REVIEW ARTICLE

Evaluation of Clinical Efficacy of Acupuncture and Moxibustion for Asthma: Systematic Review and Meta-Analysis

Qiao Wang, MS; Yufeng Xie, MS; Fang Dong, MS; Longjian Zhou, MS; Bo An, PhD; Jing Wang, PhD; Bi Chen, PhD; Nenggui Xu, PhD; Qibiao Wu, PhD

ABSTRACT

Objective • The effectiveness of manual acupuncture for treating bronchial asthma is still debatable and broad, and the effects of different acupuncture points, treatment durations, or illness trajectories have never been rigorously assessed. The objective of this revised systematic review and subgroup meta-analysis of randomized controlled trials (RCTs) is to ascertain the clinical efficacy of manual acupuncture on bronchial asthma and whether these effects varied depending on the acupuncture points, length of treatment, or course of the disease.

Materials and methods • PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria were followed for creating a systematic review and meta-analysis. From the beginning through March 25, 2022, six electronic databases were checked. For the treatment of asthma, all RCTs contrasting acupuncture therapy along with conventional treatment against conventional treatment alone were chosen. The information was examined using Review Manager version 5.3 and Comprehensive Meta-Analysis version 3. Clinical efficacy (including the effective rate and the recurrence rate) was the primary outcome, and pulmonary function (including FEV1%, PEF) and The secondary results were T-lymphocyte immunity (containing CD3+, CD4+, and CD8+). Based on the acupuncture points, length of therapy, and nature of the condition, subgroup analyses were carried out.

Results • There were a total of 21 RCTs that enrolled 2510 individuals. According to the meta-findings, analysis's manual acupuncture in addition to conventional treatment significantly increased the effective rate when compared to conventional treatment alone [OR = 5.14 95% CI 3.58-7.38, $P < .00001$], lung functions [FEV1% (MD = 6.18, 95% CI 2.40-9.96, $P = .001$) and PEF (MD = 0.45 95% CI 0.18-0.73, $P = .001$)], immune functions [CD3+ T lymphocytes (MD = 7.55 95% CI 6.55-8.56, $P < .00001$), CD4+ T-lymphocytes (MD = 5.11 95% CI 4.09-6.13, $P < .00001$), T-lymphocyte CD8+ (MD = -0.37.11 95% CI -3.62--2.51, $P < .00001$)] and noteworthy reduction in the recurrence rate (OR = 0.19 95% CI 0.10-0.38, $P < .00001$). Results from the subgroup analysis were consistent.

Conclusion • Manual acupuncture combined with Western Medicine is more effective than conventional treatment alone for bronchial asthma. Combination therapy can significantly improve clinical efficacy, lung function, and immune function while reducing the relapse rate. But to further support the results of this investigation, high-quality RCTs with long-term outcomes are still required, taking into account the inherent limitations of the included studies.

Registration number: PROSPERO (no. CRD42022357805) (https://www.crd.york.ac.uk/prospero/). (*Altern Ther Health Med.* 2024;30(10):119-127).

Qiao Wang, MS; Yufeng Xie, MS; Bo An, PhD; Jing Wang, PhD; Bi Chen, PhD; Qibiao Wu, PhD; Faculty of Chinese Medicine, Macau University of Science and Technology, State Key Laboratory of Quality Research in Chinese Medicines, Faculty of Chinese Medicine; **Qiao Wang, PhD; Yufeng Xie, MS;** Department of Acupuncture and Moxibustion, Shenzhen Hospital of Guangzhou University of Chinese Medicine, Shenzhen, China; **Fang Dong, MS;** Medical Records and Statistics Room, Shenzhen Hospital of Guangzhou University of Chinese Medicine; **Longjian Zhou, MS;** Respiratory department, Shenzhen Hospital of Guangzhou University of Chinese Medicine; **Nenggui Xu, PhD;** South China Research Center for Acupuncture and Moxibustion, Medical College of Acupuncture-Moxibustion and Rehabilitation, Guangzhou University of Chinese Medicine, Guangzhou, Guangdong Province, China.

Corresponding author: Qibiao Wu, PhD
E-mail: qbwu@must.edu.mo
Corresponding author: Nenggui Xu, PhD
E-mail: ngxu8018@gzucm.edu.cn

INTRODUCTION

One of the principal non-communicable diseases, bronchial asthma is still the most prevalent chronic condition in children.[1,2] It is caused by genetic constitution plus external environmental stimulation, such as inhalation of allergens and climatic mutations.[3,4] Different degrees of wheezing, shortness of breath, cough, progressive breathing difficulties, and blurred consciousness are common asthma symptoms.[5] According to the report of the Global Asthma Prevention and Treatment Initiative in 2022 (https://ginasthma.org/gina-reports/), mild continuous asthma patients usually rely on short-acting β2-receptor agonist (SABA) to relieve symptoms, which may lead to over-dependence. Overuse of glucocorticoids and bronchodilators is linked to a rise in adverse outcomes like COPD, ACOS, and even fatalities.[6] The medication method varies with the severity of the disease and whether it is combined with other comorbidities.[7] β_2-agonists alone,[8] low-dose inhaled corticosteroids,[9] low-dose ICS/LABA, and comprehensive Western medicine treatment[10] are often used for asthma treatment, but their side effects tend to be drug-dependent and side effects. The persistence and recurrence of asthma hurts patient's quality of life and raise the cost of treatment. Asthma therapy with acupuncture and moxibustion involves a complicated process that is regulated by several different elements. Patients with asthma who receive various forms of acupuncture and moxibustion can lower their serum eosinophil levels. Regulate the contents of IgG, IL-6, TNF, IFN, TGF, and IGF-I. The improvement of the above indexes indicates that acupuncture treatment for asthma is not the result of a single factor. Therefore, in clinical practice, only observing a single index to judge its efficacy is not consistent with the comprehensive (Overall bidirectional/benign) regulatory mechanism of acupuncture treatment for diseases. Due to the modern sciences' and technologies' rapid advancement, it is necessary to apply modern scientific and technological means to further clarify its mechanism of action. This will advance the use of moxibustion and acupuncture in asthma treatment.[44]

