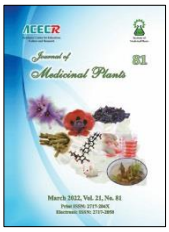
J. Med. Plants 2022; 21(81): 51-66

Institute of Medicinal Plants

Journal of Medicinal Plants

Journal homepage: www.jmp.ir



Research Article

Effects of Imfluna, an Iranian traditional polyherbal medicine, on COVID-19 symptoms: A randomized, double-blind and placebo-controlled clinical trial

Hasan Fallah Huseini[1], Mohammadreza Gholibeikian[2], Majid Shohrati[3], Afsaneh Kaffash[4], Ali Taheri[5], Hojatolah Khajepour[6], Mehdi Raei[7], Saeed Kianbakht[1], Amena Fallah Hosseini[8], Majid Ghorbani Nohooji[1], Reza Mohtashami[9,*]

[1] *Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran*
[2] *Department of Organic Chemistry, Faculty of Chemistry, University of Kashan, Kashan, Iran*
[3] *Department of Pharmacotherapy, Faculty of Pharmacy, Baqiyatallah Uiversity of Medical Sciences, Tehran, Iran*
[4] *Department of Internal Medicine, Faculty of Medicine, Sabzevar University of Medical Sciences, Sabzavar, Iran*
[5] *Faculty of Pharmacy, Baqiyatallah University of Medical Sciences, Tehran, Iran*
[6] *Department of Radiology, Baqiyatallah University of Medical Sciences, Tehran, Iran*
[7] *Health Research Center, Life Style Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran*
[8] *Department of Emergency Medicine, Tehran University of Medical Sciences, Tehran, Iran*
[9] *Medicine Quran and Hadith Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran*

ARTICLE INFO

Keywords:
Clinical trial
COVID-19
Polyherbal medicine
Iranian traditional medicine
Imfluna

ABSTRACT

Background: The current pandemic of Coronavirus disease 2019 (COVID-19) and severity of the infection and high mortality have almost unprecedented challenges in the health systems of most countries around the world. **Objective:** The present study aimed to evaluate the effect of Iranian traditional polyherbal medicine (Imfluna) containing a mixture of echinacea, stachys, artemisia, hyssopus, polybody, alpinia, ginger, and ginseng extract on symptoms of COVID-19 infected patients. **Methods:** In this placebo-controlled and double-blind clinical trial, a total of 60 voluntarily approved patients with COVID-19 were randomly assigned to the placebo and Imfluna groups. Patients in each group, in addition to receiving standard medications, took two 500 mg capsules of Imfluna or placebo every 8 hours for 2 weeks. The patient's vital signs, including the severity of shortness of breath, cough, and body temperature, were recorded during the study. Also blood ESR, liver and kidney function tests were performed at baseline and endpoint. **Results:** The results showed that patients in the Imfluna-treated group had significantly greater improvement in daily cough, shortness of breath and ESR compared with the placebo group. In addition, lung lesions improved in the Imfluna-treated group, although not significantly. **Conclusion:** Patients with COVID-19 who were treated with Imfluna for 2 weeks had better comfort and fewer symptoms associated with the disease with no any drug side effects.

Abbreviations: ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; WBC, White blood cell; RBC, Red blood cell; Hb, Hemoglobin; HCT, Hematocrit; AST, Aspartate transaminase; ALT, Alanine transaminase; ALP, Alkaline phosphatase; Cr, Creatinine; BUN, Blood urea nitrogen; Na, Sodium; K, Potassium

*Corresponding author: reza_mohtashami1979@bmsu.ac.ir

doi: 10.52547/jmp.21.81.51
Received 15 September 2021; Received in revised form 12 December 2021; Accepted 22 January 2022

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[DOR: 20.1001.1.2717204.2022.21.81.1.7]
[DOI: 10.52547/jmp.21.81.51]

1. Introduction

COVID-19 infection since 2019 is a global pandemic that has challenged the health care system worldwide. The lung is the most important organ involved by COVID-19 diseases and the common symptoms range from mild to severe illness accompanied by fever, cough and shortness of breath that can lead to hypoxemia and even death [1, 2]. The immune response interconnected with inflammatory damage is thought to play a key role in progress of infection [3].

Although the recommended treatments for COVID-19 are antiviral, anti-inflammatory, antibiotic, anti-malarial, immune-modulatory, and anticoagulant drugs, there is currently a number of drugs and natural product used for treatments of this virus, but their safety and efficacy are under investigation [4,5].

Many of the immune responses and respiratory symptoms of COVID-19 patients are common with other respiratory viral diseases [6]. In Iranian traditional medicine, several medicinal plants with imunomodelating, antipyretic, antitussive, anti-inflammatory, antioxidant and antimicrobial properties are known to improve pulmonary and systemic symptoms of viral infections, which may be effective in preventing and improving the symptoms of COVID infection [7]. Imfluna is an herbal mixtures formulation, containing *Echinacea angustifolia* DC. aerial part (echinacea), *Stachys lavandulifolia* Vahl aerial part (stachys), *Artemisia annua* L. aerial part (artemisia), *Hyssopus officinalis* L. aerial part (hyssopus), *Polypodium vulgare* L. rhizome (polybody), *Alpinia officinarum* Hance rhizome (alpinia), *Zingiber officinale* Roscoe rhizome (ginger) and *Panax ginseng* C.A.Mey. root (ginseng) [8, 9].

A number of experimental and clinical studies demonstrated several pharmacological effects for aforementioned plants including: immunomodulatory, anti-inflammatory, antiviral, antimicrobial and antifungal effects for echinacea [10], antitussive and expectorant for polybody [11]. immunomodulatory, analgesic, anti-inflammatory and antimicrobial effects for stachys [12], antiviral and antioxidant activities for alpinia [13], immunosuppressive and antiviral activities for artemisia [14], antipyretic, antiviral, anti-inflammatory and analgesic effects for ginger [11], antiviral, antioxidant and anti-viral activities for hyssopus [15] and antiviral and strengthening of host immunity effects for ginseng [16].

