RELEVANCE BETWEEN RANDOM BLOOD GLUCOSE LEVEL OF SPONTANEOUS CEREBRAL HEMORRHAGE IN ACUTE STAGE AND SEVERITY OF DISEASE AS WELL AS PROGNOSIS

GUO HUANG[1], JIANDONG ZUO[2*]
[1]Department of Military Surgery, Lianshui County People's Hospital, Lianshui County, Jiangsu Province, 223400, China - [2]Department of Neurosurgery, The Affiliated Huai'an Hospital of Xuzhou Medical University, Huai'an, Jiangsu Province, 223001, China

ABSTRACT

Purpose: *To investigate the correlations between random blood glucose, neurological score and prognosis of spontaneous intracerebral hemorrhage (SICH).*

Methods: *A total of 128 SICH patients were recruited over a 1-year period for this study and randomly assigned to two groups: control group (49 patients with random blood glucose level<6.1 mmol/L) and observation group (79 patients with random blood glucose level≥6.1 mmol/L). The observation group consisted of 37 males and 42 females aged 22 to 72 years (mean age= 62.7±11.6 years), while the control group consisted of 26 males and 23 females aged 21 to 67 years (mean age= 58.4±10.9 years). Independent and multiple risk factors influencing SICH in the two groups were analyzed. The correlations between the level of random blood glucose, neurological score and prognosis were also assessed.*

Results: *Age and National Institutes of Health Stroke Scale (NIHSS) scores were significantly higher in the observation group than in control group, and random blood glucose level after admission was positively correlated with NIHSS scores (r= 0.309, p<0.05). Modified Rankin Scale (mRS) ≤ 2 and ≥ 3 were significantly higher in the observation group than in control group, but mRS ≤ 1 and death were significantly lower in observation group than in control group (p<0.05). The results of Logistic regression analysis showed that age (OR: 1.027, 95% CI: 1.010 - 1.045) and NIHSS scores at admission (OR: 1.547, 95% CI: 1.216 - 1.968) were independent risk factors for poor prognosis of SICH (mRS≥3) (p<0.05).*

Conclusion: *Spontaneous cerebral hemorrhage, Blood glucose level, Severity, Prognosis, Correlation.*

Keywords: *Spontaneous cerebral hemorrhage, blood glucose level, severity, prognosis, correlation.*

DOI: 10.19193/0393-6384_2019_2_179

Received *November 30, 2018;* ***Accepted*** *January 20, 2019*

Introduction

Spontaneous intracerebral hemorrhage (SICH) refers to hemorrhage in brain parenchyma induced by spontaneous rupture of cerebral artery, vein and blood capillaries, and it is caused by factors such as trauma, hypertensive vasculopathy, cerebral amyloid angiopathy, and vascular malformations. It is second in the hierarchical ranking of cerebral apoplexy; the incidence is only lower than that of ischemic cerebral stroke, and it is characterized by high disability and lethality[1-3]. The incidence of SICH increases with age. Hypertension and diabetes are predictors of early death after SICH. Studies have shown that hyperglycemia induced by hemorrhage in the acute stage aggravates deterioration of cerebral tissue resulting in fatalities over 50% or higher, and it is the key factor that influences prognosis[4-6]. The aim of this study was to investigate the correlations between the level of random blood glucose, neurological score and prognosis of SICH.

Methods

Patients and clinical data

A total of 128 patients were recruited over a 1-year period for this study and randomly assigned to two groups: control group (49 patients with random blood glucose level<6.1 mmol/L) and observation group (79 patients with random blood glucose level≥6.1 mmol/L). The observation group consisted of 37 males and 42 females

aged 22 to 72 years (mean age= 62.7±11.6 years), while the control group consisted of 26 males and 23 females aged 21 to 67 years (mean age= 58.4±10.9 years).

The inclusion criteria were:

• Patients who met the diagnostic criteria of the Fourth National Cerebrovascular Disease Conference of Chinese Medical Association as confirmed by cranial CT scan[7];

• Patients who had stroke for the first time or recurrent stroke and mRS score= 0;

• Patients who were admitted in hospital within 24 h after onset;

• Patients who signed written informed consent with their family members.

The exclusive criteria were:

• Patients who had subarachnoid hemorrhage;

• Patients who had traumatic or tumor-related cerebral hemorrhage;

• Patients who had hemorrhagic infarction. The study protocol was approved by the Ethics Committee of the Affiliated Huai'an Second People's Hospital of Xuzhou Medical University.

