Article published online: 2023-03-06

Meta-analysis and Construction of Core Indicator Field of Pediatric Bronchitis Treated by Chinese Herbs Acupoint Application Therapy

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CMNP 2023;3:e15–e28.

Abstract

Objective Our objective was to explore the commonly used herbs, acupoints, and efficacy evaluation indicators of Chinese herbs acupoint application therapy in the treatment of pediatric bronchitis, screen and construct the core index field, and systematically evaluate the efficacy and safety of Chinese herbs acupoint application therapy in the treatment of this disease.

Methods Chinese periodical databases such as China National Knowledge Infrastructure, Wanfang database, VIP Information, and Chinese Biomedical Literature database were searched, and the literature information was extracted manually to establish data tables for data analysis and the key efficacy evaluation index field. The quality of the included studies was assessed using the Cochrane Systematic Bias Risk Assessment Tool and the relevant efficacy indicators were meta-analyzed using RevMan 5.3 software.

Results The most commonly used herbs in acupoint application therapy were wind-cold dispersing herbs and cough-asthma relieving herbs. Feishu (BL 13), Danzhong (RN 17), and Tiantu (RN 22) were the main acupoints. The core indicators were effective rate, improvement of main symptoms/signs, onset time, disappearance time, traditional Chinese medicine (TCM) syndrome score, and symptom score. Meta-analysis results showed that the total effective rate was 0.11 (0.08, 0.33) ($Z = 8.64$, $p < 0.00001$), $I^2 = 39\%$; due to the heterogeneity of cough, expectoration, asthma, and other indicators, the meta-analysis was abandoned.

Conclusion In terms of total efficiency, Chinese medicine acupoint application therapy is superior to conventional Western medicine in efficacy and shortening the time of symptoms of pediatric asthmatic bronchitis. However, as the quality of the evidence included in the study is medium and low, and in the selection of indicators,

Keywords
- pediatric bronchitis
- acupoint application therapy
- data mining
- core indicators
- systematic review
- meta-analysis

received
October 12, 2022
accepted after revision
December 27, 2022
article published online
March 6, 2023

DOI https://doi.org/10.1055/s-0043-1762571.
ISSN 2096-918X.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

there are more composite and relatively subjective indicators such as total effective rate, TCM syndrome score, and symptom score. Therefore, it is necessary to further standardize the efficacy indicators in this field and carry out high-quality and detailed Chinese medicine clinical randomized controlled trials.

Introduction

Bronchitis is a common disease in pediatrics. It is usually caused by biological, physical, chemical stimuli, and allergies. Cough, expectoration, and asthma are the main symptoms in clinical practice. Its pathological manifestations are congestion and edema of bronchial mucosa and infiltration of lymphocytes and neutrophils, and it can be accompanied by damage and shedding of cilia epithelial cells. When mucous glandular hypertrophy and hyperplasia are accompanied by bacterial infection, the secretion is purulent. Routine treatment of this disease mainly includes symptomatic treatment such as anti-infection and atomization.

It is classified as "cough" by traditional Chinese medicine (TCM). Regarding the records of pediatric cough, there is a saying in *Treatise on Causes and Manifestations of Various Diseases (Zhu Bing Yuan Hou Lun)* that "a person who coughs is due to invasion of wind-cold to the lung," in which exogenous pathogens, especially wind pathogen is the main pathogenic factor. The pathogenesis of the disease is mainly lung qi failing in dispersing, and the treatment is mainly ventilating lung qi and relieving cough. However, due to children's weak constitution and poor compliance, the medical compliance of oral administration is poor and this affects its clinical efficacy. Chinese herbs acupoint application therapy belongs to the external treatment. Based on the meridian theory, the herbs are grounded into fine powder, mixed with water, ginger juice, vinegar, yellow rice wine, honey, medical solution, etc., and then directly applied to the acupoints. In recent years, with the development of transdermal technology, Chinese herbs acupoint application therapy has also been valued by doctors. In the previous clinical retrospective studies, it was found that Chinese herbs acupoint application therapy had good curative effects on common clinical diseases in the primary clinics, such as fever, diarrhea, cough, and sore throat and, to some extent, the dosage of antibiotics was reduced. The purpose of this study was to provide evidence-based medical evidence for the correct clinical use of this method by conducting a meta-analysis of randomized controlled trials of Chinese herbs acupoint application therapy or conventional Western medicine in pediatric asthmatic bronchitis.

Materials and Methods

Source of Data

The Chinese periodical databases such as China National Knowledge Infrastructure, Wanfang database, VIP Information, and Chinese Biomedical Literature database were searched, and the keywords such as Xue Wei Tie Fu (acupoint application), Tie Fu Liao Fa (acupoint application therapy), Zhong Yao Tie Fu (acupoint application with Chinese herbs), Yao Tie (herbal patch), Xiao Er Zhi Qi Guan Yan (pediatric bronchitis), Xiao Er Chuan Xi Xing Zhi Qi Guan Yan (pediatric asthmatic bronchitis), and Xiao Er Ji Xing Zhi Qi Guan Yan (pediatric acute bronchitis) were searched. Retrieval time was from the establishment of the database to December 28, 2022, according to the nanofiltration standard, and 48 literature works were obtained in the preliminary examination. After removing the duplication, irrelevant literature, and unclear efficacy indicators, 36 literature works were finally included, involving 19 prescriptions, 73 Chinese herbs, 21 acupoints, and 12 efficacy evaluation indicators.

Inclusion Criteria

Inclusion criteria were based on the following factors: (1) research type: randomized controlled clinical trials (RCTs) and case-control trials; (2) research subjects: children with a definite diagnosis of bronchitis, acute bronchitis, and asthmatic bronchitis; (3) intervention: the treatment group focused on acupoint application therapy; the control group was treated with conventional Western medicine and the symptomatic treatment in the treatment group was the same as that in the control group; and (4) outcome indicators: efficacy evaluation indicators above ≥ 1.

Literature Screening and Data Extraction

The retrieved title information was imported into NoteExpress 3.0 software; the obviously irrelevant literature was screened out through the title and abstract; the full texts were downloaded, read, and screened strictly according to the inclusion criteria; and Excel form was established to prepare the document information extraction form. Extraction contents were basic information, intervention, and control measures, outcome indicators, and adverse reactions of the included research.

Literature Quality Evaluation

The Cochrane bias risk assessment tool was used to evaluate seven aspects of random sequence generation, allocation concealment, subject-blinded implementation, outcome evaluator-blinded implementation, incomplete outcome report, and selective outcome report. The literature search, literature screening, data extraction, and quality evaluation of the included literature were independently conducted by two investigators and cross-checked. The inconsistent contents were discussed and determined through consultation. If it was still uncertain, a third investigator would make the judgment.

