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Frequency and pattern of Chinese herbal medicine prescriptions for chronic hepatitis in Taiwan

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Abstract

Ethnopharmacological relevance: Chinese herbal medicine (CHM) has been commonly used in treating liver diseases in Asian countries.
Aim of study: To conduct a large-scale pharmacoepidemiological study and evaluate the frequency and pattern of CHM prescriptions in treating chronic hepatitis.
Materials and methods: We obtained the database of traditional Chinese medicine outpatient claims from the national health insurance in Taiwan for the whole 2002. Patients with chronic hepatitis were identified by the corresponding diagnosis of International Classification of Disease among claimed visiting files. Corresponding prescription files were analyzed, and association rule were applied to evaluate the co-prescription of CHM in treating chronic hepatitis.
Results: Among the 91,080 subjects treated by CHM for chronic hepatitis, the peak age was in the 40s, followed by 30s and 50s. Male/female ratio was 2.07:1. Long-dan-xie-gan-tang and *Saliva miltiorrhiza* (Dan-shen) were the most commonly prescribed Chinese herbal formula and single herbal drug, respectively. The most common two-drug prescription was Jia-wei-xia-yao-san plus *Saliva miltiorrhiza*, and the most common three-drug prescription was Jia-wei-xia-yao-san plus *Saliva miltiorrhiza* and *Artemisia capillaries* (Yin-chen-hao).
Conclusions: This study showed the utilization pattern of Chinese herbal drugs or formulae in treating chronic hepatitis. Further researches and clinical trials are needed to evaluate the efficacy of these Chinese herbs or its ingredients in treating chronic hepatitis.

Keywords: Chronic hepatitis; Chinese herbal medicine; National health insurance; Pharmacoepidemiology; Traditional Chinese medicine

1. Introduction

Chronic hepatitis and its clinical sequela are serious health problems in both Eastern and Western countries. Among subjects with chronic hepatitis, viral hepatitis B or C was the major etiology in Asian countries (Chen, 1996; Hwang, 2001). Despite the advantages of treating subjects with chronic viral hepatitis using the Western medicine, a remarkable number of patients (about 38–42% of global chronic hepatitis population) are seeking helps from complementary and alternative medicine (CAM). The reasons for this may possibly due to their culture or the concern of the side effects of interferon and/or anti-viral agents (Strader et al., 2002; Yang et al., 2002; Lok and McMahon, 2004; Yee et al., 2006). Chinese herbal medicine (CHM), an important category of traditional Chinese medicine (TCM) and CAM, has been proven to be an efficacious and safe treatment option for chronic hepatitis in some clinical trials (Schuppan et al., 1999; Langmead and Rampton, 2001; Strader et al., 2002; Yang et al., 2002; Chou et al., 2003; Liu et al., 2003). Nevertheless, there is no large-scale epidemiological study evaluating

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the prevalence and drug utilization patterns of CHM in treating chronic hepatitis so far. Despite the fact that a variety of the CHM formulae or single herbal drugs have been used to treat chronic hepatitis based on practitioner's personal experiences, it remains unclear what kind of Chinese herbal formulae or drugs used would be possibly effective in treating chronic hepatitis in clinical practice.

The studies on drug utilization and prescribing patterns can serve as an effective tool for investigating the clinical pharmacology to provide suggestive information for the way to identify the potentially effective CHM or its ingredients (Chan, 2005; Tang, 2006; Graz et al., 2007). Clinically, it is hard to reach consensus to establish general rules for CHM prescription, as the prescribing behaviors depend heavily on physicians' empirical experiences. A possible way to identify the potentially effective herbs from the variety of CHM widely used in clinical practice is through a large-scale survey of drug utilization or prescribing patterns of CHM. Once the effective Chinese herbs in treating chronic hepatitis are identified in clinical trials, further researches can be carried on to identify the effective ingredients of these herbs.

