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.

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Short Communication

Remdesivir for the treatment of coronavirus COVID-19: A meta-analysis of randomised controlled trials

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A novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing COVID-19, was identified in December 2019 and rapidly spread worldwide. Several candidate therapeutic agents have been reported for treatment of COVID-19 [1]. As there is an urgent demand for therapeutic drugs, some have been rapidly approved after a few clinical trials. However, consecutive monitoring for their effectiveness and safety is needed. A meta-analysis is a powerful and useful methodology to integrate and evaluate the effectiveness and safety of a drug based on different published trials. A report on the effectiveness of hydroxychloroquine based on systematic review and meta-analysis indicated that it was not sufficiently effective to be used alone or in combination with azithromycin [2]. Recently, results from three randomised controlled trials (RCT) using remdesivir reported its effectiveness for the treatment of COVID-19 [3–5]. Therefore, we evaluated the effectiveness and safety of remdesivir for COVID-19 treatment using a meta-analysis.

After the database search, we obtained 9414 articles to be screened, excluding 19 articles that were duplicated (Fig. S1). Of these, six were further examined in detail, excluding 9408 that did not meet the inclusion criteria. Finally, three studies [3–5] were included in the meta-analysis. A total of 1879 patients (1080 remdesivir-treated patients) were included in this analysis. The study characteristics are given in Table S2. All studies were RCTs; however, the study by Spinner et al. [4] was not blinded. Therefore, blinding risk was observed in Spinner et al. [4] (Fig. S2). In the studies by Beigle et al. [3] and Wang et al. [5], remdesivir was administered at 200 mg/day on the first day, followed by 100 mg/day for 2–10 days; however, in Spinner et al. [4], remdesivir was administered at 200 mg/day on the first day, followed by 100 mg/day for 2–5 or 2–10 days (Table S2).

In remdesivir-treated patients, the clinical improvement was significantly higher than in those treated with placebo (RR 1.16; 95% CI 1.07–1.25) (Fig. 1A). The mortality rates reported in the three studies were different. Beigle et al. [3] reported 15-day mortality rates, Spinner et al. [4] 11-day rates, and Wang et al. [5] 28-day rates. Remdesivir tended to reduce the mortality rate, but this was not significant (Fig. 1B). We compared all adverse events and total SAEs between the remdesivir and placebo groups and found a significant reduction in SAEs in remdesivir-treated groups compared with those receiving placebo (RR 0.74; 95% CI 0.62–0.90) (Fig. 1D), but the

To search the literature, we used MEDLINE, Web of Sciences, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov as electronic databases (24 August 2020). Four reviewers independently searched for literature using the following terms: 'COVID-19' and 'remdesivir' (details in Table S1). A study was considered eligible if it met the following criteria: RCT on patients with COVID-19, use of remdesivir as an interventional drug, placebo or standard care as a comparison treatment, and comparison of the effectiveness as an outcome. The exclusion criteria were as follows: no association with COVID-19 treatment and insufficient data on comparisons of the effectiveness of initial therapy as an outcome. Four reviewers independently conducted the screening. Two reviewers independently extracted data from the studies. In each study, the data of the total patient population and intention to treat were extracted. The author, country, study design, duration of study, patient age, drug administration regimens, treatment duration, follow-up duration, and disease severity were extracted. Regarding the outcome measures used to assess clinical improvement, the rates of clinical response, treatment success, and clinical improvement were used as the primary outcome measure, and the mortality rate, all adverse events, and serious adverse events (SAEs) were used as secondary outcome measures. Two authors independently assessed the risk of bias. Risk assessment was performed in reference to the Cochrane Collaboration. We performed a meta-analysis using the Review Manager for Windows (RevMan, version 5.3, The Cochrane Collaboration, 2014), and forest plots were prepared. We calculated the risk ratio (RR) and 95% confidence interval (CI) using the Mantel-Haenszel random-effects model. Statistical heterogeneity among studies was assessed using I^2.

