

Research on Influence of Clopidogrel on Life Quality in Patients with Transient Ischemic Attack and its Influencing Factors

Lanbo Chen Xiaohong Gu Bo Dong

Department of Health Management, Institute of Field Surgery, Daping Hospital, Third Military Medical University, Chongqing Municipality, Chongqing, 400042, China

Abstract: Purpose: To analyze the basic situation and health related quality of life (HRQOL) results of patients with transient ischemic attack (TIA), and to study the influencing factors of health related quality of life in patients receiving clopidogrel. Method: Divide the TIA patients into clopidogrel group, aspirin group and untreated group. Measure HRQOL scores of TIA patients using the short form 36 questionnaire (SF-36) scale and analyze influencing factors of HRQOL with one-way ANOVA and multivariate stepwise linear regression statistical methods. Results: The differences of HRQOL scores among three groups are of statistical significance ($F = 4.29$, $P = 0.00$). There is no difference in HRQOL score between clopidogrel group and aspirin group ($t = 5.35$, $P = 0.00$), but HRQOL scores of clopidogrel group and aspirin group are higher than those of the untreated group ($t = 6.14$, $P = 0.00$; $t = 5.16$, $P = 0.00$). The HRQOL scores of clopidogrel group are positively correlated with diet, exercise, gender and family harmony ($P < 0.05$), but negatively correlated with diabetes, hypertension, smoking, drinking, hyperlipidemia, age, career and ABCD2 score ($P < 0.05$). Conclusion: TIA patients who received secondary prevention with clopidogrel and aspirin show better life quality results than those who did not. There were many factors influencing clopidogrel's treatment effect. Paying attention to middle-aged and elderly, the obese, mental workers and female TIA patients, teach TIA patients to quit smoking, drinking and eating low-salt and low-fat food, actively treating their hypertension, hyperlipidemia and diabetes and laying emphasis on psychological counseling and exercise can significantly improve the treatment effect of clopidogrel.

Keywords: Transient ischemic attack; Clopidogrel; Life quality; Influencing factors

Corresponding Author: Xiaohong Gu, 286628359@qq.com

Author's Information: Xiaohong Gu, female, associate chief physician, director of Health Management Department, E-mail: 286628359@qq.com, 13527459954, Ph.D., mainly engages in Chongqing citizen physical examination big data research. Lanbo Chen, male, attending physician, E-mail: 615558459@qq.com, 13638396512, bachelor's degree, mainly engages in research of health-related quality of life of Chongqing citizens.

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1. Introduction

Transient ischemic attack (TIA) is a common ischemic cerebrovascular disease of neurology and neurosurgery, which was redefined by the American Stroke Association in 2009 as: "Transient neurological dysfunction in the brain, spinal cord, and focal

ischemia of the retina without acute infarction"^[1]. In 2011, Chinese experts reached a consensus and defined TIA as: "Transient neurological dysfunction in the brain, spinal cord, or focal ischemia of the retina without acute cerebral infarction"^[2]. There are about 23.9 million TIA patients in China. Moreover, TIA patients' medical treatment rate, prevention awareness, recognition rate, diagnosis rate

and hospitalization rate are very low. If they do not receive secondary prevention early, they are highly likely to progress to stroke^[3]. As the frontier medicine for mid to long-term secondary prevention of TIA^[4], clopidogrel has a good efficacy, low cost and small side effect and it is applied widely clinically. Health related quality of life (HRQOL) is a comprehensive evaluation of health conditions and subjective feelings of the population^[5] and can be used to observe the condition of TIA patients. In this study, we measured the HRQOL score using the short form 36 questionnaire (SF-36) scale and analyzed the influencing factors of HRQOL to provide a reference for the treatment effect of clopidogrel.

