



Use of traditional Chinese medicine reduces exposure to corticosteroid among atopic dermatitis children: A 1-year follow-up cohort study



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ABSTRACT

Ethnopharmacological relevance: Atopic dermatitis is a prevalent dermatologic disease in children. Corticosteroid is an important treatment but side effects caused by long-term and excessive use heavily concern patients. Traditional Chinese medicine (TCM) is potentially an alternative treatment and might cause less adverse effects. This nationwide retrospective cohort study aimed to examine the hypothesis that TCM use is associated with lower exposure to corticosteroid.

Materials and methods: Children under 12 years of age with ICD-9 codes 691.8 and 692.x were identified as atopic dermatitis patients from 2007/1/1 to 2007/12/31. Corticosteroid use was compared between TCM users and non-users for one-year follow-up by using a general estimation equation model with propensity-score matching.

Results: A total of 9012 TCM users were identified and the use of corticosteroid after treatment was compared with matched TCM non-users. Use of TCM significantly reduced exposure to corticosteroids after 1-year follow-up. Among TCM users, the exposure to any corticosteroids was lower (42.1% reduction in TCM users versus 34.5% increase in TCM non-users, relative risk: 0.36; *p*-Value < 0.001), the duration was shorter (relative risk for using corticosteroid more than 14 days: 0.37; *p*-Value < 0.001), and the rate of frequent visits with steroid prescription was also lower. CHM was the most commonly used TCM modality (98.5% of all visits) and Xiao-Feng-San was the most commonly used CHM (33% of all prescriptions) with extensive coverage for pathogenesis of atopic dermatitis.

Conclusions: Lower use rate of corticosteroid can be found after TCM treatment, which can be considered as an integrative therapy for atopic dermatitis. Further studies are warranted on the basis of this study.

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Abbreviations: CHM, Chinese herbal medicine; CI, Confidence interval; GEE, General estimation equation; ICD-9, International Classification of Disease, 9th revision; NHIRD, National Health Insurance Research Database; RR, Relative risk; TCM, Traditional Chinese medicine; WM, Western medicine; XFS, Xiao-Feng-San

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1. Introduction

Atopic dermatitis, characterized by severe skin itching, erythema, and lichenification, is a common chronic inflammatory skin disease among children. About 15–30% of children experience atopic dermatitis and their quality of life is usually severely impaired due to nuisance skin manifestations (Bieber, 2010; DiNicola et al., 2013). The financial burden is also high, with the increasing annual prevalence worldwide among children (Herd et al., 1996; Mancini et al., 2008). Although the epidermal barrier

defect model and the immune hypersensitivity model are used to explain its pathogenesis, its exact mechanisms are not fully understood (Bieber, 2010; Winge, 2014). For treating atopic dermatitis, anti-histamines, emollients, corticosteroids, and even immune-modulating agents are often used alone or concurrently, with topical corticosteroid as the mainstay treatment. However, the long-term and frequent use of corticosteroids on children's skin has potential adverse effects, including cutaneous atrophy, telangiectasia, hypertrichosis, drug tolerance, and possible suppression of endocrine function (Furue et al., 2003; Hengge et al., 2006; Schoepe et al., 2006). Some of these adverse events are not uncommon (> 10%) and thus make parents unwilling to use them (Buys, 2007; Aubert-Wastiaux et al., 2011). Trying to control symptoms of atopic dermatitis with topical corticosteroid as less as possible and avoid systemic corticosteroids, which should not be used for children, is the best policy to treat atopic dermatitis among children.

Traditional Chinese medicine (TCM) is an alternative therapy to western medicine (WM) and might cause less adverse effects for atopic dermatitis in children. Chinese herbal medicine (CHM) has been reported to be one of the most commonly used TCM in Taiwan (Cheng et al., 2011b; Chen et al., 2012b). The effectiveness of several CHMs has been demonstrated in relieving symptoms in clinical practice (Sheehan and Atherton, 1992, 1994; Hon et al., 2007). However, systematic reviews evaluating the efficacy and safety of CHM have only marginal benefit or even inconclusive results and information about effects of TCM on children is still lacking (Gu et al., 2013; Tan et al., 2013). Small sample size, short follow-up duration, and considerable variety in CHM all markedly biased these studies and therefore this evidence is not easily applicable in daily practice (Gu et al., 2013). Moreover, as an adjuvant therapy, whether use of TCM is beneficial to spare use of corticosteroid, the most concerned common WM drug, still remains unclear. Once corticosteroid use can be spared, especially systemic corticosteroid, the side effects may be minimized, which is particularly significant for children because atopic dermatitis is easily-relapsed and long-term use of corticosteroid should be avoided among children (Furue et al., 2003; Hanifin et al., 2004).

