The traditional Chinese medicine prescription patterns for migraine patients in Taiwan: A population-based study

Yu-Yun Chang [a], Yueh-Ting Tsai [a], Jung-Nien Lai [a,b,*], Chia-Hao Yeh [b], Shun-Ku Lin [c]

[a] Institute of Traditional Medicine, School of Medicine, National Yang-Ming University, Taipei City 112, Taiwan
[b] Department of Chinese Medicine, Taipei City Hospital, Yangming Branch, Taipei City 111, Taiwan
[c] Department of Chinese Medicine, Taipei City Hospital, Ren-Ai Chinese Medicine Branch, Taipei, Taipei City 106, Taiwan

ARTICLE INFO

ABSTRACT

Ethnopharmacological relevance: Traditional Chinese medicine (TCM), when given for symptom relief, has gained widespread popularity among migraine patients. The aim of this study is to analyze the utilization of TCM among migraine patients in Taiwan.
Materials and methods: The usage, frequency of service, and the Chinese herbal products prescribed for migraine were evaluated using a representative sample of one million subjects selected at random from the 22 million beneficiaries of the National Health Insurance scheme of Taiwan.
Results: Overall, 89.3% ($N=12,827$) migraine patients utilized TCM and 24.2% of them sought TCM with the intention of treating their migraine-related symptoms. Migraine patients who are living in urban area and those with an episodic migraine pattern (<15 days/month) ($aOR=3.18$, 95% CI: 2.75–3.67) were more likely to be TCM users than those living in a rural area and those who suffered from chronic migraine (≥ 15 days/month) ($aOR=1.00$). Overall, 81.2% of TCM visits involved the prescription of a Chinese herbal remedy or remedies and *Chuan-Xiong-Cha-Tiao-San*, *Jia-Wei-Xiao-Yao-San*, *Ge-Gen-Tang*, *Xue-Fu-Zhu-Yu-Tang*, *Ban-Xia-Bai-Zhu-Tian-Ma-Tang*, *Qing-Shang-Juan-Tong-Tang*, *Xiao-Chai-Hu-Tang*, *Tian-Ma-Gou-Teng-Yin*, *Bu-Zhong-Yi-Qi-Tang*, and *Tian-Wang-Bu-Xin-Dan* were the ten most frequently prescribed formula for treating migraine based on syndrome differentiation.
Conclusions: *Chuan-Xiong-Cha-Tiao-San*, which contains sedative and anti-inflammatory agents, is the most commonly prescribed Chinese herbal formula for the treatment of migraine-related phenomena.

1. Introduction

Migraine is the most frequent neurological disorder in the adult population worldwide and is characterized by recurrent attacks of moderate to severe unilateral headaches that are accompanied by nausea or vomiting as well as sensitivity to light and sound. Migraine affects up to 12% of the general population and is more frequent among women (Raggi et al., 2013) in both its episodic and chronic forms, with the latter imposing more substantial individual and socioeconomic burden (Lipton et al., 2001; Bigal et al., 2008; Munakata et al., 2009). Although several studies have suggested that various symptomatic migraine pharmacotherapies are effective ways of relieving pain and improving the sufferers' quality of life (Solomon and Santanello, 2000; Evers et al., 2009; Hildreth et al., 2009), migraine remains prevalent and disabling because of the side effects that are associated with the chronic administration of painkillers (Hamel, 2007; Evers and Jensen, 2011) as well as the high recurrence rate, which does not appear to be related to initial clinical efficacy (Geraud et al., 2003). Not surprisingly, complementary and alternative therapies have become increasingly popular as a symptom relief treatment among migraine patients and are quickly approaching conventional therapy in frequency of use (von Peter et al., 2002; Rossi et al., 2005).

Previous studies have revealed that some Chinese herbs have sedative and pain-alleviating properties that act via cytokine suppression and COX-2 inhibition (Kang et al., 2007; Wieser et al., 2007; Wang et al., 2011). However, evidence obtained in human studies is limited regarding patterns of use of classical traditional Chinese medicine (TCM) in relation to migraine and is an area in which complementary and alternative medicines have recently grown in popularity. Furthermore, TCMs now seem to be marketed without established efficacy or safety checks in many Western countries (von Peter et al., 2002; Xue et al., 2007). In view of the above and because there is a lack of knowledge about the biochemical profiles of Chinese herbal products (CHPs) prescribed, there is a lack of direction for researchers and doctors trained in conventional medicine when, targeting migraine, they want to explore the

* Corresponding author at: Institute of Traditional Medicine, School of Medicine, National Yang-Ming University, No.155, Sec. 2, Linong Road, Taipei 112, Taiwan . Tel.: 88 662 826 7396.
E-mail address: kareny@ms10.hinet.net (S.-K. Lin).

potential mechanisms of TCM therapy. Such an exploration would help to assess the cost-effectiveness of using TCM therapy, and allow potential interaction between Chinese herbs and conventional therapies to be observed.

