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The effects of hyssop and mullein tea on the clinical symptoms of COVID-19 patients

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Abstract

The use of medicinal herbs as treatments for different illnesses has a long history. This research aims to study the effects of hyssop and mullein tea on the clinical symptoms of COVID-19 patients. This was a triple-blind clinical trial study performed on 80 COVID-19 patients hospitalized in Khomeini's Imam Khomeini Hospital. The intervention group received 250 ccs of hyssop and mullein tea three times a day for eight days along with their normal treatment, while the witness group only received the normal treatment. All patients were monitored for coughing, dyspnea, hoarseness, sore throat, and body pain throughout the experiment. In the end, the Stata-17 statistical software was used to compare the five symptoms mentioned above among the patients.

There were no significant differences between the two groups in the five clinical symptoms (sore throat, body pain, dyspnea, cough, and hoarseness) before the intervention began. However, differences appeared after the intervention. After six days of intervention, the two groups were meaningfully different in the cases of all five clinical symptoms. Fewer patients in the intervention group reported these symptoms. Analyzing the effects of the intervention on clinical symptoms indicated that the patients in the intervention group had a significantly lower chance of experiencing the five symptoms. The use of hyssop and mullein tea as supplementary treatments can decrease clinical symptoms in COVID-19 patients and quicken recovery.

Keywords: *Hyssop, Mullein, Clinical Symptoms, COVID-19*

Introduction

The new respiratory infectious virus known as coronavirus disease (COVID-19) was identified in Wuhan, China, for the first time (1). Due to the quick spread of the virus, the World Health Organization announced a global health emergency in January 2020 (2). Currently, management of the COVID-19 virus includes a decrease in clinical symptoms. Multiple treatment methods have been used against COVID-19, and due to their effectiveness against SARS, the use of medicinal herbs is one of them (3). Medical herbs were studied during the 2003 SARS epidemic, and multiple herbs and their active compounds were identified as effective antivirus agents (4). Combined with modern treatments, these herbs can improve COVID-19 clinical symptoms such as cough, fever, body pain, chest pain, diarrhea, and vomiting with their antimicrobial and antiviral activities (5,6). Members of the mint family (Lamiaceae), such as hyssop, have long been used in medicine all around the world (7). The tea made from its leaves is good for the treatment of coughing, asthma, chronic bronchitis, and sore throats (8). Mullein flowers of the papilionaceous family have also been used alone or with other medicinal herbs to make tea (9) to treat respiratory issues such as cough, cold, inflated throat and pharynx, and tonsillitis (10). In addition to traditional and everyday uses of such herbs as anti-inflation remedies, laboratory and animal studies on asthmatic mice indicate that hyssop can play an anti-inflammatory role in this disease (11). In animals, hyssop decreases inflammatory cytokines and respiratory tract inflation (12). According to a laboratory study, mullein also has anti-inflammatory effects in respiratory diseases (13). Mullein's

chemical compounds, which are effective against COVID-19, have been identified through molecular modeling methods. Other chemical compounds of mullein that can prevent the spread of coronaviruses include apigenin, luteolin, and quercetin flavonoids. Chemical compounds in mullein flowers can fight the cytokine storm caused by COVID-19 through their anti-inflammatory and immunosuppressive characteristics (10). Many countries have performed numerous clinical studies on COVID-19 in hopes of finding effective treatment methods. Many of them are focused on herbal medicines as supplementary or even primary treatments (3). According to the WHO, 70 to 95 percent of people use traditional medicines as a sort of treatment. The benefit of traditional medicines is their effectiveness and safety, which have been proven over centuries (5). The Chinese National Healthcare Commission has recognized medical herbs as a supplementary treatment in addition to common COVID-19 treatment methods and has released multiple recommendations on medical herbs (2). Traditional medicine, especially traditional Persian medicine, has deep roots in the global healthcare system. If it is properly used, it can help overcome situations like the COVID-19 pandemic (14). Due to the long history and benefits of traditional medicine (easy access, low costs, and lack of major side effects) and the laboratory and animal studies that indicate positive effects of medicinal herbs on respiratory conditions such as asthma and respiratory infections and their clinical symptoms caused by the coronaviruses, this study was performed on the effects of hyssop and mullein tea on the clinical symptoms of COVID-19 patients.

