Study of the relationship of glycated hemoglobin levels and neurological impairment and three months prognosis in patients with acute ischemic stroke

Guo Shuangxi[1], Tan Song[1], Song Bo[1], Chandra Avinash[1], Ma Anna[2], Fang Hui [1], Chen Si[1], Xu Yuming[1]

[1.]Department of Neurology, the First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan 450052, China.
[2.]Xinxiang Medical College, Xinxiang, Henan 453003, China.
Corresponding author: XU Yu-ming, xuyuming@zzu.edu.cn

Abstract: Objective:To explore the relationship of glycated hemoglobin levels (HbA1c) and neurological impairment and three months prognosis in patients with acute ischemic stroke. Method:180 patients with acute ischemic stroke within twenty four hours after onset were included in the present analysis from the Department of Neurology of the First Affiliated Hospital of Zhengzhou University.Three milliliter of Venous blood within twenty four hours after admission to test the blood HbA1c.The patients were divided into three groups based on the glycated hemoglobin (HbA1c). These three groups designated as: Normal group (HbA1c<5.7%), Intermediate group (5.7%-6.5%) and Elevated group (HbA1c≥6.5%). Evaluation of neurological functional impairment with NIHSS scores within twenty four hours after admission, and to evaluation of the prognosis with MRS score after three months. Result:As for patients, in age, sex, hypertension, hyperlipidemia, smoking history aspects, the difference was not statistically significant among three groups (P>0.05). As for the history of diabetes, blood glucose on admission, NIHSS scores, three months MRS score, the difference was statistically significant among three groups (P<0.05). The blood HbAIc and NIHSS score and three months MRS score of 180 patients were respectively analyzed using Pearson correlation analysis, the results showed that the blood HbAlc content and NIHSS score and three months MRS score in patients with ischemic stroke were positively correlated (P <0.001). Conclusion: Different HbA1c levels in patients with acute stroke has different neurological impairment on admission and three months prognosis are also different, showing that a higher blood HbA1c levels has a more serious neurological impairment and the prognosis is worse after three months. HbA1c levels maybe is an important predictors to evaluate the neurological impairment and three months prognosis in patients with acute ischemic stroke .
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1. Introduction

Acute stroke is a limited or comprehensive brain function deficit syndrom caused by acute cerebral circulation disorder. Its incidence,morbidity and mortality rates are high[1-3], it is a serious threat to human's health. At present,Cerebrovascular disease has been one of the three diseases that seriously threaten human's health. In some areas in China,Stroke has been ranked in the first place of the fatal diseases.The existing studies [4-6] have shown that the main cause of ischemic stroke is the lesions of the vascular wall, and atherosclerosis is the most common cause which leads to the lesions of the vascular wall[7-8]. As we all know,Diabetes is one of the major risk factors of atherosclerosis,which can accelerate the process of the vascular lesions.Glycosylated hemoglobin(GHb) is a variety of non -enzymatic glycation reaction products generated by thehemoglobin in the role of continuous glucose,and their formation is irreversible,its synthesis rate is proportional to the blood glucose concentration. Its main form is HbA1c , which represents the average blood glucose levels in 2-3 months. Studies have shown[9]that the blood HbA1c levelcan be as one of the important predictors of occurrence, development and prognosis of patients with ischemic stroke. The new guidelines issued by the American Diabetes Association (ADA) [10] in 2010 takes HbA1c ≥ 6. 5% as one of the diagnosti criteria for diabetes,and takes HbA1c≥5. 7% as one of screening criteria of the diabetes.However,at present, the Correlated study of the relationship of blood HbA1c levels and neurological impairment and three months prognosis in patients with ischemic stroke has been reported little.

2. Materials and Methods

2.1Object of study

Over a period of one year from July 2010 to September 2011, From the Department of Neurology of the First Affiliated Hospital of Zhengzhou University, 180 patients with acute ischemic stroke

within twenty four hours after onset were included in the present analysis. Including 97 males and 83 cases of women, ages ranging from 45 to 81 years old, the average age was 60.5 ±8.65years old. Diagnostic criteria: All cases were in accordance with the diagnostic criteria of World Health Organization (WHO) 1976 [11]. Inclusion criteria: (1)Cases within the diagnostic criteria. (2) Stroke attack in twenty four hours. (3) Head CT to exclude hemorrhage. Exclusion criteria: exclusion of patients with diseases that lead to ischemic stroke, such as arteritis, blood system diseases, heart disease et al. Exclusion of patients who were accompanied with atrial fibrillation, cancer, generalized infection, autoimmune diseases and liver, kidney or cardiac failure.

