

Complementary and Alternative Medicine Combined with Symptomatic Treatment Improves Symptoms in COVID-19 Patients

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ABSTRACT

Introduction: The global population has been severely affected by the COVID-19 pandemic. The exploration of Complementary and Alternative Medicine (CAM) as a potential complement to standard management for COVID-19 is essential, but it requires conclusive evidence. This observational study aimed to investigate the association between CAM and improvements in COVID-19 symptoms, the incidence of such improvements, the utilization of complementary methods, and the stages of the disease.

Methods: This research involved a secondary data analysis that compared baseline characteristics, treatment modalities, symptoms, and vital signs before and after treatment in a randomized sample of 881 COVID-19 patients. Medical records from April to May 2021 were collected, and 273 participants were included in the study.

Results: Among the respondents, 131 (47.9%) received andrographis capsules alongside symptomatic treatment, 87 (31.9%) received Homeopathic medicine with symptomatic treatment, 33 (12.1%) received symptomatic treatment only, and 22 (8.1%) received Lianhua Qingwen alongside symptomatic treatment. When comparing the proportion of improvements after treatment, it was found that 28 (32.2%) of the 87 participants who received homeopathic medicine alongside symptomatic treatment exhibited the highest improvement in chest x-ray results. The highest proportion of patients receiving Lianhua Qingwen alongside symptomatic treatment showed favorable changes in vital signs, with 9 (41.0%) of the 22 participants demonstrating improvement. Strong evidence of improvement in symptoms was observed with andrographis capsules alongside symptomatic treatment, with 109 (83.2%) of the 131 participants experiencing improvement. Comorbidities among participants and the stage of the disease were found to significantly influence the effectiveness of these four treatment methods (p-value < 0.010).

Conclusion: This study suggests an association between CAM and improving COVID-19 symptoms. Homeopathic medicine showed considerable improvement in chest x-ray results, while andrographis capsules in the symptomatic treatment group demonstrated notable improvement in symptoms. The most remarkable improvement in vital signs was correlated with using Lianhua Qingwen.

Keywords: COVID-19, Complementary and alternative medicine (CAM), Andrographis capsule, Lianhua Qingwen, Homeopathic medicine

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Introduction

The COVID-19 pandemic, originating from SARS-CoV-2 infection, first surfaced in China in December 2019. SARS-CoV-2 can afflict individuals of all age groups, manifesting with symptoms that range from asymptomatic cases to severe pneumonia, often culminating in multi-organ failure and, tragically, loss of life [1, 2]. COVID-19 impacts various dimensions of an individual's existence, encompassing not only physical and mental health but also socioeconomic well-being [3].

SARS-CoV-2 is primarily transmitted through aerosol droplets, often within a radius of six feet. Measures such as covering coughs and sneezes and adhering to social distancing guidelines have been recommended to mitigate the risk of viral transmission. Frequent hand hygiene practices remain a cornerstone in minimizing the risk of infection. The most effective approach for preventing SARS-CoV-2 infection is vaccination, a pursuit being vigorously pursued by nations worldwide. Various treatment modalities for COVID-19, including antiviral drugs, convalescent plasma therapy, vaccination, and symptomatic management, are being actively explored. Monoclonal antibodies targeting SARS-CoV-2 have gained prominence and are endorsed in the COVID-19 treatment guidelines for pre-and post-exposure prophylaxis [1, 2].

Thailand encountered its first case of COVID-19 in January 2020, with the disease rapidly disseminating throughout the nation. The initial response involved a 14-day hospital or government-supported facility-based isolation for confirmed cases. In milder and moderate cases, symptomatic treatment, featuring antipyretic, antitussive, and antiallergic medications, constituted the primary therapeutic approach. Antiviral agents were reserved for severe scenarios involving pneumonia or multiorgan failure [4]. In addition to conventional pharmaceutical interventions, there is growing interest in exploring alternative and complementary medicine (CAM) for the management of COVID-19.

Notably, a study conducted in India identified commonly employed homeopathic remedies, including arsenicum album, bryonia alba, gelsemium sempervirens, and pulsatilla nigerians, for the treatment of COVID-19 [5]. In China, Lianhua Qingwen has been employed as a treatment for COVID-19 [6], and andrographis paniculata extract is currently under scrutiny in Thailand for its potential therapeutic support [7]. This study aims to investigate whether CAM treatments, including homeopathic medicines (gelsemium sempervirens, arsenicum album, bryonia alba), andrographis paniculata extract, and Lianhua Qingwen, when combined with symptomatic treatment at Ratchaphiphat Hospital, can effectively mitigate the severity of COVID-19 symptoms.

