Effectiveness of Chinese herbal medicine Ping Chuan Ke Li for the management of mild/moderate persistent asthma

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Abstract

This study assessed the effectiveness and safety of Chinese herbal medicine Ping Chuan Ke Li (PCKL) for the treatment of patients with mild/moderate persistent asthma.

A total of 108 eligible patients with persistent asthma were included and were divided into a treatment group and a control group in this retrospective study. All 108 patients underwent oral montelukast. Additionally, subjects in the treatment group also received PCKL therapy. All patients in both groups were treated for a total of 1 month. The primary outcome of lung function was evaluated by the forced expiratory volume in one second (FEV₁) and FEV₁/forced vital capacity (FVC). The secondary outcome of quality of life was assessed by St. George's Respiratory Questionnaire (SGRQ). Moreover, adverse events (AEs) were also recorded in this study. All outcome measurements were assessed after 1-month treatment.

After 1-month treatment, patients in the treatment group did not demonstrate better outcome in the improvement of lung function, measured by FEV₁ ($P=.57$, table 2), and FEV₁/FVC ($P=.29$); and enhancement of quality of life, measured by SGRQ scale (total, $P=.37$; symptom, $P=.32$; activity, $P=.39$; impact, $P=.83$). In addition, no AEs differ between 2 groups.

The results of this study showed that Chinese herbal PCKL may not benefit for patients with mild/moderate persistent asthma after 1-month treatment.

Abbreviations: AEs = adverse events, CM = complementary medicine, FEV₁ = forced expiratory volume in one second, FVC = forced vital capacity, PCKL = Ping Chuan Ke Li, SGRQ = St. George's Respiratory Questionnaire.

Keywords: asthma, effectiveness, Ping Chuan Ke Li, safety

1. Introduction

Asthma is a heterogeneous respiratory disease, and it is associated with airway inflammation.^[1–3] Its symptoms mainly

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include difficult breath, triggers coughing, wheezing, and shortness of breath.^[4–5] Its prevalence rate was reported about 4.3%, with range from 0.7% to 21.0% around the world, while this figure was 1.24% in China.^[6–7] It has been reported about 240 million people suffer from this condition worldwide.^[8] It is estimated that this number will increase to 400 million by 2025.^[9]

Inhaled corticosteroids (ICS) are reported to the main option for asthma treatment; and are highly effective for managing the asthma symptoms and also help to reduce the risk of asthma-related exacerbations, hospitalizations and death.^[10–12] On the other hand, severe adverse events (AEs) with maintenance ICS treatment remain a tricky issue and it is also reported to be associated with poor asthma-related outcomes.^[13–14] Therefore, more effective and safety treatment options are still needed to be explored.

Complementary medicine (CM) is a 1 of the most powerful potential candidates. It has been reported CM may be utilized to treat this condition effectively.^[15–16] This kind of treatment option includes Chinese herbal medicine, acupuncture, moxibustion, yoga, exercise, and so on.^[17–23] Although these options are widely recommended by the physicians, there is still insufficient evidence to support CM for treating patients with asthma. Therefore, more evidence is urgently needed to be conducted in CM for asthma.

Ping Chuan Ke Li (PCKL) is reported to treat asthma in the past decades without severe AEs.^[17,24–25] However, limited data are available to support its effectiveness and safety of PCKL for treating patients with asthma presently, especially for persistent asthma. In this retrospective study, we explored the effectiveness and safety of PCKL for the treatment of patients with mild/moderate persistent asthma.

2. Methods

2.1. Study design

This study was approved by the Medical Ethics Committee of The First Affiliated Hospital of Heilongjiang University of Chinese Medicine. All the patient cases were selected between August 2015 and November 2017. Additionally, all patients provided written informed consent.

In this retrospective study, 108 eligible patients with mild/moderate persistent asthma were included. All these patients were equally assigned to a treatment group or a control group according to the different treatment schedule they received. Patients in the treatment group underwent oral montelukast plus PCKL therapy, while subjects in the control group received oral montelukast alone. All patients in both groups received a total of 1-month treatment. After treatment, the data of lung function and quality of life were analyzed for the assessment of PCKL therapy.

3. Patients

All included patients had diagnosed as mild to moderate persistent asthma. They aged between 22 and 68 years old. However, cases were excluded if they had serious organs diseases, allergy to the medication use, or took steroid drugs and antiallergic agents 1 month before this study. In additionally, cases were also excluded if they had insufficient data.

3.1. Treatment schedule

All 108 patients in both groups received montelukast orally every night, 10 mg daily for a total of 1 month. In addition, patients in the treatment group also underwent Chinese herbal medicine PCKL, 10 g/sachet, 2 sachets each time, twice daily for a total of 1 month.^[26] PCKL was provided by the Pharmacy of First Affiliated Hospital of Heilongjiang University of Chinese Medicine.

