European Journal of Integrative Medicine 8 (2016) 609–618

Contents lists available at ScienceDirect

European Journal of Integrative Medicine

journal homepage: www.elsevier.com/eujim

Review article

Qingkailing injection for uncomplicated upper respiratory tract infection: A systematic review and meta-analysis

Linghui Li[a,b], Yanming Xie[a], Yan Chai[c,*], Xing Liao[a,d,**], Wang Pei[b]

[a] Institute of Basic Research in Clinical Medicine, China Academy of Chinese Medical Sciences, No. 16 Nanxiao Street, Dongzhimennei, Dongcheng District, Beijing 100700, China
[b] Wangjing Hospital, China Academy of Chinese Medical Science, Huajiadi Street, Beijing 100102, China
[c] Department of Epidemiology, University of California-Los Angeles, 405 Hilgard Avenue, CA 90095, United States
[d] Post Doctoral Research Station, China Academy of Chinese Medical Science, No. 16 Nanxiao Street, Dongzhimennei, Dongcheng District, Beijing 100700, China

ARTICLE INFO

Article history:
Received 28 October 2015
Received in revised form 27 June 2016
Accepted 27 June 2016

Keywords:
Qingkailing injection
Chinese herbal medicine
Upper respiratory tract infection
Meta-analysis
Systematic review

ABSTRACT

Introduction: Acute upper respiratory tract infections (URTIs) are very common diseases. Qingkailing injection (QKL) has been widely used in China for uncomplicated URTIs. However, the evidence of the effect of QKL has not been assessed systematically. We therefore performed a systematic review in an attempt to evaluate the efficacy and safety of QKL for uncomplicated URTIs in children and adults.
Methods: Eight databases (Western and Chinese) were extensively searched from inception to January 2016 for relevant randomized controlled trials (RCTs). Two reviewers independently extracted data and assessed the quality of studies according to the Cochrane standards. Meta-analysis was carried out using Review Manager Software (version 5.3), provided by the Cochrane Collaboration.
Results: Twenty-six studies involving 3121 participants were included in this systematic review. Meta-analysis showed that QKL plus western medicine significantly improved the effective rate (Heterogeneity: $\chi 2 = 17.25$, P = 0.70, $I^2 = 0\%$; RR = 1.19; 95% CI = [1.15, 1.23]; $P < 0.00001$) and the duration of clinical symptoms compared with western medicine alone. There were seventeen studies mentioned adverse drug reactions (ADRs). A pooled analysis showed that there was a slightly raised risk of ADRs in western medicine group (Heterogeneity: $\chi^2 = 7.27$, $P = 0.51$, $I^2 = 0\%$; RR = 0.39; 95% CI = [0.22, 0.69]; P = 0.001).
Conclusions: In summary, there is some encouraging evidence for the use of QKL for uncomplicated URTIs. However, we still cannot draw definitive conclusions due to the poor methodological quality of included studies. More high-quality RCTs would help to confirm the evidence.

Contents

* Corresponding author.
** Corresponding author at: Institute of Basic Research in Clinical Medicine, China Academy of Chinese Medical Sciences, No.16 Nanxiao Street, Dongzhimennei, Dongcheng District, Beijing 100700, China
E-mail addresses: yc448@ucla.edu (Y. Chai), okfrom2008@hotmail.com (X. Liao).

http://dx.doi.org/10.1016/j.eujim.2016.06.019

1. Introduction

Acute upper respiratory tract infections (URTIs), which include common cold, influenza, inflammation of the larynx and pharynx, acute otitis media and rhino sinusitis, are very common diseases and the major cause of absenteeism from work and school [1]. Typical symptoms are fever, sneezing, runny nose, cough, headache, and sore throat [2]. URTIs are often caused by viral infections. In patients with uncomplicated URTIs (common cold), viruses characteristically cause an infection that is mild, self-limited and of short duration [3,4]. However, sometimes, the infection spreads to adjacent organs, resulting in various clinical complications and an enormous economic burden on society [5,6].