Statistical Analysis

Herbal use, acupoint selection, and efficacy indicator analysis: the collected data were entered into Excel 2013 for standardized pretreatment and frequency analysis. Meta-analysis: RevMan5.3 statistical software was used, and mean difference (MD) was used for the measurement data. Relative risk was used for counting data or binary variables. Each effect size was expressed as a 95% confidence interval (95% CI). The statistical heterogeneity of the I^2 values included in the study was calculated. If $I^2 < 50\%$ and $p > 0.05$, the fixed effect model was used for meta-analysis. If $I^2 \geq 50\%$ and $p < 0.05$, the random effect model was used. When there was obvious heterogeneity, the source of heterogeneity was explored for subgroup analysis and sensitivity analysis. If the heterogeneity was too large or the source of the data could not be found, the meta-analysis was discarded and only descriptive analysis was performed. If the same control type included more than 10 studies, a backward funnel plot was used to analyze publication bias.

Results

Basic Information of Literature

Finally, 36 literature works were included, including 4,545 cases, with 2,335 cases in the acupoint application therapy group and 2,210 cases in the control group. The details are shown in ►**Table 1**. In the literature quality evaluation, it was found that only the randomized method was reported in the included studies, and the blinding, allocation concealment, and selectivity reports were not reported. See ►**Fig. 1** for details.

Medication Statistics

Finally, 36 literature works were included. The statistics of Chinese herbs for acupoint application used in the included literature showed that 73 kinds of herbs were used. The most frequently used herbs were Xixin (Asari Radix et Rhizoma), Baijiezi (Sinapis alba L.), Xingren (Armeniacae Semen Amarum), etc. A total of 18 kinds of Chinese herbs were used with herb frequency > twice. The efficacy was classified by reference to the efficacy of Chinese herbs[1] (►**Table 2**). The most common herbs were wind-cold dispersing herbs and cough-relieving and asthma-calming herbs. The specific herb efficacy radar figure is shown in ►**Fig. 2**.

Analysis of Acupoints

Statistics on the selected acupoints in the Chinese herbs acupoint application therapy for the treatment of pediatric bronchitis included in the study showed that 21 acupoints were involved. Among them, the most frequently used acupoints were Feishu (BL 13), Danzhong (RN 17), Tiantu (RN 22), etc., as shown in ►**Fig. 3**.

Analysis of Efficacy Indicators

The efficacy indicators involved in the included literature were statistically analyzed, screened, and combined, and the key efficacy indicators were screened according to the frequency. The results showed that there were 12 efficacy indicators for the evaluation of acupoint application therapy in pediatric bronchitis, among which the key efficacy indicators were the total effective rate, main symptoms/physical signs improvement, onset time, disappearance time, TCM syndrome score, and symptom score (►**Fig. 4**).

The literature with clinical symptoms/signs as efficacy evaluation indicators was further analyzed. The results showed that cough, expectoration, asthma, and pulmonary rales occurred frequently. Therefore, these four indicators were selected as efficacy evaluation indicators in the subsequent meta-analysis.

Meta-analysis

According to the screening results of the key efficacy indicators above, the total effective rate, the onset, and improvement time of main symptoms/signs were selected as the efficacy evaluation indicators based on the frequency, and the effect of acupoint application therapy on pediatric bronchitis was further meta-analyzed. Meta-analysis results showed that the I^2 value of each index was greater than 50%, indicating that the results were heterogeneous and the reasons for the heterogeneity were needed to be discussed by excluding the literature one by one. In the meta-analysis, the total effective rate I^2 value was 53% (►**Fig. 5**). After excluding one RCT, the total effective rate was 0.11 (0.08, 0.13) ($Z = 8.64$, $p < 0.00001$) and $I^2 = 39\%$, indicating that this RCT may be the source of heterogeneity.[2] Through further analysis of this literature, it was found that the therapeutic effect of the test group and the control group was significantly different 48 hours after administration, so the heterogeneity was large. In addition, the meta-analysis of cough, expectoration, asthma, rale, and other symptom indicators showed that I^2 values were greater than 90%, indicating that there was significant heterogeneity, which was not suitable for meta-analysis.

Publication Bias Analysis

A total of 36 clinical randomized controlled trials were included in this study. The risk of bias was analyzed by funnel plot according to the effective rate, as shown in ►**Fig. 6**.

Discussion

The lung is a delicate Zang organ with clear, weak, and tender features. Children are not yet fully developed and easy to be impaired by pathogens. Pediatric bronchitis is a common respiratory disease in pediatrics. Chinese herbs acupoint application therapy is a commonly used external therapy in TCM. The few adverse reactions and good acceptance increase its compliance.

In this study, the previously published TCM clinical randomized controlled trials were conducted to summarize the commonly used acupoint application herbs, selected acupoints, and evaluation indicators of efficacy in pediatric bronchitis. The results showed the following factors. (1) The selection of acupoint application herbs: wind-cold-dispersing herbs and cough-relieving and asthma-calming

Table 1 Inclusion of literature

Lead authors and publication time of the included literature	No.	Sample size (trial group / control group)	Acupoint application therapy group (herb/acupoint)	Control group	Outcome indicators	Course of treatment
Xu et al[4] [Removed ref field] 2012	1	230(115/115)	Cough-and-asthma relieving acupoint application with Chinese herbs of Jixiangcao (Reineckea carnea), Baijiezi (Sinapis alba L.), Zisuzi (Fructus Perillae), Aidicao (Herba Ardisiae Japonicae), etc.on the acupoints of Danzhong (RN 17), Feishu (BL 13) and Dingchuan(EX-B1)	Western medicine routine	Total effective rate and time of symptom improvement (breathing time, lung asthma, sputum amount, and night cough)	5 d
Kong[5] [Removed ref field] 2020	2	110(55/55)	Combination of cough-and-asthma relieving acupoint application with Chinese herbs of Baijiezi (Sinapis alba L.), Jixiangcao (Reineckea carnea), Zisuzi (Fructus Perillae), Aidicao (Herba Ardisiae Japonicae), etc., on the acupoints of Danzhong (RN 17), Feishu (BL 13), Dingchuan (EX-B1)	Western medicine routine	Total effective rate, time of symptom improvement (breathing time, lung asthma, sputum amount, and night cough)	/
Sun[6] [Removed ref field] 2015	3	60(30/30)	Acupoint application with Chinese herbs of Baijiezi (Sinapis alba L.), Yanhusuo (Corydalis Rhizoma), Gansui (Kansui Radix), Xixin (Asari Radix et Rhizoma) on the acupoints of Dazhui (DU 14), Danzhong (RN 17), Feishu (BL 13), Shenshu (BL 23), Pishu (BL 20) and Yongquan (KI 1)	Successive flash cupping therapy	Total effective rate	4 wk
Gao and Zhao[7] [Removed ref field] 2019	4	90(45/45)	Combination of child cough-relieving cold compress acupoint application on the acupoints of Shenque (RN 8), Dazhui (DU 14), Danzhong (RN 17), Feishu (BL 13), and Dingchuan (EX-B1)	Western medicine routine	Total effective rate, time of disappearance of symptoms and signs (fever, cough, asthma, pulmonary signs), hospital stay, and immune Function (IgE,$CD4^+$,$CD8^+$, $CD4^+/CD8^+$)	7 d
Zhang[8] [Removed ref field] 2015	5	60(30/30)	Combination of acupoint application with Chinese herbs of Mahuang (Ephedrae Herba), Guizhi (Cinnamomi Ramulus), Ganjiang (Zingiberis Rhizoma), Baijiezi (Sinapis alba L.), Baishao (Paeoniae Alba Radix), Banxia (Pinelliae Rhizoma), Xixin (Asari Radix et Rhizoma), Gancao (Glycyrrhizae Radix et Rhizoma) on the acupoints of Feishu (BL 13) and Gaohuang (BL 43)	Western medicine routine	Total effective rate	7 d
Li[9] [Removed ref field] 2008	6	132(67/65)	Combination of acupoint application with Chinese herbs of Xixin (Asari Radix et Rhizoma), Beixing (Armeniacae Semen Amarum) on the acupoints of Feishu (BL 13), Pishu (BL 20) and Tiantu (RN 22)	Western medicine routine	Time of symptom disappearance (asthma and pulmonary asthma), and hospital stay	/
Tian[10] [Removed ref field] 2000	7	76(38/38)	Combination of acupoint application with Chinese herbs of Baibu (Stemonae Radix), Jiegeng (Platycodonis Radix), aminophylline, chlortrimeton, fresh Shengjiang (Zingiberis Rhizoma Recens) on the acupoint of Feishu (BL 13)	Western medicine routine	Total effective rate	/