3.2. Outcome measurements

The primary outcome included lung function. It was assessed by forced expiratory volume in 1 second (FEV₁)^[27–28] and FEV₁/forced vital capacity (FVC).^[29–30] The secondary outcome was quality of life. It was evaluated by the tool of St. George's Respiratory Questionnaire (SGRQ).^[31] Additionally, any AEs were also documented in this retrospective study.

3.3. Statistical analysis

All data in this retrospective study were analyzed by the Statistical Package for the Social Sciences Software 17.0 (IBM Corp., Armonk, NY). The *t* test or Mann–Whitney rank sum test was utilized to analyze the continuous data, while Chi-square test was applied to analyze the discrete variables. *P* < .05 was regarded as statistically significant.

4. Results

A total of 108 eligible patients with mild/moderate persistent asthma were included in this retrospective study. All the outcome data and the variables of characteristics were analyzed in this study. As for characteristics, no significant differences were detected between 2 groups (Table 1).

Table 1

Comparison of characteristics of included patients between 2 groups.

Characteristics	Treatment group (n = 54)	Control group (n = 54)	P value
Mean age (year)	42.8 (11.2)	44.5 (12.4)	.45
Sex			
Male	32 (59.3)	35 (64.8)	.64
Female	22 (40.7)	19 (35.2)	—
Duration of asthma (year)	9.7 (3.3)	10.5 (2.9)	.18
Asthma category			
Mild	12 (22.2)	15 (27.8)	.46
Moderate	42 (78.8)	39 (72.2)	—
BMI (kg/m ²)	26.6 (2.9)	27.3 (3.1)	.23
Smoking history			
Smokers	18 (33.3)	25 (48.1)	.46
Non-smokers	34 (66.7)	29 (51.9)	.46
Previous medications, n (%)			
Ipratropium	31 (57.4)	27 (50.0)	.64
Albuterol	20 (37.0)	24 (44.4)	.52
Prednisone	29 (53.7)	26 (48.1)	.10
Fluticasone	18 (33.3)	21 (38.9)	.57
Zafirlukast	14 (25.9)	12 (22.2)	.57
Lung function			
FEV ₁ % (predicted)	67.3 (13.9)	69.1 (14.4)	.51
FEV ₁ /FVC(reduced),%predicted	2.8 (0.7)	2.6 (0.8)	.17
SGRQ			
Total	53.8 (13.6)	55.1 (14.5)	.63
Symptom	56.2 (12.9)	57.4 (13.3)	.62
Activity	51.0 (15.7)	52.8 (15.1)	.52
Impact	52.5 (16.0)	50.9 (16.8)	.61

Data are presented as mean ± standard deviation or number (%).

BMI = body mass index, FEV₁ = forced expiratory volume in 1 second, FVC = forced vital capacity, SGRQ = St. George's Respiratory Questionnaire.

After 1 month treatment, patients in the treatment group did not find greater effectiveness in lung function improvement, as measured by the FEV₁ (*P* = .57, Table 2), and FEV₁/FVC (*P* = .29, Table 2); as well as the quality of life enhancement, as measured by the SGRQ scale (total, *P* = .37; symptom, *P* = .32; activity, *P* = .39; impact, *P* = .83; Table 3), compared with patients in the control group.

All AEs are summarized in Table 4. The comparison of all AEs did not differ significantly between 2 groups (Table 4). Of those AEs, the most frequent adverse events included nausea, cough, and runny nose.

5. Discussion

Previous animal studies reported that PCKL can be utilized to inhibit airway inflammation and remodeling in experimental asthma animals.^[32–33] PCKL can be applied to reduce inflammatory cell infiltration in the lung tissue of asthmatic rats. In addition, it also can decrease bronchial mucosa and airway wall

Table 2

Comparison of lung function after 1-month treatment (change from pretreatment).

Lung function	Treatment group (n = 54)	Control group (n = 54)	Difference	P value
FEV ₁ /FVC(reduced), % predicted	−0.8 (−1.2, −0.3)	−0.6 (−1.0, −0.2)	−0.2 (−0.5, −0.1)	.29
FEV ₁ , % predicted	2.8 (1.5, 4.1)	2.3 (1.1, 3.7)	0.5 (0.2, 0.8)	.57

FEV₁ = forced expiratory volume in 1 second, FVC = forced vital capacity.

