The Role of Long-term Low-dose Methylprednisolone Treatment on Long Covid Patients

Long-Covid Hastalarının Tedavisinde Uzun Süre Düşük Doz Metilprednizolon Tedavisinin Rolü

Aslıhan Banu Er[1], Okan Er[2]

[1]Department of Pulmonology, Training and Research Hospital, Usak University, Usak, Turkiye
2Department of Cardiology, Training and Research Hospital, Usak University, Usak, Turkiye

ABSTRACT

Objective: To determine whether the two-month low-dose methylprednisolone therapy might improve symptomatic, radiologic, and laboratory findings of long COVID-19. Many patients have emerged to hospitals with residual symptoms due to Sars Cov-2 pneumonia in the post-COVID period. They had not enough treatment and need a novelty medical approach.
Methods: This study is single-center, retrospective, and investigated the response to methylprednisolone therapy in long COVID-19 patients with persistent symptoms between October 2020 and April 2021. The medical history, blood analysis, and current lung tomography results of 158 patients with ongoing symptoms at least one month later the acute illness were evaluated. Thirty-two patients were excluded from the study because of the exclusion criteria. After all, we wanted to assess the effects of oral methylprednisolone therapy in gradually decreasing doses of totally 680 mg on one hundred twenty-six patients had been given. But we could research ninety-seven patients' findings due to twenty-nine patients were not attending follow-up.
Results: The mean age of the patients was 50,8 years, and 52.6% were male. Each of the resistant symptoms was improved by methylprednisolone therapy. Laboratory findings were similar before and after the treatment, except for creatine and D dimer. Radiologic amelioration was promising on lung CT signs. We detected a mild-moderate positive correlation between neutrophil, ferritin, LDH, and D-Dimer levels to lung CT involvement pre-methylprednisolone treatment.
Conclusion: Low-dose methylprednisolone therapy may be an option for the symptomatic and radiological treatment of long Covid-19 patients.

Key Words: Long COVID-19, methylprednisolone, pneumonia viral

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ÖZET

Amaç: Bu çalışma, Long COVID-19'dan muzdarip hastaların semptomlarını, radyolojik bulgularını ve laboratuvar sonuçlarını iyileştirebilecek iki aylık düşük doz metilprednizolon tedavisinin etkilerini belirlemeyi amaçlamaktadır. Birçok hastanın, akut Sars-CoV-2 pnömonisi iyileştikten sonra bile semptomları devam etmektedir ve geleneksel tedaviler yetersiz kalmış, bu nedenle yenilikçi tıbbi yaklaşımlara ihtiyaç duyulmuştur.
Yöntem: Bu çalışma, Ekim 2020 ile Nisan 2021 arasında devam eden Long COVID-19 hastalarının geçmeyen semptomlarına metilprednizolon yanıtını inceleyen tek merkezli, retrospektif bir çalışmadır. Akut hastalık sonrasında en az bir ay boyunca semptomları süren 158 hastanın tıbbi geçmişi, kan analizi ve akciğer tomografisi sonuçları değerlendirilmiştir. Kriterlere uymayan 32 hasta çalışmadan çıkarıldı. Toplam 680 mg dozda kademeli olarak azalan metilprednizolon tedavisi alan 126 hasta çalışmaya alınmıştır. Ancak 29 hastanın takip muayenelerine gelmemesi nedeniyle çalışma analizi için 97 hasta kullanıldı.
Bulgular: Hastaların ortalama yaşı 50,8 yıldı ve %52,6 'sı erkekti. Metilprednizolon tedavisiyle, tüm semptomlarda iyileşme gözlendi. Laboratuvar bulguları, tedavi öncesi ve sonrası genellikle benzer kaldı. Ancak kreatin ve D-dimer seviyelerinde değişiklikler gözlendi. Sevindirici bir şekilde, akciğer BT taramalarında radyolojik düzelmeler gözlemlendi. Metilprednizolon tedavisi öncesi nötrofil, ferritin, LDH ve D-dimer seviyeleri ile akciğer BT tutulumu arasında hafif ile orta derecede pozitif bir ilişki tespit edildi.
Sonuç: Düşük doz metilprednizolon tedavisi, Long COVID-19 hastalarının semptomları ve radyolojik anormalliklerinin tedavisi için bir seçenek olarak düşünülebilir.