2.2 Research methods

Three milliliters of venous blood was taken to test blood glucose,blood lipids and glycated hemoglobin(HbAlc) in the next day morning after admission. Age, sex, past history（hypertension，diabetes）, smoking history of selected patients were recorded. The patients weredivided into three groups based on the glycated hemoglobin (HbA1c).These three groups designated as: normal group (HbAlc <5.7%), intermediate group (5.7%-6.5%) and elevated group(HbA1c ≥ 6. 5%).The degree of neurological inpairment (NIHSS score) was evaluated within twenty four hours after admission, The prognosis (MRS score) was evaluated after three months,by a neural physician who was trained. According to NIHSS score , the patients were divided into three groups:mild(<4score),moderate(4~15score),severe (> 15 score). According to MRS score ,the patients were divided into two groups: independence(0~2score) and dependence(3~5score and death).

2.3 Statistical Methods

All continuous variables were expressed as mean± standard deviation.All data were analyzed using one-way ANOVA or the X^2 test by the spss 13.0 software package,The blood HbAIc and NIHSS score and three months MRS score of 180 patients were statistically analyzed using Pearson correlation analysis, P <0.05 was statistically significant.

3. Result

3.1 The clinical data of three groups

As for patients, in age, sex,hypertension hyperlipidemia,smoking history aspects, There was not statistically difference (P > 0.05) among three groups, As for the history of diabetes, blood glucose on admission, NIHSS scores, three months MRS score, The difference was statistically significant (P <0.05) among three groups. In diabetes aspects, elevated group accounts for 48 cases (90.57%), intermediate group accounts for 21cases (38.18%), normal group accounts for 12 cases (16.67%),elevated group is higher than the intermediate group and normal group. In the same time, in NIHSS score on admission,elevated group was 8.60 ± 3 27points, it was higher than the intermediate group (6.71 ±3.29 score) and normal group(4.09±3.14 score).In three months MRS score aspects,elevated group(3 79 ± 0.97 score) was higher than the middle group(2.97 ± 1.36 score) and normal group (2 81 ± 0 87score),as shown in the Table1.

Table 1 General characteristics of three groups

Characteristics	Normal group （n=72）	Intermediate group （n=55）	Elevated group （n=53）	X^2/F	P value
Age（Years）	59.68±3.868	61.26±1.281	60.264±4.073	0.590	0.556
Hypertension（case）	40	35	37	2.707	0.258
Hyperlipidemia（case）	23	25	21	2.460	0.292
Diabetes（case）	12	21	48	68.848	<0.001
Smoking history（case）	28	21	23	0.3680	0.832
NIHSS（score）	4.090±3.140	6.710±3.290	8.600±3.270	18.190	<0.001
MRS（score）	2.810±0.870	2.970±1.360	3.790±0.970	13.350	<0.001
Glycated hemoglobi（%）	5.270±0.303	6.180±0.390	7.950±0.640	536.300	<0.001
Blood glucose（mmol/l）	5.610±0.780	6.690±1.940	7.650±3.250	524.410	<0.001

3.2 Comparison of the severity of neurological impairment and three months prognosis of three groups

The severity of neurological impairment on admission and three months prognosis of three groups of patients were analyzed respectively by the X^2 test, the difference was statistically significant (P<0.05).In neurological impairment aspect on admission,severe patient of elevated group accounted for 26.40%, that is higher than intermediate group(12.70%) and normal group (5.55%). In three months prognosis aspects, dependent patients of elevated group accounted for 33.96%, that is higher than the intermediate group (21.82%) and normal group (13.89%). The blood HbAIc and NIHSS score and three months MRS score of 180 patients were respectively analyzed using Pearson correlation analysis. The results showed that the blood HbAlc content and NIHSS score in patients with acute ischemic stroke was positively correlated (r = 0.384, P <0.001), the blood HbAlc content and NIHSS score in patients with acute ischemic stroke was also positively correlated (r = 0.326, P <0.001).That is to say: a higher blood HbA1c levels has a more serious neurological impairment and the prognosis is worse after three months.as shown in the Table 2,Table 3, Figure1, Figure2.

Table 2. Comparison of the severity of neurological impairment of three groups

Group	Case（n）	Mild（%）	Moderate（%）	Severe（%）
Normal group	72	37（51.39）	31（43.06）	4（5.55）
Intermediate group	55	23（41.80）	25（45.50）	7（12.70）
Elevated group	53	21（39.60）	18（34.00）	14(26.40）

Note: X^2 = 11.74, P =0.019

Table 3. Comparison of three months prognosis of three groups

Group	Case（n）	independent（%）	dependent（%）
Normal group	72	62（86.11）	10（13.89）
Intermediate group	55	43（78.18）	12（21.82）
Elevated group	53	35（66.04）	18（33.96）