Clinically, asthma can be categorized according to age, triggers, inflammatory features of the respiratory tract, and clinical symptoms. It can also be classified according to the acute and chronic staging of asthma and according to the severity of asthma onset. Efficacy, relapse rate, lung function, and T-lymphatic immunity were selected as outcome indicators. These indices were chosen because asthma control is considered separately from symptoms and lung function.[11] Lung function is mainly useful in the evaluation of the increased risk of asthma attacks and prognosis.[12] The proportion of forced vital capacity that is represented by the forced expiratory volume in the first second (FEV1%; FEV1/FVC) is used by the National Asthma Education and Prevention Program to classify the severity of asthma. The purpose of evaluating PEF is to assess triggers, airway patency, and response to treatment.[13] T-lymphocytes can regulate the body's immune activity, maintain tolerance to autoantigens, and hinder the development of autoimmune diseases.[14]

Acupuncture is recommended for a wide range of clinical conditions in China and is an important part of complementary and alternative medicine in Western countries.[15] The least confusing method of treatment is manual acupuncture, and it is currently commonly used to treat various stages and degrees of asthma as well as varied asthma severities. Although many desirable case reports examining the efficacy and safety of acupuncture have been documented,[16] few studies have estimated the efficacy, the effect on pulmonary function, and immune factors of manual acupuncture therapy. Manual acupuncture reduces other acupuncture techniques to stimulate acupuncture points and places more emphasis on reinforcing and reducing techniques to dredge the meridians and regulate the viscera. According to recent studies, the negative effects of existing traditional asthma treatments, like long-term glucocorticoid use and beta2 agonists, can be avoided.[17] A persistent inflammatory response of the airways known as bronchial asthma involves a range of cells and cellular constituents, resulting in airway hyper-responsiveness and extensive and variable reversible airflow limitation. At present, the main method of modern medical treatment for acute exacerbation of bronchial asthma is the inhalation of β2 receptor agonist to dilate the bronchus. There are many disadvantages, such as recurrent attacks, and repeated drug use. Long-term use is easily tolerable and aggravates asthma symptoms, resulting in greater adverse responses.[43] Moxibustion and acupuncture have both been used for a very long time to treat bronchial asthma, with definite efficacy, and no side effects, and are widely used in clinical practice.

According to a few meta-analyses, acupuncture is more successful at treating asthma than sham acupuncture, other acupuncture techniques, and medication therapy alone.[3,16,18] A different meta-analysis failed to provide evidence that acupuncture can lessen asthma.[19] Therefore, whether manual acupuncture is useful for treating bronchial asthma is still debatable. Additionally, the effects of manual acupuncture vary depending on the acupuncture sites used, the length of the therapy, or the progression of the ailment. To provide evidence for clinical decision-making, this updated systematic review and subgroup meta-analysis of randomized controlled trials (RCTs) sought to ascertain the clinical effects of manual acupuncture on bronchial asthma and whether those effects varied depending on the acupuncture points, treatment durations, or disease course.

MATERIALS AND METHODS

Six popular databases were looked up between the database's creation and March 25, 2022, per Preferred Reported Items for Systematic Review and Meta-analysis (PRISMA) guidelines.[20] RevMan version 5.3 and Comprehensive Meta-Analysis version 3 were used for data synthesis and analysis.

Study Types

RCTs investigated acupuncture therapy and without regard to publication status, blinding, or language, combined treatment (manual acupuncture combined with conventional treatment) was compared to conventional treatment alone for the management of asthma, and outcomes covering efficacy, pulmonary function, and immunological variables were chosen. Animal studies, reviews, case reports, and non-randomized trials are all excluded.

Types of participants

Inclusion criteria. The RCTs considered in this research fulfilled the following requirements: (a) Patient characteristics: All the patients met the diagnostic criteria of asthma. The onset age was between 6 months and 70 years old. There were no restrictions on the time of onset, disease severity, or symptom phenotype. (b) Intervention characteristics: Patients in the experimental group received normal Western medical care whereas those in the control group received just manual acupuncture (either applied alone or in conjunction with Western medicine). Additionally, western medicine treatment between the two groups should be similar and comparable. (c) Outcome measures: Efficacy and recurrence rate were the primary outcomes. The percentage of forced vital capacity was explained by pulmonary function, which includes forced expiratory volume in the first second (FEV1%-FEV1/FVC), and peak expiratory flow (PEF). Immune factors (CD3+, CD4+, CD8+) were the secondary outcomes.

Exclusion Criteria. Studies were disqualified if they fell under one of the following categories: (a) Manual acupuncture treatment excludes electro-acupuncture, auricular acupuncture, scalp acupuncture, moxibustion, cupping, acupoint injection and other acupuncture therapies; (b) The main supplemental treatment therapy (either used alone or in conjunction with western medicine) for the treatment of asthma is manual acupuncture; different western medicine therapies are not compared in this intervention; (c) Intervention is not conventional western medicine alone, combined with oral Chinese medicine as well; (d) Studies are nonrandomized controlled trials (non-RCTs), including cells or animals studies, randomized crossover trials; (e) Literature with incomplete outcome indicators, repeatedly detected or republished papers, review papers and graduation papers, literature like conference unable to obtain the full text; (f) The sham acupuncture technique either involved piercing the skin at various acupoints or did not involve piercing the skin at all while choosing the identical acupoints for the control group.

Types of Interventions

The manual acupuncture technique was used on the treatment group (either used alone or combined with conventional treatment). The control group received just traditional medical care (including inhaled corticosteroids, β2-agonists, anticholinergic drugs, leukotriene receptor antagonists, aminophylline, oxygen therapy, antibiotics, and other supportive treatment). Interventions except manual acupuncture are similar between the two groups.

Types of outcome measures

Clinical efficacy, which includes both effectiveness and recurrence rates, is the main outcome variable. Pulmonary functions, such as forced expiratory volume in one second, which represents a fraction of forced vital capacity, are the secondary outcome variables (FEV1%, FEV1/FVC), and peak expiratory flow (PEF), immune functions (CD3+, CD4+, CD8+).

