
2) Prabhakar P, Chandra SR, Supriya M, Issac TG, Prasad C, Christopher R. Vitamin D status and vascular dementia due to cerebral small vessel disease in the elderly Asian Indian population. J Neurol Sci 2015; 359: 108-111.
3) Conway KS, Forbang N, Beben T, Criqui MH, Ix JH, Rifkin DE. Relationship between 24-Hour ambulatory blood pressure and cognitive function in Community-Living older adults: The UCSD ambulatory blood pressure study. Am J Hypertens 2015; 28: 1444-1452.
4) Yamashiro K, Tanaka R, Okuma Y, Shimura H, Ueno Y, Miyamoto N, Urabe T, Hattori N. Cerebral microbleeds are associated with worse cognitive function in the nondemented elderly with small vessel disease. Cerebrovasc Dis Extra 2014; 4: 212-220.
5) Kececi SD, Cengiz M, Yavuzer H, Yavuzer S, Sulu C, Doventas A, Beger T. Relation of ambulatory blood pressure measurement and cognitive functions in hypertensive elderly patients. Aging Clin Exp Res 2016; 28: 699-704.
6) Komori T, Eguchi K, Saito T, Nishimura Y, Hoshide S, Kario K. Riser blood pressure pattern is associated with mild cognitive impairment in heart failure patients. Am J Hypertens 2016; 29: 194-201.

7) Huijts M, Duits A, Staals J, Kroon AA, de Leeuw PW, van Oostenbrugge RJ. Basal ganglia enlarged perivascular spaces are linked to cognitive function in patients with cerebral small vessel disease. Curr Neurovasc Res 2014; 11: 136-141.

8) Huijts M, Duits A, van Oostenbrugge RJ, Kroon AA, de Leeuw PW, Staals J. Accumulation of MRI markers of cerebral small vessel disease is associated with decreased cognitive function. A study in first-ever lacunar stroke and hypertensive patients. Front Aging Neurosci 2013; 5: 72.

9) Sun J, Yu X, Jiaerken Y, Song R, Huang P, Wang C, Yuan L, Mao Y, Guo Y, Yu H, Zhang M. The relationship between microvasculature in white matter hyperintensities and cognitive function. Brain Imaging Behav 2016 march: doi: 10.1007/s11682-016-9531-8.

10) Wong A, Xiong YY, Kwan PW, Chan AY, Lam WW, Wang K, Chu WC, Nyenhuis DL, Nasreddine Z, Wong LK, Mok VC. The validity, reliability and clinical utility of the Hong Kong Montreal Cognitive Assessment (HK-MoCA) in patients with cerebral small vessel disease. Dement Geriatr Cogn Disord 2009; 28: 81-87.

11) Abraham HM, Wolfson L, Moscufo N, Guttmann CR, Kaplan RF, White WB. Cardiovascular risk factors and small vessel disease of the brain: blood pressure, white matter lesions, and functional decline in older persons. J Cereb Blood Flow Metab 2016; 36: 132-142.

12) Yamaguchi Y, Wada M, Sato H, Nagasawa H, Koyama S, Takahashi Y, Kawanami T, Kato T. Impact of ambulatory blood pressure variability on cerebral small vessel disease progression and cognitive decline in community-based elderly Japanese. Am J Hypertens 2014; 27: 1257-1267.

13) Klarenbeek P, van Oostenbrugge RJ, Rouhl RP, Knottnerus IL, Staals J. Ambulatory blood pressure in patients with lacunar stroke: association with total MRI burden of cerebral small vessel disease. Stroke 2013; 44: 2995-2999.

14) Ji AL, Chen WW, Huang WJ. Clinical study on influences of enteric coated aspirin on blood pressure and blood pressure variability. Eur Rev Med Pharmacol Sci 2016; 20: 5017-5020.