2. Data and Methods

2.1 Survey Object

This study includes 168 TIA patients admitted to the Department of Health Management of Daping Hospital of the Third Military Medical University from September 2012 to September 2014. All subjects were investigated before admission and after treatment. The study was approved by Daping Hospital Ethics Office and informed consent forms were signed with the subjects. The diagnosis of TIA is based on the criteria set by the American Stroke Association in 1990^[1]: Repeated attack of transient neurological deficits caused by transient ischemic brain damage; the typical clinical symptoms would last for no more than 24 hours; cerebral infarction is excluded by imageological examination, and the course of disease is up to 1 year. Exclusion criteria: (1) cerebral infarction and other organic nerve injury; (2) non-cerebrovascular disease-induced symptoms; (3) patients who cannot participate in the survey and refuse to receive the questionnaire due to physical reasons. A total of 59 subjects who took clopidogrel before admission are included in the clopidogrel group; 37 subjects taking aspirin for a long term are included in the aspirin group; 72 subjects without secondary prevention are included in the untreated group.

2.2 Survey Method

2.2.1 Survey Tool

SF-36 scale^[6]: It is used to evaluate the life quality, the evaluation of the clinical treatment effect and the feedback evaluation of health policy in related testing population. As a concise health questionnaire, SF-36 includes 36 entries and 8 dimensions, each dimension scoring between 0-100 and a total score of 800. The higher the score, the better the life quality, vice versa.

2.2.2 Data Collection Method

SF-36 scale shall be filled by the patient in person and

collected back immediately; at the same time, the basic information of clopidogrel group is recorded, including age (< 45, 45-60, ≥ 60), occupation (manual workers, mental workers, the unemployed), gender, diet (low-salt and low-fat diet refers to sodium intake < 2 g / day, fat intake < 50 g / day, cholesterol intake < 300 mg / day), history of smoking (defined by lifetime smoking or cumulative smoking for 6 months or longer by WHO), drinking (drinking means more than 300 mg of alcohol intake per week), exercise (refer to aerobic exercise for more than half an hour per day), and education (junior high school and below, senior high school and secondary vocational school, junior college and undergraduate, master and above), TIA secondary prevention (long-term uninterrupted administration of anti-platelet drugs, anti-hyperlipidemia drugs), body mass index (BMI, < 18.5, 18.5-28, ≥ 28), with or without hypertension (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg), with or without diabetes (any blood glucose ≥ 11.1 mmol / L, fasting blood glucose ≥ 7.0 mmol / L or OGTT2h blood glucose ≥ 11.1 mmol / L), with or without hyperlipidemia (fasting serum total cholesterol ≥ 6,145 mmol / L, triglyceride ≥ 1,153 mmol / L), TIA severity score (ABCD2 score, 0-3 points for low-risk group, 4-5 points for middle-risk group, 6-7 points for high-risk group), family per capita monthly income (< RMB 1,500, RMB 1,500-4,000, ≥ RMB 4,000), whether the family is harmonious.

2.3 Statistical Analysis

SPSS13.0 statistical software is used for statistical analysis, the data are expressed in $\bar{x} \pm s$, and one-way ANOVA is employed for HRQOL score comparison of different groups; multivariate stepwise linear regression method is used to analyze the influencing factors of clopidogrel group's HRQOL score. If $P < 0.05$, it means the difference is of statistical significance.

3. Results

3.1 HRQOL Score Comparison

The average HRQOL score of clopidogrel group is 494.15 ± 125.45 , the average HRQOL score of aspirin group is 491.34 ± 107.33 , and the average HRQOL score of untreated group is 462.17 ± 97.15 . The differences of HRQOL scores among three groups are of statistical significance ($F = 4.29$, $P = 0.00$). Through comparison among groups, it is found that there is no difference in HRQOL score between clopidogrel group and aspirin group ($t = 5.35$, $P = 0.00$), and HRQOL scores of clopidogrel group and aspirin group are higher than those of the untreated group ($t = 6.14$, $P = 0.00$; $t = 5.16$, $P = 0.00$).

