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Characteristics of traditional Chinese medicine use in patients with rheumatoid arthritis in Taiwan: A nationwide population-based study



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ABSTRACT

Ethnopharmacological relevance: Large-scale study of traditional Chinese medicine (TCM) usage among patients with rheumatoid arthritis (RA) is lacking. The aim of this study is to evaluate the TCM usage among RA patients in Taiwan.

Materials and methods: We examined the "registry for catastrophic illness patient dataset" of the National Health Insurance Research Database (NHIRD; n=23 million people) in Taiwan. Patients (n=25,263) newly diagnosed as RA in 2001–2009 were included and then followed-up until the end of 2011. Based on the medical utilization, they were further categorized into TCM users (n=6891; 27.3%) and non-TCM users (n=18,372; 72.7%). The demographic data and core prescription patterns of the TCM users were analyzed.

Results: Compared to non-TCM user, TCM users were younger (mean age: 49.6 versus 54.0 years), had a higher female/male ratio (82.7%/17.3% versus 74.1%/25.9%), resided in more urbanized area. Herbal remedies were the most commonly used therapeutic approach (76.4%), followed by combining acupuncture (21.1%). The frequency of outpatient visits in TCM users was higher across all disease categories except circulatory system. The most commonly prescribed formula and herb was Shang-Jong-Shiah-Tong-Yong-Tong-Feng-Wan and Rhizoma Corydalis, respectively. The analysis of core pattern revealed that Dang-Gui-Nian-Tong-Tang, Shu-Jing-Huo-Xie-Tang, Gui-Zhi-Shao-Yao-Zhi-Mu-Tang, Myrrha and Olibanum, were among the most frequently used combinations. RA patients who had anxiety and depression, allergic rhinitis, osteoporosis, menstrual disorder, and menopausal syndrome were prone to have more TCM visits compared to non-TCM users.

Conclusions: Our population-based study revealed the high prevalence and specific usage patterns of TCM in the RA patients in Taiwan. The information could be used for further pharmacological investigation and clinical trials.

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1. Introduction

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http://dx.doi.org/10.1016/j.jep.2015.10.024 0378-8741/© 2015 Elsevier Ireland Ltd. All rights reserved. Rheumatoid arthritis (RA) is a common disorder among autoimmune diseases affecting approximately one percent of worldwide population (Spector, 1990). Although the annual incidence in Taiwan was only 15.8 per 100,000 people (Lai et al., 2012), lower than the data extracted from other countries (Maradit-Kremers et al., 2006), it could lead to significant synovial inflammation,

Taiwan

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bone erosion and progressive disability. Even more, it also hampers somatic systems, resulting in cardiovascular disease, interstitial lung disease, osteoporosis (Gorter et al., 2010; Saag et al., 2008; Sesin and Bingham, 2005; Smolen et al., 2010) and mortality (Gonzalez et al., 2007; Mok et al., 2011). Non-steroid anti-inflammation drugs (NSAIDs) and Disease-modifying antirheumatic drugs (DMARDs) are conventionally used to suppress inflammation and modulate immunity (O'Dell, 2004; Saag et al., 2008; Smolen et al., 2010). Biologic agents that inhibit tumor necrosis factor α (TNF- α), interleukin-1 (IL-1) and interleukin-6 (IL-6) are also available to reduce the ongoing inflammation that is refractory to conventional therapy (Smolen et al., 2010). Despite the fact that conventional and biological therapies are effective to inhibit the inflammation; there are still some unmet needs and concerns (Giacomelli et al., 2014; McInnes et al., 2013; Smolen and Aletaha, 2015). The economic burden of using biologic products may also delay the treatment if the patient could not afford it.

Utilization of complementary and alternative medicine (CAM) was not uncommon in patients with RA (Jacobs et al., 2001). However, current knowledge of the usage of CAM among RA patients is limited by research methodologies such as telephone interview and questionnaires. Although there are some international studies on RA, including the RAISE survey (McInnes et al., 2013), as well as national studies including the Swedish Rheumatology Quality Register (SRQ) (Eriksson et al., 2014), the Consortium of Rheumatology Researchers of North America (CORRONA) registry (Curtis et al., 2014; Kremer, 2006), the American Rochester Epidemiology Project (REP) (Maradit-Kremers et al., 2006), the Italian RAPSODIA study (Giacomelli et al., 2014) and the Hong Kong study (Mok et al., 2011), there is a lack of large-scale surveys on the adjunctive CAM usage specifically among RA patients.