Table 3**Comparison of quality of life after 1-month treatment (change from pretreatment).**

SGRQ	Treatment group (n=54)	Control group (n=54)	Difference	P value
Total	-5.1 (-8.6, -2.4)	-3.9 (-7.2, -1.8)	-1.2 (-2.0, -0.3)	.37
Symptom	-6.6 (-9.2, -4.3)	-5.0 (-7.9, -2.8)	-1.6 (-2.5, -0.9)	.32
Activity	-4.7 (-7.5, -2.2)	-3.8 (-6.7, -1.5)	-1.0 (-1.8, -0.3)	.39
Impact	-4.5 (-7.1, -2.0)	-3.6 (-5.1, -1.7)	-0.9 (-1.5, -0.4)	.83

SGRQ = St. George's Respiratory Questionnaire.

Table 4**Comparison of adverse events between 2 groups.**

Adverse events	Treatment group (n=54)	Control group (n=54)	P value
Nausea	4 (7.4)	5 (9.3)	.73
Vomiting	2 (3.7)	1 (1.9)	.57
Cough	3 (5.6)	1 (1.9)	.33
Runny nose	3 (5.6)	2 (3.8)	.65
Diarrhea	1 (1.9)	2 (3.8)	.57
Mild stomach pain	1 (1.9)	0 (0)	.50
Stomach upset	2 (3.8)	1 (1.9)	.57

Data are presented as number (%).

thickening, as well as the reduction of blood vessel wall thickening, and vascular proliferation.^[32–33]

Our previous study was designed as a randomized controlled trial to explore the efficacy and safety of PCKL as an adjunctive therapy to montelukast for patients with chronic asthma.^[17] In that study, 72 patients with chronic asthma were included. The results of that study found that PCKL as an adjunctive intervention can effectively alleviate symptoms of chronic asthma.^[17] However, the major limitation of that study was its relative small sample size.

In the present study, we included 108 patients specifically with mild/moderate persistent asthma. It investigated the effectiveness and safety of PCKL for the treatment of persistent asthma. The results of this study are inconsistent with the previous study, which specifically focused on the PCKL treatment for chronic asthma.^[17]

In this study, after 1-month treatment, patients in the treatment group showed neither the improvement of lung function, measured by FEV₁ and FEV₁/FVC nor the enhancement of quality of life, measured by SGRQ scale. The results indicated that PCKL may not benefit patients with mild/moderate persistent asthma after 1-month treatment.

This retrospective study has several following limitations. First, the treatment period is relatively short in this study, which is far less than the previous study, and may accounts for the negative results of this study. Second, the outcome results and AEs were the combination of PCKL and montelukast, but not the PCKL alone, although the both groups underwent the same dose of montelukast. Third, this retrospective study could not control the drug administration of patients as the prospective study. Finally, no previous study specifically investigated the effectiveness of PCKL for patients with acute asthma, but on chronic asthma.

6. Conclusion

The results of this study demonstrated that PCKL may not provide promising effectiveness for mild/moderate persistent asthma after 1-month treatment.

Author contributions

Conceptualization: Zhu-ying Li, Chun-yan Tian, Xue-hui Wang, Ya-fang Liu.

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References

- [1] Sorino C, Scichilone N, D'Amato M, et al. Asthma-COPD overlap syndrome: recent advances in diagnostic criteria and prognostic significance. *Minerva Med* 2017;108(suppl 1):1–5.
- [2] Castillo JR, Peters SP, Busse WW. Asthma exacerbations: pathogenesis, prevention, and treatment. *J Allergy Clin Immunol Pract* 2017; 5:918–27.
- [3] Carr TF, Altisheh R, Zitt M. Small airways disease and severe asthma. *World Allergy Organ J* 2017;10:20.
- [4] Patadia MO, Murrill LL, Corey J. Asthma: symptoms and presentation. *Otolaryngol Clin North Am* 2014;47:23–32.
- [5] Zhao J, Zhai YK, Zhu WJ, et al. Effectiveness of telemedicine for controlling asthma symptoms: a systematic review and meta-analysis. *Telemed J E Health* 2015;21:484–92.
- [6] To T, Stanojevic S, Moores G, et al. Global asthma prevalence in adults: findings from the cross-sectional world health survey. *BMC Public Health* 2012;12:204.
- [7] Lin J, Wang W, Chen P, et al. Prevalence and risk factors of asthma in mainland China: the CARE study. *Respir Med* 2018;137:48–54.
- [8] Global Burden of Disease Study 2013 collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;386:743–800.
- [9] Braman SS. The global burden of asthma. *Chest* 2006;130(suppl 1):4S–12S.
- [10] Sobieraj DM, Baker WL, Nguyen E, et al. Association of inhaled corticosteroids and long-acting muscarinic antagonists with asthma control in patients with uncontrolled, persistent asthma: a systematic review and meta-analysis. *JAMA* 2018;319:1473–84.
- [11] Heffler E, Madeira LNG, Ferrando M, et al. Inhaled corticosteroids safety and adverse effects in patients with asthma. *J Allergy Clin Immunol Pract* 2018;6:776–81.
- [12] Takemura M, Nishio M, Fukumitsu K, et al. Optimal cut-off value and clinical usefulness of the adherence starts with knowledge-12 in patients with asthma taking inhaled corticosteroids. *J Thorac Dis* 2017;9:2350–9.
- [13] Williams LK, Pladevall M, Xi H, et al. Relationship between adherence to inhaled corticosteroids and poor outcomes among adults with asthma. *J Allergy Clin Immunol* 2004;114:1288–93.

