Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Infection 82 (2021) e34–e35

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Letter to the Editor

Sofosbuvir/daclatasvir in the treatment of COVID-19 infection: A meta-analysis

To the Editor,

We read with great interest with the review article by Tu et al.,[1] in which several potential anti-viral agents, including lopinavir/ritonavir, ribavirin, arbidol, remdesivir, oseltamivir, nafamostat, favipiravir, nitazoxanide and sofosbuvir could be considered as treatment options. However, the studies investigating the usefulness for most of these agents is lack. Recently, four studies[2-5] which investigated the efficacy of sofosbuvir plus daclatasvir in combination for COVID-19 patients with mild to severe diseases. All of them[2-5] demonstrated the beneficial effect of sofosbuvir-daclatasvir on the outcomes of COVID-19 patients; however, most of the differences between sofosbuvir-daclatasvir and comparator in terms of these clinical outcomes, such as clinical recovery, length of hospital stays and mortality did not reach statistical significance. These insignificant differences may be attributed to the small case number in each study[2-5], so all three studies concluded that further large-scale study is warranted. Before that, we believe an integrated analysis of these four studies[2-5] can provide more strong evidence than each of them. Therefore, we conducted this pooled analysis of these studies.

After literature search, only four studies[2-5] which compared the clinical efficacy of sofosbuvir-daclatasvir-based treatment and standard care or other alternative treatment were included in this analysis. The outcomes including clinical recovery rate, mortality, intensive care unit (ICU) admission, requirement of mechanical ventilation (MV) and the length of hospital stay were extracted from the original studies for analysis.

Among three included studies, three studies[2,4,5] were randomized control trials, and one[3] was open-label parallel trial. Three studies[2,3,5] were conducted in a single institute and one[4] was multicenter study. Overall, 118 and 112 received sofosbuvir/daclatasvir-based treatment and standard care or alternative treatment, respectively. In Abbaspour Kasgari et al's study,[2] they assessed the uses of 400 mg sofosbuvir, 60 mg daclatasvir and 1200 mg ribavirin twice daily as intervention ($n = 24$), compared to standard care ($n = 24$) for hospitalized COVID-19 patients with moderate disease. In Eslami et al's study,[3] they assessed the efficacy of sofosbuvir/daclatasvir ($n = 35$) with ribarivin ($n = 27$) for severe COVID-19 patients. In Sadeghi et al's study,[4] they compared the outcomes of treatment arm receiving sofosbuvir/daclatasvir plus standard care, and control arm receiving standard care alone for each 33 moderate or severe COVID-19 patients. In Roozebeh et al's study,[5] they compared the outcomes of treatment arm receiving sofosbuvir/daclatasvir plus hydroxychloroquine, and control arm receiving hydroxychloroquine alone for outpatients with mild COVID-19 infections.

In the pooled analysis of four studies,[2-5] the clinical recovery rate was 88.9% (105/118) in the group receiving sofosbuvir/daclatasvir-based treatment, and only 73.2% (82/112) in the control group. The overall clinical recovery rate in the sofosbuvir/daclatasvir-based treatment was significantly higher than those of control group (risk ratio [RR], 1.20; 95% CI, 1.04–1.38; $I^2 = 23\%$, Fig. 1A). The significant difference was also observed between those receiving sofosbuvir/daclatasvir-based treatment and standard care/other alternative treatment in terms of mortality (5.4% [5/92] vs 20.2% [17/84]; RR, 0.31; 95% CI, 0.12–0.78; $I^2 = 0\%$, Fig. 1B). Only two studies[2,3] reported the rate of ICU admission and the pooled analysis showed sofosbuvir/daclatasvir-based treatment group was associated with lower rate of ICU admission than standard care/other alternative treatment group (10.2% vs 33.3%; RR, 0.33; 95% CI, 0.15–0.72; $I^2 = 0\%$). Another two studies[2,4] reported the rate of MV. Although sofosbuvir/daclatasvir-based treatment group was associated with lower rate of MV uses than standard care/other alternative treatment group, the difference did not reach statistical significance (5.3% vs 15.8%; RR, 0.40; 95% CI, 0.10–01.73; $I^2 = 15\%$). The similar trend was observed regarding the length of hospital stay in the pooled analysis of three studies.[2-4] Those receiving sofosbuvir/daclatasvir-based treatment was associated with numerically shorter length of hospital stay than control group, but the difference did not reach statistical significance (mean difference, −1.86; 95% CI, −3.88 to 0.16; $I^2 = 81\%$).