Anahtar Sözcükler: Long COVID-19, Metilprednizolon, Viral Pnömoni

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ORCID IDs: A.B.E.0000-0002-7832-6233,O.E.0000-0003-1264-7947

Address for Correspondence / Yazışma Adresi: Okan Er, MD, Usak University Faculty of Medicine, Cardiology Department, Usak, Turkiye E-mail: erokan2005@gmail.com

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INTRODUCTION

As of 2021, we understand that it is possible for various presentations of Covid-19 disease. The symptomatic patients have more often upper or lower respiratory complaints. They rarely have musculoskeletal, gastrointestinal, or neurological signs. In Turkey, the national medical program for SARS CoV-2 has been applied since March 10, 2020. It has been updated many times according to the medical literature. Some success has been achieved in the treatment of this mortal pandemia. It is advised to take a five-day favipiravir (first day a loading dose, 1600 mg twice a day and then thorough four-day 600 mg twice a day) and five-day hydroxychloroquine (Hq 200 mg twice a day) for all cases proved virologically. After a long time, in May 2021, Hq has been discontinued to use. In this period, survivors have been accepted as treated. Unfortunately, clinicians have been meeting lots of inadequately treated patients with Covid 19 day-to-day. We must clearly understand who is fully recovered and who needs medical treatment in the following days.

We want to introduce you to this paper's authors: Mrs. Er, pulmonologist, and the case's wife; Mr. Er, cardiologist, had a positive polymerase chain reaction of Sars-Cov2 on October, 11th 2020. Six days after the diagnosis, progressive respiratory distress occurred when he was at home in quarantine. He was admitted with an oxygen saturation of 65% to the emergency service and hospitalized in intensive care unite (ICU) of Usak University Traning and Searching Hospital, Turkey. He was treated with high-flow oxygen, continuous positive airway pressure, a ten-day prolonged favipiravir therapy, subcutaneous enoxaparin (0,6 cc twice a day), intravenous (iv) vitamin C (4 mg/day for four days), iv methylprednisolone (MP 250 mg three days in a row, then 40 mg/day for five days), iv furosemide (20 mg/day for six days), convalescent plasma (three times), iv immunoglobulin (totally 150 mg), remdesivir (totally 600 mg in five days), and finally tocilizumab (totally 800 mg). It was gradually achieved a clinic improvement.

After all, computerized tomography (CT) was done for the lungs. Near 80% involvement of lungs became a big concern for us in the recovery period. Mr. Er had a second chance for his life, but the question was whether lungs sequelae could be avoided. There was a slight increase in heart dimensions, severe thick fibrotic bands, atelectasis specifically in the left lower lobe, interlobular septal thickening, and patchy bilateral areas of ground-glass opacification (ggo) in lower and middle lobes. We decided to use a low-dose decreasing MP (total 680 mg, mean 11,3 mg/day) during the sixty-day post-Covid recovery period. After discharged, MP; 48 mg for the first five days, 32 mg for the second five days, 16 mg for the third five days, 8 mg for the fourth five days, rest ten days from the first month, and the second month was given 4 mg in a day. We added just for the first month orally furosemide (40 mg twice a week, totally 320 mg), rivaroxaban (10 mg/day), and low-salt dietary (2 gr/day). After ninety-five days from the diagnosis, a thorax CT scan was done again. (see figure 1). As a satisfactory result, there was seen neither sign of fibrosis nor sequelae. Symptoms like fatigue, cough, dyspnea, chest discomfort, or palpitation did not accompany recovery. Thank God, complete health and well-being happened. On the increasing outpatient applications in our daily practice of long Covid-19 patients defined in the NICE guideline published in December 2020 (1), we decided to give the same MP therapy to the cases with ongoing symptoms based on Mr.Er' successful treatment.