National health insurance (NHI), the only national and official health insurance program in Taiwan has established since 1995, covers nearly all inhabitants (22,520,776 beneficiaries at the end of 2002) (Cheng and Chiang, 1997; Cheng, 2003). People in Taiwan are freely to choose any kind of medical services (eq. TCM or Western medicine), as both are reimbursed by the NHI. Because all claimed data are available to researchers in electronic form, a large-scale survey of the pharmacoepidemiology can be conducted. The aim of this study is to survey the frequency and pattern of CHM use in chronic hepatitis patients by analyzing the NHI database.

2. Methods

2.1. Data sources

In this study, we analyzed the complete database of TCM claims (CM_CD2002.DAT and CM_OO2002.DAT) of the year 2002, which represented the linked visit and prescription files, respectively, from the National Health Insurance Research Database supplied by National Health Research Institute, Taipei in November 2003. The visit files, CM_CD2002.DAT, recorded the date of encounter, the medical care facility and specialty, the patients' gender, date of birth, and at most three diagnoses in coding of International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) (Chen et al., 2006, 2007; Kung et al., 2006). For privacy protection, the identification data of patients and institutions had been scrambled cryptographically to attain anonymity. The prescription files, CM_OO2002.DAT, contained corresponding prescriptive orders and Chinese herbal drugs or formulae. A prescription may contain one or more Chinese herbal drugs or formulae. The Chinese herbal formulae or drugs were made in concentrative powder or fine granules in Taiwan. These can be easily mixed and dispensed into small packages to take one prescription at a time (Chan, 2005).

All TCM were provided only in ambulatory clinics within the coverage of NHI; there was no inpatient care. In addition, only licensed TCM physicians were qualified for reimbursement. The insurance benefits of TCM in Taiwan included CHM, acupuncture and traumatology manipulative therapy especially for joint dislocation.

2.2. Study design

Although the concept of disease entities in TCM is different from those in Western medicine, the TCM physicians in Taiwan are requested to make the diagnoses based on ICD-9-CM coding for claims (no more than three diagnostic codes at each visit). In the current study, we used the data from the claims and prescriptions with the single diagnosis of chronic hepatitis (ICD-9-CM code of 070, 571 or 573).

We first identified the numbers of the patients with chronic hepatitis who had used TCM in Taiwan during 2002 by picking up the single diagnostic code 070, 571 or 573 of ICD-9-CM. Then, we sampled the numbers of subjects using CHM. Thus, we could analyze the corresponding prescriptions of CHM for chronic hepatitis.

According to the TCM theory, a single prescription may contain a single Chinese herbal drug or multiple herbal drugs of various dosages, namely a compound (Fu-Fang), or a classical formulae (regimen, remedy, or Fang-Ji) which is a combination of compatible herbal drugs in fixed dosages ascribed to classical or well-known Chinese textbooks of medicine, or a classical formula plus some herbal drugs, called Chia-Chien-Fang, or even several formulae put together with or without one or several herbal drugs, for different symptoms and signs a patient manifests (Yi and Chang, 2004; Chan, 2005). In 2004, Yi and Chang reported that 92% of total 11,810 traditional Chinese herbal formulae contain a single to 13 herbs (Yi and Chang, 2004).

2.3. Statistical analysis

The database software, IBM DB2 8.1, was used for data linkage and processing (Chen et al., 2003a,b). The regular statistics display the frequency of utilization. The association rule of data mining, originally developed in 1990s to identify which groups or sets of items were likely to be purchased together, was applied to calculate the prescription of the Chinese herbal drugs or formulae for chronic hepatitis (Berry and Linoff, 1997; Han and Kamber, 2001). Association rules were applied to evaluate the co-prescriptions of CHM. In brief, when a physician prescribes drug A (or drugs {A1, A2}, drugs {A1, A2, A3} and so forth), he will also prescribe drug B in X% of cases, and this co-prescribing is present in Y% of all prescriptions. The support factor is the ratio of co-prescriptions of all prescriptions (i.e., Y% in the above example). The confidence factor is the ratio of co-prescriptions to prescriptions for drug A (i.e., X% in the above example). Data mining is an interactive, exploratory process. In executing the program to identify association rules in our data set, we chose 0.5% as the minimum support factor and 30% as the minimum confidence level (Chen et al., 2003a,b; Kung et al., 2006).