

The prevalence and risk factors of stroke in patients with chronic schizophrenia

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Objective: To investigate the stroke risk and risk factors in patients with chronic schizophrenia.

Patients and methods: This study was a large-sample, cross-sectional survey. A total of 363 patients with chronic schizophrenia were selected from the Changping Traditional Chinese Medicine Hospital, Beijing, in August 2014. The patients were divided into either stroke group or control group based on the presence of stroke. Clinical evaluation included positive and negative syndrome scale assessment and a detailed questionnaire to collect the general information and disease-related conditions.

Results: The prevalence of stroke was 16.5% (60 cases). Stroke and control groups showed a significant difference in age, sex, smoking, combined medication, doses, negative factor score in positive and negative syndrome scale, body mass index, waist circumference, and systolic blood pressure. Multivariate analysis showed that a number of factors are significantly related to stroke, including age, sex, smoking, combined medication, doses, body mass index, and systolic blood pressure.

Conclusion: The prevalence of stroke is relatively higher in Chinese patients with chronic schizophrenia. Chronic schizophrenia patients are more likely to suffer from stroke; meanwhile, a number of risk factors were identified, including old age, female sex, smoking history, combined medication with a variety of drugs, high doses, obesity, and high blood pressure.

Keywords: schizophrenia, stroke, risk, risk factors

Introduction

The risk of premature death in schizophrenia patients is two to three times that in the general population, resulting in a reduction in life expectancy of 15–20 years. It is well known that cerebrovascular diseases are one of the leading causes of premature death in schizophrenia patients.^{1,2} In recent years, more and more scholars began to focus on the association of cerebrovascular diseases in patients with schizophrenia, and they found that the prevalence of such cerebrovascular diseases was significantly higher than that in the general population.^{3,4}

At present, stroke is the second leading cause of death in the People's Republic of China, as well as a major cause of disability. There is an annual increase of ~2 million patients who are newly diagnosed with stroke, which brings a heavy burden to both society and individuals. However, till now, only few studies in Mainland China have focused on the stroke-associated issues in patients with schizophrenia.

In this study, a large-sample, cross-sectional survey was conducted, aiming at 1) exploring the stroke risk in patients with chronic schizophrenia and 2) investigating the risk factors for stroke in patients with chronic schizophrenia.

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Patients and methods

Subjects

Patients with schizophrenia admitted to the psychiatric ward of Changping Traditional Chinese Medicine Hospital in August 2014 were included in this study. Inclusion criteria were 1) meeting the diagnostic criteria for schizophrenia by International Classification of Mental and Behavioral Disorders Diagnostic Criteria (ICD-10)⁵ 2) with disease duration ≥ 10 years. In addition, stroke was confirmed by the diagnostic criteria for cerebrovascular disease classification revised by Chinese Academy of Neurology and Chinese Academy of Neurosurgery in 1995.⁶

The study protocol and written informed consent were in accordance with the Guideline for Good Clinical Practice of the International Conference on Harmonisation,⁷ which was approved by the Ethics Committee of Peking University, Institute of Mental Health. Prior to the enrollment, written informed consent was obtained from the subjects or their legal guardians. A total of 704 cases of subjects were screened, of which 363 cases were qualified for our study.

Clinical assessment

Positive and negative syndrome scale (PANSS) was measured,⁸ which is an evaluation scale of 30 disparate items scored from 1 to 7 for psychopathological symptoms. A total of three subscores (positive, negative, and general psychopathology) were obtained with this evaluation tool. A questionnaire was used for collecting the general information and disease conditions, including age, sex, date of birth, education level, ethnicity, marital status, age of onset, disease duration, previous disease history, medication history, family history of cerebrovascular disease, smoking and drinking history, body mass index, fasting glucose levels, lipid levels, and current medication list; in addition, the current dose of antipsychotic was converted to equivalent doses of chlorpromazine.⁹

Statistical methods

Data were analyzed using the SPSS 17.0 statistical package for Windows. The comparison between the two groups with regard to sociodemographic and clinical characteristics was performed by independent samples *t*-test for data of normal distribution, by the Mann–Whitney *U*-test for continuous variables, and by the chi-square test for categorical variables. Multiple logistic regression analysis was carried out to adjust for relevant covariates and to determine the risk factors of stroke. The one-sample Kolmogorov–Smirnov test was used to check the normality of distributions for

continuous variables. Level of significance was set at 0.05 (two-tailed).