The efficacy evaluation of asthma should be based on the symptoms, lung functions, etc. Asthma evaluation is a key link in asthma control. It is evaluated through the following four aspects: the first is symptoms. The second is the patient's lung function. The third is asthma control test evaluation. The fourth is the measurement of airway nitric oxide. Symptoms: the symptoms of asthma patients, such as coughing, wheezing, shortness of breath, or pressure in the chest can appear day and night. However, the patients often wake up in the middle of the night because of the above symptoms, which often indicate that asthma is aggravated. In terms of lung function, the ventilation function indicators used in the diagnosis and evaluation of asthma mainly include FEV1% and PEF. FEV1% and PEF can reflect the severity of airway obstruction and are the most commonly used evaluation indicators to objectively judge asthma. The peak flow meter is convenient to carry and easy to operate. Patients can self-detect PEF at home and adjust drugs in time according to the detection results. The third is the asthma control test, which is often called the act questionnaire score. This is mainly about the daytime symptoms, nighttime symptoms, the application of relief drugs, and the self-evaluation of the control situation in the past four weeks. There are five questions. Patients need to score each question according to their actual situation. The final total score of all questions is considered. The more control, the higher the score, generally speaking, 20 to 25 points indicate good control, 16 to 19 points indicate poor control, and 5 to 15 points indicate poor control. The fourth is the exhaled nitric oxide. The monitoring of nitric oxide is what we routinely call NO. The determination of NO can be used to evaluate the level of airway inflammation and asthma control. The normal reference value of FeNO in adults is 4 to 25 parts per billion. When asthma is controlled, nitric oxide increases and can be decreased after glucocorticoid treatment.

Information sources

Two writers independently searched and retrieved information from the databases China National Knowledge Infrastructure, Wanfang Data, China Science Technology Journal Database, PubMed, EMBASE, and Web of Science. Between the database's creation and March 25, 2022, six databases were searched.

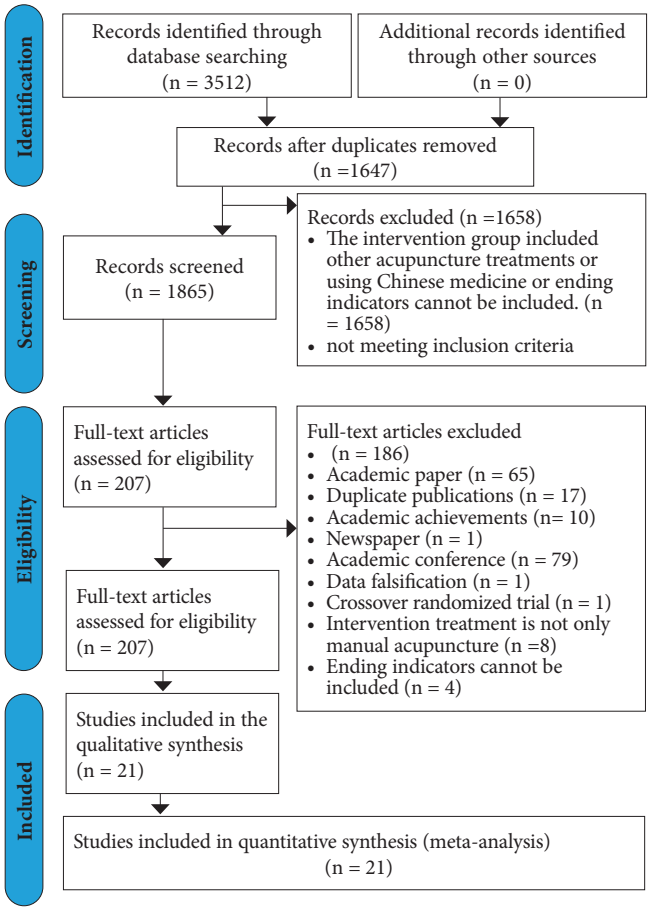
Search strategy

The Chinese descriptors from three databases (CNKI, Wanfang Database, Chongqing VIP), for example: ["Zhen Jiu/Zhen Ci (acupuncture)" OR "Shou Zhen (manual

acupuncture)" OR "Zhen (needle)" OR "Zhen Fa(acupuncture therapy)" OR "Zhong Yi Zhi Liao (Chinese treatment)" OR "Wai Zhi (external therapy)" OR "Zhen Yao Jie He (Combination of Acupuncture and Medicine) " OR "Zhong Xi Yi Jie He Zhi Liao (Integrated Traditional Chinese and Western Medicine Treatment)"] AND ["Xiao Chuan/Xiao Zheng/Chuan Zheng/Ke Chuan (Asthma/Bronchial Asthma/ Asthmatic)"]AND ["Lin Chuang Fen Xi/Lin Chuang Guan Cha/Lin Chuang Zheng Zhuang/Liao Xiao Guan Cha/Liao Xiao/Lin Chuang Yan Jiu/Ji Bing Kong Zhi (curative effect/ therapeutic efficacy)" OR "Fei Gong Neng (Pulmonary function)"].

The English descriptors from three databases (Web of Science, PubMed, Embase), for example ("Acupuncture" [MeSH] / "Manual acupuncture" / "Acupuncture therapy" / "Needling" / "External therapy" / "Adjunct therapy") and ("Asthma" [MeSH] / "Bronchial Asthma" / "Asthmatic") and ("Randomized controlled trial"[MeSH] / "Clinical trial" / "Randomized controlled study" / "Clinical study" / "Randomized pilot study"). In case the relevant RCTs were missed, the listings in the references were found manually. Any publication language or status may be included (Figure 1).

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram of the search



Study selection

Following the search strategy, two reviewers (Wang Q and An B) independently reviewed all of the candidate publications based on their titles and abstracts. Full-text studies were then retrieved for additional evaluation following the inclusion and exclusion criteria. Conflicts were arbitrated by a third party (Zhou LJ).