TCM, which includes acupuncture, traumatology, manipulative therapies and Chinese herbal products, has been an important part of health care in Taiwan for hundreds of years and is fully reimbursed under the current National Health Insurance (NHI) system. CHPs, defined as composed of several herbs (formula) are most widely accepted by TCM users. According to Taiwan's laws, to ensure manufacturing quality, all CHPs must comply with good manufacturing practice (GMP) standards, and can only be prescribed by licensed TCM doctors. We downloaded all detailed of reimbursed CHPs, including the proportion of each single herb, the date and period of drug approval, and the name of manufacturer from the Department of Chinese Medicine and Pharmacy website, which is the competent authority of Chinese medicine in Taiwan. Because strict production quality control, only minor differences exist between each CHPs. We classified CHPs with the same components in the same category, regardless of slight variations of pharmaceutical manufacturing company. The unique approach used for TCM diagnosis involves gathering clinical symptoms and signs and then a treatment principle is put forward in accordance with the aforementioned diagnostic process. In this situation, researchers in Taiwan have found that symptoms, signs and ill-defined conditions are one of the most common reasons for TCM visits across various different patient populations (Yang et al., 2009; Fang et al., 2012; Lai et al., 2012). Accordingly, the claims database, part of the Taiwan National Health Insurance Research Database, is able to provide a platform for understanding the utilization of TCM therapies by licensed TCM doctors (Hsieh et al., 2008). The aim of our study is to analyze a random sample from this comprehensive database and to determine the TCM utilization patterns of newly diagnosed migraine patients in Taiwan. The results of this study should provide valuable information that will enable physicians to respond to patient use of the TCM in an informed way. This will, in turn, strengthen further the patient–physician relationship when treating migraine and migraine-related symptoms.

2. Materials and methods

2.1. Data resources

This study was designed as a population-based study analyzing a sample of one million subjects selected at random from the 22 million beneficiaries of the National Health Insurance scheme of Taiwan. It was aimed at determining the prevalence of use of prescribed Chinese herbal products among adults with migraine between January 1, 1997, and December 31, 2008. All data were obtained from the National Health Insurance Research Database (NHIRD), which includes all the reimbursement data of the NHI with the identification numbers of all individuals encrypted and transformed; this database is maintained by the National Health Research Institutes of Taiwan (Institutes). The NHIRD database contained patient gender, patient date of birth, all records of clinical visits and hospitalization, drugs prescribed and their dosages (including Chinese herbal products (CHPs)) and three major diagnoses codes which are to effectively depict the whole picture of a patient staying within a typical health service area as included in the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM).

2.2. Study subjects

The selection of study subjects from the random sample of one million individuals was performed as follows (Fig. 1). Firstly, all
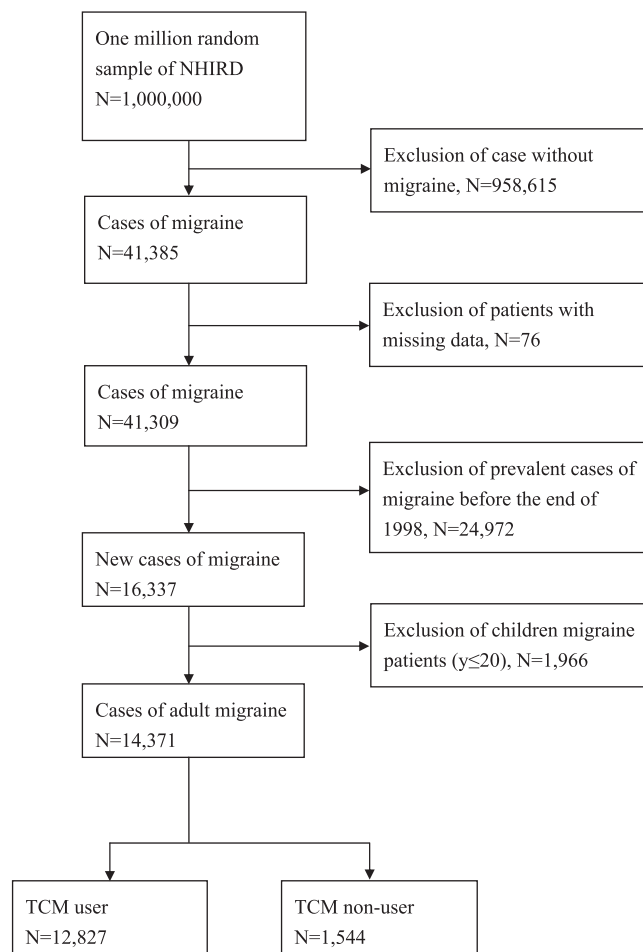

Fig. 1. Flow recruitment chart of subjects from the one million random samples obtained from the National Health Insurance Research Database (NHIRD), 1998 to 2008, in Taiwan.

beneficiaries without migraine ($n=958,615$) as well as those with missing information concerning gender ($n=76$) were excluded. Secondly, migraine patients ($n=24,972$) that had been diagnosed before the end of 1997 were also excluded to ensure that all the subjects included were newly diagnosed with migraine in the time period 1998–2008. Thirdly, subjects under 20 years of age ($n=1966$) were also excluded to limit the study sample to adults. Finally, 14,371 study subjects remained and these were included in the study cohort.

2.3. Study variables

To determine the key independent variables for utilization of TCM among migraine patients, we selected a series of demographic factors based on previous studies (Lipton et al., 2001; Bigal et al., 2008; Chang et al., 2008; Evers et al., 2009; Smitherman et al., 2013). The ages of individuals were categorized into four groups: 21–30, 31–40, 41–50, and > 51 years; the geographic areas of Taiwan were classified into seven regions: Taipei city, Kaohsiung city, Northern region, Central region, Eastern region, Southern region, and Outlying islands; and we split the monthly wage levels of the individuals into four levels: New Taiwan Dollars (NT$) 0, 1–19,999, 20,000–39,999 and > 40,000.

We also searched the NHIRD database for clinical features and treatment records related to migraine as independent variables. The clinical features associated with migraine included episodic migraine, which is defined as those individuals with migraine who have 0 to 14 headache days per month and chronic migraine, which is defined as those individuals with migraine who have 15 or more