Results

Stroke risk

Among the 363 patients with chronic schizophrenia, the prevalence of stroke was 16.5% (60 cases); the majority of these stroke patients had cerebral infarction (59 cases), whereas one case had cerebral hemorrhage. The prevalence rates of stroke were 11.2% (20/178) and 21.6% (40/185) in male and female patients, respectively.

Risk factors for stroke

Patients were divided into stroke group and control group according to the presence of stroke. The following information was significantly different between the two groups, such as age, sex, smoking, combined medication, doses, negative factor score in PANSS, body mass index, waist circumference, and systolic blood pressure (Table 1). Multivariate analysis found that age, sex, smoking, combined medication, doses, body mass index, and systolic blood pressure were significantly related to stroke (Table 2).

Discussion

To our knowledge, this is the first study in Mainland China that investigates the prevalence and risk factors of stroke in the patients with schizophrenia. We found that 16.5% of patients with chronic schizophrenia had stroke, and this value was significantly higher than that reported by Taiwan (1.7%)¹⁰ and Canada (7.9%),³ which might probably be due to the fact that the schizophrenia patients included in our study were much older and their disease were more heavy, while with longer disease duration. However, it could also be related to the recent changes in disease spectrum in Mainland China. A previous study had shown that the stroke prevalence in the community residents of Beijing was 4.8%,¹¹ significantly higher than the figures reported by Taiwan (1.2%)¹⁰ and Canada (4.3%).³ With the recent improvement of socioeconomic conditions of Mainland China, the life patterns and diet structures have great changes; therefore, obesity, hypertension, hyperlipidemia, and other chronic diseases have become a major threat to the health of residents, while the prevalence of cerebrovascular disease was also increased every year.¹¹ However, what is consistent with the previous findings is that schizophrenia could greatly enhance the risk of stroke,^{3,10,12} suggesting that the psychiatric researchers in Mainland China should pay special attention to the issues of stroke in patients with chronic schizophrenia.

Table 1 Comparison of general population information and clinical data between the stroke group and control group

| | Whole sample (n=363) | | Stroke group (n=60) | | Control group (n=303) | | P-value |
|--|-------------------------|------|------------------------|------|--------------------------|------|---------|
| | N | % | N | % | N | % | |
| Age | | | | | | | 0.00 |
| ≥65 years | 106 | 29.2 | 34 | 56.7 | 72 | 2.8 | |
| Sex (female) | 185 | 60.0 | 40 | 66.7 | 145 | 47.8 | 0.01 |
| Duration of illness in schizophrenia (years) | | | | | | | 0.10 |
| <20 | 40 | 11.0 | 4 | 6.7 | 36 | 11.9 | |
| 20–30 | 114 | 31.4 | 14 | 23.3 | 100 | 33.0 | |
| >30 | 209 | 57.6 | 42 | 70.0 | 167 | 55.1 | |
| Family history of cerebrovascular disease | 142 | 39.1 | 25 | 41.7 | 117 | 38.6 | 0.66 |
| History of smoking | 61 | 16.8 | 22 | 36.7 | 39 | 12.9 | 0.00 |
| History of alcohol abuse | 39 | 10.7 | 10 | 16.7 | 29 | 9.6 | 0.11 |
| Antipsychotic polypharmacy | 208 | 57.3 | 49 | 81.7 | 159 | 52.5 | 0.00 |
| Type of APs | | | | | | | 0.16 |
| Only typical APs | 25 | 6.9 | 1 | 1.7 | 24 | 7.9 | |
| Only atypical APs | 293 | 80.7 | 53 | 88.3 | 240 | 79.2 | |
| Combination | 45 | 12.4 | 6 | 10.0 | 39 | 12.9 | |
| Doses of antipsychotic drugs (CPZ) | | | | | | | 0.00 |
| <300 mg | 89 | 6.7 | 4 | 6.7 | 85 | 28.1 | |
| 300–600 mg | 118 | 30.0 | 18 | 30.0 | 110 | 36.3 | |
| >600 mg | 146 | 63.3 | 38 | 63.3 | 108 | 35.6 | |
| | Mean | SD | Mean | SD | Mean | SD | P-value |
| PANSS score | 49.3 | 13.7 | 52.0 | 14.7 | 48.8 | 13.5 | 0.10 |
| PANSS positive factors | 12.1 | 5.1 | 11.7 | 4.5 | 12.2 | 5.2 | 0.54 |
| PANSS negative factors | 13.1 | 5.8 | 14.7 | 5.3 | 12.8 | 5.8 | 0.02 |
| Body mass index (kg/m ²) | 25.5 | 6.2 | 28.2 | 3.3 | 25.0 | 6.5 | 0.00 |
| Waist circumference (cm) | 81.9 | 13.1 | 85.0 | 8.7 | 82.0 | 13.5 | 0.04 |
| Systolic blood pressure (mmHg) | 118.5 | 9.5 | 122.2 | 14.4 | 117.8 | 8.6 | 0.01 |
| Diastolic blood pressure (mmHg) | 74.6 | 6.1 | 74.9 | 7.4 | 74.5 | 5.8 | 0.69 |
| Fasting glucose levels (mmol/L) | 4.8 | 1.4 | 4.9 | 1.6 | 4.7 | 1.3 | 0.41 |
| Total cholesterol (mmol/L) | 3.9 | 1.1 | 4.1 | 1.6 | 3.9 | 1.0 | 0.29 |
| Triglyceride (mmol/L) | 1.5 | 0.9 | 1.5 | 0.9 | 1.4 | 0.9 | 0.79 |