The aim of this study is to examine whether use of TCM is associated with reducing corticosteroid use among atopic dermatitis children using a large-scale nationwide database in Taiwan with a 1-year follow-up period. Furthermore, to understand how TCM treatments work, analysis on prescriptions is conducted. By using nationwide database, the results of this study can be regarded as the consensus treatment for atopic dermatitis made by nearly all TCM doctors in Taiwan, thereby providing valuable information about summary of CHM pharmacological mechanisms as our previous reports (Chen et al., 2013; Lin et al., 2013; Yang et al., 2013).

2. Materials and methods

2.1. Data source and study subjects

The detailed flow diagram of this study is illustrated in Fig. 1. Data was obtained from the National Health Insurance Research Database (NHIRD), which was made publicly available for researchers to perform nationwide analysis in Taiwan (Chen et al., 2010, 2012b; Cheng et al., 2011a), and a retrospective cohort study was conducted. The NHIRD was composed of information about treatments reimbursed by the National Health Insurance (NHI) since 1996 including detailed clinical information on the use of WM and TCM. With de-identified and encrypted personal information, the NHIRD contained nearly all of the patients' medical records due to the high coverage of the NHI (98.3% of entire population) (Chen et al., 2012b). The International Classification of Disease, Ninth

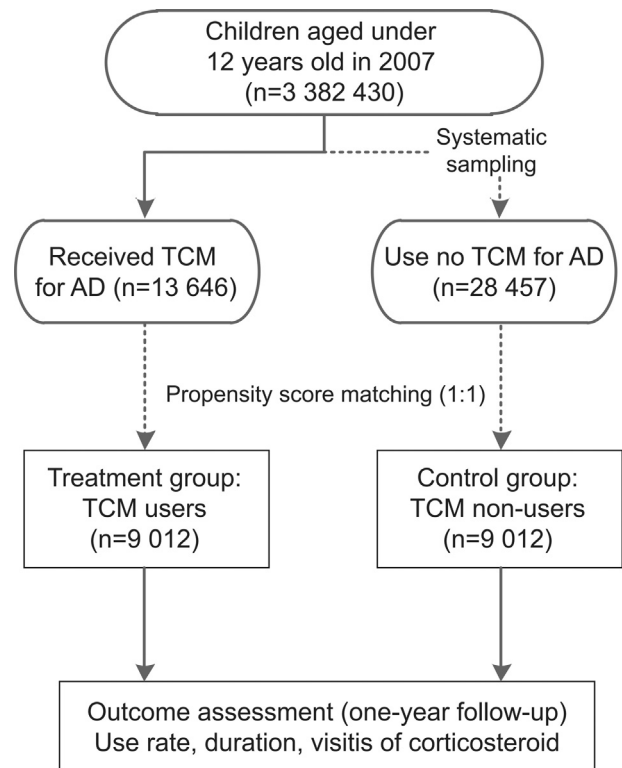


Fig. 1. Flow diagram of this study.

Revision (ICD-9) was used as a diagnosis code and each outpatient visit could have three ICD-9 codes at most.

To identify patients who visited a TCM doctor for atopic dermatitis, children aged 0–12 years with out-patient visits for atopic dermatitis (ICD-9 code: 691.8 and 692.x) were enrolled. Clinically, the diagnosis of atopic dermatitis in Taiwan was based on the criteria published by the United Kingdom working group (Williams, 2005). All patients had evidence of pruritic skin, including report by parents of the child rubbing or scratching. The age limit was set at 12 years old since most atopic dermatitis patients were diagnosed before adolescence. Patients with missing data were excluded.

TCM user was defined as children who used TCM at least once in 2007 and TCM non-user was defined as children who never used TCM. TCM non-users were extracted from the NHIRD by systematic sampling, in which these patients' characteristics were same as the general population. The index date of WM and TCM was defined as the first date when they received treatment.

2.2. Study covariates

Demographic features such as patient sex, age, combined allergic diseases, geographic location, and urbanization status were used as covariates. Moreover, utilization of corticosteroid, such as use rate, duration and visit frequency is also used as covariates in this study. Patient's age was classified into four groups according to the difference between index date and birthday. Asthma and allergic rhinitis (ICD-9 codes 493.x and 477.x, respectively) were associated with atopic dermatitis and used to identify past history of allergic diseases. Since allergic diseases were highly related to the living location and urbanization status, both were used as potential covariates (Robinson et al., 2011). In Taiwan, urbanization status was divided into seven levels according to location. Level 1 was the most urbanized and level 7 was the least urbanized. Levels 4–6 were combined as level 4 because few children lived in these areas (Chen et al., 2012b).

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