Data extraction

In the complying literature, the data were extracted and entered by two researchers (Dong F and Wang J). When available, intention-to-treat (ITT) outcomes were used. The extraction includes baseline characteristics, intervention features, and outcome indicator characteristics, per the summary of the studies in Table 1. The effectiveness, lung function, and immunological aspects of manual acupuncture for treating asthma are the main topics of this meta-analysis.

Risk of bias in individual studies

Two reviewers (Chen B and Xie YF) independently evaluated the risk of each RCT following the Cochrane Collaboration Network Risk of Bias Assessment Tool.[21] Conflicts were arbitrated by a third party. the blinding of participants and staff (performance bias); the blinding of outcome assessment (detection bias); the incomplete outcome data addressed (attrition bias); the selective reporting (reporting bias); and other types of bias. These seven components made up the particular assessment criteria. The risk of bias was labeled as "low," "unclear," or "high" for each criterion item.

Summary measures and data synthesis

The efficacy and recurrence data of the treatment were binary variables, and the statistical analysis was performed using RevMan version 5.3 and Comprehensive Meta-Analysis V3. There are continuous variables for the remaining outcome indicators. Therefore, odds ratios (ORs) and mean differences (MDs), along with their 95% confidence intervals, were used to express the data (CIs). The chi-squared test was used to measure heterogeneity. Data with clear heterogeneity ($P \leq .1$, $I^2 > 50\%$) and without obvious heterogeneity ($P > .1$, $I^2 < 50\%$) were analyzed using the fixed effects model combined analysis and the random-effects model, respectively.

Risk of bias across studies

Using RevMan version 5.3 software, forest plots, and funnel diagrams were created and examined. To carry out Begg's test, Comprehensive Meta-Analysis V3 was utilized, Egger's test, and fail-safe number analysis to investigate whether there was publication bias.

Additional analyses

Outcome indicators with high heterogeneity were subgroup-analyzed to determine the heterogeneity. For sensitivity analysis, the data were split up into various subgroups to ensure the reliability of the findings.

Table 1. The main features of the studies included in the meta-analysis

Reference	Patients type	Design	Sample size (T/C)	Age (years) (T/C)	Male/female ratio (T; C)	Disease duration (T; C)	Outcome measure(s)	Interventions		Acupuncture Features	Treatment duration
								Treatment group	Control group		
Wang, 1999[23]	BA	RCT	146 (74/72)	0.5-13	38/36; 43/29	2-10d	CE	MA+ CT	CT	EO	15-30min,Qd
Liu, 2002[24]	BA	RCT	80 (40/40)	4-11	21/19; 19/21	3-10d	CE, IF	MA+ CT	CT	EO	Qd,30days
Zhang, 2005[25]	BA	RCT	90 (60/30)	27.4±9.2/26.8±8.7	28/32; 14/16	10.7±8.9/11.2±8.6y	CE, PEF	MA+ CT	CT	ME+SCB	30min, Bid,10 days
Zhang, 2006[26]	BA	RCT	104(59/45)	44.5±13.9/44.2±14.6	15/44; 12/33	1-15y,+15y	CE,FEV1%,RS	MA+ CT	CT	EO	30min, Qd,10 days
Zhou, 2009[27]	BA	RCT	60 (30/30)	12-65,13-67	12/18; 14/16	1-25/1-33y	CE	MA+ CT	CT	CBO	30min,Qd,24 days
Wang, 2010[28]	BA	RCT	70 (35/35)	15-65,14-69	18/17; 17/18	2-15/2-13y	CE,FEV1%	MA+ CT	CT	MCB+SE	20-30min,Qd,10 days
Han, 2012[29]	BA	RCT	577(289/28)	42.1±17.6/43.5±16.4	174/115; 169/119	18.7±10.4/19.2±9.8y	FEV1%,PEF	MA+ CT	CT	EO	60min,Once
Lv, 2012[30]	BA	RCT	90 (30/30)	15-68,16-67	13/17	1-35y	CE	MA+ CT	CT	EO	30min,Qd,10 days
Jia, 2013[31]	BA	RCT	98 (48/50)	48.1±12.8/46.9±12.6	28/20; 29/21	8.7±3.6/8.4±3.3y	RS	MA+CT	CT	CBO	20min,Qd,90 days
Tang, 2014[32]	BA	RCT	90 (30/20)	25±21/40±18	16/14;13/7	8±7.2/7±6y	CE,PEF	MA+CT	CT	ME+SCB	30min,Qod,36 days
Xie 2015[33]	BA	RCT	180 (90/90)	40±12	50/40; 47/43	9.2±5.0/9.2±5.2y	CE,FEV1%,IF	MA	CT	MCB+SE	30min,Qod,28 days
Zhu, 2016[34]	CVA	RCT	120 (40/40)	36.78±2.75/38.05±3.25	25/15; 23/17	9.26±4.19/10.25±3.16m	CE	MA+CT	CT	ME+SCB	Qod,12 days
Li, 2016[35]	BA	RCT	60 (30/30)	55.57±13.67/57.3±13.35	12/18; 13/17	25.97±15.04/31.8±11.96d	CE,PEF	MA	CT	MCB+SE	30min,Qd,130 days
Zhang,2017[36]	CVA	RCT	80 (40/40)	37.98±2.98/36.95±3.15	25/15; 23/17	10.25±3.48/9.85±4.53m	CE	MA+CT	CT	MCB+SE	Qod,12 days
Zhang, 2017[17]	CVA	RCT	100 (50/50)	41.95±5.73/40.67±5.33	33/17; 30/20	16.08±5.01/15.98±4.88m	CE	MA	CT	ME+SCB	Qod,24 days
Qin, 2018C[38]	BA	RCT	128 (64/64)	47.94±8.03/48.23±8.16	37/27; 39/25	4.61±2.15/5.15±2.07y	CE,FEV1%,IF	MA+CT	CT	MCB+SE	30min,Qod,12 days
Wang, 2019[39]	BA	RCT	60 (30/30)	38.46±16.21/36.68±14.57	19/11; 17/13	11.78±6.54/10.53±6.24y	CE	MA+CT	CT	MCB+SE	30min,Qd,10 days
Liu, 2020[40]	CVA	RCT	80 (40/40)	40.22±4.31/40.37±4.84	24/16; 25/15	15.37±3.74/15.98±3.82m	CE	MA	CT	ME+SCB	Qod,24 days
He, 2020[41]	BA	RCT	94 (47/47)	38±5/37±5	25/22; 27/20	2.73±0.34/2.56±0.42y	CE,RS	MA+CT	CT	CBO	30min,Qod,12 days
Zhang, 2020[42]	BA	RCT	67 (34/33)	45.12±5.65/44.36±6.47	16/18; 18/15	Not reported	PEF	MA+CT	CT	MCB+SE	20min,Qd,10 days
Chen, 2020[43]	BA	RCT	156 (78/78)	56±4	43/35;41/37	5.61±1.21/5.63±1.23y	PEF,IF	MA+CT	CT	ME+SCB	30min,Qd,21 days