Due to the various pathogenetic mechanisms caused by a multitude of different virus types, no effective universal treatment is available at present [7]. Although being widely used in the treatment of uncomplicated viral URTIs, antibiotics are not effective against viruses [8,9]. Early antibiotic treatment of URTIs does not appear to prevent pneumonia or acute otitis media in children [10]. According to recent meta-analyses, there is no evidence of benefit from antibiotic treatments for uncomplicated URTIs in children and adults [11]. Routine use of antibiotics for nonspecific URTIs is not recommended [12,13].

Angong Niuhuang Pill, a well-known compound formula of Traditional Chinese Medicine (TCM), consists of *Acidum cholicum*, *Acidum hyodesoxy-cholicum*, *Cornu Bubali*, *Concha Margaritifera*, *Flos lonicerae*, *baicalinum*, *Fructus gardenise* and *Radix Isatidis* [14]. Qingkailing injection (QKL) is extracted from *Angong Niuhuang Pill* and has been widely used in the clinic for treating stroke, cardiovascular disease, acute hepatitis, chronic hepatitis and URTIs [15]. It was approved by China Food and Drug Administration (CFDA) since 2002 and was included in "National Essential Drug List" (2004 Edition) [16,17]. In mainland China, QKL was well known for its remarkable effect of antipyretic action and enormous market share [18–21]. Clinical trials reported that QKL could alleviate the symptoms of uncomplicated URTIs. Pharmacological studies proved that QKL could reduce fever, anti-viral and anti-bacterial and it also could inhibit the metabolic behavior of *S. aureus*. Animal studies indicated that QKL probably exerted its antipyretic effect by repairing the perturbed metabolism of amino acids [22].

The availability of scientific evidence is the major obstacle for the acceptance of TCM in western countries. Previous meta-analyses have been conducted to evaluate the effect of QKL in treating acute stroke [23–26]. So far, there has been no systematic review of randomized controlled trials of QKL in treating uncomplicated URTIs or common cold. Therefore, we performed a systematic review in an attempt to better define the efficacy and safety of QKL in the treatment of uncomplicated URTIs.

2. Materials and methods

The current review was performed following the criteria of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [27] and AMSTAR (Assessment of Multiple Systematic Reviews) [28] through all stages.

2.1. Data sources and search strategy

For this systematic review we searched the following 8 databases: Cochrane Central Register of Controlled Trials, Medline (via PubMed), Science Citation Index (SCI), Clinicaltrials.gov, Chinese National Knowledge Infrastructure (CNKI), Wanfang Data, Sino-Med database, the VIP Chinese Scientific Journal database (CQVIP). The last search was updated on January 2016. Search term 'Qingkailing' was combined with the following keywords respectively: 'upper respiratory tract infection'; 'URTI'; 'common cold'; 'cold'; 'shang feng'; 'wai gan'; 'feng han' and 'random*'. We also searched for these terms in the titles and abstracts. When an abstract did not contain such data; but the presence of such data was expected in the full-text paper; the full-text paper was screened as well.

2.2. Study selection criteria

All studies were included for this systematic review if they met the following inclusion criteria: (1) The study was a randomized controlled trial. (2) Participants in the studies were diagnosed with URTIs or common cold, without other specifically defined respiratory conditions, for example tonsillitis, laryngitis, pneumonia, bronchitis and asthma. Diagnostic criteria and treatment efficacy evaluation system followed the Guidelines for Clinical Research of New Chinese Medicine (GCRNCM) and Criteria of the Diagnosis and Curative Effect of Common Diseases (CDCECD) [29]. Given the definition of URTIs is hard to apply rigidly, the researchers also accepted trials in which the diagnosis was made on textbooks and clinical grounds. (3) QKL was used in the experimental group without other TCM. We included trials allowing concurrent use of western medicine if they equally used in both experimental group and control group. Western medicine