Traditional Chinese medicine (TCM), including Chinese herbal remedies, acupuncture and manipulative therapies, is commonly used as an adjunctive therapy in different diseases in Asian countries (Park et al., 2012). In Chinese pollution, TCM has been used as an adjunctive therapy for autoimmune and rheumatologic diseases. RA was viewed as the Bi Syndrome (Impediment Syndrome) and treated according to the stages of the disease, onset symptoms, and condition of whole body (Zhang et al., 2011). For example, Chinese herbs might play a role in modulating cytokine networks in inflammatory response of RA (Xi Bao et al., 2006) or have analgesic effects (Li et al., 2007). In Taiwan, more than 99% of the total population (23 million people) were enrolled in the mandatory National Health Insurance (NHI) program since 1995 (BoNH, 2010). Not only Western medicine, but also TCM treatment -including Chinese herbal products, acupuncture/moxibustion and manipulative therapy, were reimbursed by this program (Huang et al., 2014). We have also identified the specific pattern of TCM usage in patients with Sjögren's syndrome (Chang et al., 2015), asthma (Huang et al., 2013), allergic rhinitis (Yen et al., 2015b), rhinosinusitis (Yen et al., 2015c), uterine fibroids (Yen et al., 2015a) and fracture (Liao et al., 2015).

To explore the characteristics of TCM usage in patients with RA, we analyzed the registry for catastrophic illness patients of the National Health Insurance Research Database (NHIRD) of Taiwan. This dataset comprehensively included all clinical and laboratory confirmed RA patients with long-term follow-up and thus could reduce the potential for sampling bias. The results of this study should provide valuable information for patients, rheumatologists, and the government concerning the healthcare of patients with RA. The Chinese herbal prescription patterns should also serve as a candidate list for further pharmacological investigation and clinical trial.

2. Materials and methods

2.1. Data source

Taiwan established the NHI program in March 1995. Nearly all of the necessary Western medical services were reimbursed since 1995 and TCM services (Chinese herbal remedies, acupuncture/ moxibustion, and manipulative therapy) since 1996. Any other treatment such as mediation, Qigong and tai chi were not covered. Only licensed TCM doctors are qualified for reimbursement. In 2010, there were 23 million people, equaled to 99.89% of the total population, enrolled in the NHI program (BoNH, 2010). The registry and original data comprising demographic characteristics. outpatient and inpatient visits, diagnostic codes, assessments, procedures, prescriptions and medical expenditure for reimbursement were included in the NHRID. The NHIRD also established a "registry for catastrophic illnesses patient database (RCIPD)", including about 30 disease categories such as cancer, schizophrenia, end-stage renal disease, lupus and rheumatoid arthritis. RA patients who received complete clinical and laboratory evaluation, followed by careful and routine review by rheumatologists commissioned by the National Health Insurance Administration, were granted for catastrophic illness certificates. This accuracy of the diagnosis of the RA patients enrolled in this study is thus highly reliable (Chung et al., 2014).

2.2. Data availability statement

All data are deposited in an appropriate public repository. The study examined datasets from the NHIRD (http://w3.nhri.org.tw/ nhird//date_01.html), which are maintained by National Health Research Institutes (http://nhird.nhri.org.tw/en/index.htm), Taiwan.

2.3. Study subjects and variables

The flow chart for selection of RA cases was shown in Fig. 1. First, all the patients (n=47,809) with diagnosis of RA (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code: 714.0) in the RCIPD of NHIRD were included in this study. Ultimately, individuals with newly diagnosed RA between January 2001 and December 2009 were included for this study (n=25,263) and then followed-up until the end of 2011. After a confirmed diagnosis of RA, those consulted with TCM doctors were grouped as TCM users (n=6891), while the others non-TCM users (n=18,372). The demographic characteristics and claims data of this study cohort were collected and analyzed. Therapeutic actions and indication of TCM prescription was recorded based on TCM theory (Bensky et al., 2004; Scheid et al., 2009).

Urbanization of the residence areas was described previously (Liu et al., 2006; Yen et al., 2015c). In brief, the residence areas of Taiwan township were divided into 4 levels of urbanization which were defined by population density (people/km²), the population ratio of different educational level, ratio of elderly people, ratio of people of agriculture workers, and the number of physicians per 100,000 people. Level 1 had the highest degree of urbanization and level 4 had the lowest. Urbanization levels 1 and 2 were defined as urban areas, while levels 3 and 4 were classified as rural areas.

2.4. Statistical analysis

All statistical analyses were performed using SAS software, version 9.2 (SAS Institute Inc., Cary, NC, U.S.A.). Univariate analysis was used to compare the TCM users with the non-TCM users. The

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