High blood pressure in acute ischemic stroke and clinical outcome

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Abstract

This study aimed to evaluate the prognostic value of acute phase blood pressure in patients with acute ischemic stroke by determining whether or not it contributes to clinical outcome. We studied 515 consecutive patients admitted within the first 48 hours after the onset of ischemic strokes, employing systolic and diastolic blood pressure measurements recorded within 36 hours after admission. High blood pressure was defined when the mean of at least 2 blood pressure measurements was ≥200 mmHg systolic and/or ≥110 mmHg diastolic at 6 to 24 hours after admission or ≥180 mmHg systolic and/or ≥105 mmHg diastolic at 24 to 36 hours after admission. The high blood pressure group was found to include 16% of the patients. Age, sex, diabetes mellitus, hypercholesterolemia, atrial fibrillation, ischemic heart disease, stroke history, carotid artery stenosis, leukoaraiosis, NIH Stroke Scale (NIHSS) on admission and mortality were not significantly correlated with either the high blood pressure or non-high blood pressure group. High blood pressure on admission was significantly associated with a past history of hypertension, kidney disease, the modified Rankin Scale (mRS) on discharge and the length of stay. On logistic regression analysis, with no previous history of hypertension, diabetes mellitus, atrial fibrillation, and kidney disease were independent risk factors associated with the presence of high blood pressure [odds ratio (OR), 1.85 (95% confidence interval (CI): 1.06-3.22), 1.89 (95% CI: 1.11-3.22), and 3.31 (95% CI: 1.36-8.04), respectively]. Multi-organ injury may be presented in acute stroke patients with high blood pressure. Patients with high blood pressure had a poor functional outcome after acute ischemic stroke.

Introduction

It is well-known that blood pressure is often elevated in the early stage of acute ischemic stroke.[1] This early elevation in blood pressure is considered to play an important role in maintaining the cerebral circulation and collateral blood circulation in the penumbra region; however, the mechanism is not fully understood.[2-4] Some reports suggest that an initially high blood pressure is associated with a poor prognosis,[5-8] while other reports suggest that it contributes to a more favorable prognosis[9] or does not affect the prognosis,[10] and evaluations have not been adequately conducted.

In this study, we evaluated the clinical characterics of acute ischemic stroke cases with very high blood pressure in acute phase.

Materials and Methods

We studied 515 consecutive patients (309 male and 206 female patients, mean age: 73 years old) admitted within the first 48 hours after the onset of ischemic stroke between April 2003 and December 2007 from our hospital. Those who showed a mean of at least 2 blood pressure recordings of ≥200 mmHg systolic and/or ≥110 mmHg diastolic at 6 to 24 hours after admission or ≥180 mmHg systolic and/or ≥105 mmHg diastolic at 24 to 36 hours after admission were assigned to Group 1,[11] and the remaining patients were assigned to Group 2 (≥90 mmHg systolic or ≥48 mmHg diastolic). We excluded patients who received thrombolysis or intra-arterial therapies. We compared the clinical entity of the stroke, the site of the infarct, risk factors, carotid artery stenosis, cerebral white matter lesions, severity, and mortality between the two groups. The study protocol was acknowledged and authorized by the Institutional Review Board of Okayama Medical Center in Japan.

Clinical entities were classified into lacunar, atherothrombotic and cardioembolic infarctions according to the 3rd Edition of Cerebrovascular Disease Classification by the National Institute of Neurological Disorders and Stroke (NINDS-III).[12] The site of the infarct was classified into supratentorial small vessels, supratentorial cortical branches, as well as supratentorial and supra- and sub-tentorial lesions. Risk factors were defined as follows: high blood pressure – those who had been diagnosed with hypertension, and had already taken anti-hypotensive drugs; diabetes mellitus – those who had a fasting glucose level above 126 mg/dL and HbA1c higher than 6.5%, or those who had been taking antihyperglycemic drugs; hypercholesterolemia – those who exhibited a total cholesterol level higher than 220 mg/dL during hospitalization, or those who had been taking antihyperlipidemic drugs; degree of severity – according to the NIH stroke scale (NIHSS) and the modified Rankin Scale (mRS); carotid artery stenosis of more than 70% as assessed by the NASCET index was considered significant; cerebral white matter lesions were divided into grade 0-3 based on the study by Fazekas et al.[13] Grade 0, no cerebral matter lesions; Grade 1, periventricular hyperintensities (PVH) on the bilateral anterior or posterior horn or patchy lesions; Grade 2, enlarged, patchy lesion and early confluent stage; Grade 3, enlarged PVH surrounding the lateral cerebral ventricle. Grade ≥2 on cerebral white matter lesion scoring indicates significant white matter disease. Although the general recommendation in Japan is not to treat elevated blood pressure during the first day of ischemic stroke, antihypertensive (a calcium antagonist) was administered only when extreme hypertension of ≥220 mmHg systolic and/or ≥130 mmHg diastolic continued or patients had aortic dissection, acute myocardial infarction, heart failure or kidney failure.