Table 1 (*Continued*)

Lead authors and publication time of the included literature	No.	Sample size (trial group / control group)	Acupoint application therapy group (herb/acupoint)	Control group	Outcome indicators	Course of treatment
Li et al[11] [Removed ref field] 2019	8	98(20/19–19–20–20)	Acupoint application with Chinese herbs of honeyed Mahuang (Ephedrae Herba), Kuxingren (Armeniacae Semen Amarum), Shigao (Gypsum Fibrosum), Gancao (Glycyrrhizae Radix et Rhizoma), Dilong (Pheretima), Tinglizi (Lepidii Semen), Chenpi (Pericarpium Citri Reticulatae), Ziwan (Asteris Radix et Rhizom), Baibu (Stemonae Radix), Baiqian (Cynanchi Stauntonii Rhizoma et Radix), Shegan (Belamcandae Rhizoma) on the acupoints of Tiantu (RN 22) and Danzhong (RN 17), bilateral Feishu (BL 13), Dingchuan(EX-B1) and Shenque (RN 8)	Western medicine routine	Total effective rate, time of symptom disappearance (panting, cough, and lung asthma)	/
Deng[12] [Removed ref field] 2020	9	160(80/80)	Huatan Zhike Patch with Chinese herbs of Houpo (Magnoliae Officinalis Cortex), Beixing (Armeniacae Semen Amarum) and Xixin (Asari Radix et Rhizoma) on the acupoints of Zhiyang (DU 9), Tiantu (RN 22), Feishu (BL 13), Dazhui (DU 14) and Danzhong (RN 17)	Budesonide aerosol inhalation	Total effective rate	2 wk
Hong[13] [Removed ref field] 2019	10	52(26/26)	Combination of self-made Phlegm-resolving and Cough-relieving Plaster with Chinese herbs of Beixing (Armeniacae Semen Amarum), Xixin (Asari Radix et Rhizoma), Houpo (Cortex Magnoliae Officinalis) on the acupoints of Feishu (BL 13), Dazhui (DU 14), Zhiyang (Du 9), Danzhong (RN 17) and Tiantu (RN 22)	Western medicine routine	Total effective rate, time of improvement of symptoms and signs (cough, expectoration, asthma, lung symptoms, respiratory rate, tidal volume, and maximum expiratory flow)	1 wk
Lin et al[14] [Removed ref field] 2017	11	96(48/48)	Combination of acupoint application on the acuponits of Feishu (BL 13), Tiantu (RN 22), Danzhong (RN 17) and Zusanli (ST 36)	Western medicine routine	Total effective rate, time of symptom improvement (cough, expectoration, and lung symptoms)	/
Li et al[15] 2020	12	60(30/30)	Combination of acupoint application with Chinese herbs of Beixing (Armeniacae Semen Amarum), Xixin (Asari Radix et Rhizoma) on the acupoints of Pishu (BL 20), Feishu (BL 13) and Tiantu (RN 22)	Western medicine routine	Lung function (tidal volume per kg, inspiratory time, respiratory time, respiratory rate, and TPTEF/TE, VPEF/VE)	/
Wang[16] [Removed ref field] 2021	13	70(35/35)	Combination of Lung-clearing Plaster with Chinese herbs of Jinyinhua (Lonicerae Japonicae Flos), Qianhu (Peucedani Radix), Ziwan (Asteris Radix et Rhizom), Kuandonghua (Farfarae Flos), Baibu (Stemonae Radix), Zhebeimu (Fritillariae Thunbergii Bulbus), Aidicha (Ardisiae Japonicae Herba), Zhiqiao (Aurantii Fructus), Yuxingcao (Houttuyniae Herba) on the acupoints of Feishu (BL 13), Tiantu (RN 22), Danzhong (RN 17) and Zusanli (ST 36)	Western medicine routine	Total effective rate	/

(*Continued*)

Table 1 (*Continued*)