Abbreviations: BA, bronchial asthma; CVA, Cough Variant Asthma; T/C, Treatment group/Control group; CE, Clinical Effective; MA, Manual Acupuncture; CT, Conventional treatment (including inhaled corticosteroids, β_2-agonists, anticholinergic drugs, leukotriene receptor antagonists, aminophylline, oxygen therapy, antibiotics, and other supportive treatment); PEF, Peak Expiratory Flow; FEV1%, FEV1/FVC, Forced expiratory volume in the first second accounted for the proportion of forced vital capacity; Immune Factors, CD3+, CD4+, CD8+; RS, Recurrence Situation; EO, Extremities Only; CBO, Chest and back only; ME+SCB, Extremities as the main + Chest and back as the secondary; MCB+SE, Chest and back as the main +Extremities as the secondary; RCT, randomized controlled trial.

RESULTS

Study selection

1647 duplicate records were removed, leaving 3512 records in total. Title and abstract criteria were used to eliminate a further 1865 publications, which included interventions involving other acupuncture treatments, herbal treatments, and outcome indicators that were not consistent with the target setting. Further eligibility evaluations of the 207 candidate articles' entire texts were conducted. The following factors led to the exclusion of 186 articles: scholarly papers (n = 65), duplicate publications (n = 17), scholarly achievements (n = 10), newspapers (n = 1), academic conferences (n = 79), data falsification (n = 1), cross-randomized trials (n = 1), interventions that were not only manual acupuncture (n = 8), ending indicators cannot be included (n = 4). Finally, the meta-analysis included 21 trials. (Figure 1).

Study Characteristics

Table 1 provides an overview of the 21 included studies' features. There were 2510 patients engaged in all, 1238 of whom were in the experimental class while the remainder were in the control category. Twenty-one Chinese studies. The years of publication ranged from 1999 to 2020. The patient sample size was focused on 60 to 577 individuals. The study population was spread across infants, adolescents, and adults. The control group was not included in the sham acupuncture therapy combined with Western medicine. Manual acupuncture was categorized as extremity only, chest and back only, extremities mainly plus chest and back second, and chest and back mainly plus extremities second. At the beginning of each study, there were no notable differences.

According to the different phenotypes, all patients in the included literature had a diagnosis of asthma, 19 RCTs on bronchial asthma, and 4 RCTs on cough variant asthma. Seven articles had a disease duration of fewer than 2 years, 1 article had an unknown disease duration, and 13 articles had a disease duration of more than 2 years. There were 17 articles with fewer than 30 treatments and 4 articles with more than 30 treatments. In terms of intervention characteristics, Manual acupuncture mixed with traditional Western medical care was compared to traditional Western medical treatment in 17 intervention therapies. There were 4 interventions in the literature comparing manual acupuncture alone with Western medicine. Eleven articles reported the Qd acupuncture frequency, 8 articles reported the Qod acupuncture frequency, 1 article reported the Bid acupuncture frequency and 1 article reported the acupuncture frequency immediately. The outcome indicators were efficacy, including relapse events involved in 18 articles, lung function involved in FEV1% (FEV1/FVC), PEF in 10 articles, and immune factors in 4 articles.

Risk of bias and methodological quality

Each included trial's methodological quality was evaluated to create a risk of bias graph, and the risk of bias summary is depicted in Figures 2 and 3. Most of the included studies were of low to moderate quality. Two trials failed to clearly describe the method of random allocation. In 6 trials, there was allocation concealment, and the allocation method was determined by the order of treatment or parity of participants. Five trials described exclusions and missing cases from the treatment process. The article omitted to mention biased reporting and other hazards, such as selective reporting. In conclusion, all of the included RCTs had complete data.

Figure 2. Risk of bias graph.

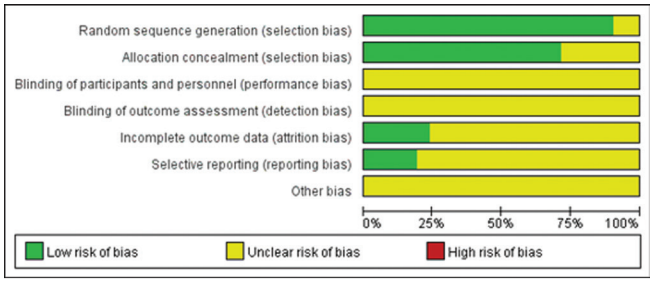


Figure 3. Risk of bias summary

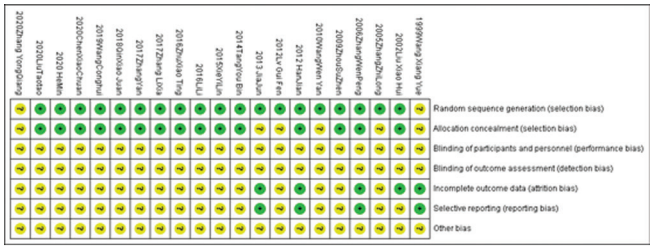


Figure 4. When compared to the control group, forest plots in the therapy group demonstrated a considerable increase in the effective rate.