3.2 General Data Analysis of Clopidogrel Group

The general data statistics of the clopidogrel group (see Table 1) show that the difference of HRQOL score arising from different age groups, occupations, gender, diet, smoking history, drinking history, exercise, BMI, ABCD2 scores, family harmony are statistically significant ($P < 0.05$), and whether the patient is associated with hypertension, diabetes and hyperlipidemia would also cause HRQOL score changes ($P < 0.05$). However, different educational level and household income have no impact on HRQOL scores ($P > 0.05$). The higher the ABCD2 score, the higher the age and the higher the BMI, and the lower the HRQOL score. The HRQOL scores of manual workers are higher than those of mental workers and the unemployed; women's HRQOL scores are lower than men's; HRQOL scores of those who have a low-salt and low-fat diet are higher than those who don't; the HRQOL scores of smokers and alcoholics are relatively low; family harmony and regular exercise can significantly improve the HRQOL score; concomitant hypertension, diabetes and hyperlipidemia will reduce the HRQOL score. (See Table 1)

3.3 Multivariate Stepwise Linear Regression Analysis on HRQOL-Related Factors in the Clopidogrel Group

According to the results of one-way ANOVA, statistically significant variables (excluding education level and monthly income) are screened out, and the HRQOL scores are assigned as dependent variables using these variables as independent variables: Age: ($< 45 = 1, 45-60 = 2, \geq 60 = 3$); Occupation: (Manual worker = 1, mental worker = 2, unemployed = 3); Gender: (Male = 1, Female = 2); Diet: (Non-low-salt and low-fat diet = 1, low-salt and low-fat diet = 2); Smoking condition: (Non-smoking = 1, smoking = 2); Drinking condition: (Non-drinking = 1, drinking = 2); Exercise: (No exercise = 1, exercise = 2); BMI ($< 18.5 = 1, 18.5-28 = 2, \geq 28 = 3$); Concomitant hypertension: (No = 1, Yes = 2); Concomitant diabetes: (No = 1, Yes = 2); Concomitant hyperlipidemia: (No = 1, Yes = 2); ABCD2 score (0-3 points = 1, 4-5 points = 2, 6-7 points = 3); Whether the family is harmonious (No = 1, Yes = 2). The data are analyzed through multivariate stepwise linear regression. The results (Table 2) indicate: the HRQOL scores are positively correlated with diet, exercise, gender and family harmony ($P < 0.05$), but negatively correlated with diabetes, hypertension, smoking, drinking, hyperlipidemia, age, career and ABCD2 score ($P < 0.05$). Five most important factors affecting the HRQOL score of the clopidogrel group include: diabetes, diet, hypertension, smoking and drinking. Multivariate linear regression equation: $HRQOL = 634.85 - 22.35 \times \text{diabetes} + 18.34 \times \text{diet} - 16.20 \times \text{hypertension} - 15.56 \times \text{smoking} - 14.37 \times \text{drinking}$ ($P < 0.05$).

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4. Discussion

TIA is a clinical syndrome characterized by multiple factors and symptoms and usually presents with transient limb stiffness and weakness accompanied by headache, dizziness, speech and visual impairment^[7]. The current prevalence of cardio-cerebrovascular disease in China continues to increase, and the incidence of TIA becomes more common. TIA is a risk factor for cerebral infarction, threatening the patient's health. In essence, TIA and cerebral infarction are ischemic brain injury; they are different stages of the dynamic process of ischemic lesions, if timely prevention and treatment is not in place, TIA has a higher probability of conversion to cerebral infarction, making disease worse^[8]. According to the "Guidelines for Secondary Prevention of Ischemic Stroke and Transient Ischemic Stroke in China 2010", classical solutions of secondary prevention with clopidogrel can significantly improve the prognosis of patients with TIA and reduce the incidence of cerebral infarction^[9]. Clopidogrel is an ADP receptor antagonist that blocks platelet activation and inhibits platelet aggregation with minimal side effects; and it is a frontier medicine for treatment of TIA^[10]. However, due to the lack of medical knowledge and awareness of the risk of TIA, the living habit and living environment of TIA patients have a greater impact on the treatment effect of clopidogrel. Diagnosis and prognosis of TIA via routine imaging examination are ineffective; while HRQOL employs overall and comprehensive indexes to assess the health, which places more emphasis on the roles of individual and social adaptive capacity in health, and pays more attention to individual subjective feelings^[11], and is particularly suitable for the observation of clopidogrel treatment effect.