Lead authors and publication time of the included literature	No.	Sample size (trial group / control group)	Acupoint application therapy group (herb/acupoint)	Control group	Outcome indicators	Course of treatment
Deng and Zhou[17] [Removed ref field] 2020	14	108(54/54)	Combination of Jianfu Massage Cream on acupoints of Tiantu (RN 22), Danzhong (RN 17), Zusanli (ST 36) and Feishu (BL 13)	Western medicine routine	Total effective rate, time of symptom improvement (lung symptoms, asthma, expectoration, cough), lung function (respiratory rate, tidal volume, and maximum expiratory flow)	1 wk
Huang et al[18] 2019	15	100(50/50)	Lung-Clearing acupoint application with Chinese herbs of Mahuang (Ephedrae Herba), Xingren (Armeniacae Semen Amarum), Huangqin (Scutellariae Radix), Shengjiang (Zingiberis Rhizoma Recens), Bingpian (Borneolum Syntheticum), Niuhuang (Bovisc Alculus), Gancao (Glycyrrhizae Radix et Rhizoma) on the acupoints of Feishu (BL 13), Tiantu (RN 22) and Danzhong (RN 17)	Western medicine routine	Total effective rate, time of symptom disappearance (cough, expectoration, and pulmonary rale)	5 d
Wang[19] [Removed ref field] 2013	16	61(31/30)	Combination of infrared Cough-Relieving acupoint application on the aupoints of Dazhui (DU 14), Feishu (BL 13) and Danzhong (RN 17)	Oral administration of Chinese Medicine + Western medicine antibiotics	Total effective rate	/
Chen et al[20] [Removed ref field] 2018	17	108(54/54)	Combination of Phlegm-Resolving and Cough-Relieving acupoint application with Chinese herbs of Mahuang (Ephedrae Herba), Baijiezi (Sinapis alba L.), Rougui (Cinnamomi Cortex), Banxia (Pinelliae Rhizoma), Chishao (Paeoniae Radix Rubra), Dingxiang (Caryophylli Flos), Ruxiang (Olibanum) on the acupoints of Tiantu (RN 22), Shenque (RN 8), Feishu (BL 13) and Dingchuan(EX-B1)	Western medicine routine	Total effective rate, TCM syndrome score, C-reactive protein, time of disappearance of clinical symptoms (fever, asthma, cough, and lung symptoms)	7 d
Li and Huang[21] [Removed ref field] 2019	18	200(100/100)	Combination of acupoint application of Phlegm-Resolving and Cough-Relieving Prescription with Chinese herbs of Baijiezi (Sinapis alba L.), Banxia (Pinelliae Rhizoma), Mahuang (Ephedrae Herba), Dingxiang (Caryophylli Flos), Rougui (Cinnamomi Cortex), Chishao (Paeoniae Radix Rubra), Ruxiang (Olibanum) on the acupoints of Feishu (BL 13), Shenque (RN 8) and Tiantu (RN 22)	Western medicine routine	The total effective rate, time of disappearance of clinical symptoms (cough, rale, expectoration), and TCM syndrome score (red throat and dry tongue)	1 wk
Ma and Liu[22] [Removed ref field] 2019	19	80(40/40)	Combination of acupoint application with Chinese herbs of Baijiezi (Sinapis alba L.), Yanhusuo (Corydalis Rhizoma), raw Gansui (Kansui Radix), Xixin (Asari Radix et Rhizoma), Guizhi (Cinnamomi Ramulus), Laifuzi	Western medicine routine	The total effective rate, time of disappearance of clinical symptoms (cough,	3–5 d

Table 1 (*Continued*)

Lead authors and publication time of the included literature	No.	Sample size (trial group / control group)	Acupoint application therapy group (herb/acupoint)	Control group	Outcome indicators	Course of treatment
			(Semen Raphani), Qingdai (Indigo Naturalis) on the acupoints of Tiantu (RN 22), Dazhui (DU 14), Danzhong (RN 17) and Feishu (BL 13)		expectoration, fever, and pulmonary rales)	
Li and Wang[23] [Removed ref field] 2009	20	120(60/60)	Jiezi Kechuan Paste acupoint application with Chinese herbs of Baijiezi (Sinapis alba L.), Shengjiang (Zingiberis Rhizoma Recens), Yanhusuo (Corydalis Rhizoma), Xixin (Asari Radix et Rhizoma), Gansui (Kansui Radix), Bingpian (Borneolum Syntheticum) on the acupoints of bilateral Feishu (BL 13), Gaohuang (BL 43) and Dingchuan (EX-B1)	Western medicine routine	Total effective rate, onset time of symptoms/signs, symptom/sign score	3 d
Ding and Zhou[24] [Removed ref field] 2021	21	76(38/38)	Jiezi Kechuan Paste acupoint application with Chinese herbs of Baijiezi (Sinapis alba L.), Yanhusuo (Corydalis Rhizoma), Xixin (Asari Radix et Rhizoma), Rougui (Cinnamomi Cortex), Ganjiang (Zingiberis Rhizoma) on the acupoints of Danzhong (RN 17), Feishu (BL 13), Gaohuang (BL 43) and Dingchuan (EX-B1)	Western medicine routine	Total effective rate, bed symptoms and signs score, hospital stay, parental satisfaction	7 d
Mo and Luo[25] 2017	22	108(54/54)	Lung-Clearing Plaster acupoint application with Chinese herbs of Jinyinhua (Lonicerae Japonicae Flos), Qianhu (Peucedani Radix), Ziwan (Asteris Radix et Rhizom), Kuandonghua (Farfarae Flos), Baibu (Stemonae Radix), Zhebeimu (Fritillariae Thunbergii Bulbus), Aidicha (Ardisiae Japonicae Herba Herba), Zhiqiao (Aurantii Fructus), Yuxingcao (Houttuyniae Herba) on the acupoints of Feishu (BL 13), Danzhong (RN 17), Tiantu (RN 22) and Fenglong (ST 40)	Western medicine routine	Total effective rate, HAMD score, TCM syndrome score, disappearance time of main symptoms (expectoration, cough, rale)	5 d
Li et al[26] 2011	23	60(30/30)	Lung-Clearing Plaster acupoint application with Chinese herbs of Mahuang (Ephedrae Herba), Xingren (Armeniacae Semen Amarum), Huangqin (Scutellariae Radix), Shengjiang (Zingiberis Rhizoma Recens), Bingpian (Borneolum Syntheticum), Niuhuang (Bovisc Alculus), Gancao (Glycyrrhizae Radix et Rhizoma) on the acupoints of Feishu (BL 13), Tiantu (RN 22) and Danzhong (RN 17)	Western medicine routine	Total effective rate, disappearance time of symptoms and signs (cough, expectoration, pulmonary rale), TCM syndrome score	/
Du et al[27] 2017	24	420(300/120)	Heat-Clearing and Lung-Dispersing Plaster acupoint application for Children with Chinese herbs of Zhizi (Gardeniae Fructus), Xingren (Armeniacae Semen Amarum), Taoren (Persicae Semen), Honghua (Carthami FlosA) on the acupoints of Danzhong (RN 17), with the back application site corresponding to the chest	Acute bronchitis syrup	The total effective rate, symptom and sign score, main symptom score, number of cases and time of disappearance of main symptoms and signs (number of disappearance	/

(*Continued*)

Table 1 (*Continued*)