Methodology

Study Design, Population, and Sample

This observational study collected secondary data from Ratchaphiphat Hospital of COVID-19 patients treated in April and May 2021. All study protocols were approved by the Mae Fah Luang University Ethics Committee (COA: 120/2022) and the Bangkok Metropolitan Administration Human Research Ethics Committee (COA: 110). Data were collected after receiving ethical approval. Study samples were determined using a random number table with systematic random sampling. Every third patient who met the inclusion criteria was randomly assigned among 881 asymptomatic, mild, and moderate COVID-19 patients, resulting in 294 initially selected participants. Subsequently, to meet the predetermined sample size of 273 participants, a random elimination of 21 participants was carried out from the initially selected 294 patients using a random sampling method.

Sample size calculation

Key aspects of this observational study included the incidence of symptoms, vital signs, and chest x-ray improvements, the rate of CAM treatment, the stage of disease, and the associations between CAM and COVID-19 symptom improvement. Sample size determination used the following medical and public health observational formula for estimating the proportion of COVID-19 patients showing symptom improvement, receiving Homeopathic medicine, Andrographis capsule, Lianhua Qingwen, and Symptomatic treatment based on two months of medical records:

$$n = \frac{z_{\alpha/2}^2 pq}{d^2}$$

n = Sample size for this study
 $Z_{\alpha/2}$ = The standard normal variate at 5% type 1 error ($\alpha = 0.050$); which is 1.96
d = Absolute error or precision of 5%
p = Proportion of COVID-19 patients whose symptoms improved after treatment with homeopathic medicine in the reference study by Fujino, et al [8] was 82% or 0.82 [8].
q = 1 - p
d = Acceptable margin of error = 0.05
n = $\frac{(1.96)^2 (0.82)(1-0.82)}{(0.05)^2} = 226.8$

Thus, n = 226.8, which was rounded up to 227 participants. After factoring in a potential 20% risk of incomplete data from participants, the final sample size was calculated as 273 participants required.

Selection criteria

Inclusion criteria were positive reverse transcription polymerase chain reaction (RT-PCR) for novel coronavirus 2019, both male and female, aged 18 years or older, and COVID-19 patients with asymptomatic and mild-to-moderate symptoms. The exclusion criteria were incomplete data.

Instruments

Data were collected from medical records, encompassing gender, age, height, weight, medical history, underlying diseases, disease severity, symptoms, vital signs, chest x-ray findings, and the treatment administered at Ratchaphiphat Hospital.

Symptoms: Severity scores on a scale of 0 to 10 were assigned to each symptom, with 0 indicating normal or no symptoms and 10 indicating the most severe symptom. Improvement, stability, or worsening of symptoms was assessed by comparing scores before and after treatment.

Vital signs: Vital signs, including temperature, blood pressure, pulse rate, respiratory rate, and oxygen saturation, were measured. The change in vital signs before and after treatment determined whether they improved, remained stable, or worsened.

Chest x-ray: Chest x-ray results before and after treatment were compared to ascertain improvement, stabilization, or worsening by specialists.

Complementary and Alternative Medicine (CAM) with Symptomatic Treatment: CAM was administered with symptomatic treatment, which prescribed medication based on the presenting symptoms. For moderate-severity patients, such as those with pneumonia, Favipiravir and steroids were also prescribed. *Andrographis paniculata* with symptomatic treatment: Patients received 3 tablets thrice daily for 5 days alongside symptomatic treatment.

Homeopathic medications with symptomatic treatment: *Gelsemium sempervirens*: 5 ml administered once daily in the morning with symptomatic treatment. *Arsenic Album*: 5 ml administered once daily at noon with symptomatic treatment. *Bryonia alba*: 5 ml administered once daily before bed with symptomatic treatment. Lianhua Qinwen with symptomatic treatment: Patients received 4 tablets thrice daily for 7 days alongside symptomatic treatment. Symptomatic treatment: This involved the administration of medications targeting distressing symptoms, including analgesics (e.g., Paracetamol), allergy medications (e.g., Cetirizine), anti-tussives (e.g., mucolytics), and expectorants.

Data collection

Data collection took place at Ratchaphiphat Hospital between April and May 2021, involving a total of 273 males and females aged 18 and above with asymptomatic, mild, or moderate COVID-19 infections.

Data encompassing gender, age, weight, height, comorbidities, disease stage, pre-treatment and post-treatment outcomes related to symptoms, vital signs, chest radiographs, and treatment methods were extracted from medical records. All collected data were recorded in an Excel file for subsequent analysis.

