Clinical Infectious Diseases

CORRESPONDENCE

Influence of Corticosteroid Dose on Viral Shedding Duration in Patients With COVID-19

To the Editor—Coronavirus disease 2019 (COVID-19) is a newly emerged disease that is now spreading globally. Severe acute respiratory syndrome (SARS)–associated coronavirus 2 (SARS-CoV-2) has been identified as the causative agent, which has affected more than 6 million patients in over 200 countries, causing 400 000 deaths between December 2019 and June 2020. So far, there has been no proven effective therapies for COVID-19. Since proinflammatory cytokine storms may play a prominent role in the pathogenesis of COVID-19, corticosteroid use was recommended by Chinese guidelines [1]. However, routinely administering systemic corticosteroids was not suggested by the World Health Organization for patients with COVID-19 because of potential adverse outcomes such as prolonged viral shedding duration, as observed in SARS [2, 3]. In our previous paper, patients with early RNA clearance had a lower prevalence of corticosteroid use than patients with late RNA clearance. However, corticosteroid use was not an independent risk factor for prolonged viral RNA shedding in the multivariable model [4]. Using least absolute shrinkage and selection operator analysis, Li et al [5] demonstrated that high-dose (80 mg/d) but not low-dose (40 mg/d) corticosteroids potentially delayed viral shedding in patients with COVID-19.

Considering the potential influence of corticosteroid dosage on viral clearance, we conducted supplemental analysis on the previous data. Since COVID-19 is an emerging infectious disease, the treatment experience was lacking. During the course of treatment, different corticosteroid dosages were tried. Basically, the use of corticosteroids in these patients could be categorized into 2 types: glucocorticoid pulse therapy for 3 days (intravenous methylprednisolone: 200–400 mg/d) and low- to medium-dose corticosteroids for 21 days. The low- to medium-dose corticosteroid regimen included intravenous methylprednisolone 0.5–2 mg/kg body weight (bw) daily for 3 days, which was reduced to half for 3–5 days, then replaced with oral methylprednisolone (half of previous dosage) for 3–5 days. The dose is halved every 3 days until therapy is discontinued. The whole course of corticosteroids therapy lasts approximately 21 days. The influence of corticosteroid therapy and dose on viral shedding duration and treatment outcomes was evaluated in this study.

The data on 113 patients enrolled in our previous study were analyzed [4]. Among 113 patients, corticosteroids were used in 56.6% of patients (64 cases). The 64 patients were divided into 3 groups: 1 group with patients treated with low-dose corticosteroid (0.5–1 mg/kg bw daily), 1 group with patients treated with medium-dose corticosteroid (1–2 mg/kg bw daily), and another group with patients who received high-dose corticosteroid (glucocorticoid pulse therapy; intravenous methylprednisolone: 200–400 mg for 3 days). Clinical characteristics and treatment outcomes of these 3 groups and patients without corticosteroid use were summarized and compared.

There were 4 groups: patients without corticosteroids (n = 49), those with low-dose corticosteroids (n = 21), those with medium-dose corticosteroids (n = 19), and those with high-dose corticosteroids (n = 24). A comparison of illness severity and treatment responses is shown in Table 1. The ratio of male patients and comorbidity with hypertension were comparable among the 4 groups. The high-dose-group patients were older than the patients in the other 3 groups ($P = .0004$). The percentage of patients diagnosed as having severe/critical illness at admission was significantly higher in the medium-dose group than in the group without corticosteroid use and the high-dose group ($P = .0006$). The medium duration from illness onset to hospital admission was longer in the low-dose and medium-dose groups than in the no-corticosteroid group ($P = .008$). Patients treated with medium-dose and high-dose corticosteroids showed prolonged duration of viral shedding ($P = .003$) in comparison with the no-corticosteroid group, while there was no significant difference between the low-dose group and other groups. The rate of invasive mechanical ventilation in the high-dose group was significantly higher than that in the other groups ($P = .003$), as well as delayed recovery on chest computed tomography (CT) ($P = .0004$). The duration from illness onset to temperature recovery was apparently longer in the low-dose and high-dose groups, while no significant difference was observed between the medium-dose group and the no-corticosteroid group. The only 2 deaths occurred in the high-dose group. However, no statistical significance of mortality was observed among the 4 groups.

The use of corticosteroids in COVID-19 is controversial. However, studies on the influence of corticosteroid treatments in COVID-19 are limited. This study investigated the associations of corticosteroid use and dosage on SARS-CoV-2 viral shedding duration and treatment outcomes. We found that virus clearance could be delayed in patients with medium- and high-dose corticosteroid therapy. This was in line with the results of Li et al [5]. In particular, there was no evidence of clinical benefit for patients receiving high-dose corticosteroids (glucocorticoid pulse therapy; intravenous methylprednisolone: 200–400 mg for 3 days), which suggests that high-dose corticosteroids should not be

Table 1. Comparison of Clinical Characteristics and Treatment Responses Between Groups With Different Corticosteroid Dosages

	No Corticosteroids (n = 49)	Low-dose Corticosteroids (0.5–1.0 mg/kg bw) (n = 21)	Medium-dose Corticosteroids (1.0–2.0 mg/kg bw) (n = 19)	High-dose Corticosteroids (200–400 mg for 3 Days) (n = 24)	*P*
Age, years	47 (36, 58)[b]	51 (38, 61)[b]	51 (45, 62.5)[b]	64 (59, 67.5)[a]	.0004
Male sex, % (n)	49.0 (24)	52.4 (11)	73.7 (14)	70.8 (17)	.141
Hypertension, % (n)	16.3 (8)	23.8 (5)	36.8 (7)	25.0 (6)	.34
Severe patients at admission, % (n)	10.2 (5)[b]	38.1 (8)[a,b]	57.9 (11)[a]	29.2 (7)[b]	.0006
Duration from illness onset to hospital admission, days	4 (3, 6)[b]	7 (4, 10)[a]	7 (5.5, 9)[a]	5 (2, 7)[a,b]	.008
Duration of viral shedding, days	15 (10, 18)[b]	18 (14, 21)[a,b]	21 (15, 24)[a]	20 (14, 27.25)[a]	.003
Duration from illness onset to radiologic recovery, days	14 (11, 16)[b]	13 (11.5, 17)[b]	13 (10, 15)[b]	21 (16, 27)[a]	.0004
Duration from illness onset to temperature recovery, days	8.5 (6.25, 11.75)[b]	12 (11, 15)[a]	10 (10, 11.25)[a,b]	12 (9.25, 25.25)[a]	.004
Invasive mechanical ventilation, % (n)	2.0 (1)[b]	19.0 (4)[b]	15.8 (3)[b]	41.7 (10)[a]	.003
In-hospital mortality, % (n)	0.0 (0)	0.0 (0)	0.0 (0)	8.3 (2)	.198

Data are presented as medians with interquartile ranges in parentheses unless otherwise indicated. Chi-square (χ^2) test or Fisher's exact test was used, with $P < .05$ as significant. The superscript letters "a" and "b" were used to indicate statistic difference among groups. Values sharing the same superscript letter are not significantly different at the $P < .05$ level.
Abbreviation: bw, body weight.

used. Low-dose corticosteroids may be used, as there was no obvious influence on viral clearance, although there were also no beneficial responses to treatment. However, patients treated with corticosteroids usually had more clinical symptoms, a higher inflammation index, and more abnormalities on chest CT. Such observational studies do not account for patients' clinical condition at the time of corticosteroid therapy initiation. Ideally, randomized controlled trials should be designed to study the effects of corticosteroids systematically in further studies.

Notes

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