Note: X^2=7.12 P=0.028

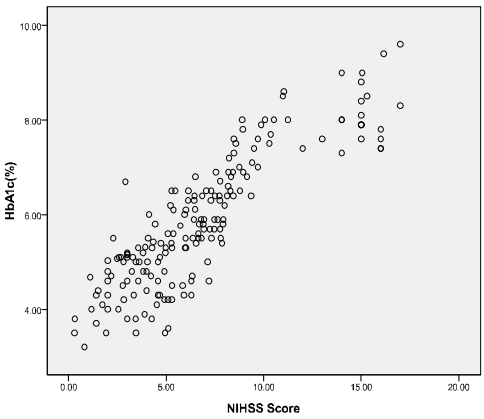

Figure 1. Scatter chart of HbA1c and NIHSS score

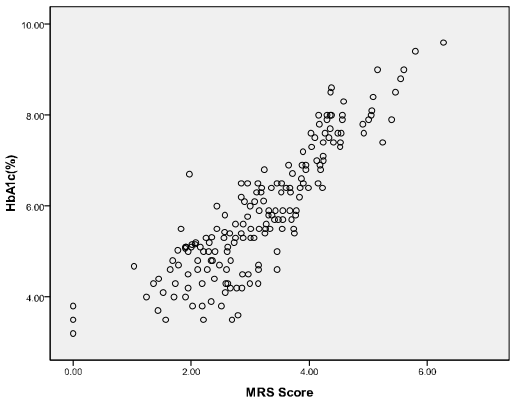

Figure 2. Scatter chart of HbA1c and 3months prognosis score

4. Discussion

Studies[12] have shown that HbAlc rise in the blood and HbAlc continually accumulate in the vessel wall, which lead to increase of thromboxane A_2 and protein kinase, which lead to excessive collagen fibers cross-link by reducing release of nitric oxide, this course results in hardening of the blood vessel wall and decline of artery compliance, and a higher content of HbA1c allows oxygen dissociation curve to the left, resulting in oxygen dissociation barrier, nerve tissue ischemia and hypoxia,myelin loss,nerve degeneration,dysfunction and necrosis.

Kizer et al[13-16]. studied the relationship glycated hemoglobin (HbA1c) and stroke (average follow-up of 9.2 years),in 1691 cases of patients with diabetes.The results showed that after adjusting age, gender, smoking, blood lipids and other variances, HbA1c and stroke risk was significantly associated.They emphasized that strict control of glycated hemoglobin(HbA1c) might be benefit for stroke prevention for the patients with diabetes. Our study showed that in the history of diabetes, blood glucose on admission, NIHSS scores, three months MRS score, among three groups of patients, the difference was statistically significant ($P<0.05$). The blood HbAlc content and NIHSS score in patients with acute ischemic stroke was positively correlated ($r=0.384$, $P<0.001$), the blood HbAlc content and NIHSS score inpatients with acute ischemic stroke was also positively correlated ($r=0.326$, $P<0.001$). Thant is to say, a higher blood HbA1c levels has a more serious neurological impairment, and the condition might be more serious. So,HbA1c levels on admission might be an important predictors to evaluate the neurological impairment in patients with acute ischemic stroke.

The results also showed that the severity of neurological impairment on admission and three months prognosis of three groups of patients were analyzed respectively by the X^2 test, the difference was statistically significant ($P<0.05$). In neurological impairment aspects on admission,severe patients of elevated group accounted for 26.40%, that is higher than intermediate group (12.70%) and normal group (5.55%).In three months prognosis aspects,dependent patients of elevated group accounted for 33.96%,that is higher than the intermediate group (21.82%) and normal guoup (13.89%).and a higher blood HbA1c levels has a more serious neurological impairment on admission and the prognosis is worse after three months.The mechanism might be associated with long-term high blood glucose and high blood HbA1c,which lead to lesions of large blood vessels and micrangium and which lead to oxygen dissociation curve to the left, resulting in oxygen dissociation barrier, nerve tissue ischemia and hypoxia, that is not benefit for the recovery of neurological function, and the prognosis is worse. This result is in line with the result of Kamouchi et al[17],who studied 3627 patients,the result showed that neurological improvement is lower relevant to age and sex and is higher relevant to the blood HbA1c level on admission. namely,a higher blood HbA1c levels has a more serious neurological impairment and the prognosis is worse in three months.

In summary, Our study suggests that blood HbA1c levels on admission may influence severity in patients with acute ischemic stroke when stroke attack and may predict three months prognosis. So,HbA1c levels maybe is an important predictors to evaluate the neurological impairment and three months prognosis in patients with acute ischemic stroke, Therefore, effectively lowering blood HbA1c levels may reduce the severity of neurological impairment in patients with acute ischemic stroke, and maybe can improve the life quality of patients with acute ischemic stroke.

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