Lead authors and publication time of the included literature	No.	Sample size (trial group / control group)	Acupoint application therapy group (herb/acupoint)	Control group	Outcome indicators	Course of treatment
					cases, onset and disappearance time)	
Huang et al[28] 2017	25	400(200/200)	Chinese medicine acupoint application with Chinese herbs of Xingren (Armeniacae Semen Amarum), Xixin (Asari Radix et Rhizoma) on the acupoints of Danzhong (RN 17), Feishu (BL 13) and Tiantu (RN 22)	Western medicine routine	Total effective rate	7 d
Liu[29] 2009	26	120(60/60)	Shenque (RN 8) Plaster acupoint application on the acupoints of Tiantu (RN) 22) and Shenque (RN 8) during the day and Feishu (BL 13) and Gaohuang (BL 43) at night.	Western medicine routine	Total effective rate	2–4 wk
Li et al[30] 2014	27	200(100/100)	Cough-Relieving and Phlegm-Resolving Paste acupoint application with Chinese herbs of Xixin (Asari Radix et Rhizoma) and Xingren (Armeniacae Semen Amarum) on the acupoints of bilateral Feishu (BL 13), Tiantu (RN 22) and Danzhong (RN 17)	Western medicine routine	Total effective rate	3–6 d
Li[31] 2019	28	72(36/36)	Self-made Sanfu Plaster acupoint application with Chinese herbs of Baijiezi (Sinapis alba L.), Xixin (Asari Radix et Rhizoma), Ganjiang (Zingiberis Rhizoma) and Huajiao (Zanthoxyli Pericarpium) on the acupoints of Tiantu (RN 22) and Feishu (BL 13)	Western medicine routine	Total effective rate	1 wk
Zhang[32] [Removed ref field] 2015	29	72(36/36)	Self-made Sanfu Plaster acupoint application with Chinese herbs of Dahuang (Rhei Radix et Rhizoma), Huanglian (Coptidis Rhizoma), Wugong (Scolopendra), Tianma (Gastrodiae Rhizoma), Huangbai (Phellodendri Chinensis Cortex), Sanqi (Notoginseng Radix et Rhizoma), Yujin (Curcumae Radix), Awei (Ferulae Resina), Zhishi (Aurantii Fructus Immaturus), Danggui (Angelicae Sinensis Radix), Sanleng (Rhizoma Sparganii), Rougui (Cinnamomi Cortex), Huangqin (Scutellariae Radix), Shengdihuang (Rehmanniae Radix), Mahuang (Ephedrae Herba), Ruxiang (Olibanum), Houpo (Magnoliae Officinalis Cortex), Baizhi (Radix Angelicae Dahuricae), Fangfeng (Saposhnikoviae Radix), Taoren (Persicae Semen), Xingren (Armeniacae Semen Amarum), Xiangfu (Cyperi Rhizoma), Binlang (Semen Arecae), Tianhuafen (Trichosanthis Radix), Wubeizi (Galla Chinensis), Qianghuo (Notopterygii Rhizoma et Radix) and Duhuo	Western medicine routine	Total effective rate	1 wk

Table 1 (*Continued*)

Lead authors and publication time of the included literature	No.	Sample size (trial group / control group)	Acupoint application therapy group (herb/acupoint)	Control group	Outcome indicators	Course of treatment
			(Radix Angelicae Pubescentis) on the acupoints of Tiantu (RN 22) and Feishu (BL 13)			
Pang[33] [Removed ref field] 2019	30	80(40/40)	Combination of Jiezi Kechuan Plaster acupoint application with Chinese herbs of fried Baijiezi (Sinapis alba L.), Yanhusuo (Corydalis Rhizoma), Shengjiang (Zingiberis Rhizoma Recens), Xixin (Asari Radix et Rhizoma), Gansui (Kansui Radix) and Bingpian (Borneolum Syntheticum) on the acupoints of Feishu (BL 13), Gaohuang (BL 43) and Dingchuan (EX-B1)	Western medicine routine	Total effective rate and symptom score	7 d
Huang et al[34] [Removed ref field] 2014	31	200(100/100)	Combination of Chinese medicine acupoint application with Chinese herbs of Xixin (Asari Radix et Rhizoma) and Xingren (Armeniacae Semen Amarum) on the acupoints of Feishu (BL 13), Danzhong (RN 17) and Tiantu (RN 22)	Western medicine routine	Total effective rate	7 d
He[2] [Removed ref field] 2014	32	60(30/30)	Combination with Cough-Asthmatic Plaster acupoint application on the acupoints of Feishu (BL 13), Xinshu (BL 15), Geshu (BL 17) and Danzhong (RN 17)	Western medicine routine	Total effective rate, main symptoms, secondary symptom score, and time of remission of symptoms and signs	/
Zeng[35] [Removed ref field] 2017	33	106(53/53)	Shunkening Plaster on the acupoints of Tiantu (RN 22), Danzhong (RN 17), Feishu (BL 13), Bailao (EX-HN 15) and Dingchuan (EX-B1)	Western medicine routine	Total effective rate and symptom improvement time	7 d
Guo[36] [Removed ref field] 2015	34	140(70/70)	Application of Kening Powder with Chinese herbs of Baijiezi (Sinapis alba L.), Suzi (Perillae Fructus), Xiangfu (Cyperi Rhizoma), Xixin (Asari Radix et Rhizoma), Wuzhuyu (Euodiae Fructus) on the acupoints of Feishu (BL 13), Dazhui (DU 14), Tiantu (RN 22), Pishu (BL 20), Fengmen (BL 12), Danzhong (RN 17) and Fenglong (ST 40)	Western medicine routine	Total effective rate	6 d
Ren[37] [Removed ref field] 2020	35	110(55/55)	Combination with the acupoint application with Chinese herbs of Baijiezi (Sinapis alba L.), Wuzhuyu (Euodiae Fructus), Zisuzi (Fructus Perillae), Xixin (Asari Radix et Rhizoma) and Xiangfu (Cyperi Rhizoma) on the acupoints of Feishu (BL 13), Danzhong (RN 17), Fengmen (BL 12), Pishu (BL 20), Tiantu (RN 22) and Dazhui (DU 14)	Western medicine routine	Total effective rate, symptom score (cough, expectoration, asthma, lung rales, asthma times), and family satisfaction	7 d
Liu[38] [Removed ref. field] 2016	36	250(125/125)	Application of far-infrared antitussive plaster on the acupoints of Feishu (BL 13), Tiantu (RN 22), Danzhong (RN 17), Dazhui (DU 14), Pishu (BL 20), and Geshu (BL 17)	Western medicine routine	Total effective rate, time of symptom improvement, and serum immunoglobulin	7 d

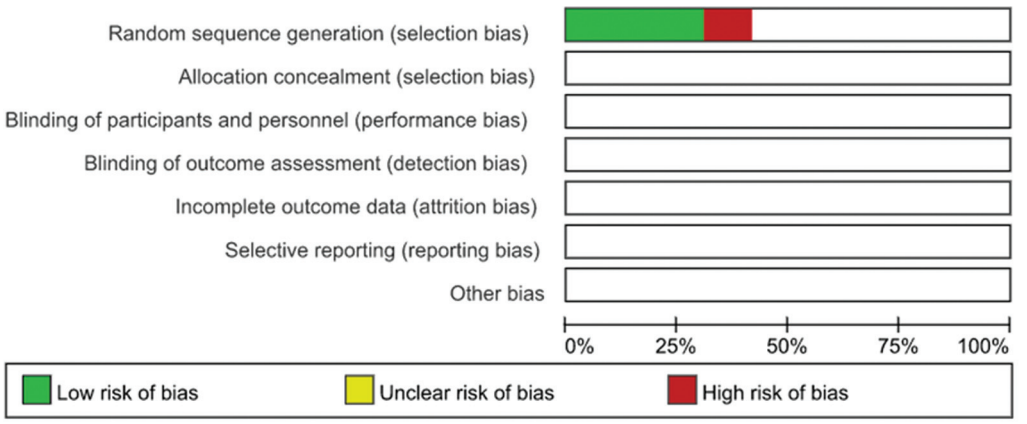

Fig. 1 Quality evaluation chart of literature.

