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Characteristics of traditional Chinese medicine usage in patients with stroke in Taiwan: A nationwide population-based study

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ABSTRACT

Ethnopharmacological relevance: Stroke has been the leading causes of death worldwide. Traditional Chinese medicine (TCM) has been used for stoke patients for thousands of years. This study aimed to investigate TCM usage and prescription patterns in stroke patients in Taiwan.

Materials and methods: We analyzed a random sample of one million individuals representing the 23 million enrollees selected from the National Health Insurance Research Database in Taiwan. Demographic characteristics, TCM usage, prescription patterns and mortality rate among stroke patients were analyzed.

Results: We identified 23,816 patients who were newly diagnosed with stroke between 2001 and 2009 by their diagnostic codes (ICD-9-CM 430–438). Among them, 4302 patients had hemorrhagic stroke while 19,514 patients had ischemic stroke. Overall, 12% of the stroke patients (n=2862) were TCM users. The median interval between stroke onset to the first TCM consultation is 12.2 months. Among the TCM users, more than half (52.7%) of the patients received both Chinese herbal remedies and acupuncture/traumatology treatment. Bu-yang-huan-wu-tang and Dan-shen (*Radix Salviae Miltiorrhizae; Salvia miltiorrhiza* Bunge) was the most commonly prescribed Chinese herbal formula and single herb, respectively. TCM users had a higher incidence rate ratio in myalgia, myositis, fasciitis and insomnia than non-TCM users. Mental disorders such as anxiety and depression are common in both TCM and non-TCM users. Comparing with the non-TCM users, the TCM users had a lower mortality rate (adjusted hazard ratios were 0.44 in overall stroke, 0.50 in ischemic stroke and 0.25 in hemorrhagic stroke).

Conclusion: Adjunctive TCM use may reduce the risk of mortality rate among stroke patients. Bu-yang-huan-wu-tang and Dan-shen are the most common prescribed Chinese herbal formula and single herb for stroke patients, respectively. Future study investigating the anti-inflammatory and neuroprotective efficacy of Bu-yang-huan-wu-tang and Dan-shen in stroke is warranted.

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1. Introduction

Stroke has been one of the leading causes of death worldwide. There are approximately 5.5 million deaths per year worldwide (Mukherjee and Patil, 2011). Sequels of stroke also pose significant impact on the quality of life and economic burdens of the patients and their family. The survivors from stroke, about 44 million

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disability-adjusted life-years estimated, are the major sauce of long-term disability, costing huge amount of social economy and medical resource (Chiu et al., 2013; Mukherjee and Patil, 2011). In Taiwan, more than US$ 400 million was spent per year for cerebrovascular accident and its related healthcare (Chang et al., 2012). Current management of acute stroke is to stabilize vital signs and rescue brain damage. Although the overall stroke-related mortality rate is decreasing, the stroke-related disability rate remains high (Feigin et al., 2014). Neurological deficits such as conscious disturbance, cognitive and behavioral changes, paralysis, dysphagia and aphasia are the major sequels of stroke. Rehabilitation is the standard treatment to help patients to improve daily self-care function (Kumar et al., 2010). However, long-term disability and highly recurrent rate are still concerned and unsolved, driving patients and family to seek complementary therapies for help (Mukherjee and Patil, 2011).

Traditional Chinese medicine (TCM) has been used for patients with stroke for thousands of years. Acupuncture has been proved to lower the risk of stroke recurrence (Shih et al., 2015) and might be beneficial for muscle spasticity, joint pain, and dysphagia after stroke (Lee et al., 2012; Long and Wu, 2012; Zhao et al., 2009). TCM doctors prescribe different TCM formulas and herbs based on individual's clinical presentation, so called as “Syndrome Differentiation and Pattern Diagnosis”.(Jhong et al., 2013) Although there are a few studies on the use of TCM in stroke patients (Xu et al., 2015), there is a lack of large-scale ethnopharmacological surveys on TCM usage in stroke patients.

Taiwan launched the mandatory National Health Insurance (NHI) program in 1995 and reimbursed TCM service since 1996. In addition to acupuncture, the NHI program also reimburses Chinese herbal medicine and Chinese traumatology therapy. All claims data were collected in the National Health Insurance Research Database (NHIRD) and managed by the National Health Research Institutes in Taiwan. We have investigated the TCM usage in a variety of diseases, such as asthma (Huang et al., 2013b), fracture (Liao et al., 2015), rheumatoid arthritis (Huang et al., 2015), uterine fibroid (Yen et al., 2015a) and allergic rhinitis (Yen et al., 2015b) in Taiwan. The datasets provided a nationwide population-based claims database with long-term follow-up. The data from this claims database can represent the whole population, and thus reduces the potential for sampling bias (Huang et al., 2014).