METHODS

This is a single-centered, retrospective study between December 2020 to May 2021. The clinical trials ethics committee of the Usak University Training and Research Hospital in Turkey approved it with a decision no 15 on June 30, 2021. According to the national guidelines for Covid-19, the patients who had had a positive polymerase chain reaction test for Sars CoV2 or radiological and clinical illness and, still symptomatic at the end of one month after the diagnosis, were enrolled in the study. The asymptomatic patients at discharge or the quarantine's end but who had recurrent symptoms later were also included in this study. Our focus was on optimal long Covid-19 treatment for persistent or recurrent symptoms after at least one month later from the acute infection.

Cohort Identification

Ongoing dyspnea, fatigue, chest discomfort, palpitation, and cough complaints following one month after the first diagnose were named as "ongoing symptomatic Covid 19" (residual complaints from 4 weeks up to 12 weeks) and "Post-Covid 19 Syndrome" (persisting complaints over 12 weeks). Both groups are defined as "long Covid-19" together. We searched the patients' medical history, previous and current medical therapy about Covid-19 and noted their arterial tensions, pulses, oxygen saturation in room air from the records. Blood samples including complete blood count, creatine, sodium, potassium, high sensitive troponin I (hs Trop I), lactate dehydrogenase (LDH), d-dimer, ferritin, procalcitonin, C reactive protein (CRP), Brain-type natriuretic protein (BNP) at admission, and after the two-month steroid therapy were registered. Exclusion criteria were at least one value of hs Trop I above the 99% upper reference limit, BNP level more than 400 mc/L, hemoglobin level less than 10 gr/dl, perimyocarditis, congestive heart failure, moderate or severe valvular disease, history of cardiac arrhythmias, history of thyroid gland disorders, liver failure, renal failure, primer pulmonary disease. 32 of 158 symptomatic patients had at least one exclusion criterion and were excluded from the study. One hundred twenty-six long Covid cases were re-evaluated with symptomatic, laboratory findings, and radiologically after a two-month low-dose MP therapy. Twenty-nine subjects' follow-up data were not found. Of the remaining 97 patients with long Covid-19, 49 were included in the study as ongoing symptomatic Covid-19, namely group 1, and 48 as Post-Covid 19 Syndrome, or group 2. Ninety-seven patients' CT signs were noted as ggo, consolidation, crazy paving, air bronchogram, broncho-vascular dilatation, peribronchial thickening, atelectasis, honeycomb lung, fibrotic changes, subpleural interstitial changes, and other nonspecific signs (pleural effusion, nodules) as defined by the glossary of terms of the Fleischner Society (2). At the end of two months, we assessed the MP therapy on improving symptoms, laboratory findings, and CT signs. The study diagram data provides additional detail on the method for making these measurements (see Figure 1).