Notes: Results are in response to an independent *t*-test and where appropriate the chi-square test. *P*-values were considered significant at the α 0.05 level.

Abbreviations: APs, antipsychotics; PANSS, positive and negative syndrome scale; CPZ, chlorpromazine.

Our study found that the prevalence of stroke in female patients with schizophrenia is much higher than that of male patients, which is consistent with two previous studies conducted in Taiwan;^{10,12} however, it was contrary to the

findings in general population,¹³ which might be because obesity and metabolic syndrome are more commonly seen in female patients with schizophrenia.¹⁴

This study shows that stroke risk in elderly patients was significantly higher, similar to the findings observed in the general population; the reason might be that such aging population is closely associated with hypertension, hyperlipidemia, hypercoagulable state and cytotoxicity. Elderly patients with schizophrenia should obviously be viewed as a major focus in the prevention of stroke.¹⁵

Compared with the nonstroke patients, stroke patients with schizophrenia have more risk factors such as obesity, smoking, and high blood pressure, which is in line with the findings in the general population.¹¹ Interestingly, our study did not find that the involvement of family history of cerebrovascular disease could have a significant effect on stroke patients with schizophrenia, suggesting that compared

Table 2 Multivariate analysis of risk factors for stroke

| Factors | P-value | Odds ratio | 95% CI |
|--------------------------------------|---------|------------|------------|
| Aged ≥65 years | 0.003 | 2.87 | 1.42–5.79 |
| Sex (female) | 0.016 | 2.35 | 1.17–4.70 |
| History of smoking | 0.001 | 3.72 | 1.76–7.88 |
| Antipsychotic polypharmacy | 0.005 | 3.06 | 1.41–6.66 |
| Drug doses | 0.001 | – | – |
| <300 mg | | | |
| 300–600 mg | 0.039 | 3.68 | 1.07–12.68 |
| >600 mg | 0.000 | 8.39 | 2.55–27.62 |
| Body mass index (kg/m ²) | 0.014 | 1.07 | 1.01–1.12 |
| Systolic blood pressure (mmHg) | 0.004 | 1.05 | 1.01–1.08 |

Notes: Results are in response to a multiple logistic regression analysis. *P*-values were considered significant at the α 0.05 level.

to genetic history, environmental factors could play a larger part in stroke onset of the patients with schizophrenia.

This study shows that a larger number of schizophrenia patients diagnosed with stroke are more likely to use the combination therapy of antipsychotics, with higher doses, which has not been reported in previous studies. It should be noted that combination therapy using multiple drugs often needs larger doses, with more prominent adverse reaction.¹⁶ In particular, it has been widely proven that antipsychotics cause issues such as weight gain, obesity, and metabolic syndrome,¹⁷ which are clear risk factors for stroke.

Conclusion

Patients with chronic schizophrenia have a high risk of stroke in Chinese population. A number of risk factors were associated with stroke in chronic schizophrenia, including old age, female sex, smoking history, combined medication with a variety of drugs, high doses, obesity, and high blood pressure. Hence, special attention should be paid by clinical psychiatrists.

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Disclosure

The authors report no conflicts of interest in this work.

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