Therefore, due to the lack of effective drugs for COVID-19 and the history of using Imfluna plants in traditional Iranian medicine to modulate the immune system and treat pulmonary viral infections, this study was performed to evaluate the effect of Imfluna in controlling the symptoms of patients with Covid-19.

2. Materials and Methods

2.1. Plant materials

The plant materials echinacea and hyssopus were collected in June from Institute of Medicinal Plants farm in Karaj, Iran. The stachys was collected in July from Azarbaijan province Iran. The polypody and artemisia were collected

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in June from Guilan province Iran. The alpinia and ginger rhizomes and ginseng root were purchased from local market. The plants were identified by botanist Dr. M. Ghorbani Nohooji and a voucher specimen of the plants was deposited in the central herbarium of the Institute of Medicinal Plants, Karaj, Iran with code no for echinacea (108-IMPH), stachys (7129-IMPH), artemisia (1421-IMPH), hyssopus (7077-IMPH), polypody (7125-IMPH), alpinia (7127-IMPH), ginger (7128-IMPH) and ginseng (7126-IMPH).

The plant materials were dried in the shade at room temperature and then mixed according to the dosage used in traditional medicine. The plant material was extracted with 80% hydroalcoholic solvent and dried by spray drying system.

2.2. Standardization of herbal extract

The extract was standardized by determination of artemisinin, total phenolic and flavonoids contents. The artemisinin content was determined using HPLC method [17], total flavonoids using previously developed method [18] and total phenol by method described by Kim et al. [19].

2.3. Preparation of the herbal and placebo capsules

The extract powder were granulated and filled in 500 mg hard gelatin capsule. The placebo capsules were also prepared similarly using toasted powder.

2.4. Trial design and participants

This placebo-controlled double-blind randomized clinical trial, began in May 2020 at Baqiyatallah Hospital. A total of 60 COVID-19 approved Iranian volunteer patients who were admitted to the COVID-19 ward in Baqiyatallah Hospital on the same day were selected and participated in the study if the inclusion and exclusion criteria were met. This clinical trial was approved by the Ethics Committee of Baqiyatallah University of Medical Sciences (IR.BMSU.REC.1399.036 dated: 29.03.2020) and the trial was registered in the Iranian Registry of Clinical Trials (IRCT 20080901001157N16 dated: 08.04.2020).

2.4.1. Inclusion criteria

Inclusion criteria for selecting patients were the COVID-19 infected patients with positive chest Computed tomography (CT) scan and PCR diagnostic test; ages 20 to 70 years, who are able to use oral medications; declare consent to participate in the study and give written informed consent.

2.4.2. Exclusion criteria

The exclusion criteria were patients with severe shortness of breath; difficulty in swallowing or the possibility of aspiration of food; patients who are unable to take the drug orally; patients with refractory hypoxemia; decreased level of consciousness; hemodynamic instability; hypercapnia; respiratory fatigue who require hospitalization in intensive care units; patients with respiratory failure requiring mechanical ventilation; patients with immunodeficiency, including patients treated with corticosteroids, and chemotherapy; patients

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with malignancies, organ transplants and HIV; patients with underlying diseases including: cardiovascular disease, uncontrolled hypertension, uncontrolled diabetes and underlying respiratory diseases; patients known to have history of seasonal allergic rhinitis or allergy to asteraceae (compositae) family plants; patients with BMI > 40 and pregnant or breastfeeding women.

2.4.3. Sample Size

A statistical power analysis using GPower 3.1.97 software was performed for sample size estimation, based on shortness of breath as primary outcome, comparing two means and the effect size (ES) equal to 0.8, with an alpha = 0.05 and power = 0.80, the projected sample size needed with this effect size is approximately N = 52 (26 in each group) for this simplest between/within group comparison. Thus, our proposed sample size of 52 + 8 = 60 will be more than adequate for the main objective of this study and should also allow for expected attrition and our additional objectives of controlling for possible mediating/moderating factors/subgroup analysis.

2.4.4. Intervention

After confirmation of COVID-19 infection, sixty male and female volunteer Iranian patients who met the inclusion criteria signed a written-informed consent form before participating in the study. Patients in both groups received standard COVID-19 medications, including antiviral and antimalarial drugs, and any supportive therapy as required. In addition to standard COVID-19 medications (routine treatment according to the latest national guideline for the treatment of COVID-19), patients in Imfluna group received 2 Imfluna capsules and patients in placebo group received 2 placebo capsules every 8 hours daily for 14 days. The trial was performed in accordance with the Declaration of Helsinki. The adherence of the participants to the treatment regimen was assessed by checking the number of capsules remaining in boxes at end of the study.

2.4.5. Randomization

A random number table and block randomization method were used. In this method 60 eligible patients were assigned to 30 blocks of 2 patients. Then, each of the 2 patients in the block was randomly assigned to take Imfluna or placebo, so that 30 patients were assigned to each group.

2.4.6. Blinding

Package for herbal and placebo capsule were identical in all specifications and labeled with code B or A. No one except technician who performed the capsules packaging was aware of the contents of the packages or what was code A or B. Patients were aware that they were either in the Imfluna or placebo groups, but they were not aware of the type of group they were in.

2.4.7. Outcomes

The daily shortness of breath and day and night cough were measured during 14 days of the study as primary outcomes. The Shortness Of

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Breath With Daily Activity Questionnaire and Cough Symptom Scoring Questionnaire were used for data collection of cough and shortness of breath respectively during the study [20, 21]. The patient's vital signs, including: blood pressure, heart rate, body temperature, respiratory rate and oxygen saturation were recorded at baseline and then every 12 hours during the study as secondary outcomes. The complete blood count (CBC), aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), blood urea nitrogen (BUN) and creatinine (Cr) as secondary outcomes were determined at baseline, day 3, day 8 and endpoint for any hematological, hepatic and renal drug's probable adverse effects. Other secondary outcomes including chest computed tomography (CT) scan, erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP) were determined at baseline and endpoint.

2.4.8. Side effects

Echinacea and artemisia are members of the Asteraceae (Compositae) family that may cause transient allergies in patients who are allergic to the Asteraceae plant family. Although no documented side effects were reported for this combination in our pilot study, in the present study, patients were advised to report any adverse events such as urticaria, hot flashes, wheezing, nasal congestion, and gastrointestinal upset.