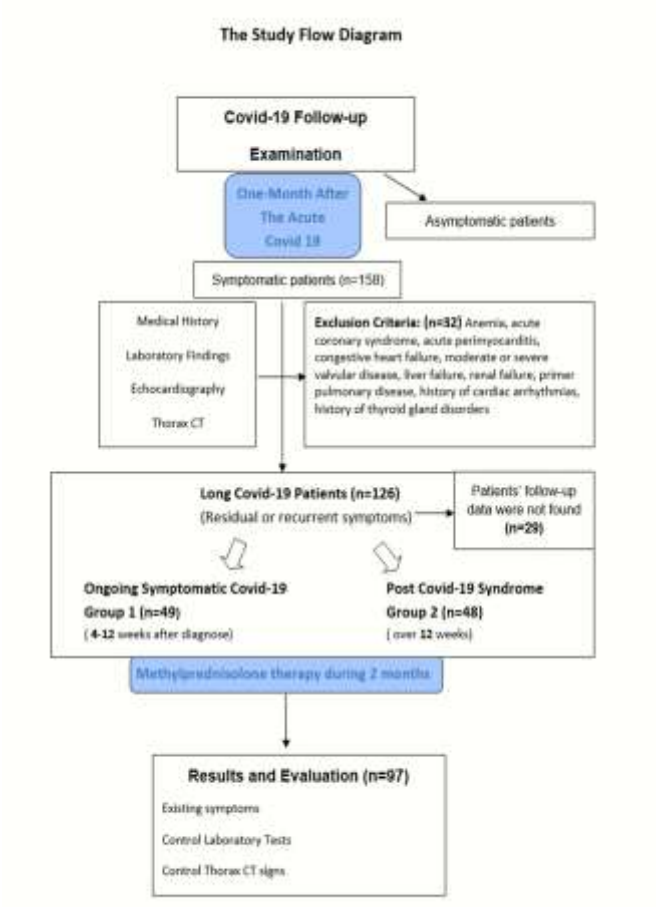

Figure 1: The Study Diagram

Statistical Analysis

Continuous measurements were reported as mean ± standard deviation(SD) or median (min-max), according to whether samples are drawn from a normally distributed data set. Data is denoted as numbers (n) and percentages (%). The descriptive statistical analysis included tests for data distribution (Kolmogorov–Smirnov test, and density blot/histogram analysis), and 2-way parametric or nonparametric tests were applied. Wilcoxon signed-rank or Mann–Whitney U-tests were used for the group comparisons of continuous data. Binary and categorical data were analyzed with the McNemar, Chi-squared, or Fisher's exact test. Correlations were assessed with Spearmen correlation coefficient rank for nonparametric data. SPSS Statistics version 22.0 IBM (Armonk, NY, USA) was used for all analyses.

RESULTS

The mean age of the cases was 50,88 ± 13,49 years. Male patients comprised 52.57% of all patients, hypertensives 17,52%, and diabetes 12,37%. Other clinical characteristics of long Covid-19 patients are in Table 1.

Table 1. Clinical Characteristics of Long Covid-19 Patients

Demographics and cardiopulmonary data	mean±SD or median(min-max) n/Σn (%)	
Age, year	50.88 ± 13.49	
Female	46/97 (47.42)	
Male	51/97 (52.57)	
Ongoing Symptomatic Covid-19 (Group 1)	49/97 (50.52)	
Post-Covid 19 Syndrome (Group 2)	48/97 (49.48)	
Diabetes mellitus	12/97 (12.37)	
Hypertensive	17/97 (17.52)	
Systolic tension, mmHg	125.47 ± 15.14	
Diastolic tension, mmHg	78.43 ± 8.98	
	Pre-treat	**Post-treat**
Heart rate in rest, beat/minute	80.61 ± 14.10	75.70 ± 12.06
Saturation with pulse oximeter, in-room air, %	95.97 ± 3.24	97.09 ± 1.05
Sat ≥ 93%	91/97 (93.8)	97/97 (100)
Previous treatments during acute COVID-19	median (min-max) or n/Σn (%)	
Time in quarantine / outpatients	14.00(6.00-45.00), 63/97(64.94)	
Time in hospital / hospitalized patients	0.00(0.00-23.00), 27/97(27.83)	
Time in ICU / ICU patients	0.00 (0.00-7.00), 7/97 (7.21)	
Favipiravir	95/97 (97.9)	
Hydroxychloroquine	2/97 (2.06)	
Convalescent plasma	6/97 (6.18)	
Intravenous immunoglobulin	10/97 (10.30)	
Tocilizumab	9/97 (9.27)	
Remdesevir	3/97 (3.09)	
Dexamethasone	0/97 (0.00)	
Methylprednisolone	17/97(17.52)	
Total dose, mg	0.00 (0.00-1310.00)	
Duration, day	0.00 (0.00-13.00)	
Mean dose, mg/day	40.00 (40.00-107.50)	

Of all long-term Covid-19 cases, 64.94% were outpatients, 35.06% were inpatients (just 7.2% were in the ICU). Long Covid-19 has also been reported among people with mild symptomatic outpatients (3). Expectingly, inpatients' CT involvement percentages were higher than outpatients' (p <0,001, mean rank respectively 67,96 to 38,77, Z Skor -4,93).