Statistical analysis was conducted using SPSS16.0 (SPSS Inc.). We employed the χ^2 test to compare the backgrounds of the patients, and non-parametric Mann-Whitney test to compare the clinical evaluation scales between the two groups. Logistic regression analysis was conducted to evaluate the association of the risk factors and presence of a high blood pressure, and the odds ratio and 95% confidence interval (CI) were evaluated. $p < 0.05$ was considered significant.

Results

A total of 83 patients (16%) belonged to Group 1. No significant differences in mean age, sex and clinical entities were noted between the groups. In both groups, the most common site of the infarct was supratentorial cortical branches.

Concerning the risk factors, the percentage of patients with a history of hypertension was 75.9% and 57.6%, and that of kidney disease was 12.0% and 3.5% in Groups 1 and 2, respectively, with significant differences. There was no significant difference regarding other risk factors; however, the incidence of risk factors was higher in Group 1. Concerning the degree of severity, mRS on discharge and the length of stay were significantly higher in Group 1. There was no significant difference in NIHSS on admission and the mortality rate, but it was higher in Group 1 (Table 1).To clarify the association of the risk factors and the presence of a high blood pressure, logistic regression analysis was conducted. Regarding the factors excluding a history of hypertension, a history of diabetes mellitus, arterial fibrillation, and kidney disease were significantly associated with an odds ratio (OR) of 1.85 (95% confidence interval (CI): 1.06-3.22, p=0.02), 1.89 (95% CI: 1.11-3.22, p=0.02), and 3.31 (95% CI: 1.36-8.04, p=0.01), respectively, and they were independent risk factors for having elevated blood pressure during the acute phase of stroke. Other factors did not show a significant correlation (Table 2).

Discussion

In this study, Group 1 indicated the very high blood pressure group; the size of this group (n=83) was relatively small although the entire study group as a whole was large at n=515. The rates of patients with a history of high blood pressure, and kidney disease were significantly higher in Group 1, and they were more likely to have a history of being prescribed several kinds of antihypertensive drugs. They were also more likely to show atrial fibrillation and diabetes mellitus, although the difference was not significant. Their mRS scores on discharge and the length of stay were significantly higher, though NIHSS on admission was not significant between the two groups, which suggested that they were more likely to have a poorer prognosis. On logistic regression analysis with no previous history of hypertension, diabetes mellitus, arterial fibrillation, and kidney disease were independent risk factors associated with the presence of a high blood pressure. In patients without a history of hypertension, patients with diabetes, atrial fibrillation, and kidney disease were more likely to have elevated blood pressure early during stroke. Atrial fibrillation and kidney disease are common complications of late hypertensive disease and hypertension is more prevalent among patients with diabetes. These results suggest that multi-organ injury may be present in patients with high blood pressure, and thus acute phase high blood pressure is related to a poor prognosis. Generally, the blood pressure is elevated in the early stage of stroke, and it reaches a plateau within 24 hours, and then gradually starts to decrease in a week. In this study, only 28 (5.4%) and 10 (1.9%) acute inpatients spontaneously had a blood pressure of higher than 180/105 mmHg one week and two weeks after admission, respectively. The acute phase elevation in blood pressure is considered to play an important role in maintaining cerebral and collateral blood circulation in the penumbra region. However, the continuation of an elevated blood pressure has been suggested to lead to brain edema and reinfarction of ischemic lesions.[14-16] Large epidemiological studies of acute ischemic stroke patients have demonstrated a U-shaped curve with respect to pre-

Table 1. Baseline characteristics of subjects.