Table 2 Efficacy of Chinese herbs used in treating children's bronchitis with Chinese herbs acupoint application ≥ twice

No.	Name of Chinese herbs	Efficacy	Frequency/ times	No.	Name of Chinese herbs	Efficacy	Frequency/ times
1	Xixin (Asari Radix et Rhizoma)	Wind-cold dispersing herb	16	17	Ruxiang (Olibanum)	Blood-activating and pain-relieving herb	3
2	Baijiezi (Sinapis alba L.)	Warmly resolving cold-phlegm herb	13	18	Zisuzi (Fructus Perillae)	Cough-relieving and asthma-calming herb	3
3	Xingren (Armeniacae Semen Amarum)	Cough-relieving and asthma-calming herb	12	19	Chishao (Paeoniae Radix Rubra)	Heat-clearing and blood-cooling herb	2
4	Mahuang (Ephedrae Herba)	Wind-cold dispersing herb	6	20	Dingxiang (Caryophylli Flos)	Interior-warming herb	2
5	Yanhusuo (Corydalis Rhizoma)	Blood-activating and pain-relieving herb	5	21	Kuandonghua (Farfarae Flos)	Cough-relieving and asthma-calming herb	2
6	Baibu (Stemonae Radix)	Cough-relieving and asthma-calming herb	1	22	Guizhi (Cinnamomi Ramulus)	Wind-cold dispersing herb	2
7	Bingpian (Borneolum Syntheticum)	Orifices-opening herb	4	23	Jixiangcao (Reineckea carnea)	Heat-clearing and toxin-removing herb	2
8	Gancao (Glycyrrhizae Radix et Rhizoma)	Qi-tonifying herb	4	24	Niuhuang (Bovis Calculus)	Wind-calming and spasm-relieving herb	2
9	Rougui (Cinnamomi Cortex)	Interior-warming herb	4	25	Qianhu (Peucedani Radix)	Heat-clearing and phlegm-dissolving herb	2
10	Shengjiang (Zingiberis Rhizoma Recens)	Wind-cold dispersing herb	4	26	Taoren (Persicae Semen)	Blood-activating and menstruation-regulating herb	2
11	Aidicao (Herba Ardisiae Japonicae)	Cough-relieving and asthma-calming herb	4	27	Wuzhuyu (Euodiae Fructus)	Interior-warming herb	2
12	Banxia (Pinelliae Rhizoma)	Warmly resolving cold-phlegm herb	3	28	Xiangfuzi (Cyperi Rhizoma)	Qi-regulating herb	2
13	Gansui (Kansui Radix)	Expelling water retention with drastic purgative herb	3	29	Jinyinhua (Lonicerae Japonicae Flos)	Heat-clearing and toxin-removing herb	2
14	Ganjiang (Zingiberis Rhizoma)	Interior-warming herb	3	30	Yuxingcao (Houttuyniae Herba)	Heat-clearing and toxin-removing herb	2
15	Houpo (Magnoliae Officinalis Cortex)	Dampness-resolving herb	3	31	Zhiqiao (Aurantii Fructus)	Qi-regulating herb	2
16	Huangqin (Scutellariae Radix)	Heat-clearing and dampness-drying herb	3	32	Ziwan (Asteris Radix et Rhizoma)	Cough-relieving and asthma-calming herb	2

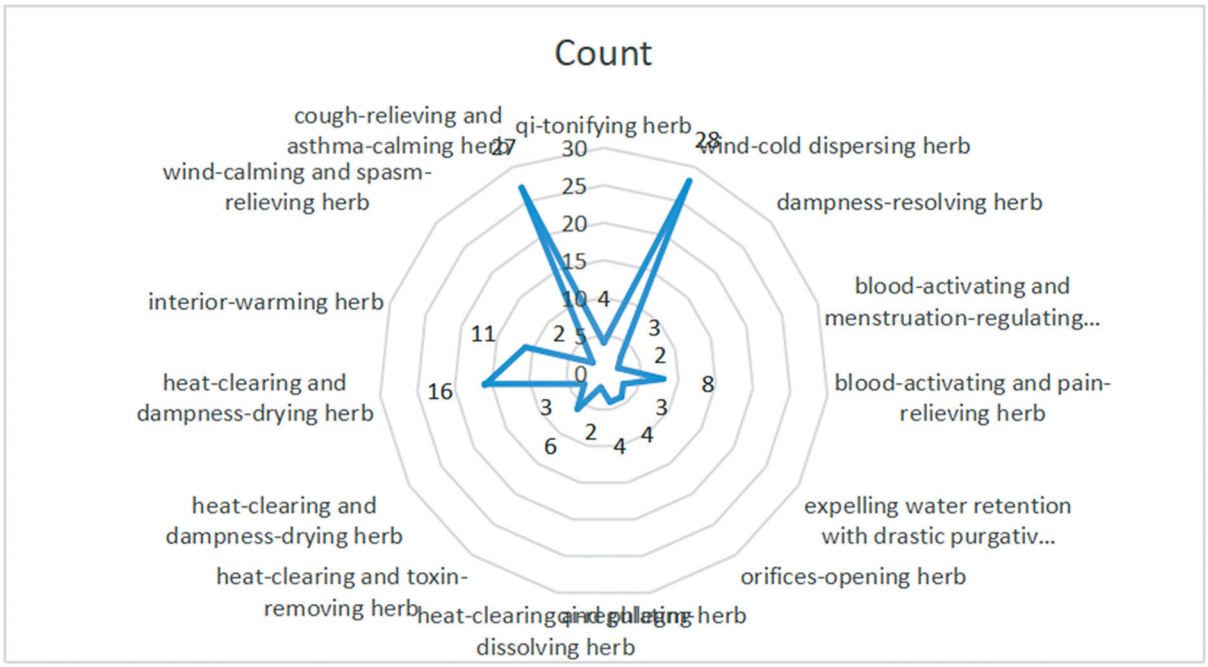

Fig. 2 Herb efficacy radar map.