2.4.9. Preventive measures

Imfluna or placebo was discontinued if the patient's health or symptoms worsened.

2.5. Statistical analysis

The SPSS software (version 17, IBM Corporation) was used for analysis of data. Baseline and post intervention data were analyzed using independent t test, paired sample t test and chi-square test. Generalized estimating equation (GEE) model with identity link function and exchangeable correlation matrix was used to compare the groups, adjusted for other covariates such as age, BMI and sex. $P < 0.05$ was considered as significant. The data were analyzed by the intention-to-treat approach.

3. Results

3.1. Phytochemical analysis

Phytochemical analysis showed that Artemisinin concentration was 1.56 ± 0.06 mg/1000 mg in plants dry extract. The extract also contained total flavonoid as 65.49 ± 6.36 milligrams of catechin equivalents per gram and total phenolic content 102.48 ± 8.37 milligrams of gallic acid per gram of dry extract.

3.2. Clinical trial

The study, was started in May 2020 in Baqiyatallah Hospital and competed in October 2020. A total of 60 volunteer patients 30 in each group completed the trial (Fig. 1). Three patients were lost to follow-up as one left the study at his own request, one did not take herbal medicine regularly and the other was shifted to home quarantine and stopped herbal medication.

The baseline characteristics of the study participants are given in Table 1. There was no significant difference between age, sex and body mass index of patients (BMI) in the two groups at baseline.

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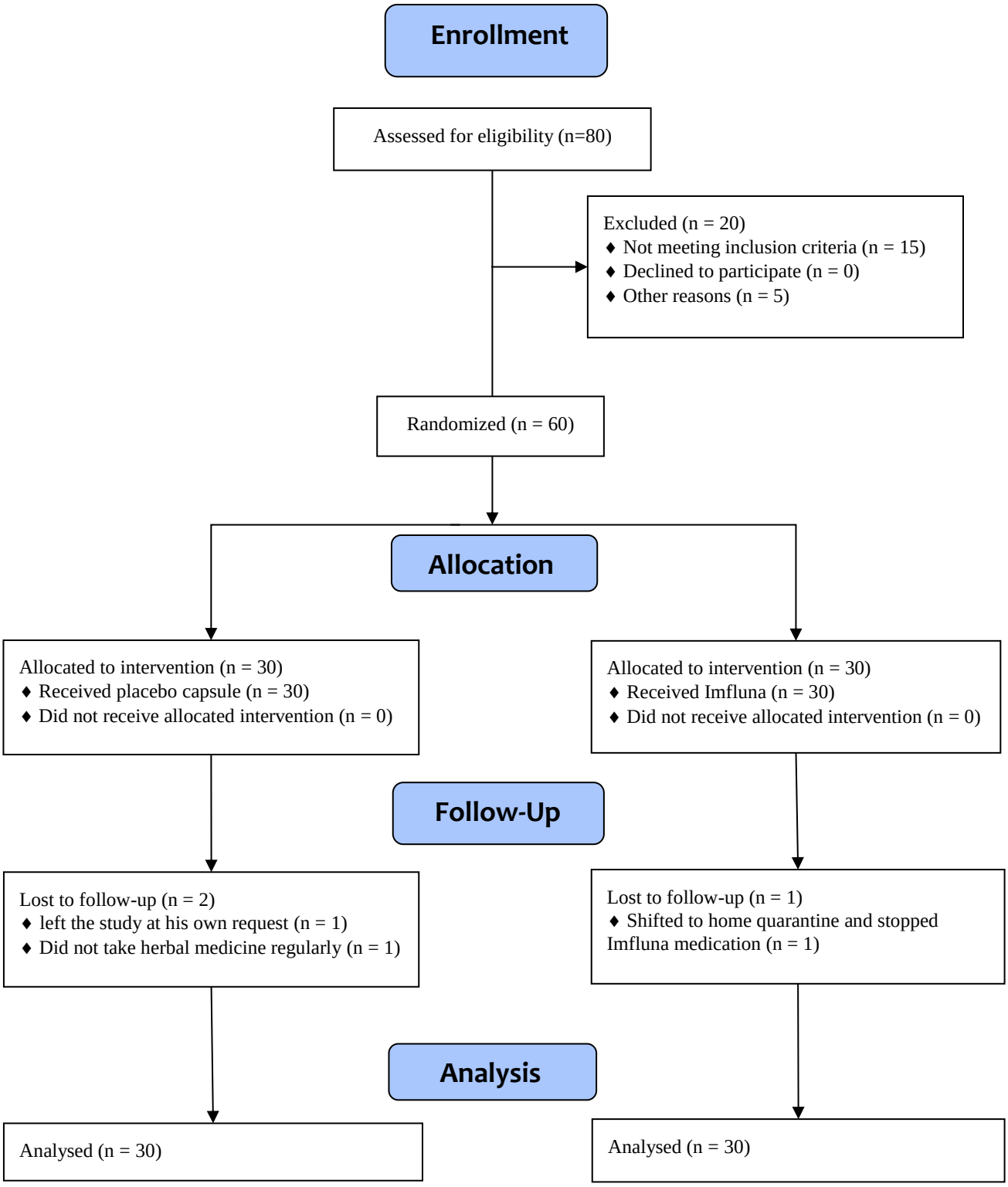


Fig. 1. CONSORT 2010 flow diagram showing the entry and exit of patients in the two study groups from the beginning to the end of the intervention