Methods

This was a triple-blind clinical study conducted in 2020 at the COVID-19 Unit of Imam Khomeini Hospital in Khomein. Participants were selected using the convenient sampling method from COVID-19 patients hospitalized at Imam Khomeini Hospital based on the following inclusion criteria: being over 18 years of age; conscious; the ability to swallow (to swallow herbal tea); must be hospitalized and receive positive PCR test results; Lung infection should be confirmed with ground-glass chest CT scans by infection experts and interns, the 5 symptoms (sore throat, body aches, dyspnea, cough, and hoarseness) should be moderate; must have no history of heart, liver, or kidney disease or diabetes; not be pregnant or breastfeeding; and must be willing to participate in the study. Exclusion criteria included refusal to continue the study, worsening of symptoms and hospitalization in the intensive care unit, allergic reactions to herbal tea, and elevation of systolic blood pressure to 160 or more during the intervention.

The sample size was set at a 5 percent fault level and 80 percent power of a test (80 participants, 40 in each group). Sampling was performed through the convenience method and according to the inclusion criteria mentioned above from December until March 2020. After entering the study, participants were separated into two groups (intervention and control) through simple random selection using a coin. If the coin landed heads, the patient would join the control group. If it landed on tails, the patient would join the intervention group.

To prepare the tea, fresh hyssop, and mullein plants were collected from mountain regions and approved by a traditional medicine expert. The flowers were then washed and cleaned. The hyssop flowers and mullein leaves were then dried using the traditional and completely healthy method. The tea was prepared in a sterilized laboratory overseen by a traditional medicine expert. Fifteen grams of hyssop flowers and 5 grams of mullein leaves were boiled in 0.5 liters of water for 20 minutes. After the tea cooled down, it was separated into clean 250-cc bottles. The placebo was prepared from light-colored black tea, and it looked identical to the real tea. As a measure of concealment, the bottles were labeled with random 3-digit letters. Only the main researcher, who had no part in the measurement, knew what the bottles contained.

After receiving the research license and the morality code from Khomeini's medical university (code number: IR.KHOMEIN.REC.2020.012), the patients were provided with detailed explanations about the goal of the study and the security of their personal and clinical information by the researchers. The participants signed legal "willingness to participate" documents. Three times a day for the next 8 days, the control group received the placebo and the intervention group received the tea. Each drink was 250 cc. The participants did not know if they were drinking real tea or not. Neither did the staff who distributed the bottles, the staff who measured the participants' clinical symptoms every day, the nurses, the specialist doctor, and the analyzer. Also, a psychologist colleague was used to control the feeling of pain and frustration and to motivate the patients of both groups. To achieve this goal, the psychologist used motivation-enhancing therapeutic methods, which included an emphasis on empathic listening, repeated affirmation of the patient, calm and gentle persuasion, and avoiding arguments.

The tools used to gather information included a survey of demographic characteristics (age, sex, educational level, occupation, and relationship status) and surveys of clinical symptoms (sore throat, body pain, dyspnea, cough, and hoarseness). The results measured in this study included five COVID-19-caused clinical symptoms (body pain, dyspnea, hoarseness, sore throat, and cough). The symptoms were measured by trained specialists before the

intervention and on the second, fourth, sixth, and eighth days. The existence or lack of symptoms would be checked in each participant and recorded on separate checklists.

The study was performed over eight days. If a participant was released from the hospital before the study ended, they would still be given the tea and examined, depending on their willingness. Patients of both groups received the same doses of the hospital's normal treatment, which included Dexamethasone, Enoxaparin, Remdesivir, and Pantoprazole. It should be mentioned that the traditional medicine expert was always close at hand to control possible side effects of the tea. This study is registered in Iran's clinical trial database with the following code: IRCT20100130003227N15.