There is no statistically significant difference between group 1 and group 2 in terms of age (p=0,837). However, neutrophil, NLR, LDH, D-Dimer, and ferritin values were higher in group 1 patients without surprise (respectively; p=0,003, p=0,006, p=0,040, p=0,026, p=0,002). We can explain as follows: these values are high in the acute infection period and tend to decrease over time.

When the percentages of involvement in lung tomography before the MP treatment were examined, the involvement of the patients in group 1 was statistically significantly higher.

At the same time, there was no difference between the groups after the MP treatment. Regardless of which group they were in, the patients gave a similar response to MP treatment.

Each symptom of long Covid-19 patients, fatigue, dyspnea, chest discomfort, palpitation, and cough, has significantly improved with MP treatment (p<0,001). The most seen residual symptom was fatigue (93%), and the second was dyspnea (92%). (see Table 2). The most common complaint, fatigue, was found at a 63% frequency by Huang C and colleagues (4). A trial from Italy, consisting of 143 patients followed up after hospitalization with acute COVID-19, reported that 87% had at least one persisting symptom (fatigue or dyspnea) at two months. Only fatigue was found at 53% (5). Our study saw many higher symptom rates because our cohort consisted of patients who applied for a reason to the post-covid follow-up service.

Table 2. Symptoms of Long Covid-19 Patients

Before MP Treatment		*After MP Treatment n(%)*			p
		+	-	Total	
Fatigue	+	52(53.60)	39(40.20)	91(93.81)	
	-	0(0.00)	6(6.18)	6(6.18)	**<0,001**
	Total	52(53,60)	45(46.39)	97(100)	
Dyspnea	+	13(13.40)	77(79.38)	90(92.78)	
	-	1(1.03)	6(6.18)	7(7.21)	**<0,001**
	Total	14(14.43)	83(85.56)	97(100)	
Chest Discomfort	+	3(3.09)	62(63.91)	65(67.01)	
	-	2(2.06)	30(30.92)	32(32.98)	**<0,001**
	Total	5(5.15)	92(94.84)	97(100)	
Palpitation	+	1(1.03)	69(71.13)	70(72.16)	
	-	1(1.03)	26(26.80)	27(27.83)	**<0,001**
	Total	2(2.06)	95(97.93)	97(100)	
Cough	+	1(1.03)	70(72.16)	71(73.19)	
	-	0(0.00)	26(26.80)	26(26.80)	**<0,001**
	Total	1(1.03)	96(98.96)	97(100)	

Table 3. Laboratory Findings of Long Covid-19 Patients

	Before MP Treatment mean±SD,median(min-max)	**After MP Treatment** mean±SD,median(min-max)	p
Hemoglobin, gr/dl	13.94 (10.00-18.60)	14.60 (10.10-16.50)	0.227
Platelets, x10^3/µl	257.84 (87.00-616.60)	254.00 (120.00-473.00)	0.464
Neutrophil,x10^3/µl	4.39 (1.43-12.00)	4.00 (1.90-14.23)	0.825
Lymphocyte,x10^3/µl	2.30 (0.61-5.69)	2.18 ± 0.66	0.388
NLR	1.97 (0.68-8.89)	1.98 (1.09-8.09)	0.499
Creatine, mg/dl	0.84 ± 0.18	0.89 ± 0.24	**0.003**
GFR, ml/min	94.00 (66.00-139.00)	92.00 (65.00-111.00)	0.055
Na,mEq/L	138.06 ± 2.29	136.29 ± 1.07	0.792
K, mEq/L	4.12 ± 0.81	4,07 ± 0,79	0.621
Ferritin, ng/ml	64.00 (3.00-1085.00)	60.00 (5.00-447.00)	0.231
LDH, U/L	197.00 (109.00-573.00)	183.50 (137.00-304.00)	0.344
D-Dimer, ng/ml	377.00 (169.00-4241.00)	326.03 ± 183.34	**0.001**
CRP, mg/L	1.00 (0.1-93.00)	1.30 (0.10-10.00)	0.568
Procalcitonin, ng/ml	0.01 (0.01-1.00)	0.03 (0.02-0.08)	0.286
hs Troponin I, ng/ml	0.003 (0.002-0.06)	0.006 (0.004-0.09)	0.283

* There are not enough cases, and the p-value is not checked

† Due to the recovery of all cases, we could not control the Mcnemar test p-value.