Observation indices

After examining the patients using an endoscope within 24 h of admission, their fasting blood glucose levels were determined using glucose oxidase method. Blood glucose levels ranging from 3.9-6.1 mmol/L were taken as normal. Neurologic impairment was evaluated using National Institute of Health stroke scale (NIHSS)[8]. Insulin treatment was given to patients with blood glucose≥10 mmol/L, and monitored intermittently.

Evaluation criteria

After 90 days of follow-up, the patients were scored using mRS[9]. The prognosis was classified into three: extremely good prognosis, good prognosis, and death. The conditions applicable to each classification were:

Extremely good prognosis:

• mRS≤1;

Good prognosis:

• mRS≥2;

And death:

• mRS≥3.

Follow-up

The follow-up was by telephone calls and lasted 90 days after onset of diabetes. The data collected were recorded and analyzed.

Statistical analysis

Data are expressed as mean ± SD, and the statistical analysis was performed using SPSS (22.0). Groups were compared using Student t-test and chi-squared test. Multiple factors were analyzed using logistic regression analysis, while correlation analysis was performed using Spearman rank test. Values of $p<0.05$ were considered statistically significant.

Results

Outcomes of single factor analysis of factors influencing poor prognosis of SICH patients

Age and NIHSS scores were significantly higher in the observation group than in control group ($p<0.05$: Table 1).

Factors	Groups		χ^2	p
	Observation (n = 79)	Control (n = 49)		
Sex (male)	37 (46.83)	26 (53.06)	0.469	0.493
Age (years)	62.7 ± 11.6*	58.4 ± 10.9	2.085	0.039
Smoking room	32 (40.50)	19 (38.77)	0.096	0.756
Drinking history	52 (65.82)	34 (32.65)	0.174	0.676
Hypertension history	36 (45.56)	15 (30.61)	2.822	0.092
Hyperlipidemia	21 (26.58)	7 (14.28)	2.675	0.101
Diabetes	28 (35.44)	12 (24.48)	1.688	0.193
Concurrent infection	31 (39.24)	18 (36.73)	0.080	0.776
Systolic pressure at admission (mmHg)	169.7 ± 18.6	168.6 ± 17.9	0.329	0.742
Diastolic pressure at admission (mmHg)	102.4 ± 16.5	101.2 ± 15.8	0.406	0.685
INR	1.4 ± 0.2	1.3 ± 0.1	2.064	0.051
NIHSS scores at admission	11.64 (7.30, 15.78) *	7.03 (2.13, 9.51)	-4.471	< 0.001

Table. 1: Single factor analysis of factors that influence poor prognosis of spontaneous hemorrhage in acute stage (n, %). **p<0.05, when compared to control group.*

Correlation of random blood glucose levels after admission with NIHSS scores

The results of Spearman test showed that random blood glucose level after admission was positively correlated with NIHSS scores ($r= 0.309$, $p<0.05$). The result is shown in Figure 1.

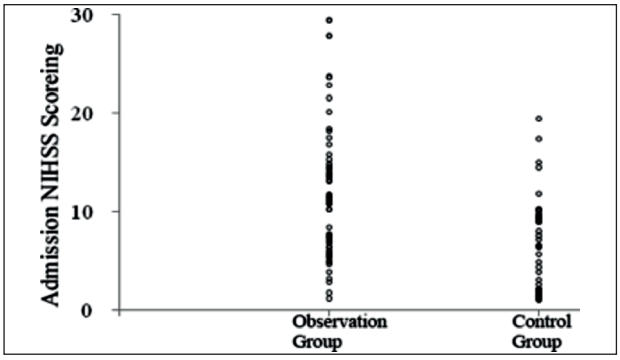

Figure 1: Distribution of NIHSS scores after admission under different severities of cerebral hemorrhage.

Influences of random blood glucose after admission on prognosis

Modified Rankin Scale (mRS) ≤2 and ≥3 were significantly higher in the observation group than in control group, but mRS ≤1 and death were significantly lower in observation group than in control group (p<0.05: Table 2).

mRS	Groups		*t*	*p*
	Observation (n = 79)	Control (n = 49)		
0 - 1	9 (11.39)*	21 (42.85)	16.685	<0.001
0 - 2	12 (15.18)*	4 (8.16)	1.365	0.242
≥ 3	20 (25.31)*	5 (10.20)	4.394	0.036
Death	38 (48.10)*	18 (36.73)	1.587	0.027

Table. 2: Influence of random blood glucose after admission on prognosis (n, %).
**p<0.05, when compared to control group.*

Outcomes of multiple factor analysis of factors that influence prognosis of SICH patients

The results of logistic regression analysis showed that age (OR: 1.027, 95 % CI: 1.010 - 1.045) and NIHSS score at admission (OR: 1.547, 95 % CI: 1.216 - 1.968) were independent risk factors for poor prognosis of SICH (mRS≥3) (p<0.05). These results are shown in Table 3.