Statistical Analysis

To compare the two groups before the intervention, independent sample T-tests, and Chi-Square statistical methods were used. Chi-Square and Fisher's exact test statistical methods were used to compare the two groups' clinical symptoms in each measurement session. To examine the effects of the intervention on clinical symptoms and compare them to those of the control group, the following statistical methods were used: Population-averaged panel-data models by using generalized estimating equations (GEE) with an exchangeable correlation structure. Since the study's result distribution (body pain, dyspnea, hoarseness, sore throat, cough) was binomial (to have or not to have), a GEE with a binomial family model and logic link function was used. Data analysis was performed using the Stata-17 software at the meaningful level of ($a = 0.05$).

Results

Table 1 shows the baseline characteristics of the participants. The age averages in the control and intervention groups were, respectively, 1.76±48.98 and 15.57±48.48. Most of the participants in both groups were female, married, uneducated, and housewives. The average onset-to-hospitalization time was longer for the intervention group. Despite that, no statistically significant differences in baseline characteristics were observed (Table 1). The clinical symptoms studied in this research were dyspnea, hoarseness, body pain, sore throat, and cough. The existence or lack of these symptoms in participants in both groups was examined before the intervention and on days 2, 4, 6, and 8. Table 2 compares these symptoms between the two groups. According to this table, there were no significant differences between the symptoms of the two groups before the intervention. However, on the second day of the intervention, there were meaningful differences between the two groups in the cases of body pain, sore throat, and hoarseness. Fewer patients in the intervention group reported these symptoms compared to the control group. On the fourth day of the intervention, the two groups were different in the cases of body pain, dyspnea, sore throat, and cough. On the sixth day of the intervention, the two groups were different in the case of all five clinical symptoms. Fewer patients in the intervention group reported the symptoms. As Table 2 shows, the two groups had meaningful differences in all clinical symptoms except body pain on the last day of the intervention. While examining the effects of the intervention on the clinical symptoms during the study, it became clear that participants in the intervention group had a significantly lower chance of reporting the clinical symptoms compared to the control group participants. The chance of having body pains in the intervention group was 0.23 in the control group (OR = 0.23, 95% CI = 0.12-0.45, P<0.001). The chances of experiencing a sore throat, cough, hoarseness, and dyspnea were also meaningfully lower in the intervention group (Table 3).

Discussion

According to the results of numerous studies, the COVID-19 virus harms many organs, including the respiratory tract, heart, liver, kidneys, etc. Unfortunately, there's yet to be a full-proof COVID-19 treatment or effective anti-virus medicine introduced (15). We can say that treating the clinical symptoms of COVID-19 is one of the main aspects of its management. This study aimed to examine the effects of hyssop and mullein tea on five clinical symptoms of COVID-19. The five symptoms (cough, hoarseness, body pain, dyspnea, and sore throat) were chosen due to their common occurrence. Symptoms such as fever and shivering were not studied due to their short-term nature (2–3 days) and the fact that most patients only visit doctors and get hospitalized a few days after the symptoms appear. According to the literature, cough, body pain, dyspnea, and sore throat are the most common COVID-19 symptoms (16–18). Hoarseness has also been reported by 20 to 40 percent of COVID-19 patients (19–21). In this study, coughing was the most common symptom (reported by 85 percent of patients). According to our results, we can say that hyssop and Mullein tea can help improve clinical symptoms and speed up the healing process of COVID-19 patients. In traditional medicine, hyssop is used to cure respiratory issues including cough, bronchitis, inflammation, and asthma (22,23). Mullein flowers are also used to cure hoarseness, cough, asthma, and bronchitis inflammation. These effects have been confirmed by pharmacology studies. According to the study performed by Ma et al. on mice, hyssop's anti-inflammatory effects equal those of dexamethasone. This plant can also regulate Cytokine levels (Interleukin 17, 6, and 4) and Interferon- γ (12). Regarding the pain-killing effects of these herbs, studies performed on mice