Data analysis

Data entered into the Excel file from medical records were analyzed using descriptive statistics, which included percentages, means, and standard deviations. To explore associations, the chi-square test was employed to determine the relationship between patient factors, disease stage, treatment methods, and improvements in COVID-19 symptoms. The analysis was conducted using SPSS version 23.0 Passport Advantage Agreement Number 000020378.

Results

Between April and May 2021, Ratchaphiphat Hospital admitted a total of 881 patients with asymptomatic, mild, and moderate COVID-19 infections. This analysis focused on 273 participants: 55.3% were male and 44.7% were female, with an average age of 38.41 ± 14.22 years and an average body mass index of 24.44 ± 4.82 kg/m². 34.1% of the participants had a body mass index within the normal range, while 58.6% had a body mass index higher than the normal threshold of 23 kg/m². The 'comorbidity' variable encompassed several factors that may influence disease progression and were not mutually exclusive, as a patient could have more than one of these conditions. 35.2% had no comorbidities, while 64.8% had comorbidities (including health problems, obesity, and being over 60 years old). 78.4% of participants were classified as asymptomatic and mild. The largest proportion (47.9%) received andrographis capsules alongside symptomatic treatment (Table 1).

Table 1 Participants baseline characteristics

Characteristics	n	%
Gender		
Male	151	55.3
Female	122	44.7
Age (years)		
18-39	148	54.2
40-60	103	37.7
>60	22	8.1
<i>Mean ± SD = 38.4 ± 14.2</i>		
BMI		
Underweight (<18.5)	20	7.3
Normal (18.5-22.9)	93	34.1
Overweight (23-24.9)	51	18.7
Obesity (25-29.9)	74	27.1

Characteristics	n	%
Morbid obesity (>30)	35	12.8
Comorbidity presenting		
Yes, including obesity and >60	177	64.8
Hypertension	39	
Diabetes Mellitus	19	
Dyslipidemia	17	
Cardiac and vascular disease	13	
Respiratory disease	21	
HIV	3	
Smoking	54	
No	96	35.2
Stage of disease		
Asymptomatic and Mild	214	78.4
Moderate	59	21.6
Treatment		
Homeopathic medicine and symptomatic treatment	87	31.9
Andrographis capsule and symptomatic treatment	131	47.9
Lianhua Qingwen and symptomatic treatment	22	8.1
Symptomatic treatment	33	12.1

Symptoms

Participants were classified with 12 symptoms before and after their treatment, regardless of the treatment method used. Cough was the most prevalent symptom (48.9%) before treatment. Rhinorrhea and headache affected 37.9% and 27.8%, respectively. Following treatment, cough remained the most common symptoms (16.8%) (Table 2).

Vital Signs

The average temperature and respiratory rate did not exhibit substantial differences before and after treatment. This study reported changes in the proportion with normal blood pressure, increasing from 65.6% to 96%, and a decrease in those with abnormal blood pressure, from 34.4% to 4% (Table 2).

Table 2 Symptoms and vital signs before and after treatment

Symptoms and vital signs	Before n (%)	After n (%)
Symptoms	Fever	20 (7.3%)
	Cough	136 (49.8%)
	Rhinorrhea	87 (31.9%)
	Sore throat	62 (22.7%)
	Dyspnea	66 (24.2%)
	Loss of smell	45 (16.5%)
	Loss of taste	35 (12.8%)

Symptoms and vital signs	Before n (%)	After n (%)
Conjunctivitis	10 (3.7%)	2 (0.7%)
Rash	13 (4.8%)	2 (0.7%)
Diarrhea	60 (21.9%)	24 (8.8%)
Headache	76 (27.8%)	16 (5.9%)
Muscle pain	70 (25.6%)	24 (8.8%)
Temperature (Degree Celsius)	36.475 ± 0.2694	36.453 ± 0.1871
Blood pressure: Normal	179 (65.6%)	262 (96%)
	94 (34.4%)	11 (4%)
Vital signs		
Abnormal		
Pulse (Beats/min)	92.78 ± 14.061	83.68 ± 10.478
Respiratory rate (Breaths/min)	21.35 ± 15.580	20 ± 0.171
SpO ₂ >95	268 (98.2%)	273 (100%)

Chest x-ray

Before treatment, chest x-rays indicated pneumonia (lung infiltration) in 21.6% of participants. It is important to note that chest x-ray data only reflected the 'before' condition, as pulmonary infiltration persisted despite symptom improvement.