Factors	OR	95 % CI	*p*
Sex (male)	0.765	0.211 - 2.780	0.684
Age (years)	1.027	1.010 - 1.045	0.002
Smoking room	0.687	0.232 - 2.031	0.497
Drinking history	0.537	0.140 - 2.056	0.364
Hypertension history	1.74	0.648 - 4.674	0.272
Hyperlipidemia	1.426	0.701 - 2.899	0.327
Diabetes	1.027	0.989 - 1.066	0.164
Concurrent infection	1.637	0.329 - 8.135	0.547
Systolic pressure at admission (mmHg)	0.834	0.608 - 1.145	0.261
Diastolic pressure at admission (mmHg)	1.054	0.979 - 1.135	0.162
INR	1.674	0.665 - 4.213	0.274
NIHSS scores at admission	1.547	1.216 - 1.968	< 0.001

Table. 3: Results of multiple factor analysis (n, %).

Discussion

Studies have shown that high blood glucose is an independent risk factor that influences acute ischemic stroke and subarachnoid hemorrhage, and that it is related to ischemic stroke hemorrhagic infarction and hemorrhagic complications of thrombolytic therapy. Although studies on the correlation between high blood glucose level and SICH are scanty, it is generally believed that the level of blood glucose increases after cerebral hemorrhage, infection and cerebrovascular diseases[10-11].

The incidence of diseases associated with high blood glucose and blood glucose stress increases after cerebral hemorrhage. Elevated blood glucose causes cerebral hemorrhage hematoma, cell apoptosis, and nerve damage. Studies have shown that there are high incidence of other diseases when blood glucose is elevated after cerebral hemorrhage, thus adversely affecting the quality of life of patients[12]. Recent studies have also shown that high blood glucose level is an independent risk factor for acute ischemic stroke and that prognosis after subarachnoid hemorrhage is related to hemorrhagic transformation of ischemic stroke and thrombolytic therapy[13]. Studies on the correlation between high blood glucose and SICH are scanty, and most authors have speculated that elevated blood glucose level after cerebral hemorrhage increases the incidence of other diseases. In the present study, age and NIHSS scores were significantly higher in the observation group than in control group, and random blood glucose level after admission was positively correlated with NIHSS scores. These results suggest that the disease may become more severe and prognosis poor with elevation in the level of blood glucose. Spontaneous intracerebral hemorrhage is accompanied by cytokine-induced generation of free radicals, which promotes the permeability of blood-brain barrier, thereby causing cerebral edema. High blood glucose after an inflammatory reaction directly stimulates cells to undergo apoptosis and the uncontrolled release of calcium ion, thus severely injuring mitochondria[16].

In this study, mRS≤2 and ≥3 were significantly higher in the observation group than in control group, but mRS≤1 and death were significantly lower in observation group than in control group. These results suggest that high blood glucose might be an effective index for predicting the severity of SICH. Previous studies have shown that the level of glycosylated hemoglobin in the initial stage of

cerebral stroke is an effective index for diagnosing stress-induced high blood glucose[15]. Immediately following the elevation of blood glucose in SICH patients, metabolic changes occur, and the severity of the disease can be assessed by measuring the blood glucose level. The higher the blood glucose, the more severe the cerebral injury, and the higher the complications such as stress ulcer, metabolic acid toxicity and azotemia.

In this study, there was no association between random blood glucose level and poor prognosis, an indication that random blood glucose alone may not be able to assess prognosis of SICH. The results of this study showed that age and NIHSS scores at admission were independent risk factors for poor prognosis of SICH, and are in agreement with those previously reported[14]. Regulation of blood glucose in patients with elevated blood glucose level and secondary injury induced by cerebral hemorrhage is reduced by optimizing prognosis of patients. As a growth factor, insulin promotes cerebral growth, stimulates vascular endothelial cells to synthesize prostacyclin (PGI_2), which exhibits high vascular dilation property. Stress-induced cerebral hemorrhage causes secretion of cortisol, which in turn increases the level of blood glucose and insulin, thereby accelerating the synthesis of PCI2 and causing further dilation of blood vessels. This causes neurological deterioration, and increases cranial pressure and rapid invasion of cells. Elevated blood glucose causes accumulation of lactic acid in cerebral tissue space, and favors the formation of permeable reaction wall. Chemotaxis of the cells leads to cerebral edema, which causes cerebral injury, and it is accompanied by high fatality[17-20].