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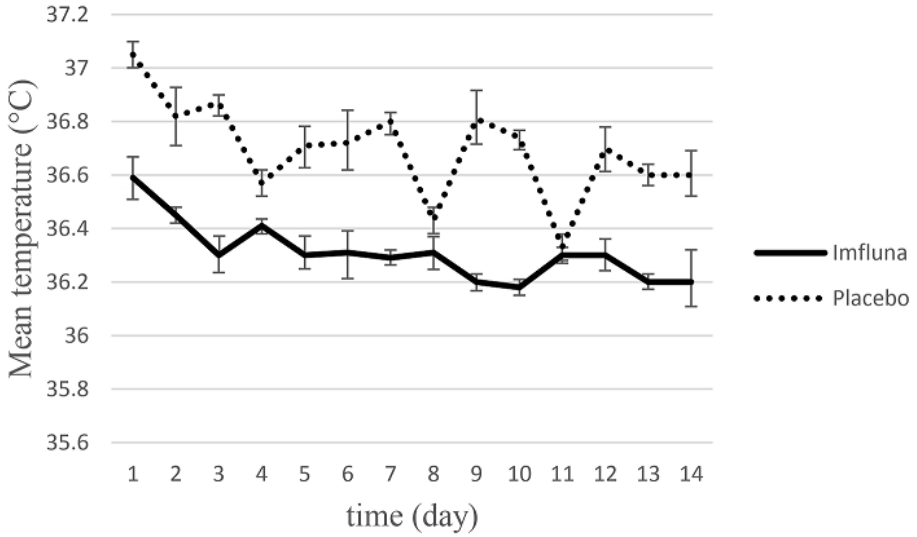


Fig. 2. The mean body temperature in Imfluna and placebo groups during 14 day study

Table 1. Baseline demographic data of the study population in Imfluna and placebo groups

Variable		Imfluna	Placebo	
		Mean ± SD		P-Value
Age (year)		58.37 ± 12.97	54.14 ± 13.58	0.25*
BMI		28.04 ± 4.23	27.31 ± 4.52	0.63*
		N (%)		
Gender	**Male**	19 (63.3)	22 (73.3)	0.40#
	Female	11 (36.7)	8 (26.7)	

*P-value calculated by two independent sample t test

#P-value calculated by Chi-squared test

3.3. Assessment of the patients' vital signs

3.3.1. Body temperature

The mean daily body temperature recorded during 14 days of the study showed that the mean body temperature in the Imfluna group improved significantly (P = 0.008) compared to the placebo group. The body temperature was reduced on average by 0.02 for each visit. Although, there was no significant time effect (P = 0.12) when controlling for age, BMI, sex and group membership (Fig. 2.).

3.3.2. Oxygen saturation

The mean daily oxygen saturation recorded during 14 day study showed that, patients in the Imfluna group had insignificantly (P = 0.87) higher mean oxygen saturation than the placebo group (Fig. 3). There was no significant time effect (P = 0.21) when controlling for age, BMI, sex and group membership.

3.3.3. Blood pressure

The mean systolic (P = 0.37) and diastolic (P = 0.36) blood pressures recorded during 14 day study were not significantly different between the Imfluna and placebo groups. The systolic (P = 0.09) and diastolic (P = 0.06) blood pressures were increased on average by 0.51 and 0.62 for each visit, respectively (Fig 4.).

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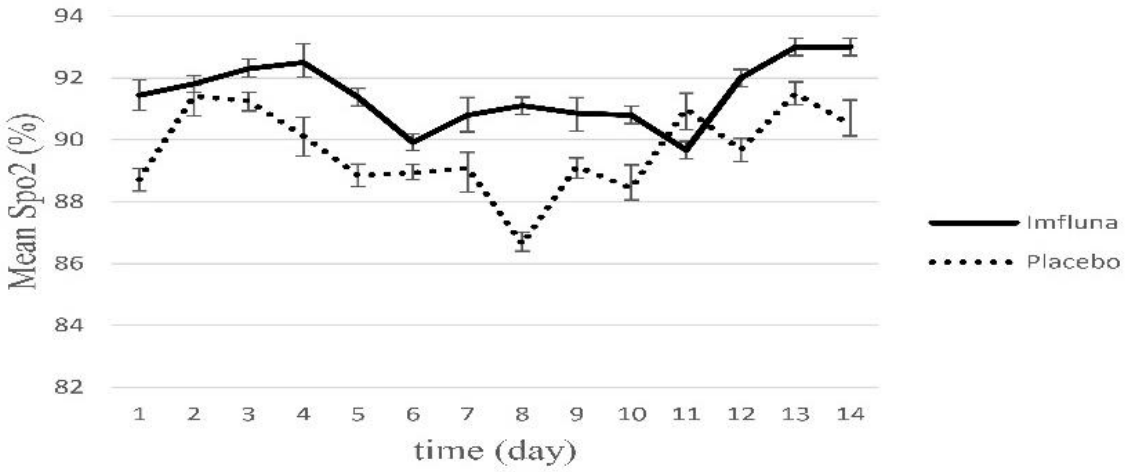


Fig. 3. The mean blood oxygen saturation in Imfluna and placebo groups during 14 day study