This study shows that there are more patients in the 45-60 years old group, indicating that middle-aged people are high incidence group. In terms of occupational factor, the higher incidence of mental workers may be related to the lack of movement of copywriters. The higher prevalence of males than females may be related to the greater stress on men's lives. This study shows that the higher the ABCD2 score, the lower the HRQOL, showing a negative correlation between stroke risk and life quality; therefore, more attention should be paid to those with higher ABCD2 score. The HRQOL of patients in harmonious families is much better, indicating that a good family environment will help to improve the secondary prevention effect of patients treated with clopidogrel.

Table 1. General Data Analysis of Clopidogrel Group ($\bar{x} \pm s$)

Factor	Case (proportion)	HRQOL score	F value	P value
Age			4.08	0.00
< 45	12 (18.1%)	513.06±96.34		
45-60	35 (53.0%)	489.38±77.84		
≥ 60	19 (28.9%)	471.25±64.18		
Occupation			3.35	0.00
Manual worker	13 (19.8%)	508.95±82.14		
Mental worker	28 (42.4%)	493.25±73.73		
Unemployed	58 (37.8%)	478.36±83.22		
Gender			4.15	0.00
Male	48 (72.8%)	497.14±65.16		
Female	18 (27.2%)	468.01±48.17		
Diet			3.93	0.00
Low-salt and low-fat diet	27 (40.9%)	505.77±73.89		
Non-low-salt and low-fat diet	39 (59.1%)	475.67±68.31		
Smoking history			3.93	0.00
Smoking	21 (31.8%)	468.53±95.14		
Non-smoking	45 (68.2%)	499.53±40.05		
Drinking history			3.24	0.00
Drinking	19 (28.7%)	468.10±86.35		
Non-drinking	47 (71.3%)	493.47±74.16		
Exercise			3.57	0.00
Exercise	29 (43.9%)	516.16±93.36		
No exercise	37 (56.1%)	465.21±56.32		
Educational level			2.31	0.24
Junior high school and below	26 (39.3%)	489.62±74.15		
Senior high school and secondary vocational school	21 (31.8%)	487.17±97.17		
Junior college and undergraduate	12 (18.1%)	479.10±68.14		
Master degree and above	7 (10.8%)	492.33±73.17		
BMI			3.57	0.00
< 18.5	15 (22.7%)	497.32±58.07		
18.5-28	18 (27.3%)	484.41±86.71		
≥ 28	33 (50.0%)	474.14±61.00		
Concomitant hypertension			3.78	0.00
Yes	20 (30.3%)	468.56±41.67		
No	46 (69.7%)	501.35±93.31		
Concomitant diabetes			4.26	0.00
Yes	24 (36.3%)	473.15±64.15		
No	42 (63.7%)	498.00±90.27		
Concomitant hyperlipidemia			3.38	0.00
Yes	18 (27.2%)	463.18±79.62		
No	48 (72.8%)	497.37±57.16		
ABCD2 score			3.65	0.00
0-3 points	21 (31.8%)	501.35±74.36		
4-5 points	29 (43.9%)	483.53±61.24		
6-7 points	16 (24.3%)	473.11±90.75		
Monthly income			2.09	0.34
< RMB 1500	14 (21.3%)	487.14±77.35		
RMB 1500-4000	37 (56.0%)	489.09±65.87		
≥ RMB 4000	15 (22.7%)	491.35±89.16		
Whether the family is harmonious			4.05	0.00
Yes	49 (74.2%)	506.13±73.43		
No	17 (25.8%)	467.64±48.66		

Table 2. Multivariate Linear Stepwise Regression Analysis on HRQOL-Related Factors

