EVIDENCE-BASED INTEGRATIVE MEDICINE

Songling Xuemaikang Capsule (松龄血脉康胶囊, SXC) for Primary Hypertension: A Systematic Review of Randomized Controlled Trials*

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ABSTRACT Objective: To evaluate the effectiveness and safety of Songling Xuemaikang Capsule (松龄血脉康胶囊, SXC) for the treatment of primary hypertension. Methods: An extensive search including Cochrane Library, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Chinese Biomedical Literature Database (CBM), Chinese National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), KoreaMed, Japanese database, and online clinical trial registry websites was performed up to February 2013. Randomized controlled trials (RCTs) regarding SXC for the treatment of primary hypertension were searched without no language restrictions. The quality of each trial was assessed according to the Cochrane Reviewers’ Handbook 5.0, and RevMan 5.0 provided by the Cochrane Collaboration. Result: A total of 17 RCTs involving 1,778 patients were included. Meta-analysis showed that there was no significant difference between SXC and antihypertensive agents on systolic blood pressure [mean difference (MD): –0.10 [–4.83, 4.63]; P=0.97] and diastolic blood pressure (MD: 1.00 [–1.16, 3.16]; P=0.36), but SXC combined with antihypertensive drugs was more effective in lowering systolic blood pressure (MD: –6.17 [–7.86, –4.49]; P<0.00001) and diastolic blood pressure (MD: –7.24 [–8.62, –5.85]; P<0.00001) compared with the antihypertensive drugs alone. Conclusions: SXC used alone or combined with antihypertensive drugs appear to be an effective treatment for lowering elevated blood pressure and improving symptoms in patients with primary hypertension. However, the conclusion cannot be drawn definitely due to the poor quality of the included studies. There is still an urgent need for well-designed, long-term studies to address the benefits of SXC for treating primary hypertension. KEYWORDS Songling Xuemaikang Capsule, primary hypertension, Chinese patent medicine, systematic review, randomized controlled trials

Hypertension is a global public health problem that is associated with serious morbidity and mortality. Arterial hypertension is an important risk factor for the development and progression of cardiovascular disease (CVD). Prospective cohort studies have established a strong, graded, and independent positive association between blood pressure (BP) levels and risk of CVD and premature death.1,2 Despite the broad use of several antihypertensive drugs BP control often remains inadequate.3 CVD risk increases beginning at systolic blood pressure (SBP) levels of 120 mm Hg. The percentage of patients who achieve the targets of BP treatment can be as low as 25%. Due to the aging of the population the incidence of hypertension is projected to rise by approximately 60% by 2025.4,5 Recent national surveys report that more than 30% of the general adult population in the United States, Korea, and China has prehypertension, among which 90% have at least one risk factor above optimal levels for CVDs including coronary heart disease (CHD), congestive heart failure (CHF), ischemic and hemorrhagic stroke, renal failure, and peripheral arterial disease.6–10

Conventional antihypertensive agents are usually associated with many adverse effects. However, about 75% to 80% of the population, especially in developing countries, preferred to treat with herbal remedy, for its better acceptability with human body and less side effects.11–13 Songling Xuemaikang Capsule (松龄血脉康胶囊, SXC) is a traditional Chinese patent medicine containing 3 commonly used herbal medicines (Radix

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Puerariae Lobatae, Pinus densiflora, and powdered nacre), which has been authorized recommended by Chinese Pharmacopoeia. Radix Puerariae Lobatae, also named kudzu vine root, contains puerarin which has a substantial antihypertensive effect on spontaneously hypertensive rats, and its mechanism may be related to reducing sensitivity of the vessels to catecholamines, protecting vascular endothelium, increasing endothelium-dependent relaxation and improving the disequilibrium between vasodilating and vasoconstricting substances. Pine needles (Pinus densiflora) have long been used as a traditional health-promoting medicinal food in China. Studies show that pine needle ethanol extract (PNE) has strong antioxidant, antimutagenic, and antiproliferative effects on cancer cells. Another herbal medicine powdered nacre, from Pinctada maxima, is a composite consisting of calcium carbonate crystals in an aragonite structure, embedded in an organic matrix. It has been shown that feeding powdered nacre to rats resulted in reduced body weight, visceral fat amount, and blood triglyceride level without influencing the food intake, body length, or amount of muscular tissue, suggesting that it could decrease visceral fat.

SXC has been widely used to treat hypertension-related symptoms in clinical practice in China. The most common symptoms include headache, dizziness, giddiness, irritability, and insomnia. Recently, many researches showed that SXC had potential effect in lowing BP in vitro and in vivo. For instance, SXC has a good effect in improving plasma levels of endothelin and nitric oxide, regulating rennin-angiotensin system. A large number of researches showed that SXC as monotherapy and in combination with other antihypertensive agents could contribute to BP control and slow the progression of end-organ damage in hypertension. However, few meta-analysis examining the efficacy and safety of SXC has been performed. This systematic review without restricting the language of publication was conducted to critically assess evidence from randomized controlled trials (RCTs) of SXC for treating hypertension.

METHODS

Search Strategy
Two authors (Yang XC and Yang GY) searched online databases including PubMed (1950 to week 4 of February 2013), the Cochrane Central Register of Controlled Trials (CENTRAL, 2013), Chinese Biomedical Literature Database (CBM), Chinese National Knowledge Infrastructure (CNKI), and Chinese Scientific Journal Database (VIP). In addition, we also searched the databases of clinical trials such as Current Controlled Trials (http://www.controlled-trials.com/isrctn/). The searching terms were “Yuan fa xing gao xue ya (primary hypertension)”, “Gao xue ya (hypertension)”, “Songling Xuemai Kang (Songling Xuemaikang Capsule)”. No language restriction was applied. The titles and abstracts of potentially relevant references were identified through the literature search and reviewed independently by 2 investigators (Yang XC, Xiong XJ) to determine whether they met eligibility criteria for inclusion. Discrepancies regarding whether to include or exclude a study were resolved by consensus with other investigator (Wang J).

Types of Studies
All the RCTs based on SXC used alone or combined with anti hypertensive drugs versus antihypertensive drugs in patients with primary hypertension were included. Quasi-RCTs were not considered.

Types of Participants
The participants must be diagnosed according to the 1999 World Health Organization-International Society of Hypertension (WHO-ISH) Guidelines for the Diagnosis and Management of Hypertension (1999 WHO-ISH GMH), or according to the corresponding diagnostic criteria in China. Trials that included patients with other serious conditions were excluded. There were no restrictions on age, gender, and race.

Types of Interventions
The medicine of the treatment group was SXC used alone or combined with conventional drugs for patients with primary hypertension regardless of manufactures, dose and duration. The study was designed to compare the effectiveness and safety of SXC versus antihypertensive drugs alone or plus placebo.

Data Extraction
Data abstraction was conducted according to predefined criteria, which included authors and title of study, study size, age and sex of the participants, details of methodological information, year of publication, treatment process, details of the control