H-type Hypertension and Recurrence of Ischemic Stroke

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Abstract: Both hypertension and hyperhomocysteinemia are important risk factors of ischemic stroke. The hypertension with hyperhomocysteinemia is defined as "H-type hypertension", with a prevalence of 75% among Chinese hypertensive population. The correlation between H-type hypertension and recurrence of ischemic stroke needs to be confirmed. In this study, we prospectively recruited and followed up 602 ischemic stroke patients in Henan province, China. The average age of patients was 59.33±13.20 years and 67.3% being male. Average level of homocysteine was 19.09±11.19 mmol/L and 57% patients had hypertension. There were 310 (51.5%) H-type hypertension patients and 292 (48.5%) non H-type hypertension patients. 23.5% patients had past stroke history in H-type hypertension group and 15.1% in non H-type hypertension group. Stroke recurrence was recorded in 6.1% patients with H-type hypertension and in 1.7% patients non H-type hypertension group at 6-month follow-up. Multivariate Logistic analysis demonstrated a weak association between the H-type hypertension and stroke recurrence at 6-month follow-up. Thus, H-type hypertension could be a risk factor for stroke recurrence in Henan Chinese population.

Keywords: H-type hypertension; ischemic stroke; recurrence

1. Introduction

The strong interaction between hypertension and hyperhomocysteinemia has been reported [1], which increased 11 times risk of cardiovascular and cerebrovascular diseases more than the sole hypertension. In 2008, Dayi Hu et al proposed "H-type hypertension" in China, whose definition is hypertension with hyperhomocysteinemia [2]. H-type hypertension takes 75% among all Chinese hypertensive patients. A nested case-control study[3] in China, with a sample of 40 000 during an average of more than 6 years follow-up, revealed that the risk of the first cardiocerebrovascular events in patients with H-type hypertension was 12.1 times more than those of controls. However, we don't know whether H-type hypertension affect recurrence of stroke. This study was to investigate the association between H-type hypertension and recurrence of ischemic stroke by prospectively recruiting the ischemic stroke inpatients during a 30-month period and recording recurrence by 6-month follow-up. The inpatients were from the department of Neurology of the First Affiliated Hospital of Zhengzhou University.

2. Methods

The Stroke diagnosis is based on the stroke diagnostic criteria of World Health Organization 1976 [4]. Cerebral hemorrhage was excluded by CT/MRI. The time from onset to registry was less than 15 days. Patients with hematological diseases or severe renal failure or hepatic failure and patients with dependence caused by any reason before onset as well as patients who could not cooperate to registry were excluded. Plasma homocysteine level was measured 2～5 days after stroke onset. The level of homocysteine >10μmol/L were set as the hyperhomocystemia [5]. Consecutive ischemic stroke patients were registered prospectively. Registry forms were filled by neurologists with unified training. The forms contain gender, age, National Institute of Health Stroke Scale (NIHSS) score after admission, hypertension, diabetes, hyperlipidemia, history of atrial fibrillation and coronary heart disease and TIA and smoking, previous stroke, fasting blood glucose, blood pressure on admission, the level of homocysteine and other laboratory tests and examinations, and the treatments. Patients were followed-up to document recurrent stroke and medication at 6 months. Multivariate logistic regression analysis was used to identify factors that increased the risk of recurrent stroke. Factors that contributed to the recurrence in the initial univariate analyses at P＜0.1 were included in the multivariate model. In the final multivariate analyses, statistical significance was achieved if P＜0.05. The Statistic Package for Social Science version (SPSS) 10.0 was used for statistical analysis.

3. Results
3.1 General profiles
634 patients who met the inclusion criteria were enrolled consecutively, and 32 (5%) patients missed the follow-up. Thus the final analysis involved 602 patients with acute ischemic stroke. Average level of homocysteine was 19.09±11.19 mmol/L. Table 1 and table 2 demonstrate general data of the patients.

3.2 Baseline characteristics of patients with H-type hypertension or without H-type hypertension
There are 310 (51.5%) patients in H-type hypertension group and 292 (48.5%) in non H-type hypertension group. Diabetes and Coronary heart disease were more in H-type hypertension group than in non H-type hypertension group (p<0.05). The patients in H-type hypertension group were obviously older and had more previous strokes than in non H-type hypertension group (p<0.01). There was no significant difference in gender, history of hyperlipidemia and atrial fibrillation and TIA and moking, severity of

stroke on admission, treatment after onset (p>0.05). (Table 3).

Table 1. Categorical variables

Variables	n	%
Male	405	67.3
Hypertension	343	57.0
Hyperhomocysteinemia	525	87.2
H-type hypertension	310	51.5
Diabetes	163	27.1
hyperlipidemia	142	23.4
Atrial fibrillation	24	4.0
Coronary heart disease	17	2.8
TIA	37	6.1
Previous stroke	117	19.4
smoking	208	34.6
Antiplatelet	523	86.9
Anticoagulation	35	5.8
Chinese traditional medicine	514	85.4
Rehabilitation	127	21.1

Table 2. Continuous variables

Variable	Minimal value	Maximal value	Mean±SD	Median
Age(years)	19	92	59.33±13.20	
NIHSS on admission	1	39		6
Fast blood glucose on admission（mmol/L）	3.0	25.57	6.11±2.69	
SBP on admission(mmHg)	90	210	143.85±20.79	
DBP on admission(mmHg)	57	160	87.37±13.56	

Table 3. Basline characteristics of patients with H-type hypertension or without H-type hypertension