Conclusion

The results of this study have shown that random blood glucose level is positively correlated with SICH, and that NIHSS score is an independent risk factor for poor prognosis of patients.

References

1) Karmann A, RãSel F, Schneider M. ProduktivitÃ¤tsmotorGesundheitswirtschaft: Finanziertsich der medizinisch-technischeFortschrittselbst? Perspektiven Der Wirtschaftspolitik 2016; 17: 54-67.
2) Ding ZJ, Chen ZX, Liu M. Relationship between prognosis of acute spontaneous intracerebral hemorrhage in diabetic patients. Diabetes New World 2018; 13: 4.
3) Lueg A. High fasting blood sugar levels in gestational diabetes. Der Diabetologe 2017; 13: 1-4.
4) Fahl C. ZurStrafbarkeit der IS-Heimkehrerinnenwegen-Sich-BeteiligensalsMitglied an einerausländischenterroristischenVereinigung. Juristische Rundschau 2018; 2018: 276-280.
5) Wang F, Chen PP, Wu X. Study progress of spontaneous cerebral hemorrhage patients in aucte stage without surgical treatment. Chin J Integr Med Cardio/Cerebrovasc Dis 2016; 14: 2782-2784.
6) Liao JM, Chen QX. Study progress of spontaneous cerebral hemorrhage inn acute stagewith drug treatment. Chin J Clin Neurosurg 2017; 18: 857-859.
7) Zhao QH, Xu XQ, Jin ZC, Sun ML, Dai LZ, et al. Diagnosis value of electrocardiogram in patients with pulmonary artery hypertension. Chin Circ J 2010; 38: 346-349.
8) Li KK, Diong J. National Institutes of Health Stroke Scale (NIHSS). J Physiother 2014; 60: 61.
9) Rivero-Arias O, Ouellet M, Gray A, Wolstenholme J, Rothwell PM, et al. Mapping the modified Rankin scale (mRS) measurement into the generic EuroQol (EQ-5D) health outcome. Med Decis Making 2010; 30: 341.
10) Hu ZX, Lin LQ, Zhang J, Cheng YF, Cheng J. Analysis of clinical prognosis of spontaneous cerebral hemorrhage. Chin J Crit Care Med 2016; 36: 11-13.
11) Klein A. Sweet tears help keep an eye on blood sugar level. New Sci 2018; 237: 9.
12) Park C, Pagnini F, Reece A, Phillips D, Langer E. Blood sugar level follows perceived time rather than actual time in people with type 2 diabetes. Proc Natl Acad Sci U S A 2016; 113: 8168.
13) Zhang S, Ma S, Li WS, Feng J, Guo Y. The SICH score for prediction of short-term clinical outcome in spontaneous intracerebral hemorrhages. J Clin Pathol 2016; 5:7-11.
14) Muengtaweepongsa S, Prapaanantachai P, Dharmasaroja PA. Not only the Sugar, Early infarct sign, hyperDense middle cerebral artery, Age, Neurologic deficit score but also atrial fibrillation is predictive for symptomatic intracranial hemorrhage after intravenous recombinant tissue plasminogen activator. J Neurosci Rural Pract 2017; 8: 49.
15) Kang JF, Huang Q, Liu YH. Advance in research on the genetic etiology of spontaneous intracerebral hemorrhage. Chin J Med Genet 2016; 33: 702-707.
16) Muengtaweepongsa S, Prapaanantachai P, Dharmasaroja PA. Not only the Sugar, Early infarct sign, hyperDense middle cerebral artery, Age, Neurologic deficit score but also atrial fibrillation is predictive for symptomatic intracranial hemorrhage after intravenous recombinant tissue plasminogen activator. J Neurosci Rural Pract 2017; 8: 49.
17) Kong J, Rong JH, Yan J, Lu PS, Zhan LP, et al. Analysis of relevant factors to prognosis of spontaneous intracerebral hemorrhage in young adults. J Clin Neurosurg 2016; 13: 231-233.

18) Fortuna JL. Sweet preference, sugar addiction and the familial history of alcohol dependence: shared neural pathways and genes. J Psychoactive Drugs 2010; 42: 147-51.
19) Roden JA, Jakob S, Roehrig C, Brenner TJ. Preparing graduate student teaching assistants in the sciences: An intensive workshop focused on active learning. Biochem Mol Biol Educ 2018; 46: 318-326.
20) Liu QJ. Analysis of relevance between inflammatory factors of cerebral hemorrhage patients in acute stage and changes of C-reaction protein as well as recovery of nerve function. J Clin Emerg Call 2017; 1: 55-57.

Corresponding Author:
Jiandong Zuo
Email: xv1318@163.com
(China)