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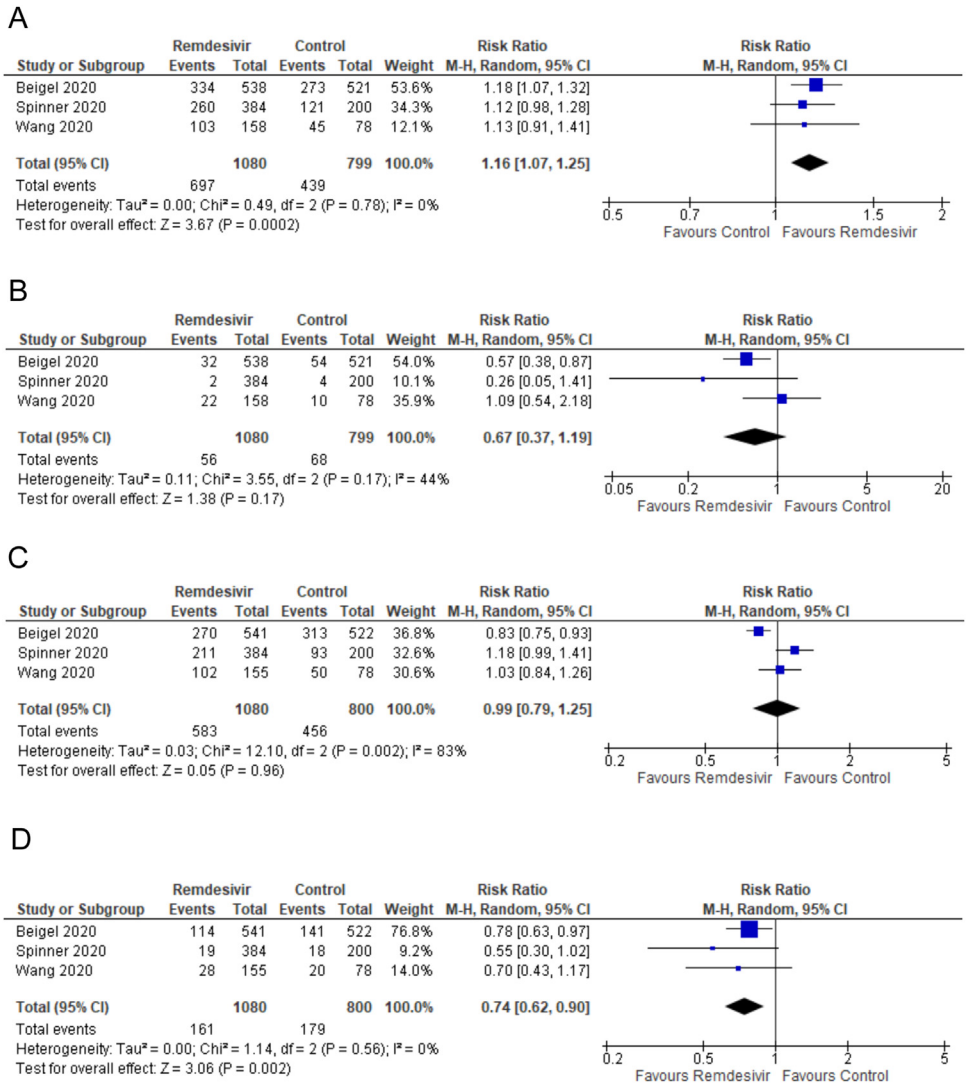

Fig. 1. Forest plot of the clinical improvement, mortality, all adverse events, and serious adverse events. The vertical line indicates no significant difference between the groups. RRs are represented by diamond shapes and 95% CIs by horizontal lines. Squares indicate point estimates, and the size of each square indicates the weight of each study included in this meta-analysis. (A) Clinical improvement. (B) Mortality. (C) All adverse events. (D) Serious adverse events.

comparison was not significant for all adverse events (Fig. 1C).

We conducted a meta-analysis of the effectiveness and safety of remdesivir for COVID-19 treatment and revealed that remdesivir improved the clinical symptoms in COVID-19; however, it did not significantly improve all adverse events. Remdesivir has been proposed as a promising therapeutic drug because there are currently no available drugs or vaccines for COVID-19, but further evidence of other drugs, combination therapy, and development of new drugs and vaccines are needed to combat the COVID-19 crisis.

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Competing interests

None declared.

Ethical approval

Not required.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jgar.2020.11.022.

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