In order to understand the characteristics of TCM usage in stroke patients, we analyzed a randomly selected sample of one million enrollees in the NHIRD. This study is important to understand the TCM utilization patterns. The results of this study will provide useful information for pharmacological investigations or clinical studies in the future.

2. Materials and methods

2.1. Data resources

The NHI program has provided reimbursement for Western medicine since 1995 and TCM since 1996. Reimbursed TCM service includes Chinese herbal products, acupuncture/moxibustion, and Chinese traumatology therapy in ambulatory clinics. All registry data in the NHIRD consist of demographic characteristics, clinical visits, hospitalizations, diagnosis, assessments, procedures, prescriptions, and the medical costs for reimbursement. A randomly selected sample consisted of a one million individual who were enrolled the NHI program in 2000 was analyzed. We also acquired the first three diagnostic codes in the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) formats. The randomly selected sample was released by the National Health Research Institutes in Taiwan. All of the datasets of the NHIRD were de-identified and encrypted before release. It is not possible to identify any individuals in the datasets. This study was approved by the Research Ethics Committee of China Medical University and Hospital (CMU-REC-101-012).

2.2. Study subjects and study variables

We identified all stroke patients (N=43,027) in the one million individuals between 2001 and 2009 by their diagnostic codes (ICD-9-CM 430-438). We excluded patients younger than 18 years old or patients who had old stroke before 2000. Among them, 23,816 of the stroke patients were newly diagnosed. We further categorized them into hemorrhagic stroke (n=4302) and ischemic stroke (n=19,514) patients according to their clinical subtypes of stroke. For each category of stroke patients, those who had at least one TCM outpatient clinical record were defined as TCM users (n=719 in hemorrhage stroke and n=2143 in ischemic stroke), whereas those who had no TCM outpatient records were defined as non-TCM users (n=3583 in hemorrhage stroke and n=17,371 in ischemic stroke). These patients and their prescriptions were followed-up until 2011 (Fig. 1). Herbal formulas were listed in pin-yin name and English name. Single herbs were listed in pin-yin name, Latin name and botanical plant name. The TCM indications of the Chinese herbal formulas and single herbs were based on TCM theory (Bensky et al., 2004; Scheid et al., 2009). Full botanical names comply with the *International Plant Names List* (IPNI; http://www.ipni.org) and *The Plant List* (http://www.theplantlist.org/) (Chan et al., 2012).

2.3. Statistical analysis

All statistical analyses were performed using SAS software, version 9.2 (SAS Institute Inc., Cary, NC, U.S.A.). Data analysis comprised descriptive statistics, including patient demographic characteristics, modalities of treatment and the frequency of prescribed Chinese herbal formulas and single herbs. The diagnoses were based on the ICD-9-CM codes. Univariate analysis was used to compare TCM users with the non-TCM users. A chi-square test was performed to examine the relationships between the categorical variables and to examine the differences between TCM users and non-TCM users. The incidence rate ratio indicated the extent of the prevalence of disease in the TCM user group relative to the non-TCM users. A P value of <0.05 was considered statistically significant. To compare the TCM and non-TCM cohorts, we estimated the risk and 95% confidence intervals of mortality by using Cox's proportional hazard regression.

3. Results

There were 23,816 newly diagnosed stroke patients between 2001 and 2009, consisting of 18% of hemorrhagic stroke (n=4302) and 82% of ischemic stroke (n=19,514) (Table 1). Their average age was 67.6 years old; the attack age was lower in hemorrhagic stroke (average=61.1 y/o) than ischemic stroke (average=69.0 y/o). Prevalence in males was higher than females in both groups. Overall, 12% (n=2862) of people sought for TCM treatment. The median interval between stroke diagnosis to the first TCM consultation was 12.2 months. Hypertension was the most common comorbidity.

Among the TCM users of stroke patients, more than half (52.7%) of the patients received both Chinese herbal remedies and acupuncture/traumatology treatment; 32.1% of the patients received Chinese herbal remedies only and 15% received acupuncture treatment alone. Treatment courses for more than six times were acceptable for 45.9% of the patients (Table 2).

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