Laboratory findings before and after MP treatment, hemoglobin, platelets, neutrophils, lymphocytes, NLR, creatinine, GFR, sodium, potassium, ferritin, LDH, D-dimer, CRP, procalcitonin, hs Trop I, BNP values are listed in Table 3. They were similar before and after the treatment, except for creatine and D dimer. The slight increase in creatinine levels, similarly decrease in GFR, was attributed to furosemide 80 mg/week given in the first month. A significant decreased in D dimer levels was accepted as a spontaneous fall response over time. We think that was not associated with MP treatment. The long Covid-19 patients were given a standard low-dose MP (mean 11,3 mg/day, total 680 mg as decreasing doses gradually in two months) and < 2 gr sodium diet; therefore, no patient complained of any adverse steroid effects like weight gain, hirsutism, acne, adrenal suppression symptoms, hypertension, new-diagnosed serious infections. All patients easily tolerated the treatment.

Just three of them (3,09%) had dyspeptic complaints, passed through with a proton pump.Radiologic amelioration on lung CT signs was promising. Although, serial CT scans at the post-Covid period showed gradual healing of pulmonary injuries (6). Lung fibrosis developed after the acute COVID-19 could be reversed spontaneously in about a third of the patients after four months from the diagnosis (7). CT scans unveiled persisting lung pathologies in 63% of patients, mainly bilateral ggos and subpleural interstitial changes in the lower lung lobes, without radiological signs of pulmonary fibrosis (8). We found that the ggo appearance, indicative of viral pneumonia, disappeared in 50 of 90 cases (p<0.001). It was also partially decreased in the other 40 of 90 patients. Consolidation in 18 of 19, peribronchial thickening in 9 of 13, and subpleural interstitial changes in 15 of 18 patients fully recovered (p<0.001). The p-value was not checked because there were not enough crazy paving cases to evaluate. We should note that the recovery of all air bronchogram (in 6 patients) and broncho-vascular dilatations (in 4 cases) were cured, so we could not control the Mcnemar test p-value. No effects of MP on atelectasis, honeycomb lung, fibrotic changes, pleural effusion, and nodules were observed (p> 0,05). Finally, we found a significant reduction of radiological lung involvement percentages with MP treatment. [median (min-max) from 25,00 (3,00-80,00) to 1,00 (0,00-50,00) (p< 0,001)) (See Table 4).

57 of 63 outpatients and 33 of 34 inpatients had ggo lesions on pre-treatment lung tomography (Fisher's exact test p-value=0,416). In 63 long Covid-19 outpatients, two crazy paving, three air bronchograms, six peribronchial thickening, eight atelectasis, two honeycomb lung, seven fibrotic changes, seven other nonspecific changes were observed. In 34 long Covid-19 inpatients, changes were observed in zero, three, seven, two, four, four, and two patients for similar lung CT lesions, respectively. There was no significant difference between outpatients to inpatients regarding the findings mentioned above on pre-treatment lung CTs. (Fisher's exact test p-value respectively p=0,540, p=0,420, p=0,210, p=0,486, p=0,180, p=1,000, and p=0,487). 15 of 63 outpatients and 3 of 34 inpatients had subpleural interstitial changes on pre-treatment lung tomography (Pearson Chi-Square p-value <0,070).

Just consolidation and broncho-vascular dilatation were significantly more common in long Covid-19 inpatients. 4 of 63 outpatients and 15 of 34 inpatients had consolidation on pre-treatment lung tomography (Pearson Chi-Square p value<0,001). 0 of 63 outpatients and 4 of 34 inpatients had broncho-vascular dilatation on pre-treatment lung tomography (Fisher's exact test p-value <0,013).

