



# Chuanxiong chadiao powder, a famous Chinese herbal prescription, for headache: A systematic review and meta-analysis



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## ABSTRACT

**Background:** Headache have been recognized as major causes of public ill-health, whereas there currently are the limitations of conventional therapies available. Chuanxiong Chadiao Powder (CXCP) is a well-known classic TCM herbal prescription with respect to treating headache for more than 1000 years. The objective of this study is to systematically assess the clinical efficacy and safety of CXCP for headache.

**Methods:** A systematic literature search in four databases, up to May of 2014, was performed to identify randomized controlled trials (RCTs), which compared CXCP monotherapy or adjunct therapy with western conventional medicine (WCM) or placebo for headache. The primary outcome measures were headache frequency, headache duration, pain intensity scales, globe assessment, patients self report outcomes, and quality of life. The second outcome measures were the total clinical effective rate and adverse events. The methodological quality of RCTs was assessed independently based on the 7 criteria recommended by the Cochrane Back Review Group.

**Results:** A total of 3680 participants were included in 37 eligible studies. The methodological quality was generally poor and there was only one high quality trial. Meta-analyses of the studies found that significant effects of CXCP for improving headache frequency and headache duration and the total clinical effective rate compared with WCM or placebo control in treating headache ( $P < 0.01$ ). Adverse event monitoring was reported in 22 studies (59%), while the other 15 studies (41%) did not mentioned.

**Conclusions:** The evidence from present study is supported but limited for CXCP clinical use in the management of headache because of methodological flaws. Larger sample-sizes and rigorously designed RCTs are required in the future.

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## 1. Introduction

The term “headache” is used to refer to pain which located above the orbitomeatal line.<sup>1</sup> According to the International Classification of Headache Disorders (ICHD)-3 beta, headache can be classified into the primary headaches, the secondary headaches, painful cranial neuropathies and other facial pains and other headaches, and then the primary headaches can be further categorized into migraine, tension-type headache, trigeminal autonomic cephalalgias and other primary headache disorders.<sup>1</sup> Headache, the common primary complaint of patients, is experienced by 96% of people in their whole life.<sup>2</sup> A recent population-based survey of nine countries in Europe<sup>3</sup> demonstrated that headache affects 15–17% of adults aged 18–65 years on any day and removes at least 0.7% from workforce capacity. The Global Burden of Disease Survey 2010<sup>4</sup> indicated that estimates of the global prevalence of tension-type headache and migraine were 20.1% and 14.7%, which ranked as second and third most common diseases worldwide in both males and females, respectively. In addition, headache carries a tremendous individual, societal, and economic burden in the world. The economic burden of primary headache disorder was enormous both in Europe and in China which the total estimated annual cost was €173 billion<sup>5</sup> and CNY 672.7 billion<sup>6</sup>, respectively. Despite a great number of general population who suffered from headaches, available acute and preventive treatment options are limited. In September 2012, the National Institute for Health and Care Excellence guidance for the acute treatment of adult migraine offered combination therapy with an oral triptan and an nonsteroidal anti-inflammatory drug, or an oral triptan and paracetamol according to the person's preference, comorbidities and risk of adverse events.<sup>7</sup> Treatment options for cluster headache that is considered to be the most severe type of headache, are also extremely limited. The only drug approved by the US Food and Drug Administration (FDA) for its acute treatment was sumatriptan injection. However, many headache patients are unable to tolerate the adverse effects of triptan, have contraindications to their use, or cannot afford them.<sup>8</sup> Triptans are FDA-labeled as contraindicated in hemiplegic or basilar migraine, and their use should be avoided by patients with hypersensitivity to specific components or with severe hepatic impairment or with uncontrolled hypertension.<sup>9,10</sup> The management of chest and central nervous system-related adverse events can add substantial costs to a treatment with triptans.<sup>11</sup> Thus, an increasing number of patients with headache resort to various kinds of complementary and alternative medicine (CAM).

According to American Academy of Neurology and the American Headache Society,<sup>12</sup> Herb *Petasites* (*butterbur*) is effective for migraine prevention and should be offered to patients with migraine to reduce the frequency and severity of migraine attacks (Level A). Furthermore, the constituents of several herbals such as

the feverfew extracts, *Petasites hybridus* and Ginkgolide B have shown effective for prophylaxis of headache in clinical studies.<sup>13</sup> Traditional Chinese medicine (TCM), a form of CAM, is one of the oldest medical systems in the world. In China, the important characteristic of China's national medical system is that TCM and Western medicine complement and cooperate with each other, being responsible together for the health care of Chinese people.<sup>14</sup> Based on Liu's literature review, Chinese Hospital Knowledge Database was searched for relevant articles evaluating the efficacy and safety of TCM for headache from 1994 to 2005, and they identified 300 out of 967 articles used ancient prescription or modified ancient prescription.<sup>15</sup> Among them, Chuanxiong Chadiiao Powder (CXCP) listed the top most frequently used prescription. CXCP,<sup>15</sup> originated from Taiping Huimin Heji Jufang (Prescriptions of the Bureau of Taiping Peoples Welfare Pharmacy), is a well-known classic TCM herbal prescription with respect to treating headache for more than 1000 years written by Huimin Heji Ju, an Imperial Medical Bureau in Song Dynasty. Nowadays, CXCP still used widely in China and elsewhere around the world.

Owing to the significant health risk of headache and the limitations of currently available conventional therapies, unprecedented attention has been attached to CXCP in modern time due to its potential efficacy on headache. Therefore, the objective of this study is to systematically assess the efficacy and safety of CXCP in treatment of headache.

## 2. Methods

We conducted a systematic review and meta-analysis. The design, implementation, and reporting of outcomes was preformed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>16</sup>

### 2.1. Database and search strategies

We systematically searched PubMed, CNKI, VIP and Wanfang database using the following keywords: (Chuan-xiong or Chuanxiong or Sichuan lovage rhizome) and Headache. All of the searches were performed from inception to 15 May 2014. Chinese databases were also searched using the above search terms in Chinese correspondingly. In addition, we examined reference lists from retrieved articles and reference literature.

#### 2.1.1. Eligibility criteria

**2.1.1.1. Types of studies.** We included RCTs evaluating the efficacy and safety of CXCP for headache in this review. There were no restrictions on population characteristics, blinding, language and publication type.

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