The participants were categorized into four groups according to the treatment methods employed. Of the women, 52.9% received homeopathic medicine with symptomatic treatment, and 59.1% received Lianhua Qingwen with symptomatic treatment. Among men, 66.7% received symptomatic treatment, and 60.3% received andrographis capsules with symptomatic treatment. No significant association was found between gender and treatment methods (Table 3). Andrographis capsules with symptomatic treatment were administered to 47.98% of the sample, while 31.86% received homeopathic medicine with symptomatic treatment. A relatively low percentage of underwent symptomatic treatment, 12.08%, and Lianhua Qingwen group with symptomatic treatment, 0.08%. Average age did not demonstrate a significant association with different categories of treatment methods (Table 3).

Homeopathic medicine with symptomatic treatment exhibited the highest percentage of comorbidity, present in 78.2%. Further statistical tests indicated a significant difference in the proportion of comorbidity among treatment methods (p-value < 0.010) (Table 3).

In terms of disease stage, Lianhua Qingwen with symptomatic treatment had the highest percentage of asymptomatic and mild cases, 95.5%, while 4.5% presented with moderate cases. Moderate cases were most prevalent in the group receiving homeopathic medicine with symptomatic treatment, at 32.2%, while 67.8% were asymptomatic and mild cases (Table 3).

Table 3 Comparisons of participants' baseline characteristics and treatments

Characteristics		Homeopathic medicine with symptomatic treatment (n=87)	Andrographis capsule with symptomatic treatment (n=131)	Lianhua Qingwen with symptomatic treatment (n=22)	Symptomatic treatment (n=33)	p-value
Gender	Male	41 (47.1%)	79 (60.3%)	9 (40.9%)	22 (66.7%)	0.064
	Female	46 (52.9%)	52 (39.7%)	13 (59.1%)	11 (33.3%)	
Age		40.56 ± 14.308	38.87 ± 14.335	30.55 ± 7.269	36.15 ± 15.417	0.305
Comorbidity	Present	68 (78.2%)	80 (61.1%)	7 (31.8%)	22 (66.7%)	<0.001*
	Absent	19 (21.8%)	51 (38.9%)	15 (68.2%)	11 (33.3%)	
Stage of disease	Asymptomatic and mild	59 (67.8%)	105 (80.2%)	21 (95.5%)	29 (87.9%)	0.009*
	Moderate	28 (32.2%)	26 (19.8%)	1 (4.5%)	4 (12.1%)	

* Statistical significance at $\alpha=0.05$

Andrographis capsules with symptomatic treatment demonstrated the highest rate of symptom improvement, affecting 83.2%. In contrast, the lowest rate of symptom improvement was observed in the Lianhua Qingwen with symptomatic treatment group, at 68.2%. Lianhua Qingwen with symptomatic treatment had the highest proportion of cases with stable symptoms, 27.3%, while andrographis capsules with symptomatic treatment had the lowest, at 13%. Symptomatic treatment exhibited the largest percentage of cases with worsening symptoms, at 6%, while the smallest percentage was in the andrographis capsules with the symptomatic treatment group, at 3.8%. No significant association was identified between symptom categories and the four treatment methods (Table 4).

The highest percentage of cases displaying improvement in vital signs was observed in the group that received Lianhua Qingwen with symptomatic treatment, accounting for 41% of cases. In contrast, the lowest percentage of improvement was observed in those who received symptomatic treatment, at 27.3%. Simultaneously, the group receiving symptomatic treatment exhibited the highest percentage of stable vital signs, with 72.7%, while the lowest percentage was noted in the Lianhua Qingwen with symptomatic treatment group, at 59%. Notably, only one treatment method, andrographis capsules with symptomatic treatment, had cases with worsened vital signs, at 1.5%, whereas no such cases were reported in the other three treatment groups. There was no significant association found between vital signs and treatment methods (Table 4).

Regarding chest x-ray, the highest percentage of cases with improvement was observed in the group receiving homeopathic medicine with symptomatic treatment, comprising 32.2% of cases. The smallest percentage of cases with improvement, at 4.5%, was observed who received Lianhua Qingwen with symptomatic treatment. The same group, Lianhua Qingwen with symptomatic treatment, demonstrated the most significant percentage of cases with stable chest x-ray results, at 95.5%, while the group receiving homeopathic medicines and symptomatic treatment had the lowest percentage, at 67.8%. It is worth highlighting that no cases of worsening chest radiographs were observed in any of the four treatment methods. A statistically significant difference in proportions was observed in chest x-ray results when comparing the four treatment methods (Table 4).