Variable	H-type hypertension （310）	No H-type hypertension （292）	P value
Male,n(%)	212(68.4)	193(66.1)	0.549
Age（years）	60.87±12.46	57.68±13.782	0.003
NIHSS on admission	6.47 ±7.88	5.41 ±6.904	0.081
Diabetes,n(%)	97(31.3)	66(22.6)	0.017
Hyperlipidemia,n(%)	83(26.8)	59(20.2)	0.101
Atrial fibrillation,n(%)	13(4.2)	11(3.8)	0.789
Coronary heart diseas,n(%)e	13(4.2)	4(1.4)	0.037
TIA,n(%)	22(7.1)	15(5.1)	0.317
Previous stroke,n(%)	73(23.5)	44(15.1)	0.009
Smoke,n(%)	100(32.3)	108(36.9)	0.223
Antiplatele,n(%)	294(94.8)	273(93.4)	0.481
Anticoagulation,n(%)	16(5.2)	19(6.5)	0.481
Chinese traditional medicine,n(%)	262(84.5)	252(86.3)	0.811
Rehabilitation,n(%)	73(23.5)	54(18.6)	0.129

3.3 Relationship between H-type hypertension and stroke recurrence
6.1% (19/310) patients with H-type hypertension had recurrent stroke and 1.7% (5/292) patients without H-type hypertension had recurrent stroke at 6-month follow-up. We defined gender, age,

NIHSS on admission, H-type hypertension, diabetes, hyperlipidemia, history of atrial fibrillation and coronary heart disease and TIA, smoking history, antiplatelet, anticoagulation, Chinese traditional medicine and rehabilitation as concomitant variables, and recurrence at 6 month follow- up as dependent

variable. We used univariate logistic regression analyzing the data. Result showed that H-type hypertension was significantly associated with recurrence (P=0.006). Other variables associated with 6 month recurrence were age, NIHSS on admission, Diabetes, Hyperlipidemia and atrial fibrillation (Table 4). Then, we put all variables whose p value were less than 0.1 into multivariate logistic regression analysis. The results demonstrated that H-type hypertension had the weak association with stroke recurrence (P=0.037, OR=1.031, 95%CI 1.069-8.245)(Table 5)

Table 4. Results of univariate logistic regression analysis

Variable	Recurrence (n=24)	No recurrence (n=578)	Wald	P value
Male	16	389	0.004	0.948
Age（years）	65.58±9.103	59.07±13.28	-2.379	0.018*
NIHSS on admission	8.83±5.67	5.84±7.48	-2.371	0.026*
H-type hypertension	19	291	7.663	0.006*
Diabetes	11	152	4.454	0.035*
Hyperlipidemia	11	131	6.884	0.032*
Atrial fibrillation	3	21	4.733	0.030*
Coronary heart disease	1	16	0.145	0.704
TIA	3	34	1.749	0.186
smoke	12	196	2.638	0.104
Antiplatelet	19	504	1.303	0.254
Anticoagulation	2	33	0.259	0.611
Chinese traditional medicine	5	79	0.954	0.329
Rehabilitation	18	457	0.229	0.632

Table 5. Results of multivariate logistic regression analysis

Variable	OR	95%CI	P value
Age	1.031	0.993-1.069	0.104
H-type hypertesion	2.969	1.069-8.245	0.037**
Diabetes	1.855	0.777-4.429	0.164
Hyperlipidemia	2.750	1.174-6.442	0.020**
Atrial fibrillation	2.996	0.711-12.61	0.135
NIHSS on admission	1.018	0.970-1.067	0.470

4. Discussion

In China, within every 4 hypertensive patients, there will be 3 cases with hypercysteinemia[6]. Previous study suggested that homocysteine might elevate blood pressure and increased the risk of hypertension[7]. Also, homocysteinemia had interaction with hypertension for stroke risks[1].Thus, the terms of H-type hypertension was proposed in 2008 [8,9]. High frequency of H-type hypertension in China is one of important characteristics of Chinese hypertensive population different from other ethic populations, which should be paid attention. Our hospital-based study showed that more than half of ischemic stroke inpatients in Henan province is with H-type hypertension.

American and European national stroke guidelines have identified hyperhomocysteinemia is an independent risk factor for stroke in its primary prevention. Identifying stroke patients with H-type hypertension who may be more prone to have a second stroke than others is crucial and may affect the policy of secondary prevention. Our prospective study result indicated weak association of H-type hypertension with stroke recurrence. This result was independent of other risk factors such as age, atrial fibrillation, diabetes, hyperlipidemia and severity on admission. Above result indicated that H-type hypertensive stroke patients might be considered as high risk patients as compared to non H-type hypertensive stroke patients. The present analysis can't give a conclusion of an independent association because OR=1.031, which showed the association strength is weak. The reason for weak association is probably that the sample size is relatively

small and follow-up time is short (only 6 months). However, more H-type hypertension patients had previous stroke history, which is therefore complementary and supports above findings. Our analysis result supports an earlier published study that found a high plasma homocysteine level was associated with history of hypertension and recurrent stroke among patients presenting with acute ischemic stroke [10].

In conclusion, the present study demonstrates a tendency of association of H-type hypertension with recurrent stroke. This might have therapeutic implications for reducing the risk of recurrent stroke. Although the efficacy of stroke prevention by combination of lowering both high plasma homocysteine levels and blood pressure is still unproven, secondary prevention studies are needed. Once such interventions prove efficient, routine detection of plasma homocysteine levels in stroke patients may be advised and appropriate measures taken to prevent recurrent stroke especially for H-type hypertensive stroke patients.

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6/9/2011