ARTICLE

HERBAL MEDICINE AND PULMONARY DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF UPDATED CLINICAL TRIALS

Hamid Rouhi-Boroujeni¹, Soheila Mosharrafat², Ehsan Bakhshian Dehkordi³, Hojjat Rouhi-Boroujeni⁴*

¹Pulmonologist, Associate professor of Clinical Biochemistry, Shahrekord University of Medical Sciences, Shahrekord, IRAN
²General Practitioner, Isfahan University of Medical Sciences, Isfahan, IRAN
³PhD student, Research Committee, Medical plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, IRAN
⁴Cellular and Molecular Research Center, Shahrekord University of Medical Sciences, Shahrekord, IRAN

ABSTRACT

Background: Recently, particular attentions have been focused on the effective role of herbal drugs in chronic disease conditions, malignancies, and also allergic and inflammatory diseases. The current systematic review and meta-analysis attempted to summate recent evidences on the use of herbal drugs to treat various types of lung diseases in different nations. Methods: Studies were identified by searching electronic databases including Cochrane Library, Medline, Embase and Cinahl databases, and the Social Sciences Citation Index, scanning reference lists of included articles and consultations with experts in the field. Our sample is based on data published during recent five years from 2009 to 2014. Among 215 studies reviewed based on the included keywords, 48 met the study criteria and finally reviewed. Results: Overall, 15061 patients included into the analysis that among them 11852 had COPD, 1324 were diagnosed to have non-obstructive pulmonary lung disease (NOSCLD), 1012 suffered asthma, 492 had pneumonia, 172 had ARDS, 146 had radiation-induced pneumonitis, and 63 had lung contusion. The used herbal drugs could affect by different mechanisms including increase of pulmonary functional parameters including FEV1/FVC, PaO2/FiO2, and peak expiration flow rate as well as lowering inflammatory biomarkers such as cytokines of interleukin-6 (IL-6), interleukin-8, tumor necrosis factor-alpha, and transformation growth factor-beta1 leading improvement of clinical manifestations (indicated by lowering symptom score), increase of survival rate (in malignant states), reduce of ICU stay, reduce of ventilation time, improvement of quality of life, and lowering level of depression and anxiety. Conclusion: According to the pointed beneficial effects of herbal therapy, this option can be a good alternative for treatment with chemical drugs in various types of malignant, inflammatory, obstructive, and sensitivity-based pulmonary disorders.

INTRODUCTION

A long history of herbal medicine has been recorded to treat various types of diseases. By developing drugs derived from medicinal plants, the use of chemical drugs has been relatively declining [1]. In any individual culture, the materials used were those that were available within the geographical location and addressed local health concerns; however with exposing cultural traditions as well as overwhelming traditional medicine by modern scientific concepts, the use of herbal remedies is global regardless of geographic, ethnic, or cultural aspects [2,3]. The developments of chemically synthesized drugs have revolutionized healthcare services in whole of the word, but large sections of the population in developing countries still rely on traditional and herbal medicines for their primary care [4]. In Africa, up to 90% and in India 70% of the population tend to use traditional medicine to achieve healthcare needs. Besides, in China, herbal medicine accounts for about half of healthcare delivered and more than 90% of general hospitals in this country have especial units for herbal medicine [5]. Most importantly, using traditional medicine is not limited to developing countries so that during the recent decades, the interest in applying natural medicine has greatly increased in developed countries [6, 7]. This tendency has also expanded remarkably even in American and European countries so that about one-third of Americans [8, 9] and approximately 20% of Europeans [10, 11] tend to use herbal therapy. The most frequent reasons for applying herbal medicine include more affordability, more closely corresponding to the individual’s ideology, allaying concerns about the adverse effects of chemical synthetic drugs, satisfying a desire for more personalized healthcare, and allowing greater public access to health information [12]. However, the use of herbal medicines is mostly considered unfortunately when conventional medicine is ineffective in the treatment of disease.

Recently, particular attentions have been focused the effective role of herbal drugs in chronic disease conditions, malignancies, and also allergic and inflammatory diseases. Recent investigations have been demonstrated beneficial effects of herbal medicine in many types of pulmonary diseases such as obstructive pulmonary lung disease (COPD), lung cancer, asthma, and even pneumonia in both children and adults. The current systematic review attempted to summate recent evidences on the use of herbal drugs to treat various types of lung diseases in different nations.