indicate that hyssop contains pain-killing compounds including flavonoids, the pain-killing effects of which are similar to those of morphine (by affecting Opioid receivers) (24). Studies performed on lab animals also indicate painkilling and anti-inflammatory effects for mullein (25). Mullein flowers can cure respiratory issues caused by inflammation like cough, hoarseness, and bronchitis inflammation due to their mucilage (26). Mullein flowers also contain Ursolic acid which works as the primary phytochemical inhibitor of the COVID-19 virus' main proteae (27). The flavonoids of mullein flowers have also stopped COVID-19 multiplication in laboratory conditions (10). From a clinical standpoint, Fallah Hosseini's study found that using traditional Iranian medicine ingredients containing hyssop can relieve COVID-19 clinical symptoms such as coughing (28). The usage of Iranian medicinal herbal components reduced the hospitalization length of COVID-19 patients and alleviated clinical symptoms such as dyspnea, according to Setayesh et al. (29). In another clinical trial, a faster recovery pace in COVID-19 patients was reported after herbal medicines such as hyssop were prescribed (30). The results of these studies confirm the effects of these medicinal herbs in clinical situations.

Conclusion

The use of traditional medicine, especially medicinal herbs, has a very long history in Iran due to its cost-effectiveness, cultural acceptance, and effectiveness against many diseases. According to studies, people tend to reach for supplementary treatments during situations like pandemics. That can be due to the easy access and low costs of such treatments. Due to Iran's unique climate, numerous medicinal herbs can be found in different regions. These herbs can be used as supplementary treatments in addition to common and modern treatments. In this study, the use of herbal tea in addition to other treatments helped improve clinical symptoms and speed up the healing process. No side effects were observed in the patients. In this study, long-term follow-up on patients' clinical symptoms was not possible. For future studies, we recommend long-term follow-ups and bigger sample sizes.

Ethics approval and consent to participate: All the ethical considerations based on the international ethical protocols were considered by the authors, and the work was approved by the ethics committee of the Khomein University of Medical Sciences (Approval code: IR.KHOMEIN.REC.2020.012). This study has also been registered in the Iranian Registry of Clinical Trials (IRCT20100130003227N15).

Consent for publication

Written informed consent was obtained from the patients to publish this article and any accompanying images. A copy of the written consent is available for review by the journal's Editor-in-Chief.

Availability of data and materials

Please contact the corresponding author (MA) for data requests.

Competing interests

The authors declared that they had no competing interests.

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Authors' contributions

MT and AS proposed the original concept. MT designed the treatment and collected the data. MT and MS prepared the herbal tea. MT and MA equally participated in the data analysis. All authors contributed to writing the manuscript.

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Limitations

The subjects in this study were people over 18, and we couldn't study the effect of this drug on people under 18. Therefore, its effect on this age group can be investigated in future studies.

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Table 1. Baseline Characteristics of Participants

Variables	Control group (n=40)	Intervention group (n=40)
Gender (No (%))[a]		
Female	21 (52.5)	21 (52.5)
Male	19 (47.5)	19 (47.5)
Marital status (No (%))[a]		
Single	7 (17.5)	5 (12.5)
Married	33 (82.5)	33 (82.5)
Divorced	0 (0)	2 (5)
Job (No (%))[a]		
Employee	15 (37.5)	12 (30)
Farmer	5 (12.5)	10 (25)
Housewife	18 (45)	16 (40)
Others	2 (5)	2 (5)
Education level (No (%))[a]		
Illiterate	13 (32.5)	12 (30)
Primary	4 (10)	2 (5)
Middle	11 (27.5)	4 (10)
Diploma	4 (10)	11 (27.5)
Bachelor	8 (20)	11 (27.5)
Age (mean±sd)[b]	48.98±1.76	48.48±15.57
Onset-to-hospitalization time (mean±sd)[b]	8.95±4.40	9.30±4.39