Table 4 Comparisons of the improvement of symptoms, vital signs, and chest x-ray between treatment methods

Characteristics		Homeopathic medicine with symptomatic treatment (n=87)	Andrographis capsule with symptomatic treatment (n=131)	Lianhua Qingwen with symptomatic treatment (n=22)	Symptomatic treatment (n=33)	p-value
Symptom	Improved	71 (81.6%)	109 (83.2%)	15 (68.2%)	25 (75.8%)	0.700
	Stable	12 (13.8%)	17 (13%)	6 (27.3%)	6 (18.2%)	
	Worsen	4 (4.6%)	5 (3.8%)	1 (4.5%)	2 (6%)	
Vital sign	Improved	34 (39.1%)	37 (28.3%)	9 (41%)	9 (27.3%)	0.440
	Stable	53 (60.9%)	92 (70.2%)	13 (59%)	24 (72.7%)	
	Worsen	0 (0.0%)	2 (1.5%)	0 (0.0%)	0 (0.0%)	
Chest x-ray	Improved	28 (32.2%)	26 (19.8%)	1 (4.5%)	4 (12.1%)	0.009*
	Stable	59 (67.8%)	105 (80.2%)	21 (95.5%)	29 (87.9%)	
	Worsen	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

* Statistical significance at $\alpha=0.05$

Discussion

In terms of symptom improvement, our study found that *Andrographis* capsules were the most effective. This observation is in line with a study by Mahajaroensiri et al [7] which reported that *andrographis* capsules helped reduce inflammation by targeting the production of inflammatory substances, resulting in a reduction of COVID-19 symptoms. Similarly, Wanaratna et al [10] discovered that the use of *Andrographis paniculata* extract in the treatment of COVID-19 with mild symptoms was safe and effective. It was associated with a reduction in viral shedding time, inflammation suppression, and pneumonia prevention. However, it's important to note that some symptoms, such as cough, loss of smell, diarrhea, and muscle pain, did not improve as significantly after treatment.

Blood pressure and oxygen saturation showed significant improvements. Notably, Lianhua Qingwen with symptomatic treatment demonstrated the most significant improvement in patients' vital signs among the treatment methods. This finding is supported by Jeon et al. [11] who found that Lianhua Qingwen reduced fever symptoms, accelerated recovery time, and prevented the progression of the disease to a severe level. There is a growing body of evidence indicating that using Lianhua Qingwen with symptomatic treatment is effective in managing COVID-19 due to its antiviral, anti-inflammatory, and immune-enhancing properties [12]. Moreover, studies such as the one by Hu et al [13] have shown that Lianhua Qingwen can lead to a higher rate of symptom recovery and shorter recovery times in COVID-19 patients. However, it's worth noting that in our study, some patients' vital signs did not improve post-treatment, possibly due to underlying conditions present before treatment, such as high blood pressure.

The significant improvement in chest x-ray results, with the most pronounced improvements seen in patients treated with homeopathic medicines alongside symptomatic treatment. This observation aligns with a study by Takacs et al [14] which reported improved chest x-ray findings in COVID-19 patients following treatment with homeopathic medicines. Importantly, the results from our study could be influenced by the fact that most patients treated with homeopathic medicines were classified as moderate cases, which could lead to abnormal chest x-ray findings. Notably, none of the patients in our study exhibited worsening chest x-ray findings, irrespective of the treatment method used.

The differences between treatment methods and the stage of COVID-19 patients' disease, data indicate an association between the four treatment methods and the disease stage. As observed, a higher number of asymptomatic and mild cases were present for all four treatment methods, with moderate cases predominantly associated with homeopathic medicine treatment. This observation can be attributed to the

hospital's screening protocols, which specified that moderate cases should be treated with homeopathic medicines. The differences observed between the four treatment methods and the disease stage were statistically significant. 14

Conclusion

This study found a statistically significant association between comorbidity, stage of diseases, and treatment methods at Ratchaphiphat Hospital in April-May 2021. Strong evidence of improvement percentage of symptoms, vital signs, and chest x-rays between treatment methods. Notably, *andrographis* capsules combined with symptomatic treatment showcased the most substantial improvement in symptoms, while Lianhua Qingwen, in conjunction with symptomatic treatment, revealed the most remarkable enhancement in vital signs. Homeopathic medicine, when used alongside symptomatic treatment, exhibited the most noteworthy improvements in chest x-ray findings.

Competing interests

The authors had no competing interests to declare.

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