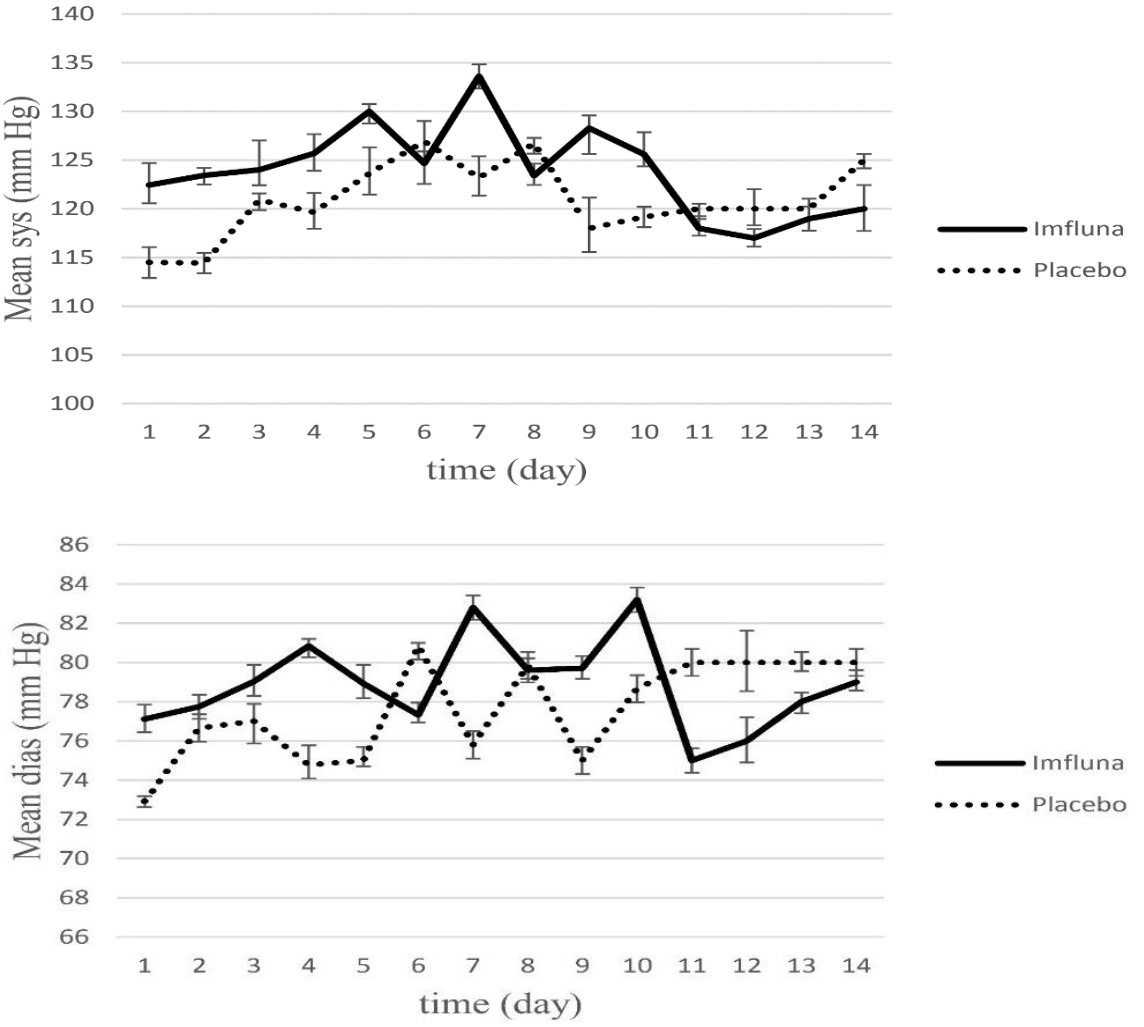


Fig. 4. The mean systolic and diastolic blood pressures recorded during 14 days in the Imfluna and placebo groups

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3.3.4. Respiratory rate

The mean daily respiratory rate recorded during 14 day study were not significantly different (P = 0.35) between patients in the Imfluna and placebo groups (Fig. 5). The trend of average respiration rate was almost steady over time and there was no significant time effect (P = 0.98) when controlling for age, BMI, sex and group membership.

3.3.5. Cough criteria & Shortness of breath

The mean score of night cough recorded in the Imfluna group at baseline was significantly higher than the placebo group but it was significantly reduced in the Imfluna group compared with placebo group at endpoint (Table 2). The mean score of cough per day in two groups at baseline was not significantly different, but it was significantly reduced in the Imfluna group compared with placebo group at endpoint (Table 2). The mean score of shortness of breath in the Imfluna group at baseline was significantly higher than the placebo group but it was significantly reduced at endpoint compared with placebo (Table 2).

In the Imfluna group, the mean score of the shortness of breath (P < 0.001), the mean score of night cough (P < 0.001) and mean score of cough per day (P < 0.001) were significantly lower than the baseline scores.

3.3.6. Patients CT

Out of a total of 60 patients, 11 in the placebo group and 13 in the drug group underwent CT scan at endpoint. Comparing the first and last CTs, the radiologist reported that 38.5 % of the patients in the Imfluna group and 9.1 % in the placebo group improved, but 61.5 % in the Imfluna group and 91.9 % in the placebo group did not (Table 3).

3.4. Blood biochemical analyses

Although there was no statistically significant difference between the mean ESR results of patients in the two groups at baseline, the mean ESR in the Imfluna group was significantly decreased at endpoint compared with placebo (Table 4). There were no significant differences in the mean blood parameters levels including: WBC, CRP, AST, ALT, ALP, CR and BUN in Imfluna compared with placebo group before and after intervention (Table 4).

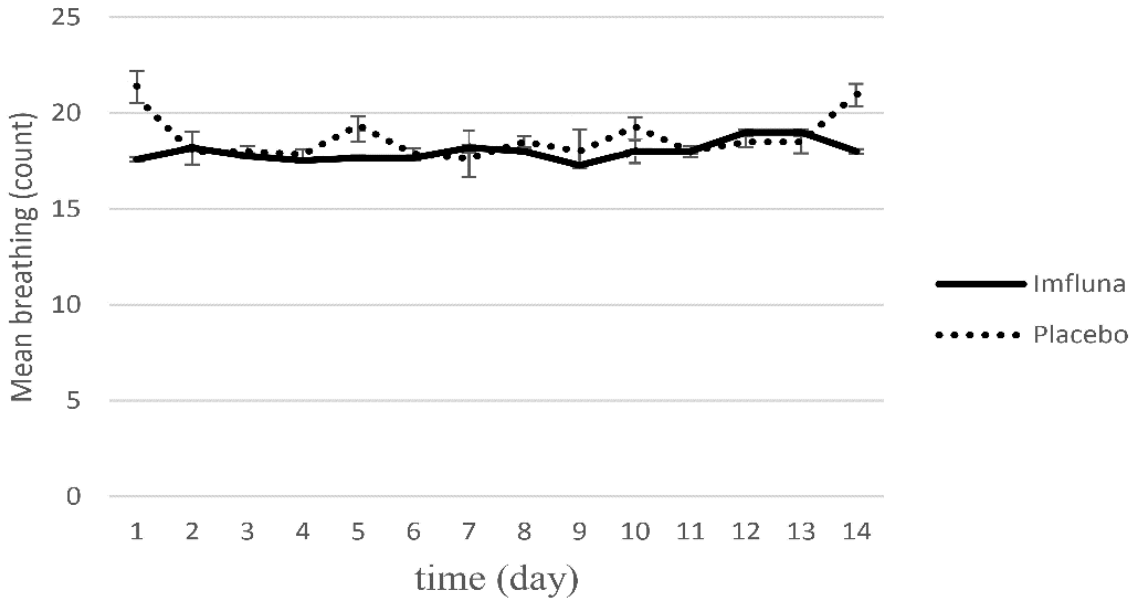


Fig. 5. The mean respiratory rate recorded in the Imfluna and placebo groups during 14 day study