Characteristic	Group 1 n=83	Group 2 n=432	p value
Mean age (years) [mean±SD]	75.0±11.1	73.1±11.9	N.S.
Male [%]	54.2	61.1	N.S.
Clinical entities [%]			N.S.
Lacunar infarction	33.7	35.5	
Atherothrombotic infarction	26.5	26.3	
Cardioembolic infarction	25.6	26.6	
Unknown cause	14.2	11.6	
The site of the infarct [%]			N.S.
Supratentrial small vessels	36.1	41.2	
Supratentrial cortical branches	51.8	40.5	
Subtentrial lesions	12.0	17.1	
Supra- and sub-tentrial lesions	0	1.2	
Hypertension [%]	75.9	57.6	0.001
Diabetes mellitus [%]	36.1	25.0	N.S.
Hypercholesterolemia [%]	26.5	25.0	N.S.
Atrial fibrillation [%]	39.8	25.7	N.S.
Ischemic heart disease [%]	18.3	14.2	N.S.
Stroke history [%]	33.7	29.4	N.S.
Kidney disease [%]	12.0	3.5	0.003
Carotid artery stenosis [%]	10.8	6.9	N.S.
Leukoaraiosis [%]	18.1	18.3	N.S.
NIHSS on admission [mean±SD]	8.7±7.0	7.5±7.8	N.S.
mRS on discharge [mean±SD]	3.1±1.8	2.4±1.8	0.005
The length of stay (days) [mean±SD]	28.2±21.4	22.7±17.5	0.007
Mortality [%]	6.0	3.5	N.S.

Group 1 represents subjects with high blood pressure. Group 2 represents the remaining patients; mRS: modified Rankin Scale; NIHSS: NIH Stroke Scale; N.S.: not significant.

Table 2. Odds ratio for an association of risk factors with the presence of a high blood pressure.

	OR	95%CL	p value
Age (>75)	1.12	0.65~1.92	0.69
Male	0.73	0.44~1.22	0.23
Diabetes mellitus	1.85	1.06~3.22	0.03*
Hypercholesterolemia	1.05	0.59~1.88	0.86
Atrial fibrillation	1.89	1.11~3.22	0.02*
Stroke history	1.11	0.66~1.89	0.69
Ischemic heart disease	1.23	0.64~2.36	0.53
Kidney disease	3.31	1.36~8.04	0.01*
Carotid artery stenosis	1.48	0.62~3.50	0.38
Leukoaraiosis	0.95	0.49~1.84	0.88
Mortality	1.40	0.46~4.20	0.55

*$p<0.05$

senting blood pressure and outcomes.[7] A low blood pressure group of patients would be put in with Group 2. Our study demonstrates that high blood pressure values were highly associated with early recurrent stroke and fatal brain edema.

Regarding the management of hypertension, the 2004 Japanese guidelines for the management of the stroke[17] states that the careful administration of antihypertensive drugs is recommended only when extreme hypertension of ≥220 mmHg systolic and/or ≥130 mmHg diastolic continues or patients have aortic dissection, acute myocardial infarction, heart failure or kidney failure. However, the grade of recommendation is C1, which means that it is not based on adequate scientific evidence.

Some studies have reported that, in patients who were administered a high-dose bolus of nimodipine, a calcium antagonist, in the acute stage of stroke, a decrease in the diastolic pressure and deterioration of neurological scores were observed, which suggests the risk of rapid blood pressure reduction.[18] However, the target blood pressure specifically related to the clinical entity, history and coexisting illnesses has not yet been proposed. The ACCESS study which was published recently reported that a 7-day course of candesartan, an angiotensin receptor II blocker (ARB), started within 36 hours rather than seven days after an acute ischemic stroke reduced the occurrence of cardiovascular events within a year after the stroke by 47.5%.[11] These findings indicate the need to re-examine the conventional management of hypertension in the early stage of acute brain stroke. In the present study, it was suggested that patients with high blood pressure were more likely to have a history of hypertension, kidney disease and carotid stenosis. In these patients, a gradual decrease in the blood pressure on careful follow-up of the clinical symptoms may be favorable.