We detected a mild positive correlation between neutrophils count, LDH, and D-Dimer levels before MP treatment and the percentages of lung CT involvement at admission respectively (p=0,024 r_s =0,23), (p<0,001 r_s =0,36) and (p=0,037 r_s =0,21). There was also a moderate positive correlation between ferritin and the percentages of lung CT involvement (p<0,001 r_s =0,42). Ongoing Symptomatic Covid-19 patients' LDH, D-Dimer, and ferritin levels are statistically significantly higher than Post Covid-19 Syndrome patients' at admission (respectively p=0,040, p=0,026, p=0,002). Elevated ferritin levels in long Covid-19 patients may indicate the severity of pulmonary involvement, and it may be rational to follow up after acute COVID-19 infection.

Table 4. Lung Computerised Tomography Findings of Long Covid-19 Patients

Before MP Treatment			***After MP Treatment n(%)***			**p**
			+	-	**Total**	
Ground-glass opacity		+	40(41.23)	50(51.54)	90(92.78)	
		-	0(0.00)	7(7.21)	7(7.21)	**<0.001**
	Total		40(41.23)	57(58.76)	97(100)	
Consolidation		+	1(1.03)	18(18.55)	19(19.58)	
		-	0(0.00)	78(80.41)	78(80.41)	**<0.001**
	Total		1(1.03)	96(98.96)	97(100)	
Crazy paving		+	1(1.03)	1(1.03)	2(2.06)	
		-	0(0.00)	95(97.93)	95(97.93)	*
	Total		1(1.03)	96(98.96)	97(100)	
Air bronchogram		+	0(0.00)	6(6.18)	6(6.18)	
		-	0(0.00)	91(93.81)	91(93.81)	†
	Total		0(0.00)	97(100)	97(100)	
Broncho-vascular dilatation		+	0(0.00)	4(4.12)	4(4.12)	
		-	0(0.00)	93(95.87)	93(95.87)	†
	Total		0(0.00)	97(100)	97(100)	
Peribronchial thickening		+	4(4.12)	9(9.27)	13(13.40)	
		-	0(0.00)	84(86.59)	84(86.59)	**0.004**
	Total		4(4.12)	93(95.87)	97(100)	
Atelectasis		+	4(4.12)	6(6.18)	10(10.30)	
		-	1(1.03)	86(88.65)	87(89.69)	0.125
	Total		5(5.15)	92(94.84)	97(100)	
Honeycomb lung		+	3(3.09)	3(3.09)	6(6.18)	
		-	0(0.00)	91(93.81)	91(93.81)	0.250
	Total		3(3.09)	94(96.90)	97(100)	
Fibrotic changes		+	5(5.15)	6(6.18)	11(11.34)	
		-	1(1.03)	85(87.62)	86(88.65)	0.125
	Total		6(6.18)	91(93.81)	97(100)	
Subpleural interstisial changes	+		3(3.09)	15(15.46)	18(18.55)	
		-	0(0.00)	79(81.44)	79(81.44)	**<0.001**
	Total		3(3.09)	94(96.90)	97(100)	
Other (pleural effusion, nodules)	+		4(4.12)	5(5.15)	9(9.27)	
		-	1(1.03)	87(89.69)	88(90.72)	0.219
	Total		5(5.15)	92(94.84)	97(100)	
Radiological lung involvement median			25.00	1.00		**<0.001**
	(min-max)		(3.00-80.00)	(0.00-50.00)		

There was no correlation between any laboratory findings after MP treatment and the percentages of lung CT involvement (p>0,05) (See Table 5).

Table 5. The Correlation Between Laboratory and Lung CT Involvement Percentage of Long Covid-19 Patients

Before MP Treatment			After MP Treatment		
Laboratory Findings	Lung CT İnvolvement (%)		Laboratory Findings	Lung CT İnvolvement (%)	
	p	r_s		p	r_s
Neutrophil,x10^3/µl	0.024*	0.23	Neutrophil,x10^3/µl	0.484	0.12
Lymphocyte,x10^3/µl	0.930	-0.01	Lymphocyte,x10^3/µl	0.949	0.01
NLR	0.081	0.17	NLR	0.257	0.20
Ferritin, ng/ml	<0.001***	0.42	Ferritin, ng/ml	0.596	0.09
LDH, U/L	<0.001***	0.36	LDH, U/L	0.058	0.33
D-Dimer, ng/ml	0.037*	0.21	D-Dimer, ng/ml	0.784	-0.05
CRP, mg/L	0.065	0.18	CRP, mg/L	0.123	0.26
BNP, pg/ml	0.942	-0.01	BNP, pg/ml	0.879	0.05