- [14] Podgórski M, Kupczyk M, Grzelak P, et al. Inhaled corticosteroids in asthma: promoting or protecting against atherosclerosis. *Med Sci Monit* 2017;23:5337–44.
- [15] Morrison JB. Alternative and complementary medicine for asthma. *Thorax* 1992;47:762.
- [16] Gamus D, Kokia I. Complementary medicine in treatment of asthma and respiratory tract infections. *Harefuah* 2008;147:777–8.
- [17] Wang X, Tian Z, Gao F, et al. Traditional Chinese medicine as an adjunctive therapy to oral montelukast for treating patients with chronic asthma. *Medicine (Baltimore)* 2017;96:e9291.
- [18] Li M, Zhang X, Bao H, et al. Acupuncture for asthma: protocol for a systematic review. *Medicine (Baltimore)* 2017;96:e7296.
- [19] Yin LM, Wang Y, Fan L, et al. Efficacy of acupuncture for chronic asthma: study protocol for a randomized controlled trial. *Trials* 2015;16:424.
- [20] Glickman-Simon R, Mukherji A. Moxibustion for asthma, acupuncture for epilepsy, psychological therapies for irritable bowel syndrome, exercise training for multiple sclerosis, and comfrey root for acute back pain. *Explore (NY)* 2015;11:67–71.
- [21] Saguil A. Effects of yoga in patients with asthma. *Am Fam Physician* 2017;96:159–60.
- [22] Bacon SL, Gibson PG. Behavioral interventions for asthma: what kind of exercise and diets should we be prescribing. *J Allergy Clin Immunol Pract* 2018;6:812–3.
- [23] Xiong J, Liu Z, Chen R, et al. Effectiveness and safety of heat-sensitive moxibustion on bronchial asthma: a meta-analysis of randomized control trials. *J Tradit Chin Med* 2014;34:392–400.
- [24] Wang YY. Preparation and manufacture of Ping Chuan Ke Li and its clinical observation on asthma. *Chin J Med Res* 2011;51.
- [25] Mao WL, Liu JQ. Effects of Ping Chuan Ke Li on miR-21 and eosinophils in chronic persistent asthma. *World Latest Med Inform Abstracts* 2016;36:237–9.
- [26] Fang XY. Clinical observation of Ping Chuan Ke Li on the chronic persistent asthma (Yang deficiency) and its effect on Th17/Treg balance. Heilongjiang University of Chinese Medicine, 2015.(Master dissertation).
- [27] Johns DP, Abramson M, Bowes G. Evaluation of a new ambulatory spirometer for measuring forced expiratory volume in one second and peak expiratory flow rate. *Am Rev Respir Dis* 1993;147:1245–50.
- [28] Krowka MJ, Enright PL, Rodarte JR, et al. Effect of effort on measurement of forced expiratory volume in one second. *Am Rev Respir Dis* 1987;136:829–33.
- [29] Morris JF, Temple WP, Koski A. Normal values for the ratio of one-second forced expiratory volume to forced vital capacity. *Am Rev Respir Dis* 1973;108:1000–3.
- [30] Vandevoorde J, Verbanck S, Schuermans D, et al. Forced vital capacity and forced expiratory volume in six seconds as predictors of reduced total lung capacity. *Eur Respir J* 2008;31:391–5.
- [31] Jones PW, Quirk FH, Baveystock CM, et al. A self-complete measure of health status for chronic airflow limitation: the St George's Respiratory Questionnaire. *Am Rev Respir Dis* 1992;145:1321–7.
- [32] Gao FL. Effects of Pingchuan Granule on VEGF, NOTCH1 and DLL4 in Chronic Asthmatic Rats according to the Vascular Regeneration/Remodeling. Heilongjiang University of Chinese Medicine, 2015. (Doctoral dissertation).
- [33] Xu J, Han D, Xu HL, et al. Effect of pingchuan granule on airway inflammation and remodeling in asthmatic guinea pigs. *Heilongjiang J Tradit Chin Med* 2012;41:58–60.