[a] Chi-Square Test

[b] Independent Samples T-test

Table 2. Comparing the status of clinical symptoms in two groups under study

Clinical symptoms	Visiting time		Control group (%)	Treatment group (%)	P-Value
Body pain	before the intervention	NO	12 (30%)	20 (50%)	0.068*
		YES	28 (70%)	20 (50%)	
	second day	NO	13 (32.5%)	22 (55%)	**0.043***
		YES	27 (67.5%)	18 (45%)	
	fourth day	NO	18 (45%)	30 (75%)	**0.006***
		YES	22 (55%)	10 (25%)	
	sixth day	NO	30 (75%)	38 (95%)	**0.012***
		YES	10 (25%)	2 (5%)	
	Eighth day	NO	35 (87.5%)	40 (100)	0.055**
		YES	5 (12.5%)	0 (0%)	
Sore throat		NO	10 (25%)	12 (30%)	0.617*

	before the intervention	YES	30 (75%)	28 (70%)	
	second day	NO	10 (25%)	22 (55%)	**0.006***
		YES	30 (75%)	18 (45%)	
	fourth day	NO	15 (37.5%)	38 (95%)	**<0.001***
		YES	25 (62.5%)	2 (5%)	
	sixth day	NO	18 (45%)	40 (100%)	**<0.001****
		YES	22 (55%)	0 (0%)	
	Eighth day	NO	34 (85%)	40 (100%)	**0.026****
		YES	6 (15%)	0 (0%)	
Cough	before the intervention	NO	8 (20%)	4 (10%)	0.210*
		YES	32 (80%)	36 (90%)	
	second day	NO	8 (20%)	4 (10%)	0.210*
		YES	32 (80%)	36 (90%)	
	fourth day	NO	8 (20%)	20 (50%)	**0.005***
		YES	32 (80%)	20 (50%)	
	sixth day	NO	12 (30%)	38 (95%)	**<0.001***
		YES	28 (70%)	2 (5%)	
	Eighth day	NO	21 (52.5%)	40 (100%)	**<0.001****
		YES	19 (47.5%)	0 (0%)	
Dyspnea	before the intervention	NO	9 (22.5%)	6 (15%)	0.390*
		YES	31 (77.5%)	34 (85%)	
	second day	NO	10 (25%)	10 (25%)	1*
		YES	30 (75%)	30 (75%)	
	fourth day	NO	14 (35%)	22 (55%)	0.072*
		YES	26 (65%)	18 (45%)	
	sixth day	NO	24 (60%)	38 (95%)	**<0.001***
		YES	16 (40%)	2 (5%)	
	Eighth day	NO	28 (70%)	40 (100%)	**<0.001****
		YES	12 (30%)	0 (0%)	
Hoarseness	before the intervention	NO	14 (35%)	10 (25%)	0.329*
		YES	26 (65%)	30 (75%)	
	second day	NO	14 (35%)	32 (80%)	**<0.001***
		YES	26 (65%)	8 (20%)	
	fourth day	NO	25 (62.5%)	38 (95%)	**<0.001***
		YES	15 (37.5%)	2 (5%)	
	sixth day	NO	27 (67.5%)	40 (100%)	**<0.001****
		YES	13 (32.5%)	0 (0%)	
	Eighth day	NO	28 (70%)	40 (100%)	**<0.001****
		YES	12 (30%)	0 (0%)	

*Chi-Square test. **Fisher's exact test

Table 3. Effect of Intervention on clinical symptoms

Groups	Odds Ratio	95% Confidence Interval	P-Value*

Clinical symptoms			Lower bound	Upper bound	
Body pain	Control (reference)				
	Treatment	0.23	0.12	0.45	**<0.001**
Sore throat	Control (reference)				
	Treatment	0.17	0.10	0.29	**<0.001**
Cough	Control (reference)				
	Treatment	0.25	0.14	0.44	**<0.001**
Dyspnea	Control (reference)				
	Treatment	0.44	0.27	0.73	**0.002**
Hoarseness	Control (reference)				
	Treatment	0.21	0.12	0.38	**<0.001**

*generalized estimating equations