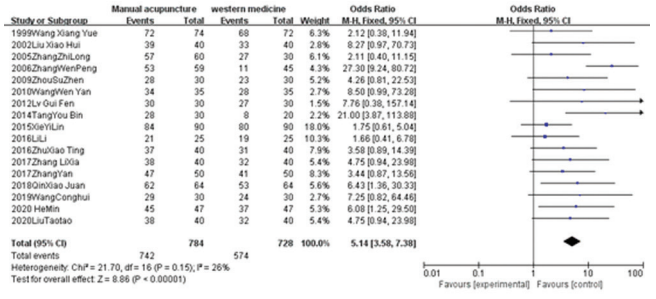


Figure 5. When compared to the control group, forest plots revealed a substantial decrease in recurrence episodes in the treatment group.

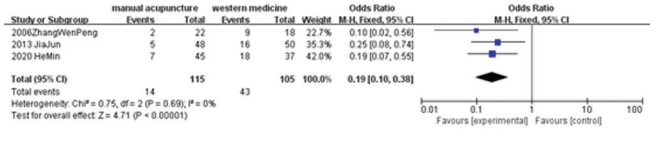


Figure 6. When compared to the control group, forest plots revealed a substantial increase in FEV1% in the intervention group.

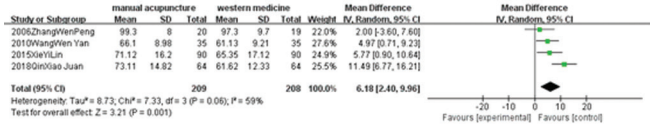
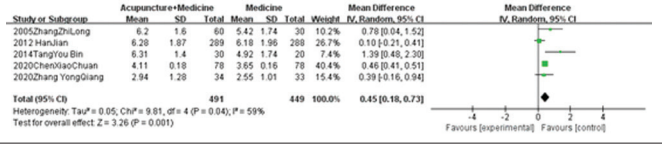


Figure 7. When compared to the control group, the treatment group's PEF on forest plots showed a substantial improvement.



Outcome measures

The effective rate. Seventeen trials[22-27,30,32-41] reported the effective rate of different interventions, The meta-findings analysis demonstrated that, when manual acupuncture was used in conjunction with Western medication to treat asthma, the effective rate was increased more than when Western medicine was used alone (OR = 5.14 95% CI 3.58-7.38, $P <$ .00001) (Figure 4). There was no discernible heterogeneity for this result, so a fixed-effects model was selected for analysis ($I^2 = 26\%$, $I^2 < 50\%$)

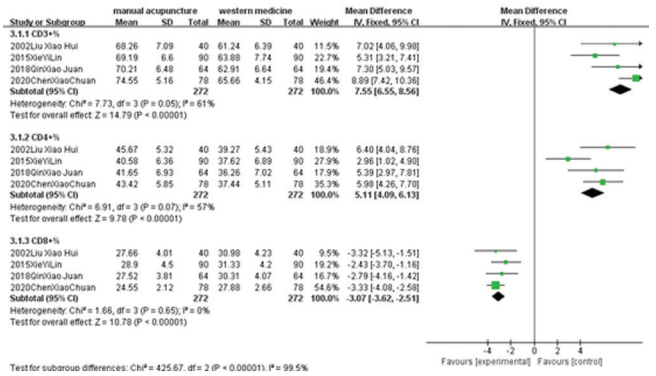
The recurrence rate. Summary estimates of 3[25,30,40] Studies found that the intervention group had a significantly lower risk of recurrence occurrences than the control category (OR=0.19, 95% CI 0.10-0.38, $P <$ .00001) (Figure 5). For this result, there was homogeneity ($I^2 = 0\%$, $I^2 < 50\%$), and a fixed-effects model was applied.

FEV1%. Four studies[27,32,37] evaluated the effect of two interventions on lung function FEV1%. According to compiled data, manual acupuncture treatment increased FEV1% lung function compared to the control group (MD=6.18, 95%CI: 2.40-9.96, P = .001). A random-effects model was used since this outcome had significant heterogeneity ($I^2 = 59\%$). Through the research of the article, it was found that the source of heterogeneity lies in Qin Xiaojuan's article.[37] The reason was that the frequency of acupuncture intervention in this article was less than 10 times, while that in other articles was more than 10 times. Different times of acupuncture intervention may be the source of heterogeneity. After excluding this article, it was shown that the efficacy of manual acupuncture in improving lung function FEV1% after more than 10 times treatments was statistically significant compared to Western medicine for asthma patients with no heterogeneity ($I^2 = 0\%$).

PEF. Pooled data from five[24,28,31,41,42] In comparison to the control group, research revealed a statistically substantial rise in the ratio of individuals with better PEF in the manual acupuncture team (MD =0.45 95% CI 0.18-0.73, P = .001). The result was statistically heterogeneous (I^2=59%, I^2>50%), the reason for the high heterogeneity might be the different acupuncture features including acupoints location and acupuncture treatment duration. Through the research of the article, it was found that the source of heterogeneity lies in Han Jian's article.[28] In this article, the acupuncture point selection was a single point (Yuji), the duration of acupuncture was over half an hour, and the frequency of acupuncture was only once. After excluding this article, it was shown that the efficacy of manual acupuncture in improving lung function PEF was statistically significant compared to Western medicine for asthma patients with no heterogeneity (I^2 = 37%) (Figure 7).

CD3+, CD4+, and CD8+. Pooled data of four studies[24,33,38,43] showed that compared to Western medicine alone, manual acupuncture with Western medicine increased CD3+ (MD = 7.55 95% CI 6.55-8.56, $P <$ .00001), CD4+ (MD = 5.11 95% CI 4.09-6.13, $P <$ .00001) and decreased T-lymphocyte CD8+ (MD = -3.07 95% CI: -3.62--2.51, $P <$ .00001, $I^2 = 0\%$). There was a

Figure 8. When compared to the control group, forest plots in the intervention group exhibited a substantial increase in CD3+ and CD4+ and a decrease in CD8+.



lot of significant outcome heterogeneity between CD3+ (I^2 = 61%, $I^2 > 50\%$) and CD4+ ($I^2 = 57\%$, $I^2 > 50\%$), the conclusion of the sources of heterogeneity led to Xie's[33] treatment group in this article being manual acupuncture therapy alone for asthma. Unlike the other groups, which used manual acupuncture together with either Western treatment or neither, which may be related to the inconsistent intervention measures included in the literature. The results of the manual acupuncture group reduced CD8%+ were statistically significant ($P < .00001$) (Figure 8).