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Table 2. The patients' daily cough and shortness of breath at baseline and endpoint in the Imfluna and placebo groups

		Baseline		Endpoint			Percent improvement
	Groups	Mean ± SD	P*	Mean ± SD	P*	P#	
Shortness of breath (score)	Imfluna	2.97 ± 0.94	< 0.001	2.00 ± 0.00	< 0.001	< 0.001	32.7 ↓
	Placebo	1.67 ± 0.95		1.55 ± 0.60		0.57	7.2 ↓
Cough during the day (score)	Imfluna	2.14 ± 1.06	0.20	1.00 ± 0.00	< 0.001	< 0.001	53.3 ↓
	Placebo	1.82 ± 0.81		1.57 ± 0.79		0.22	13.7 ↓
Cough during the night (score)	Imfluna	2.29 ± 1.10	0.03	1.00 ± 0.00	< 0.001	< 0.001	56.3 ↓
	Placebo	1.64 ± 1.06		1.57 ± 0.79		0.57	4.2 ↓

* P-value calculated by t-test, between groups

P-value calculated by paired sample t-test, Endpoint compared with baseline

Table 3. Radiologist CT improvement report of patients in Imfluna and placebo groups

Group	Number of patient	Improved		Not Improved	
		Number	Percent	Number	Percent
Imfluna	13	5	38.5 %	8	61.5 %
Placebo	11	1	9.1 %	10	90.9 %

3.5. Hospitalization period

The length of hospitalization was not fully completed by all patients due to overcrowding of the hospital. Some patients due to their request and some patients who were clinically eligible to leave the hospital were discharged earlier. The discharged patients received quarantine care at home and blood samples were taken by research team technician and data reporting was done via virtual contact. However, the patients' lengths of hospital stay were 9.35 ± 4.986 and 11.30 ± 6.600 day in Imfluna and placebo groups, respectively (Fig. 1).

4. Discussion

The present study reports the safety and efficacy of Imfluna, an Iranian traditional polyherbal medicine containing a mixture of echinacea, polybody, stachys, alpinia, artemisia, ginger, hyssopus and ginseng in controlling the symptoms of patients with COVID-19. Treatment of COVID-19 hospitalized patients with Imfluna improved daily cough, shortness of breath and ESR within 14 days of the study without any side effects. Interestingly, CT analysis of the chest showed that Imfluna treatment improved pathological lung lesions in 38.5 % of patients, while improvement was observed in only 9.1 % of patients in the placebo group.

Despite these promising findings, our study had limitations such as the small sample size and failure to perform chest CT scans for all patients at the end of the study due to reluctance of some patients. Other limitation was the earlier discharge of some patient's although they received quarantine care at home and blood samples were taken by research team technician and data reporting was done via virtual contact.

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Table 4. The patients' laboratory data at baseline and endpoint in Imfluna and placebo groups

	Group	Baseline		Endpoint	
		Mean ± SD	P* (Between groups)	Mean ± SD	P* (Between groups)
ESR (mm/hr)	**Imfluna**	39.47 ± 21.45	0.29	25.75 ± 19.46	0.01
	Placebo	31.79 ± 27.14		58.62 ± 36.50	
CRP (mg/l)	**Imfluna**	18.11 ± 28.21	0.08	8.02 ± 3.42	0.62
	Placebo	33.65 ± 31.26		7.27 ± 3.02	
WBC (cells/mcl)	**Imfluna**	7.20 ± 2.47	0.10	8.77 ± 3.72	0.08
	Placebo	6.11 ± 2.43		6.93 ± 1.59	
RBC (cells/mcl)	**Imfluna**	4.89 ± 0.76	0.73	4.67 ± 0.63	0.25
	Placebo	4.82 ± 0.78		4.29 ± 1.01	
Hb (g/dl)	**Imfluna**	15.17 ± 5.98	0.56	14.11 ± 1.72	0.11
	Placebo	16.17 ± 6.87		12.60 ± 2.82	
HCT (%)	**Imfluna**	40.74 ± 6.68	0.64	40.41 ± 4.80	0.21
	Placebo	39.71 ± 9.34		37.20 ± 7.54	
AST (U/L)	**Imfluna**	38.72 ± 29.45	0.12	39.80 ± 29.12	0.54
	Placebo	50.33 ± 27.08		43.27 ± 26.22	
ALT (U/L)	**Imfluna**	77.26 ± 37.23	0.26	72.72 ± 41.32	0.92
	Placebo	64.93 ± 48.22		71.60 ± 53.02	
ALP (U/L)	**Imfluna**	221.72 ± 79.32	0.22	231.27 ± 74.13	0.39
	Placebo	194.11 ± 96.66		212.27 ± 88.82	
CR (mg/dl)	**Imfluna**	1.15 ± 0.25	0.70	1.25 ± 0.21	0.53
	Placebo	1.18 ± 0.31		1.16 ± 0.36	
BUN (mg/dl)	**Imfluna**	16.25 ± 6.19	0.46	15.73 ± 3.40	0.92
	Placebo	19.09 ± 19.16		16.40 ± 15.14	
Na (mmol/l)	**Imfluna**	138.80 ± 4.32	0.39	140.5 ± 7.25	0.44
	Placebo	140.08 ± 4.12		137.5 ± 2.51	
K (mmol/l)	**Imfluna**	5.61 ± 6.48	0.55	4.12 ± 0.34	0.45
	Placebo	7.14 ± 8.80		3.95 ± 0.53	

* P < 0.05 was considered as significant. P value calculated by t-test.