There are some limitations to this study. First, the number of patients was relatively small. Therefore, further evaluation with a larger number of patients is required. Second, the prognosis was measured by mRS scores on discharge; thus a follow-up period of three or six months is necessary. A large randomized comparison trial to investigate indications of antihypertensive drugs in the early stage of acute stroke is awaited.

Conclusions

In this study, the rates of patients with a history of high blood pressure, kidney disease, the mRS scores on discharge and the length of stay were significantly higher in Group 1. Multiorgan injury may be present in these patients, and acute phase high blood pressure can be one of the factors indicating a poor prognosis. It was suggested that antihypertensive treatments specifically related to the history and coexisting illnesses are required.

References

1. Wallace JD, Levy LL. Blood pressure after stroke. JAMA 1981;246:2117-80.
2. International Society of Hypertension Writing Group. International society of hypertension (ISH): statement on the management of blood pressure in acute stroke. J Hypertens 2003;21:665-72.
3. Britton M, Carlsson A, de Faire U. Blood pressure course in patients with acute stroke and matched controls. Stroke 1986; 17: 861-4.
4. Willmot M, Leonardi-Bee J, Bath PM. High blood pressure in acute stroke and subsequent outcome: a systematic review. Hypertension 2004;43:18-24.
5. Leonardi-Bee J, Bath PM, Phillips SJ, Sandercock PA. IST collaborative group: Blood pressure and clinical outcomes in the international stroke trial. Stroke 2002; 33:1315-20.
6. Castillo J, Leira R, Garcia MM, et al. Blood pressure decrease during the acute phase of ischemic stroke is associated with brain injury and poor stroke outcome. Stroke 2004;35:520-7.
7. Vemmos KN, Tsivgoulis G, Spengos K, et al. U-shaped relationship between mortality and admission blood pressure in patients with acute stroke. J Intern Med 2004; 255:257-65.
8. Ahmed N, Wahlgren NG. High initial blood pressure after acute stroke is associated with poor functional outcome. J Intern Med 2001;249:467-73.
9. Chamorro A, Vila N, Ascaso C, et al. Blood pressure and functional recovery in acute ischemic stroke. Stroke 1998;29:1850-3.
10. Fiorelli M, Alpérovitch A, Argentino C, et al. Prediction of long-term outcome in the early hours following acute ischemic stroke. Arch Neurol 1995;52:250-5.
11. Schrader J, Lüders S, Kulschewski A, et al. Acute Candesartan Cilexetil Therapy in Stroke Survivors Study Group: The ACCESS Study: Evaluation of acute candesartan cilexetil therapy in stroke survivors. Stroke 2003;34:1699-703.
12. National Institue of Neurological Disorders and Stroke (NINDS) Ad hoc Committee: Classification of Cerebrovascular Diseases III. Stroke 1990; 21:637-76.
13. Fazekas F, Niederkorn K, Schmidt R, et al. White matter signal abnormalities in normal individuals: correlation with carotid ultrasonography, cerebral blood flow measurements, and cerebrovascular risk factors. Stroke 1998;19:1285-8.
14. Britton M, Carlsson A. Very high blood pressure in acute stroke. J Intern Med 1990; 228: 611-5.
15. Stead LG, Gilmore RM, Decker WW, et al. Initial emergency department blood pressure as predictor of survival after acute ischemic stroke. Neurology 2005;65:1179-83.
16. Abboud H, Labreuche J, Plouin F, Amarenco P. GENIC investigators: High blood pressure in early acute stroke: a sign of a poor outcome? J Hypertens 2006;24: 381-6.
17. Shinohara Y, Yoshimoto T, Fukuuchi Y, et al. Japanese guidelines for the management of stroke 2004. Tokyo, Kyowakikaku, 2004, pp5.
18. Ahmed N, Näsman P, Wahlgren NG. Effect of intravenous nimodipine on blood pressure and outcome after acute stroke. Stroke 2000;31:1250-5.