Factor	Regression coefficient	Standard error	Standard regression coefficient	t value	P value
Constant	634.85	3.15		13.15	0.00
Diabetes	-22.35	1.35	-0.33	-4.54	0.00
Diet	18.34	1.31	0.32	4.25	0.00
Hypertension	-16.20	1.29	-0.28	-4.13	0.00
Smoking	-15.56	1.21	-0.24	-4.04	0.00
Drinking	-14.37	1.17	-0.21	-3.89	0.00
Hyperlipidemia	-13.79	1.09	-0.19	-3.68	0.01
BMI	-12.35	0.99	-0.18	-3.54	0.00
Exercise	11.16	0.87	0.16	3.41	0.00
ABCD2 score	-10.85	0.73	-0.14	-3.26	0.00
Age	-9.67	0.71	-0.13	-3.07	0.00
Occupation	-7.18	0.59	-0.11	-2.74	0.01
Family harmony	5.14	0.52	0.10	2.45	0.00
Gender	4.25	0.48	0.06	1.43	0.01

The results of HRQOL-related factors show that low-salt and low-fat diet, exercise, gender are positively correlated with HRQOL. Low-salt and low-fat diet can reduce blood viscosity, thus improving the secondary prevention effect; as a positive factor, exercise has a significant effect on the prevention and treatment of TIA, which can significantly improve HRQOL. According to the suggestions in the "Chinese Guidelines for the Secondary Prevention of Ischemic Stroke and Transient Ischemic Attack (AHA/ASA 2014 Edition)", TIA patients with the capability and the willingness to increase their exercise amount shall be recommended to adopt the new and behavior-oriented exercise scheme^[12]. Clinically, the patients should be instructed to increase their exercise and develop a low-salt and low-fat diet, upholding healthy life habits. Men's HRQOL is significantly better than women, which may be related to female hormone endocrine changes and higher psychological sensitivity. As negative influencing factors, diabetes, hypertension and hyperlipidemia significantly reduce the secondary prevention effect of clopidogrel. AHA/ASA 2014 Guideline suggests patients with TIA and metabolic syndrome to receive treatment to lower their blood pressure, blood glucose and blood lipid^[12]. Therefore, while using clopidogrel for secondary prevention, the blood pressure, blood glucose and blood lipid shall be controlled at normal levels. Smoking and drinking would reduce the secondary prevention effect of clopidogrel significantly. Nicotine contained in tobacco, tar, and nicotine will damage the endothelial cells and cause blood viscosity, and induce vasospasm, eventually leading to tissue and organ ischemia^[13]. Long-term uncontrolled drinking can

also lead to vascular injury and cerebral ischemia exacerbation^[14]. Medical workers should inform patients of the harms of smoking and drinking on heart and cerebral vessels and urge them to quit smoking and drinking. The older the patient is, the worse the HRQOL is, indicating that age is also a risk factor for secondary prevention effect of clopidogrel. BMI is inversely proportional to HRQOL. As a risk factor for cardiovascular and cerebrovascular diseases, obesity reduces the secondary prevention effect of clopidogrel. Obese TIA patients shall be educated to lower their BMI through diet intervention and exercising. As for the occupational factor, the unemployed and mental workers lack physical movements and thus have a lower HRQOL than the manual workers. During treatment of TIA, special attention shall be paid to the mental workers and unemployed patients and urge them to exercise more.

The results of this study of TIA population HRQOL scores are statistically analyzed, showing that the life quality of TIA patients taking clopidogrel and aspirin for secondary prevention is better than that of the untreated group. There are many factors influencing the clopidogrel's treatment effect. Secondary prevention should be carried out with emphasis on the middle-aged and elderly, the obese, mental workers and female TIA patients; in the meantime, it needs to encourage them to quit smoking and drinking and develop the low-salt and low-fat diet, treat hypertension, hyperlipidemia and diabetes actively, pay attention to psychological counseling and strengthen their exercises. All above measures can significantly improve the secondary prevention effect of clopidogrel.

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