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; WBC: White blood cell; RBC: Red blood cell; Hb: Hemoglobin; HCT: Hematocrit; AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; Cr: Creatinine; BUN: Blood urea nitrogen; Na**:** Sodium; K: Potassium

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In addition, the bioactives and the mechanism of action of this herbal mixture in the treatment of COVID-19 were not investigated in the present study. One more limitation was the lack of chemical constituent determination for each plant in the mixture.

The results of the present study are in accord with the results of a clinical trial, reporting that infected COVID patients, treated with combination of ginger and echinacea had improvement of coughing, dyspnea, and muscle pain, compared with the placebo group [22]. The mechanism of action of this polyherbal combination in improving the symptoms of the COVID-19 disease can probably be related to the inhibitory effect of its ingredients on the pathophysiological mechanisms of creating and exacerbating the symptoms of the disease. Several laboratory and clinical research to date suggest that the body immunomodulatory response to COVID-19 infection is associated with a severe inflammatory response with the release of large amounts of pro-inflammatory cytokines or "cytokine storms" that are directly associated with lung damage [23].Therefore, any medication that regulates the aggravation of these two pathways can be effective in reducing the complications of COVID-19 disease. Imfluna is mixture of herbal medicines including echinacea, polybody, stachys, alpinia, artemisia, ginger, hyssopus and ginseng. Numerous studies have shown the anti-inflammatory, immunomodulating, anti-viral and antioxidant effects of herbs in this compound that may directly or indirectly affect the immune system and inflammatory infections in the respiratory system.

The available evidence suggests that echinacea has direct inhibitory effects against a wide range of viruses [24] and the mechanism of its antiviral effects may be related to the immune and anti-inflammatory effects of plant alkaline compounds [25]. As for other components, although no clinical studies have been performed to support the efficacy of polypody and stachys in the treatment of complications of COVID-19 infection, the results of previous studies show that the antipyretic, analgesic, antibacterial and antiviral effects of polypody [11, 26] and stachys analgesic, anti-inflammatory and antioxidant activities may be effective in treating COVID-19 complications [12, 27]. As for alpinia, another component of Imfluna, in vitro and in vivo studies have reported significant antiviral, anti-inflammatory, and antibacterial properties of this plant [13, 28]. However, the anti-inflammatory effects of alpinia phenolic extract have been attributed to the inhibition of COX-2 [29]. COX-2 plays a key role in the inflammatory process and a selective inhibition of COX-2 may help in decreasing the mortality and morbidity rate in COVID-19 patients [30]. Artemisia is another component of Imfluna. In agreement with our study safety and efficacy of artemisinin for treatment of patients with mild-to-moderate COVID-19 have been reported in a clinical trial. In that study, the time to reach undetectable SARS-CoV-2 was significantly shorter in artemisinin treated patients compared to control group [31]. To explain the mechanism of action of artemisia, in the previous studies, artemisinin and its derivatives such as artesunate, have been shown to exert immunomodulatory functions [14] and sterols including sitosterol and stigmasterol have been isolated from artemisia, as virus inhibitory agents [32]. Ginger, another component of Imfluna, showed a wide range of antiviral effects in experimental studies [11]. In support to our finding in a clinical trial, intake of diet supplemented with ginger in patients with

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acute respiratory distress syndrome, decreased duration of mechanical ventilation and length of stay in intensive care unit [33]. Ginger contains chemical components such as 6-gingerols, 6-shogoals, zhingerol with antioxidant and anti-inflammatory properties, that can reduce inflammatory mediators such as inflammatory cytokines and chemokines [34]. These inflammatory responses have been exaggerated in COVID-19 infected patients [30]. Hyssopus, another component of Imfluna, has demonstrated antiviral effects in laboratory studies. This antiviral effect was against herpes simplex virus and human immunodeficiency virus [35]. Researchers claim that, this antiviral effect may be due to the inhibition of oxygen free radicals by hyssopus chemical components [35]. In the case of ginseng, another component of Imfluna, in accordance to our study its antiviral effects were reported in a placebo-controlled trial in which the Korean red ginseng extract prevented influenza-like illness in healthy adults [36]. The mechanism for its antiviral effects was claimed to be due to anti-inflammatory and immunomodulatory effects in viral infection [37].

In summary, a wide range of antiviral, anti-inflammatory, immune modulating, antipyretic, analgesic and antibacterial properties of plant mixture in Imfluna induced additive and synergistic effects in improving the complications and controlling the worsening of COVID-19 infection.

5. Conclusion

Treatment of COVID-19 patients with Imfluna, an Iranian traditional polyherbal medicine, improved symptoms associated with the disease including cough, shortness of breath, and ESR within 14 days of the study without any side effects. It is suggested to conduct a further trials with larger number of patients assessing the efficacy and safety of Imfluna in the treatment of COVID-19 infection, as well as more studies addressing the mechanisms and bioactives involved in the anti-COVID effects of Imfluna seem necessary. It is also suggested to investigate the efficacy of this herbal medicine in the prevention of COVID-19 disease, especially for people who are in contact with newly diagnosed COVID-19 patients.

Author contributions

H.F.H.: Design of the work and drafting the article. M.G.: Formulation and production of herbal medicine. M.S.: Supervising the clinical trial. A.K.: Physician assistance in conducting a clinical trial. A.T.: Acquisition of data. H.K.: Performing CT scan and radiological analysis. M.R.: Analysis and interpretation of data statistical analysis. S.K.: Final approval of the version to be published. A.F.H.: Critical revision of the manuscript. M.G.N.: Collection, identification, and coding herbarium specimens. R.M.: Physician conducting the clinical trial.

Conflicts of interest

No competing financial interests exist.

Funding

This research was financial supported by Homapharmed Pharmacutical Company Tehran Iran.

Acknowledgments

We thank Dr. Morteza Khairabadi, head of Homapharmad Pharmaceutical Company, for financially supporting this study, Hadi Khairabadi for coordinating the collection of

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[DOR: 20.1001.1.2717204.2022.21.81.1.7]
[DOI: 10.52547/jmp.21.81.51]

plants and seeking the extraction and preparation of medicine, and Mehdi Khairabadi to bring together the research team and group liaison, Reza Mirzaei for consulting in the selection and dosage of medicinal plants and botanist Dr. Gorbani to identify medicinal plants. We also thank Baqiyatallah University of Medical Sciences for conducting this clinical trial and the ACECR Institute of Medicinal Plants for providing herbal medicine and placebo.