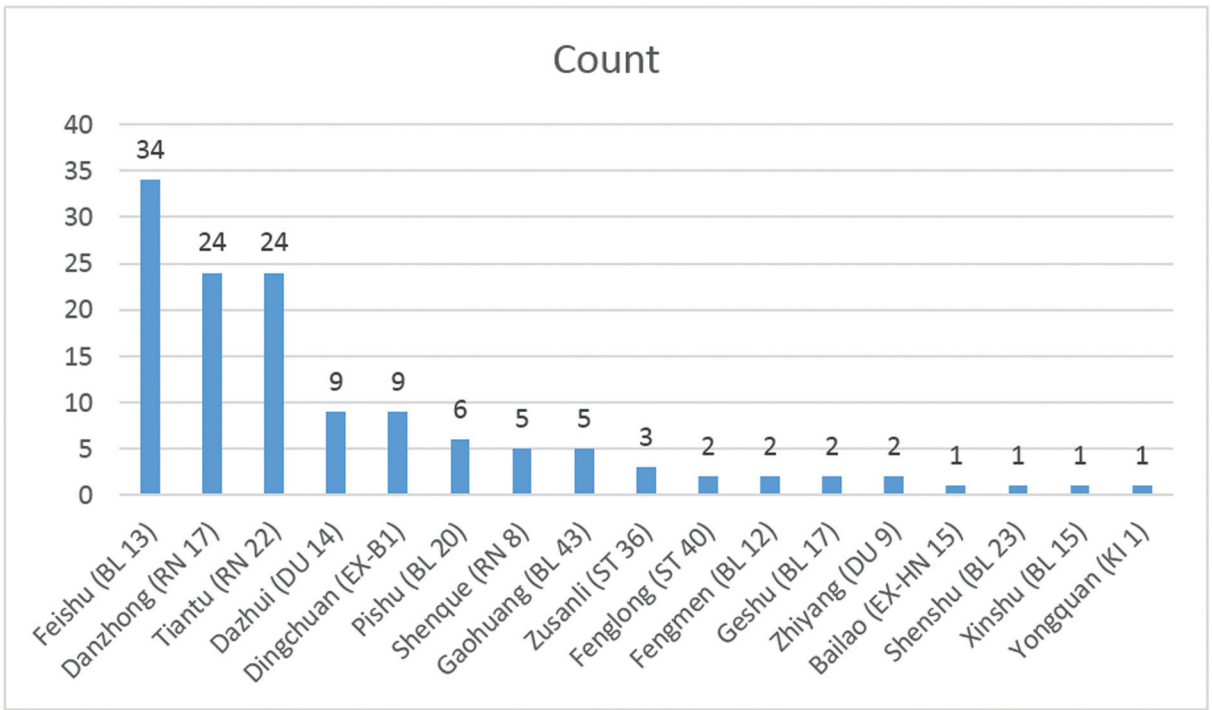

Fig. 3 Analysis of acupoint selection.

herbs were the most common. It was consistent with the pathogenesis of pediatric acute bronchitis, which was mostly due to the invasion of wind-cold pathogens and the abnormal dispersion of lung qi. (2) Selection of acupoints: Feishu (BL 13), Danzhong (RN 17), and Tiantu (RN 22) were the main acupoints, of which Feishu (BL 13) belongs to the bladder meridian of foot Taiyang, which is one of the Back-Shu acupoints along the circulation route of bladder meridian of foot Taiyang and is a conventional acupoint for treating lung diseases such as cold, cough, and asthma. Danzhong (RN 17) and Tiantu (RN 22) belongs to the conception vessel, which is located in the anterior midline and has good

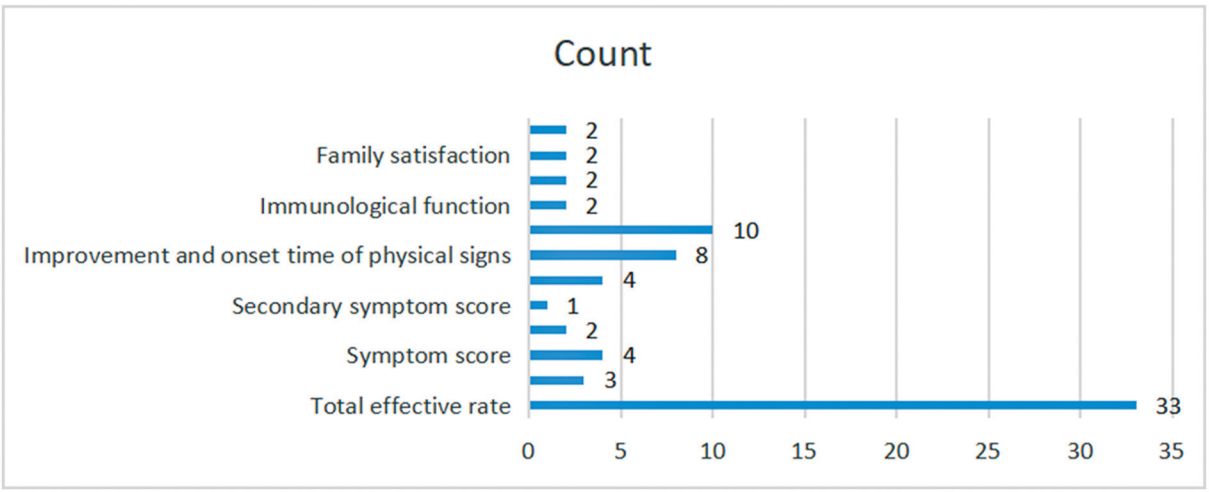

Fig. 4 Analysis of efficacy indicator selection.

