Complementary Therapies in Medicine (2015) 23, 100—115

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevierhealth.com/journals/ctim

Classic herbal formula Zhigancao Decoction for the treatment of premature ventricular contractions (PVCs): A systematic review of randomized controlled trials

Wei Liu[a,1], Xingjiang Xiong[b,1], Bo Feng[b,1], Rong Yuan[b], Fuyong Chu[a,*], Hongxu Liu[a,*]

[a] *Department of Cardiology, Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, Beijing 100010, China*
[b] *Department of Cardiology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing 100053, China*
Available online 6 January 2015

KEYWORDS
Zhigancao Decoction;
Premature ventricular contraction;
Systematic review

Summary
Background: To systematically assess the current clinical evidence of Zhigancao (ZGC) Decoction for premature ventricular contractions (PVCs).
Search strategy: PubMed, the Cochrane Center Controlled Trials Register, EMBASE, Chinese National Knowledge Infrastructure, Chinese Scientific Journal Database, and Wanfang Med Online Database were searched until June 2014. We included randomized clinical trials testing ZGC Decoction against anti-arrhythmic drugs, ZGC Decoction combined with anti-arrhythmic drugs versus anti-arrhythmic drugs alone. Study selection, data extraction, quality assessment, and data analyses were conducted according to the Cochrane standards. A meta-analysis of improving total effects and reducing number of ventricular premature beats was performed to evaluate the effects of ZGC Decoction on PVCs.
Results: A total of 25 studies (involving 2441 patients) were included. The methodological quality of the included trials was evaluated as generally low. The results of the meta-analysis showed that ZGC Decoction combined with anti-arrhythmic drugs had significant effect on improving

* Corresponding authors at: Department of Cardiology, Beijing Hospital of Traditional Chinese Medicine, Capital Medical University, No. 23 Meishuguan backstreet, Dongcheng District, Beijing, China. Tel.: +86 01052176633.
E-mail addresses: chufuyong2014@163.com (F. Chu), lhxcardiology@163.com (H. Liu).
[1] These authors contributed equally in this paper.

http://dx.doi.org/10.1016/j.ctim.2014.12.008

total effects (RR: 1.30 [1.22, 1.38]; $P < 0.00001$) and relieving number of ventricular premature beats (MD: −6.66 [−12.94, −0.37]; $P = 0.04$) compared with anti-arrhythmic drugs alone. Our review showed that ZGC Decoction was more effective in improving total effects (RR: 1.22 [1.08, 1.37]; $P = 0.0009$), compared with anti-arrhythmic drugs alone. 13 trials reported adverse events, while the others did not mention them, indicating that the safety of ZGC Decoction remains uncertain.

Conclusions: ZGC Decoction appears to have beneficial effects on improvement of total effects, reduction of number of ventricular premature beats in participants with PVCs. However, further thorough investigation, large-scale, proper study designed, randomized trials of ZGC Decoction for PVCs will be required to justify the effects reported.

Introduction

Premature ventricular contractions (PVCs) are the most common arrhythmias observed, and the majority of patients who have this arrhythmia have no structural heart disease.[1] Observational studies have documented PVCs in about 6% of the general population.[2,3] They rarely affect prognosis or management. However, they might produce bothersome symptoms and, in select individuals with a high PVC burden, they might contribute to left ventricular (LV) dysfunction and dilation, and hemodynamic deterioration.[4–7] Frequent PVCs cause severe symptoms such as dyspnea, chest pain, dizziness and palpitations and may even be incapacitating in some patients.[8,9] And not only that, more and more previous studies have shown that frequent PVCs in patients with established heart disease are associated with increased risk of cardiac mortality.[10–12] Recent meta-analysis of premature ventricular complexes demonstrated[13] that frequent PVCs are associated with a substantial increase in the risk for sudden cardiac death and total cardiac death findings from observational studies in general populations. Thus, the prevention and management of PVCs are major public health challenges. In recent decades, different classes of anti-arrhythmic were developed and tested in a variety of settings and among different patients. Clinical research finds the medical therapy of β blockers or class I or III anti-arrhythmic agents are effective and recommended to improve symptoms. However, the long-term use of western medicine will produce some side effects, even produce resistance and affect therapeutic efficacy, even with the advance of catheter ablation for ventricular tachycardia, anti-arrhythmic drugs remain an important tool for treating arrhythmias.[14] Therefore, seeking for a new effective anti-arrhythmic method is an important subject of PVCs treatment.

Complementary and alternative (CAM) therapy has become popular among patients with chronic illnesses because of its widespread use.[15,16] Traditional Chinese Medicine (TCM), as a complementary therapeutic regimen, has broad clinical prospects due to its advantages with respect to multiple targets, significant efficacy and safety.[17,18] Zhigancao (ZGC) Decoction is one kind of traditional Chinese herbal medicine, which has the function benefiting qi and nourishing yin, tonifying yang, nourishing blood and reducing the palpitation. It is a representative formula to treat almost any kind of arrhythmia in *Treatise on Febrile Diseases* (*Shang Han Lun in Chinese*) written by Zhang Zhongjing in the Eastern Han Dynasty (25—280 AD), containing nine commonly used herbs (*Radix glycyrrhizae preparata*, *Ginger*, *Cassia Twig*, *Ginseng*, *dried rehmannia*, *Donkey-hide gelatin*, *Radix Ophiopogonis*, *Fructus Cannabis*, *Fructus* Ziziphi Jujubae). Several clinical trials have shown that ZGC Decoction might have the therapeutic effect of improving symptoms of heart palpitations, shortness of breath, insomnia, fatigue in patients with PVCs.[19] Mechanism of anti-arrhythmic effect is mainly blockade effect of different ion channels to shorten ventricular muscle cells APD (action potential duration) and increase self-discipline. And, until now, a large number of randomized controlled trials (RCTs) and case series have been published but have not been evaluated according to the PRISMA systematic review standard. Understanding the effect of ZGC Decoction on PVCs could be valuable for the management of PVCs. Therefore, this study aims to assess the efficacy and safety of ZGC Decoctio alone or combined with anti-arrhythmic drugs for PVCs.

Methods

The supporting PRISMA checklist is available as supporting information; see Checklist 1.

Database and search strategies

Three authors (W. Liu, X. J. Xiong and F. Y. Chu) searched all the clinical trials about ZGC Decoction for treatment of PVCs in six electronic databases, including PubMed, the Cochrane Center Controlled Trials Register (2014), EMBASE (1980—2014), Chinese National Knowledge Infrastructure (CNKI, 1979-June 2014), Chinese Scientific Journal Database (VIP, 1989—June 2014), and Wanfang Med Online Database (WMOD, 1998—June 2014) from their inception to 31 June, 2014. We also searched the reference list of retrieved papers. We systematically searched for studies on ZGC Decoction published without language restriction. Databases in Chinese were searched to retrieve the maximum possible number of trials of ZGC Decoction for hypertension, becuase ZGC Decoction is mainly used and researched in China. The following search terms were used individually or combined: ''Zhigancao Decoction'', ''premature ventricular contractions'', ''premature ventricular beats'', ''Randomized Controlled Trial'', ''controlled clinical trial'', ''randomly'', ''trial'', ''randomised'' and ''randomized''.