Publication bias

CMA version 3 software was used to perform the Begg's test, funnel plot analysis, EGGER test, and fail-safe analysis on different subgroup outcome measurements (Table 2). For efficacy as a primary outcome indicator, the fail-safe analysis indicated that the current results would change if an additional 235 articles were included. *P* values for Begg's test were .08 and .13 for the EGGER test. For recurrence events as a primary outcome indicator, the fail-safe analysis indicated that the current results would change if an additional 15 articles were included. P values for Begg's test were 1 and 0.32 for the EGGER test. For FEV1% as a secondary outcome indicator, the fail-safe analysis indicated that the current results would change if an additional 36 articles were included. P values for Begg's test were 0.73 and 0.56 for the EGGER test. For PEF, the fail-safe analysis indicated that the current results would change if an additional 92 articles were included. P values for Begg's test were 0.73 and 0.56 for the EGGER test. For the T-lymphocyte immune factor CD3+ as a secondary outcome indicator, the fail-safe analysis indicated that the current results would change if an additional 157 articles were included. P values for Begg's test were 0.73 and 0.59 for the EGGER test. For CD4+, the failed-safe analysis indicated that the current results would change if an additional 85 articles were included. *P* values for Begg's test were .73 and .27 for the EGGER test. For CD8+, fail-safe analysis indicates the current results would change if an additional 88 articles were included. *P* values for Begg's test were .73 and .74 for the EGGER test. Based on the above data and funnel plot analysis, the current results are robust with no publication bias (Figure 9).

Table 2. Bias analysis results of the selected literature

Items	begger		egger		fail-safe
	P value	*t* value	*P* value	*t* value	
curative effect events	.08	0.31	.13	1.62	235
recurrence events	1	0	.32	1.85	15
FEV1/FVC PRED%	.73	0.17	.56	0.69	36
PEF	.73	0.17	.56	0.69	92
CD3+	.73	0.17	.59	0.63	157
CD4+	.73	0.17	.27	1.5	85
CD8+	.73	-0.17	.74	0.37	88

Abbreviaitons: PEF, Peak Expiratory Flow; FEV1%, FEV1/FVC, Forced expiratory volume in the first second accounted for the proportion of forced vital capacity; Immune Factors, CD3+, CD4+, CD8+.

Figure 9. Funnel plots of curative effect events.

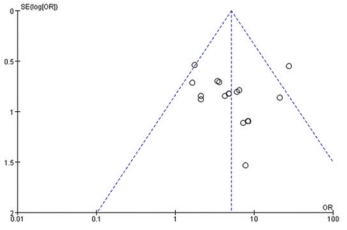


Table 3. Subgroup and sensitivity analyses

Total title	Outcome or subgroup	No. of Studies	Participants	Statistical method	Effect size	*P value*
Acupoint position	CBO	2	154	RR (fixed) 95% CI	1.22 [1.07, 1.38]	.003
				OR (fixed) 95% CI	5.14 [1.63, 16.16]	.005
				RD (fixed) 95% CI	0.17 [0.06, 0.27]	.002
	CBO	3	324	RR (fixed) 95% CI	1.16 [0.93, 1.44]	.20
				OR (fixed) 95% CI	8.53 [2.09, 34.74]	.003
				RD (fixed) 95% CI	0.23 [0.01, 0.45]	.04
	ME+SCB	5	400	RR (fixed) 95% CI	1.18 [1.03, 1.36]	.02
				OR (fixed) 95% CI	4.57 [2.26, 9.25]	<.00001
				RD (fixed) 95% CI	0.18 [0.05, 0.30]	.005
	MSB+SE	6	568	RR (fixed) 95% CI	1.13 [1.06, 1.19]	<.00001
				OR (fixed) 95% CI	3.14 [1.69, 5.83]	.0003
				RD (fixed) 95% CI	0.11 [0.06, 0.16]	<.00001
Intervention	MA	4	410	RR (fixed) 95% CI	1.10 [1.03, 1.19]	.006
				OR(fixed) 95% CI	2.45 [1.28, 4.68]	.007
				RD(fixed) 95% CI	0.09 [0.03, 0.15]	.005
	MA+CT	13	1036	RR(fixed) 95% CI	1.21 [1.15, 1.27]	<.00001
				OR(fixed) 95% CI	6.21 [3.85, 10.00]	<.00001
				RD(fixed) 95% CI	0.16 [0.13, 0.20]	<.00001
Disease duration	<2 years	7	616	RR(fixed) 95% CI	1.13 [1.07, 1.20]	<.00001
				OR(fixed) 95% CI	3.49 [1.95, 6.22]	<.00001
				RD(fixed) 95% CI	0.11 [0.06, 0.16]	<.00001
	>2years	10	830	RR(fixed) 95% CI	1.21 [1.15, 1.28]	<.00001
				OR(fixed) 95% CI	5.58 [3.37, 9.22]	<.00001
				RD(fixed) 95% CI	0.17 [0.12, 0.21]	<.00001
Numbers of treatment	≥30 times	4	326	RR(fixed) 95% CI	1.18 [1.08, 1.28]	.0002
				OR(fixed) 95% CI	4.59 [2.08, 10.13]	.0002
				RD(fixed) 95% CI	0.14 [0.08, 0.21]	<.0001
	<30 times	15	1120	RR(fixed) 95% CI	1.18 [1.13, 1.23]	<.00001
				OR(fixed) 95% CI	4.57 [2.97, 7.03]	<.00001
				RD(fixed) 95% CI	0.14 [0.11, 0.18]	<.00001

Abbreviaitons: EO, Extremities Only; CBO, Chest and back only; ME+SCB, Extremities as the main + Chest and back as the secondary; MCB+SE, Chest and back as the main +Extremities as the secondary.