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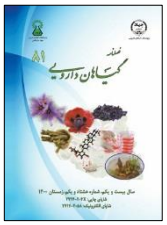
How to cite this article: Fallah Huseini H, Gholibeikian MR, Shohrati M, Kaffash A, Taheri A, Khajepour HA, Raei M, Kianbakht S, Fallah Hosseini A, Ghorbani Nohooji M, Mohtashami R. Effects of Imfluna an Iranian traditional polyherbal medicine on COVID-19 symptoms: A randomized double-blind placebo-controlled clinical trial. ***Journal of Medicinal Plants*** 2022; 21(81): 51-66. doi: 10.52547/jmp.21.81.51

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مقاله تحقیقاتی

تأثیر ایمفلونا، یک داروی سنتی چند گیاهی ایرانی، بر علائم COVID-19: یک کارآزمایی بالینی تصادفی دوسو بی‌خبر کنترل شده با دارونما

حسن فلاح‌حسینی[۱]، محمدرضا قلی‌بیکیان[۲]، مجید شهرتی[۳]، افسانه کفاش[۴]، علی طاهری[۵]، حجت الله خواجه پور[۶]، مهدی راعی[۷]، سعید کیان بخت[۱]، آمنه فلاح حسینی[۸]، مجید قربانی نهوجی[۱]، رضا محتشمی[۹،*]

[۱] *مرکز تحقیقات گیاهان دارویی، پژوهشکده گیاهان دارویی جهاد دانشگاهی، کرج، ایران*

[۲] *گروه شیمی آلی، دانشکده شیمی، دانشگاه کاشان، ایران*

[۳] *گروه فارماکوتراپی، دانشکده داروسازی، دانشگاه علوم پزشکی بقیه الله، تهران، ایران*

[۴] *گروه بیماریهای داخلی، دانشکده پزشکی، دانشگاه علوم پزشکی سبزوار، ایران*

[۵] *دانشکده داروسازی، دانشگاه علوم پزشکی بقیه الله، تهران، ایران*

[۶] *گروه رادیولوژی، دانشگاه علوم پزشکی بقیه الله، تهران، ایران*

[۷] *مرکز تحقیقات سلامت، موسسه سبک زندگی، دانشگاه علوم پزشکی بقیه الله، تهران، ایران*

[۸] *گروه فوریت های پزشکی، دانشگاه علوم پزشکی تهران، تهران، ایران*

[۹] *مرکز تحقیقات قرآن و حدیث، دانشگاه علوم پزشکی بقیه الله، تهران، ایران*

اطلاعات مقاله

گل‌واژگان:
کارآزمایی بالینی
کووید -۱۹
داروی چند گیاهی
طب سنتی ایرانی
ایمفلونا

چکیده

مقدمه: همه‌گیری فعلی بیماری کرونا ویروس ۲۰۱۹ (COVID-19) و شدت عفونت و مرگ و میر بالا، چالش‌های تقریباً بی‌سابقه‌ای در سیستم‌های بهداشتی اکثر کشورهای جهان بوجود آورده است. **هدف:** مطالعه حاضر با هدف بررسی تأثیر داروی چند گیاهی سنتی ایرانی (Imfluna) حاوی مخلوط عصاره گیاهان سرخارگل، سنبله‌ای، گندواش، زوفا، بسفایج، خولنجان، زنجبیل و جینسینگ بر علائم بیماران مبتلا به COVID-19 انجام شد. **روش بررسی:** در این کارآزمایی بالینی تصادفی دوسوکور کنترل شده با دارونما، در مجموع ۶۰ بیمار داوطلب مبتلا به COVID-19 به طور تصادفی در دو گروه دارونما و داروی گیاهی ایمفلونا قرار گرفتند. بیماران در هر گروه ، علاوه بر دریافت داروهای استاندارد، دو کپسول ۵۰۰ میلی‌گرم ایمفلونا یا دارونما را هر ۸ ساعت به مدت ۲ هفته مصرف کردند. در طول مطالعه علائم حیاتی بیمار، شامل شدت تنگی نفس، سرفه و دمای بدن بررسی شد. همچنین در شروع و پایان مطالعه سی تی اسکن قفسه سینه، آزمایش خون برای ESR، عملکرد کبد و کلیه، مورد ارزیابی قرار گرفت. **نتیجه:** نتایج نشان داد که بیماران در گروه تحت درمان با ایمفلونا در مقایسه با گروه دارونما بهبود معنی‌داری در سرفه روزانه، تنگی نفس و ESR داشتند. علاوه بر این، ضایعات ریه در گروه تحت درمان با ایمفلونا به طور غیر معنی‌داری بهبود یافت. **نتیجه‌گیری:** بیماران مبتلا به COVID-19 که به مدت ۲ هفته تحت درمان با ایمفلونا قرار گرفتند، آسایش بهتر و علائم کمتر بیماری داشتند و هیچ گونه عوارض دارویی نداشتند.

مخففها: ESR، میزان رسوب گلبول قرمز؛ CRP، پروتئین واکنشی؛ WBC، گلبول سفید؛ RBC، گلبول قرمز؛ Hb، هموگلوبین؛ HCT، هماتوکریت؛ AST، آسپارتات ترانس آمیناز؛ ALT، آلانین ترانس آمیناز؛ ALP، آلکالین فسفاتاز؛ Cr، کراتینین؛ BUN، نیتروژن اوره خون؛ Na، سدیم؛ K، پتاسیم

* نویسنده مسؤول: reza_mohtashami1979@bmsu.ac.ir

تاریخ دریافت: ۲۴ شهریور ۱۴۰۰؛ **تاریخ دریافت اصلاحات:** ۲۲ دی ۱۴۰۰؛ **تاریخ پذیرش:** ۲ بهمن ۱۴۰۰

doi: 10.52547/jmp.21.81.51

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