Turk Thorac J 2020; 21(4): 283-4 DOI: 10.5152/TurkThoracJ.2020.20.03

Editorial Comment

See article: Agrawal S, et al. Evidence based treatment of SARS-CoV2: A narrative review. Turk Thorac J 2020;21(3):221-2. DOI: 10.5152/TurkThoracJ.2020.20041

Treatment of Severe Acute Respiratory Syndrome Coronavirus 2: It Is Time to Produce Our Own Evidence Base

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Cite this article as: Sayıner A. Treatment of severe acute respiratory syndrome Coronavirus 2: It is time to produce our own evidence base. Turk Thorac J 2020; 21(4): 283-4.

Received: *28.03.2020* ***Accepted:*** *30.03.2020* ***Available Online Date:*** *16.04.2020*

Coronavirus disease 2019 (COVID-19) pandemic is a serious threat to Turkey and to the world, with rapidly rising numbers of both the newly diagnosed cases and increasing mortality. As of March 27, 2020, the total number of confirmed cases globally has exceeded 500,000 and reached 5,698 in Turkey [1, 2]. More important than the number of cumulative cases is the increasing trend in the number of new cases per day. Thus, according to the recent situation reports of the World Health Organization and the updated website of the Turkish Ministry of Health (MoH), the number of new confirmed cases in Turkey was 561 on March 26, 2020; 1,196 on March 27, 2020; and 2,069 on March 28, 2020 [2, 3]. This rapid rise in the number of cases is partly due to the recent addition of new centers performing the polymerase chain reaction (PCR) test and, consequently, the increase in the number of tests performed per day. Several hospitals in Turkey are currently facing an expanding load of patients and trying to find solutions for the high demand of diagnostic kits, computed tomography units, antiviral drugs, and hospital beds.

There are no approved drugs to treat COVID-19. However, because of the seriousness of the problem, the patients with suspected or confirmed infection are currently being treated off-label with different drugs having antiviral properties. The MoH has issued guidelines for the management of COVID-19, which are being regularly updated; it currently recommends the treatment of all confirmed and suspected cases with hydroxychloroquine and oseltamivir, with or without (depending on the decision of the attending physician) the addition of azithromycin [4].

In May issue of Turkish Thoracic Journal, Agrawal, Gupta, and Goel have reviewed the evidence for the antiviral medications used for the treatment of COVID-19 [5]. Clearly, there is very little evidence to support the use of any antiviral treatment for COVID-19. There is a dosing issue that needs clarification and there are two more agents that need to be addressed, as they have been placed among the first-line treatment options in the MoH guideline.

The optimal dose of hydroxychloroquine appears controversial. The only semi-clinical study, which is included in the review and evaluated the effectiveness of this drug, used a dose of 200 mg tid (600 mg per day) [6], differing from the dose recommended in the MoH guideline. The latter dosing schedule (400 mg bid as the loading dose, followed by 200 mg bid) is only based on an *in vitro* study [7].

Oseltamivir is recommended in combination with hydroxychloroquine as the initial therapy. Coronaviruses do not have any neuraminidases, and there is no clinical evidence that neuraminidase inhibitors have any effect on coronaviruses. However, without any microbiological evidence, it is not possible to distinguish COVID-19 from the influenza-associated respiratory tract infections using clinical and/or radiographic findings; there are rare reports of co-infections of severe acute respiratory syndrome coronavirus 2 with other respiratory viruses [8]. Thus, it may be a prudent approach to start the empiric treatment with oseltamivir. However, following the confirmation of COVID-19 diagnosis with PCR, it may be reasonable to stop the oseltamivir treatment to avoid potential adverse events and/or drug interactions.

The recommendation to combine azithromycin with the initial treatment is based on a study that investigated the effect of treatment with hydroxychloroquine alone or in combination with azithromycin on the respiratory viral load [6] There was a significantly better virologic response with the combination treatment on days 3, 4, 5, and 6. However, no clinical

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outcome was reported, thus making it difficult to recommend any treatment approach based on these findings.

The medical world is working very hard to find answers to the innumerable questions regarding the management of COVID-19; however, considering the present data, it is clear that more extensive efforts are needed to obtain the much-needed evidence. Thus, I urge all our colleagues to collect, analyze, and report their own data. The increasing number of patients is a significant threat, but also is an important opportunity to gather information.

Conflict of Interest: The author has no conflicts of interest to declare.

Financial Disclosure: The author declared that this study has received no financial support.

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