Influence of Convalescent Plasma Therapy on the Mortality in COVID-19 Patients: A Meta-Analysis

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Letter to the Editor

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Abstract

As of August15, 2020, more than 21,155,600 people were infected and about 761,264 were expired due to SARS-CoV-2 infection worldwide. The extreme spread of the emerging virus makes the disease a serious problem for public health. However, a curative treatment or effective specific vaccine againstSARS-CoV-2 infection is unavailable. Recently, several studies have been performed to evaluate the effects of COVID-19 convalescent plasma transfusion on the clinical outcomes in patients with severe/critical COVID-19 [1-5]. However, the results from these studies aredatable, and thus its useremains investigational.

Main Text

As of August15, 2020, more than 21,155,600 people were infected and about 761,264 were expired due to SARS-CoV-2 infection worldwide. The extreme spread of the emerging virus makes the disease a serious problem for public health. However, a curative treatment or effective specific vaccine againstSARS-CoV-2 infection is unavailable. Recently, several studies have been performed to evaluate the effects of COVID-19 convalescent plasma transfusion on the clinical outcomes in patients with severe/critical COVID-19 [1–5]. However, the results from these studies aredatable, and thus its useremains investigational.

In this meta-analysis, we searched the English literature library Pubmed, Embase, web of science, Chinese literature CNKI and CQVIP up to July 31, 2020, using text/word combinations. The search strategy was constructed using terms as “COVID-19”, “SARS-CoV-2” AND “convalescent plasma”. Clinical studies with more than 20 laboratory-confirmed COVID-19 patients, using convalescent plasma as intervention measure and reporting mortality outcome were included. Additionally, the references of selected studies were further reviewed to identify other eligible studies. We excluded studies from the same institutions and studies whose research type was review, meta-analysis, case reports, case series or letters. Two authors (JW and XL) independently screened every article and extracted the data. Any disagreement was resolved by discussion and consensus. Odd ratio (OR) with 95% confidence intervals (95% CI) were calculated using the package of “Meta” in R software (R version 3.6.1). Potential heterogeneity between studies was examined using I^2 judgment model. Fixed-effects model was selectedin this meta-analysis because there was no heterogeneity among the included studies ($I^2 \leq 50\%$). Egger’s and Begg’s test was used to examine potential publication bias. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

We retrieved 469 citations after duplicates removed. Besides 213 articles that were small case reports, reviews, editorials and correspondence, 181 were excluded after title/abstract review. Following manuscript review, 70 studies were excluded based on failure to meet inclusion criteria. Finally, five studies were included in the present meta-analysis [1–5]. The characteristics of the included studies were summarized in Supplement Table 1. The total number of patients was 382, which had 32 and 53 deaths in convalescent plasma treatment group (212 cases) and control group (170 cases), respectively. As the results shown in Fig. 1, COVID-19 convalescent plasma therapy could significantly reduce mortality in patients with severe or life-threatening COVID-19 (pooled OR = 0.46, 95% CI: 0.27–0.78, P < 0.01).In

addition, there was no considerable heterogeneity was observed between-study (I^2 = 0%, *P-heterogeneity* = 0.61). The results from the Egger's test (t =-2.49, *P* = 0.089) and the Begg's test (z=-1.47, P = 0.142) did not show the existence of publication bias in this meta-analysis.

Although convalescent plasma therapy has been thoroughly evaluated in the treatment of SARS, Middle East respiratory syndrome, influenza A (H1N1) and Ebola [6–9], its use has not been well studied in patients with severe/critical SARS-CoV-2 infection. Among the five studies included in the current meta-analysis, two studies suggested that convalescent plasma treatment appeared effective and safe for COVID-19 cases [1, 2]. In addition, Hegerova et al. reported that convalescent plasma use in severe and critically ill patients with COVID-19 may improve survival if given early in the course of disease [5]. Zeng et al. observed that convalescent plasma transfusion could discontinue SARS-CoV-2 shedding and contributed to longer survival in COVID-19 patients with respiratory failure, although it could not reduce mortality in critical end-stage COVID-19 patients [2]. However, the results from a Chinese randomized clinical trial showed that convalescent plasma therapy added to standard treatment did not significantly improve the time to clinical improvement in COVID-19 patients within 28 days [4]. One possible explanation is that these studies did not have a standardization and procedure control with regard to the donor selection process and the level of antibodies in convalescent plasma units. Additionally, patients with COVID-19 who were recruited in these studies were heterogeneous regarding the duration and severity of the illness, which might be another explanation for the varied therapeutic effects seen acrossdifferent studies.

After pooling included studies together, our present meta-analysis found that use of convalescent plasma from those recovered COVID-19 patients could significantly reduce mortality in patients with severe/critical SARS-CoV-2 infection. Moreover, sensitivity analysis with an exclusion of studies one-at-a-time did not change the results materially (Supplement Fig. 1), indicating that each included study did not have had a particularly strong influence on the results. However, our present analysis has limitations. The number of studies and the patients involved in this analysis was relatively small. Therefore, caution should be taken when interpreting the findings. Additionally, as the gold standard for evaluating interventions, randomized controlled trials have many advantages such as avoiding various biases that may occur in the design and implementation of clinical trials, balancing confounding factors, and improving the effectiveness of statistical tests [10]. However, only one randomized controlled trialwas included in the present study. Therefore, more multicenter randomized clinical trials should be performed to further evaluate the therapeutic effect of convalescent plasma for patients with severe or life-threatening COVID-19 in future.

Declarations

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Authors' contributions

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

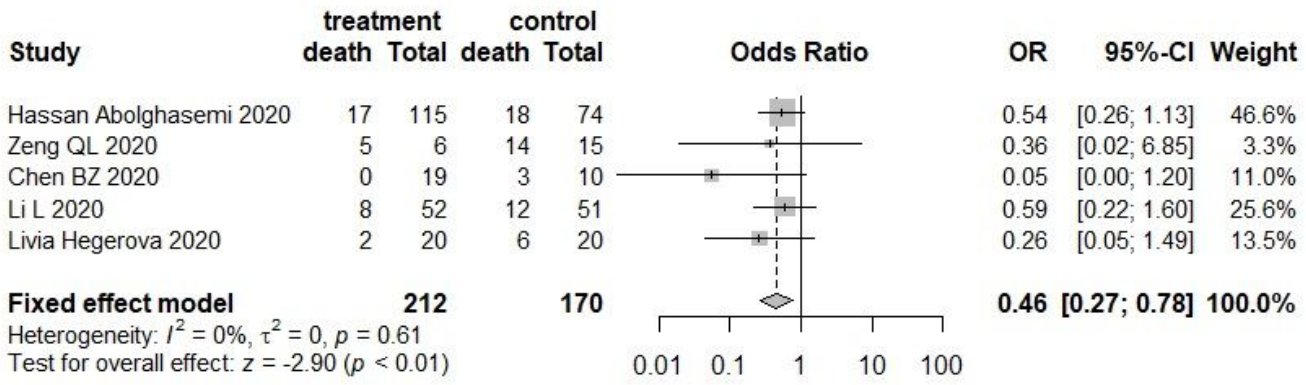

Figure 1

Forest Plot

Supplementary Files

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