Subgroup and sensitivity analyses

Based on four factors of the intervention, including the acupuncture points, the severity of the condition, and the number of manual acupuncture sessions, a sensitivity analysis of the stability of the clinical efficacy outcomes was carried out. According to the sensitivity analysis, the outcomes of the various perspective analyses were steady. (Table 3).

DISCUSSION

Asthma is of great importance to countries all over the world because of its high fatality rate and prevalence. Currently, many people are paying attention to acupuncture as an alternative intervention treatment for asthma. However, certain studies[14] do not support the effectiveness of acupuncture therapy for asthma. With a history spanning thousands of years, manual acupuncture is the most conventional kind of treatment among several acupuncture techniques. Manuel acupuncture is a treatment method that is less affected by other acupuncture interventions, and its curative effect can be seen intuitively. It can increase patient compliance and reduce adverse reactions. Pay more attention to the acupuncture method of "Bu" and "Xie" and be good at individualized treatment. There are studies on the treatment of asthma by acupuncture. Its interventions are not limited to manual acupuncture but also include electro-acupuncture, ear acupuncture, acupoint injection, cupping, Chinese medicine, and other therapies.[17] Alternatively, the research has age restrictions.[32] The intervention treatment of this research for asthma is based on the continuous updating of GINA's treatment strategy and clinical medication for asthma. The distinctions among manual acupuncture's effects on asthma, lung functioning, and T-lymphocyte immune factors and Western drug interventions have not been systematically evaluated.

Evaluation of efficacy and pulmonary function is still the main rough method of evaluation of asthma patients after treatment. There may be inconsistencies in the changes between symptoms and pulmonary function due to a variety of factors. Therefore, according to various airway patency circumstances, the impact of manual acupuncture on pulmonary function at various asthma severity levels was assessed. Lung function is mainly useful in the identification of an increased risk of asthma attacks.[12] Additionally, asthma is a diverse illness that involves chronic airway inflammation. It is crucial to research how manual acupuncture affects T-lymphocyte immunological components. The meta-analysis of 21 research revealed that in comparison to treatment using only Western medicine, manual acupuncture improved efficacy, reduced recurrent events, enhanced lung function, and positively affected T-lymphocyte immune factors.

There was heterogeneity in the total FEV1% (FEV1/FVC) and PEF index. We conducted a subgroup analysis to investigate the causes of heterogeneity, and the results revealed that there was heterogeneity within each cluster. The main result due to different asthma severities may be related to the patient's age, duration of onset, duration of treatment, and even the location of acupuncture. There was no heterogeneity in the clinical efficacy or recurrence event index. Although the statistical heterogeneity of the primary outcome was small, there could be clinical heterogeneity considering the risks of article quality, random methods, follow-up, publication bias, etc. The efficacy of treating asthma has a complex relationship with the intervention treatment. Therefore, in this paper, a sensitivity analysis of the intervention modality, location of acupuncture points, time of onset, and duration of treatment was conducted to determine the stability of manual acupuncture on the study results.

Our research has some drawbacks. (1) In addition, most studies do not directly report the HR and its 95% CI, and the data extracted from the charts may be biased from the real data, which may bias the combined results. (2) All of the included studies were RCT studies with a high probability of bias, which may affect the value of the conclusions of the meta-analysis.

The assessment findings of the clinical effectiveness of asthma are influenced by a variety of circumstances when manual acupuncture is used in conjunction with various Western medications to treat asthma. The assessment results of the clinical effectiveness of asthma will be influenced by different evaluation markers, new therapeutic acupoints and methodologies, and diverse test populations. Focusing on the current published literature on manual acupuncture combined with different Western medicines only has certain limitations. However, there was a correlation between medication strategy and asthma severity and duration of onset. However, it is not precise enough to guide clinical treatment. Furthermore, the effects of acupuncture on the timeliness of curative efficacy and the different types of asthma are also worthy of clinical observation and research as the main outcome indicators. In conclusion, manual acupuncture used in conjunction with Western medicine to treat asthma deserves to be promoted and used in clinical settings. Greater high-quality, large-sample RCTs will be required in the future to provide more proof.

CONCLUSIONS

This study showed that manual acupuncture combined with or without Western drugs had a positive effect on efficacy and relapse rate compared to Western medicine intervention alone. It has a beneficial effect on lung function in asthmatic patients. Elevated PEF and FEV1/FVC (FEV1%) in patients with airway obstruction and poor airway types. Manual acupuncture is involved in T-lymphocyte immunity, increases CD3+ and CD4+ of immune factors in serum, and decreases CD8+. This study provides a valuable complementary therapeutic regimen for the treatment of asthma. The results could, however, be further reviewed in the future based on further high-quality research because the included trials did not have good methodological quality and there were not enough high-quality double-blind studies with sizable sample sizes.

AUTHOR CONTRIBUTIONS

Wang Qiao: Conceptualization, Methodology, Investigation, Formal analysis, Writing an original draft. **Dong Fang and Wang Jing**: Investigation, Validation, Formal analysis, Writing and editing. **A Bo**: Validation, Investigation, Formal Analysis. **Chen Bi and Zhou Longjian**: Validation, Investigation. **Xie Yufeng**: Validation, Investigation. **Nenggui Xu and Qibiao Wu**: conception, method, validation, research, examination, review and editing of the manuscript, and supervision. There was no paper mill used, and all data were generated inside. All authors concur to accept responsibility for the integrity and accuracy of their work in all respects.

DATA AVAILABILITY

The data could be obtained by contacting the corresponding author.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

ACKNOWLEDGMENTS

The Science and Technology Planning Project of Guangdong Province, Macau SAR (No. 130/2017/A3, 0099/2018/A3, and 0098/2021/A2), and the Science and Technology Development Fund all provided funding for this project (2020B1212030008).

DECLARATION OF COMPETING INTEREST

No author has disclosed any conflicts of interest.

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