Decreased mortality among hospitalized coronavirus disease 2019 patients who underwent anticoagulant therapy with heparin

Letter to the Editor

Sir,

In coagulopathy, coronavirus disease 2019 (COVID-19) is correlated with high mortality due to an increased concentration of D-dimers. Patients with COVID-19 commonly develop thrombi in the tissues, as proven by laboratory and radiological data. However, to date, only few studies have reported the use of anticoagulant heparin unfractionated heparin (UFH) to manage coagulopathy related with COVID-19. Our study aimed to elucidate the correlation between the anticoagulant therapy (ACT) with UFH and the mortality rate in hospitalized COVID-19 patients.

The clinical records of 110 patients with COVID-19 admitted to the City Clinical Hospital No. 1 (Bishkek, Kyrgyzstan) until May 18, 2020, were reviewed. Nasopharyngeal and oropharyngeal samples collected from these patients between March 12 and May 11, 2020, were confirmed to be positive for severe acute respiratory syndrome coronavirus-2 infection by real-time reverse-transcription polymerase chain reaction analysis. Patients with body temperature >37°C and SaO<sub>2</sub> <90% at the time of hospitalization and those who were treated with UFH, azithromycin, lopinavir/ritonavir, corticosteroids, and hydroxychloroquine were included in the study. Among the participants were COVID-19 patients who underwent treatment with UFH, who continued to receive the treatment, or who were followed up after receiving UFH treatment. Information on mortality was documented, whereas data related to dosage, treatment duration, and method of administration were not assessed. Treatments were assigned after confirming the accuracy of the admission criteria, and all involved investigators and patients were blinded to the treatment assigned. Confidentiality was maintained concerning the data collected from the patients, who provided their informed consent. This study was approved by the City Clinical Hospital No. 1 Bioethics Committee No. HP/MR/39/536/2005-PID.

Comparisons were made for age and gender of the patients who underwent therapy with UFH versus those who did not using t-test and Chi-square test. The correlation between ACT with UFH and mortality was assessed using a logistic regression model adjusted for age and gender. Sensitivity analyses were also performed to compare the limited data on two severity markers, including the determination of whole data dropping variables without observations and a complete case study. All analyses were conducted using STATA 14 software (StataCorp, College Station, TX, USA).

Of the 110 patients, 68 were males and the study population had a mean age of 58.54 years. At the time of data collection, all patients were alive, among whom 86 had been discharged and 24 were still hospitalized. The median follow-up time was 8 days (interquartile range: 3–10 days) and all patients treated with UFH had recovered. Patients who underwent ACT with UFH were older than those who did not (P < 0.001), and the number of male and female patients treated with UFH did not differ (P > 0.05).

ACT with UFH was found to be correlated with lower mortality when the analysis was adjusted for age and gender (odds ratio (OR) [95% confidence interval]: 0.68 [0.48–0.94], P = 0.002). This correlation was significant for body temperature >37°C and SaO<sub>2</sub> <90% (OR: 0.67 [0.47–0.94], P = 0.002) as well as for other treatments added (OR: 0.54 [0.38–0.76], P < 0.001). Notably, none of the patients progressed to severe illness.

Although this study demonstrates that ACT with heparin is correlated with lower mortality in COVID-19 patients, there were some limitations. This study was not a randomized clinical study and the differences reported did not exclude the effects of other therapies, such as azithromycin, lopinavir/ritonavir, corticosteroids, and hydroxychloroquine.

We observed thrombosis during respiratory distress in COVID-19 patients. A study in Japan reported that 66.4% of patients who were treated with prophylactic UFH survived for over 28 days. Another study including 2773 hospitalized COVID-19 patients showed that the 786 patients who underwent ACT also had a lower mortality rate (22.5%) compared with those who did not (22.8%).

Currently, there is no evidence demonstrating the efficacy of anticoagulant therapy in COVID-19. UFH is simple and safe to use in critical care to prevent or...
reduce the duration of hospitalization. Despite the small number of cases investigated in this study, the potential of UFH as a COVID-19 therapy was partially confirmed. Considering that no better options are currently available, UFH may be used in COVID-19 treatment with fair outcomes. However, large-scale basic and clinical research is warranted to further understand the specific mechanism of UFH action and to optimize treatment strategies.

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Conflicts of interest
There are no conflicts of interest.

Vityala Yethindra, Tugolbai Tagaev
Department of Pathology, International Higher School of Medicine, International University of Kyrgyzstan, Bishkek, Kyrgyzstan

Address for correspondence:
Dr. Vityala Yethindra,
2-5-168, Opposite Maruthi Towers, Nakkalgutta, Warangal - 506 001, Telangana, India.
E-mail: yethindravityala10@gmail.com

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