KEY WORDS

Herbal medicine, pulmonary, meta-analysis, clinical trials

*Corresponding Author
Email: dr_rohib@yahoo.com
MATERIALS AND METHODS

Study population & data collection
Methods of the systematic review were specified in advance and documented in a published protocol in the International Prospective Register of Systematic Reviews (PROSPERO). Studies were identified by searching electronic databases including Cochrane Library, Medline, Embase and Cinahl databases, and the Social Sciences Citation Index, scanning reference lists of included articles and consultations with experts in the field. Our sample is based on data published during recent five years from 2009 to 2014 because of large volumes of studies on selected keywords and also knowledge of the latest results of studies on effects of herbal therapy in lung diseases. Only English language manuscripts and the manuscript with the available full texts were reviewed. Controlled vocabulary and keywords focused on “herbal medicine”, “pulmonary disease”, “lung”, “herb” and “clinical trial”. The clinical trial study design was only imposed. Studies were included regardless of study quality. The following data were extracted from each paper: country, description of the sample, type of pulmonary disease, type of herbal drugs, age range of patients, date of data collection, criteria measured, and standards used to judge quality, and the results. Two reviewers independently assessed studies identified by the search for eligibility based on the title and abstract. Selected full text papers were then assessed independently by the two reviewers. Among 205 studies reviewed based on the included keywords, 47 met the study criteria and finally reviewed [13-59].

Quality assessment of studies:
The selected studies were heterogeneous in terms of studied pulmonary disease, country, and scientific rigor. It was therefore inappropriate to aggregate or conduct a detailed quantitative analysis of the data. Instead, we assessed the studies using the following criteria: type of disease, patient’s age range, sampling strategy, and sample size. These criteria were applied in a structured way to each of the selected studies. As for the data extraction, the quality assessment of the study methodology was performed. The quality criteria were found to be easy to apply to the papers and no differences were found between assessors. The main reviewed endpoint was the effects of different types of herbal drugs on pulmonary function status, symptoms score, inflammatory biomarkers, survival rate, as well as quality of life and depression-anxiety status.

Statistical analysis:
In meta-analysis phase, the k statistic was used to assess the agreement between two reviewers for study selection. The pooled relative risk (RR) was calculated for each outcome using the inverse-variance method for random effect, as well as for fixed effects [14]. The data heterogeneity was assessed using the Cochrane Q test via a χ2 test and quantified with the I2 test [15]. We used the log RR as the dependent variable. The log RR standard error was used to measure the within-study variability, and the residual maximum likelihood method was used to estimate the between-study variance. All analyses were performed using STATA version 11.0 (Stata Corp; College Station, TX) and SPSS version 21.0 for windows (SPSS Inc., Chicago, IL).

RESULTS
Among 205 records retrieved from the initial search, 47 studies were reviewed in full-text that all included in the meta-analysis. The inter-reviewer agreement for the study selection was high with k = 0.93. Overall, 15061 patients included into the analysis that among those, 11852 had COPD, 1324 were diagnosed to have non-small-cell lung cancer (NSCLC), 1012 suffered asthma, 492 had pneumonia, 172 had RDS, 146 had radiation-induced pneumonitis, and 63 had lung contusion. Two studies were published in 2014, 9 in 2013, 12 in 2012, 16 in 2011, and 7 in 2010. No obvious heterogeneity was also identified among the included studies (x2 = 6.55, p for x2 = 0.428; I2 = 6.6%). In 11 studies, a combination of traditional Chinese herbal drugs was used as the intervention protocol. In studies which assessed the efficacy of herbal medicine on improvement of COPD, the use of this treatment protocol resulted in increase of FEV1/FVC, reduce of inflammatory biomarkers as well as improve level of quality of life and depression-anxiety status.

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herbal medicine on acute respiratory distress syndrome (ARDS), PaO2/FiO2 index was successfully improved.

DISCUSSION

Many herbs and their compounds have been used for Asthma, Bronchitis and COPD [60, 61]. Our review could show beneficial effects of different types of herbal drugs on a variety of inflammatory, sensitivity-based, obstructive, and even malignant pulmonary disorders in both children and adults. In this regard, reviewed clinical trials performed within recent six years showed high efficacy of herbal medicine in treatment of COPD, asthma, NSCLC, pneumonia, radiation-induced pneumonitis, and pulmonary contusion. In fact, the used herbal drugs could affect by different mechanisms including increase of pulmonary functional parameters including FEV1/FVC, PaO2/FiO2, and peak expiration flow rate as well as lowering inflammatory biomarkers such as cytokines of interleukin-6 (IL-6), interleukin-8, tumor necrosis factor-alpha, and transformation growth factor-beta1. Leading improvement of clinical manifestations (indicated by lowering symptom score), increase of survival rate (in malignant states), reduce of ICU stay, reduce of ventilation time, improvement of quality of life, and lowering level of depression and anxiety. It seems that in some trials on disorders with immunosuppressive basis, the use of herbal drugs led to increase of serum immunoglobulin. In total, according to the pointed beneficial effects of herbal therapy, this option can be a good alternative for treatment with chemical drugs.