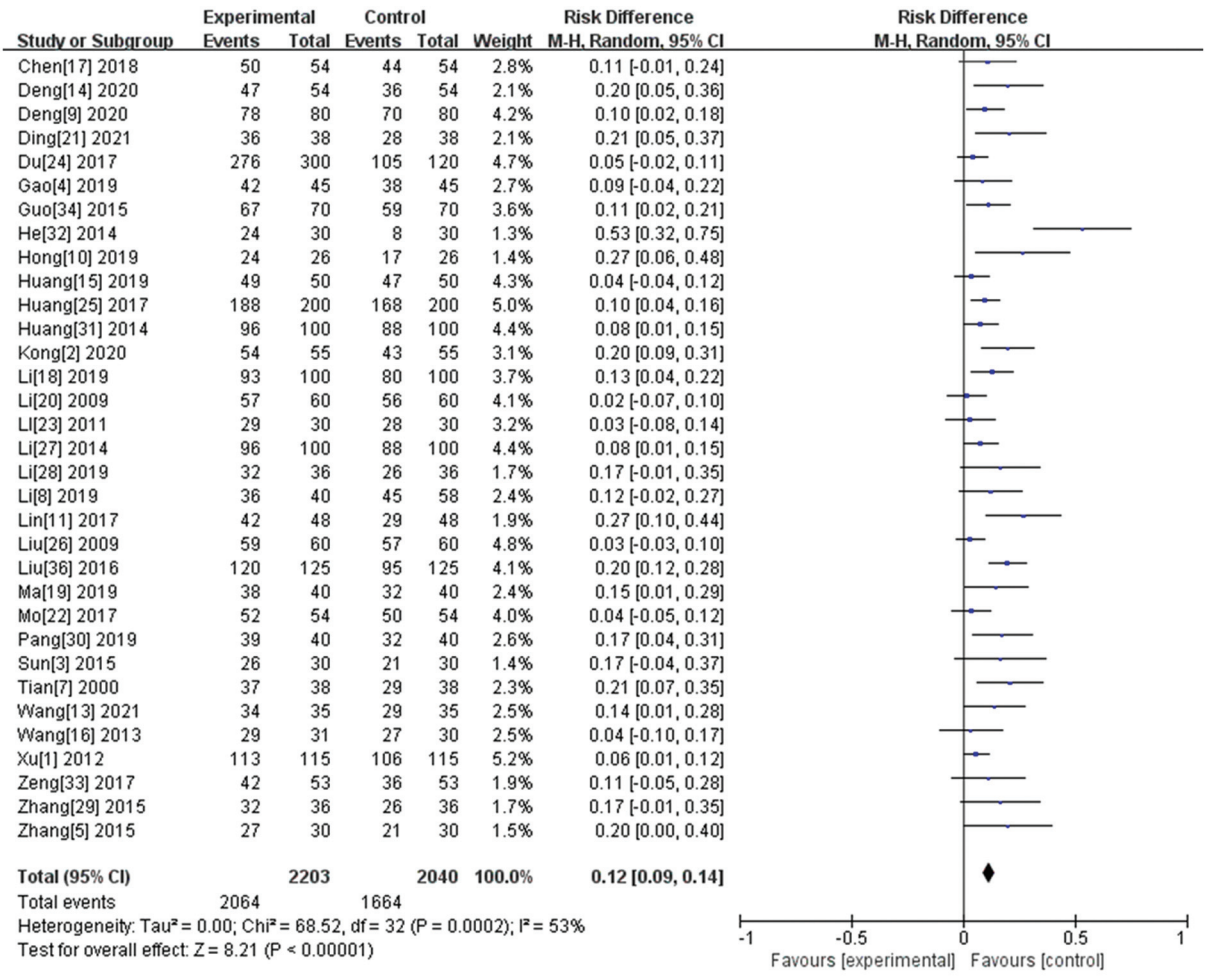

Fig. 5 Meta-analysis of the efficacy of the included study.

curative effects on panting, dysphagia, chest pain, scanty lactation, palpitations, dysphoria, and cough. (3) Construction of the core: according to previous studies, it was found that the efficacy indicators of pediatric acute bronchitis were mostly effective rate, improvement of main symptoms/signs, onset time, disappearance time, TCM syndrome score and symptom score, etc.

According to the results of the data mining, the meta-analysis of the core indicators was further performed. It was found that the therapeutic effect of Chinese herbs acupoint

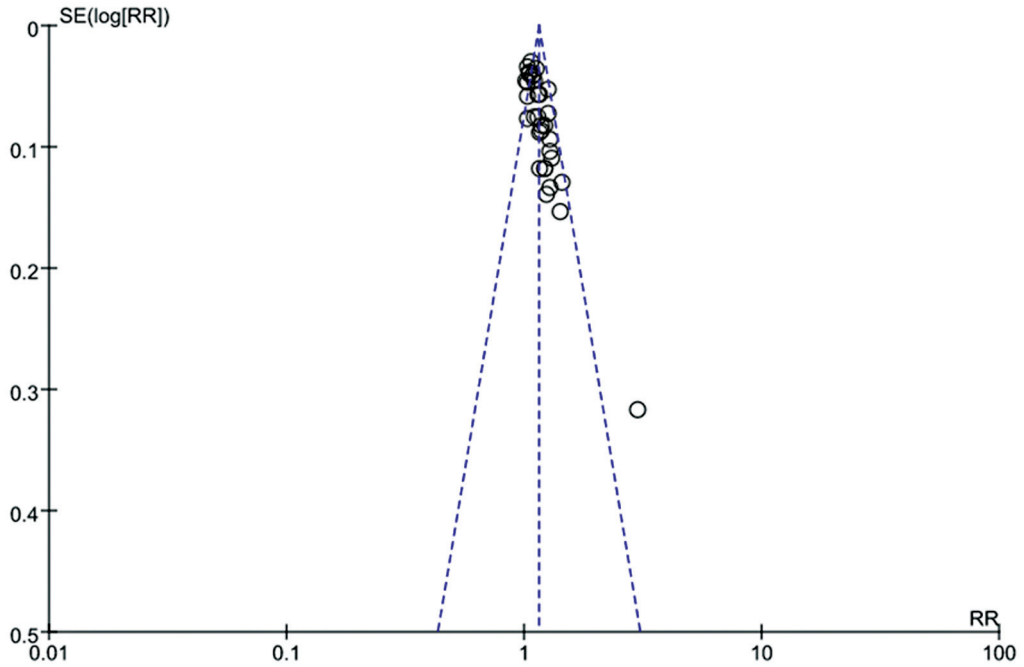

Fig. 6 Funnel plot of publication bias.

application therapy combined with Western medicine was accurate. For example, the total effective rate was 0.11 (0.08, 0.13) ($Z = 8.64$, $p < 0.00001$) after removing the heterotypicity. The symptoms of cough, expectoration, and asthma were not analyzed by meta-analysis because of obvious heterogeneity. The analysis of comprehensive results showed that when the effective rate was taken as the evaluation index of efficacy, the efficacy of combined acupoint application therapy was better than that of nonacupoint application therapy group. Regarding cough, expectoration, asthma, and other symptoms as the end point of efficacy evaluation, this study failed to reach superior conclusion through meta-analysis. In view of the fact that most of the clinical studies included in the study use a single endpoint as the main outcome indicator, and for the clinical studies of endpoint outcome indicators, the efficacy evaluation method is different from the traditional single endpoint evaluation method, so in future studies, it is better to further explore the outcome evaluation of multiple endpoints and composite endpoints.

In this study, the following problems were also found in the related TCM clinical randomized controlled trials in this field: (1) Literature quality evaluation: almost all studies only described randomized methods, but there was no hint of blinding, allocation concealment, etc., indicating that it lacks reasonable and standardized trial design in the field of TCM randomized controlled trials. (2) Efficacy evaluation indicators: according to previous studies, the core indicator field was constructed, and it was found that most of the efficacy indicators for the evaluation of pediatric acute bronchitis were effective rate, main symptoms/signs improvement, onset time, disappearance time, TCM syndrome score and symptom score, etc., which had obvious TCM characteristics. However, these "composite indicators" were poorly defined, and the judgment criteria were vague or subjective and unable to be quantified. The subjective judgment of doctors or patients could not provide a reference for other researchers. Only some studies reported objective physical and chemical examinations such as lung function and immune function, which made it easy to exaggerate the study results.[3] (3) Adverse reaction report: only a few reports have reported adverse reactions, which makes the results of the systematic review unable to clarify the safety of Chinese medicine.

CRediT Authorship Contribution Statement

Z.Q. was responsible for conceptualization, data curation, formal analysis, investigation, methodology, visualization, writing—original draft. R.L. and J.D. were responsible for methodology, writing—review and editing. Z.J. was responsible for funding acquisition, supervision, writing—review and editing. R.G. was responsible for project administration, resources, and writing—review and editing.

Funding

This work was supported by the General Project of the National Natural Science Foundation of China (82074584) National Chinese Medicine Innovative Key Professionals Improvement Program ([2019] No.128)

Conflict of Interest

The authors declare no conflict of interest.

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