MP: Methylprednisolone, CT: Computerised tomography,NLR: Neutrophil/ Lymphocyte Ratio,LDH: Lactate Dehydrogenase,CRP: C Reactive Protein,BNP: Brain-Type Natriuretic Peptide,x103/ µl = x1000/microliter,ng/ml=nanogram/milliliter,mg/L=milligram/Liter,pg/ml=picogram/milliliter,r_s:Spearmen correlation coefficient rank

DISCUSSION

We do not have enough info about the optimal medical therapy of long Covid-19 yet. While most people have uncomplicated recoveries, we do not yet know why long Covid-19 occurs in some of after acute illness (9,10). Clinicians are now forced to re-evaluate more and more long Covid-19 patients due to their residual symptoms. In addition, open-access studies are available to characterize the groups most likely to be affected by the sequelae of COVID-19 (11). Farne H. and his colleagues had underlined that only dexamethasone (DM) and remdesevir were efficacious to acute Covid-19 in May 2020 (12). DM resulted in lower 28-day mortality for those receiving invasive mechanical ventilation or alone oxygen. The results were consistent with possible harm in not receiving a respiratory support group (13).

In contrast, we found MP to be helpful in both mild or severe long Covid-19 patients. It may be a result of acute and long covid-19 causing disease with different pathophysiological mechanisms. We know that MP has a better affinity and is more effective for the lungs than DM in hypoxic Covid-19 inpatients (14-17). Although World Health Organisation declared the opposite at the beginning of the pandemia, it demonstrated the beneficial effects of corticosteroids, which are a good option for treating COVID-19, widely available, inexpensive, and easy to use (18). Sars Cov2 is a viral pathogen that affects interstitial lung tissue. The significant CT findings of patients affected by COVID-19 were previously shown to include ggos, consolidation with bilateral involvement, and peripheral and diffuse distribution (19). The American Thoracic Society (ATS) and European Respiratory Society (ERS) classification have recognized six primary idiopathic interstitial types of pneumonia(20). Long Covid-19 disease is similar to idiopathic NSIP has a subacute presentation and a better prognosis than acute Covid-19. Radiologic findings include ggos and subpleural interstitial changes with traction bronchiectasis like long Covid-19. Treatment of NSIP is with systemic corticosteroid therapy, prednisone, or MP.

The Office for UK National Statistics estimates that over a million people reported symptoms of long COVID at the beginning of March 2021. Over two-thirds of these individuals can be defined as Post-Covid Syndrome, still symptomatic 12 weeks later the first diagnose. Approximately 674,000 people complained that their symptoms have negatively impacted to daily activities. These adverse effects were seen eight times more in patients with Covid-19 than observed in the general population (21). It is an undeniable fact that the Long Covid-19 is the part of disease under the iceberg. Long Covid-19 is a disease that progresses with loss of workforce and poor quality of life in patients, rather than being fatal. Although spontaneous recovery is expected with time in lung lesions, a significant patient population also needs new and different medical treatment support. Liam Townsend and his colleagues reported that none of the measures of persistent respiratory disease were associated with initial disease severity (22). Therefore, close follow-up of patients' complaints after the acute period is required. High serum ferritin levels might be an alerting parameter used in monitoring.

Oral two-month low-dose MP therapy, which patients tolerate well, might be an option in the symptomatic and radiological recovery of patients with Long Covid-19.

We accept that this study has many limitations as it is non-randomized, retrospective, single-center, a small number of patients, and no control group consisting of long-term Covid-19 patients who did not receive MP therapy. Currently, choices for curing long Covid-19 are limited.

Conflict of interest

No conflict of interest was declared by the authors.

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