Besides the efficacy of herbal drugs on benign obstructive or inflammatory pulmonary disorders, the effects of herbs on cancer-related survival may be mediated by different mechanisms such as their anti-inflammatory effects (because inflammation is linked to increased risk of cancer), influence on carcinogenic bioactive mediators such as cytochrome P450, alteration the proliferation of several cultured cancerous cells, as well as their antioxidant effects [62-67]. Of 177 drugs approved worldwide for treatment of cancer, more than 70% are based on natural products or mimetics, many of which are improved with combinatorial chemistry. Cancer therapeutics from plants include paclitzaxel, isolated from the Pacific yew tree; camptothecin, derived from the Chinese “happy tree” Camptotheca acuminata and used to prepare irinotecan and topotecan; and combrastatin, derived from the South African bush willow [68]. More than 100 natural product-based drugs are in clinical studies [69], and of the total 252 drugs in the World Health Organization’s (WHO) essential medicine list, 11% are exclusively of plant origin [70]. However, herbal drugs against lung cancers are now under-assessed in world laboratories. Because of beneficial effects of herbal drugs, the side effects of these drugs should not be also ignored. Herbal extracts may be contaminated, adulterated, and may contain toxic compounds. The quality control of herbal medicines has a direct impact on their safety and efficacy. But, there is little data on the composition and quality of most herbal medicines not only due to lack of adequate policies or government requirements but also due to a lack of adequate or accepted research methodology for evaluating traditional medicines. In addition, there is very little research on whole herbal mixtures because the drug approval process does not accommodate undifferentiated mixtures of natural chemicals. These contents can be basis for further studies.

Table 1: literacher review

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N. of patients</th>
<th>Diagnosis</th>
<th>Herb</th>
<th>Effect</th>
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<td>2014</td>
<td>140</td>
<td>COPD</td>
<td>BuFei granule: Radix Codonopsis ssp Pericarpium Citri Reticulatae</td>
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<td>2014</td>
<td>331</td>
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<td>FEV1/FVC, Inflammatory markers, 6MWD</td>
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<td>63</td>
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<td>Xuebijing: Angelica sinensis Salvia militoriza Radix ssp</td>
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<td>75</td>
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<td>Herbal formulae: Sofora flavescnse Glycyrrhiza glabra Gonoderma lucidum</td>
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<td>352</td>
<td>COPD</td>
<td>Bu-Fei Jiang-Pi: Astragalus propinquus Codonopsis pilosula Atractylodes macrolephala Poria cocos</td>
<td>Symptom score, depression-anxiety</td>
</tr>
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</table>

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<table>
<thead>
<tr>
<th>Name</th>
<th>Year</th>
<th>Disease</th>
<th>Treatment</th>
<th>Effect</th>
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<td>2013</td>
<td>NSCLC</td>
<td>Herbal formula Tussilago farfara Rhus versini Morus alba Platycodon grandiflorum Perilla frutescens Prunus armenica</td>
<td>↑ Survival rate</td>
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<td>NSCLC</td>
<td>Scutellariae Barbatae Oregano spp</td>
<td>↓ Inflammatory marker</td>
</tr>
<tr>
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<td>Asthma</td>
<td>Ginger</td>
<td>↑ Symptom score</td>
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<tr>
<td>Cai</td>
<td>2013</td>
<td>COPD</td>
<td>Lung supportive Pulmonaria officinalis Oregano spp</td>
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<td>Pneumonia</td>
<td>TCM</td>
<td>↓ Symptom score, QOL</td>
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<td>TCM</td>
<td>↓ Bone marrow suppression, survival</td>
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<td>↓ Tumor marker, QOL</td>
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<td>Xu</td>
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<td>Magnolia flos</td>
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<td>TCM</td>
<td>↑ QOL</td>
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<td>Guo</td>
<td>2011</td>
<td>NSCLC</td>
<td>Astragalus</td>
<td>↑ Survival, QOL</td>
</tr>
<tr>
<td>Li</td>
<td>2011</td>
<td>COPD</td>
<td>Bu-Fei Yishen Condopsis pilosopa Radix Astrix Pricarpium citri</td>
<td>↓ Symptom score, QOL, 6MWD</td>
</tr>
<tr>
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CONFLICT OF INTEREST

There is no conflict of interest.

ACKNOWLEDGEMENTS

None

FINANCIAL DISCLOSURE

None

REFERENCES


Xu 2011 121 COPD Desmodium triforum Survival

Mukaida 2011 24 COPD HangAm-Dan Symptom score

Jeong 2010 82 NSCLC Symptom score

Ye 2010 82 Pneumonia Gingfeihuayu Inflammatory marker

Xiao 2010 100 Pneumonitis Liangxue KPS score, lung injury

Dou 2010 46 Pneumonitis Dixiong KPS score, dyspnea score

Li 2010 90 COPD Tanreqing Symptom score, inflammatory markers

Liu 2010 90 Pneumonitis TCM Symptom score, inflammatory markers

Rouhi 2009 76 Cough Althea officinalis Symptom score

Rouhi 2009 60 Asthma Zingiber officinalis Althea officinalis Inflammatory markers, QOL

Fazio 2009 9555 (5181 children) COPD Prospan® Ivy (Hedera helix) FEV1, peak expiration flow rate. Inflammatory markers