Based on the finding of this study, sofosbuvir/daclatasvir-based treatment was associated with a higher clinical recovery rate, a lower mortality rate and a less ICU admission than standard care or other alternative treatment in the management of patients with COVID-19 infections. In addition, we observed the trend about the less MV use and shorter length of hospital stay among the patients receiving sofosbuvir/daclatasvir-based treatment than the control group. In summary, our finding indicates that sofosbuvir/daclatasvir can a potential therapeutic agent for COVID-19 patients. This is an important finding in COVID-19 pandemic due to the truly effective weapon against SARS-CoV-2 is limited.[6,7]

However, our findings should be interpreted cautiously. Only three studies of small case number were included in this analysis and all were conducted in Iran. This issue may limit the generalizability of our findings. However, the heterogeneity regarding the clinical outcomes among these three studies were small, which could limit the bias in this study.

In conclusion, sofosbuvir/daclatasvir-based treatment can be associated with a better clinical outcome than standard care or other comparators for COVID-19 infection. However, more randomized control trials are warranted to confirm our findings and also investigate the safety of sofosbuvir/daclatasvir for treating COVID-19 patients.

https://doi.org/10.1016/j.jinf.2020.12.021

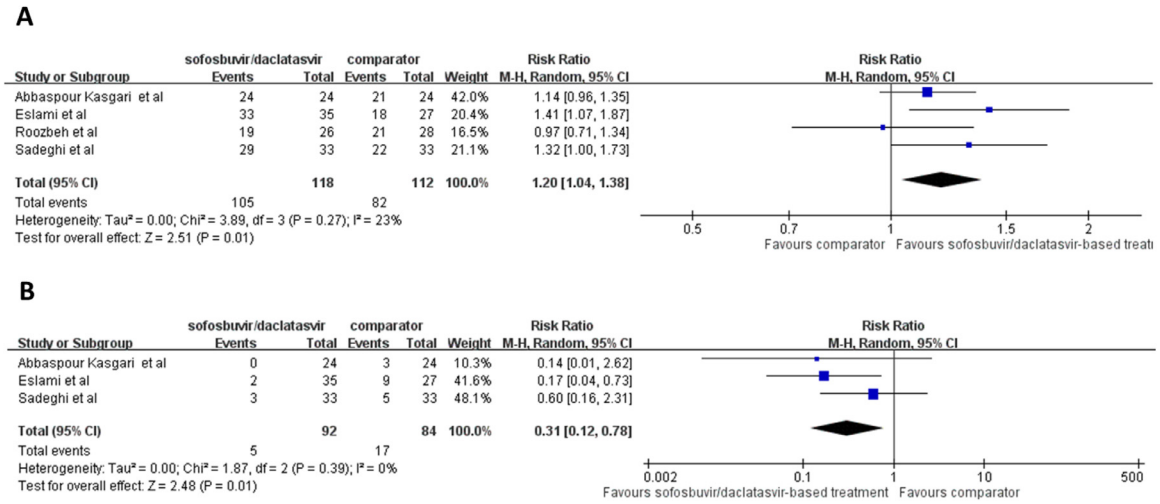

Fig. 1. (A) Forest plot about the clinical recovery rate (B) Forest plot about the mortality between sofosbuvir/daclatasvir-based treatment and comparator.

Declaration of Competing Interest

The authors declare that they have no competing interest

Author contributions

Study design: HTC, CCL; Data analysis: HTC, CCM; Writing: HTC, CCL

Acknowledgements

None

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