COCHRANE CORNER

Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19

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Convalescent plasma is being considered as a potential therapy for COVID-19. We highlight and contextualise the findings of a recent Cochrane rapid review that evaluated the effectiveness and safety of convalescent plasma or hyperimmune immunoglobulin transfusion in the treatment of people with COVID-19. The review found low-certainty evidence of the therapeutic effectiveness and safety of convalescent plasma. As the novel coronavirus continues to spread in South Africa (SA), convalescent plasma may offer a therapeutic ray of hope for mitigating the morbidity and mortality burdens of the disease. Further investigation of the clinical benefits of the therapy in well-designed studies is needed to provide more evidence that will guide COVID-19 treatment decision-making in the SA context.

As the novel coronavirus continues to spread globally, efforts are being accelerated to identify effective preventive and therapeutic measures to mitigate the impact of COVID-19.[1] As of 10 June 2020, South Africa (SA) had recorded a total of 55 421 cases and 1 210 fatalities, making it the most affected country in Africa.[2] With no licensed vaccine or definitive treatment, the clinical management of COVID-19 has been mostly supportive care.[3] Convalescent plasma is being considered as one of the potential therapies for reducing the morbidity and mortality burdens of the disease, particularly among those who are severely or critically ill.[1,3]

Objectives

To highlight and contextualise the findings of a recently published Cochrane rapid review by Valk *et al.*[1] that evaluated the effectiveness and safety of convalescent plasma or hyperimmune immunoglobulin transfusion in the treatment of people with COVID-19.

Intervention and methods

The authors considered studies that evaluated the effects of convalescent plasma or hyperimmune immunoglobulin on people diagnosed with COVID-19 in their review, irrespective of disease severity, age, gender or ethnicity. Although theirs was a rapid review, the authors followed the standard Cochrane systematic review methodology and performed all steps of study screening and selection in duplicate. They searched various research databases and trial registries for both completed and ongoing studies. They combined terms for the novel coronavirus (e.g. SARS-CoV-2 and nCoV-2019), the disease (e.g. COVID-19 and COVID19), convalescent plasma and hyperimmune immunoglobulin.

Results

The review identified 8 studies, with a total of 32 participants who were critically ill. All of these participants received only convalescent plasma at varying doses. The studies included 7 case series and 1 prospectively planned, single-arm intervention study. None was a randomised controlled trial (RCT). In addition, the authors identified 48 ongoing studies evaluating convalescent plasma (47 studies) or hyperimmune immunoglobulin (1 study) in COVID-19 patients, of which 22 are RCTs.

From the results of this review, the authors reported that there was clinical improvement in all participants, and no participant died after 37 days of follow-up. Four of the participants experienced undesirable effects: 1 had moderate fever (39ºC), and 3 had anaphylactic shock after receiving convalescent plasma. The authors judged these studies to be of low quality, with small numbers of participants; inconsistency of outcome measures; variation in outcome reporting across studies; and differences in disease severity, comorbidities, and previous or concurrent treatments across participants.

Conclusions

This Cochrane review has found limited and low-certainty evidence on the effectiveness and safety of convalescent plasma for the treatment of COVID-19. To mitigate the morbidity and mortality of COVID-19, convalescent plasma may offer a ray of hope to SA. There is therefore a need for further investigation to ascertain not only the effectiveness and safety but the practicality of this therapeutic option within the capacity of SA's local blood transfusion services.

Implications for practice

Overall, these findings represent very limited and low-certainty evidence on the effectiveness and safety of convalescent plasma therapy for people with COVID-19. In spite of these limitations, convalescent plasma transfusion may offer a therapeutic ray of hope for SA's fight against COVID-19, given its previous successes in the treatment of similar respiratory diseases such as Middle East respiratory syndrome (MERS), severe acute respiratory syndrome (SARS) and pandemic influenza A (H1N1).[4] As lockdowns and movement restrictions are being eased in SA, the threats posed to the

country's already strained health system by the possibility of further spread of the virus are dire.[5] The country must therefore brace for these threats by exploring potential therapeutic options such as convalescent plasma transfusion to mitigate the morbidity and number of deaths at the peak of the outbreak.

There is a need for further investigation of the benefits, safety and practicality of the therapy for COVID-19 patients in well-designed studies to provide more evidence that will guide clinical decisions in the SA context. Although convalescent plasma is generally thought to be safe and well tolerated, adverse events can occur.[6] As with other types of blood components, the adverse events associated with plasma transfusions are well characterised, including transfusion-related acute lung injury and transfusion-associated circulatory overload, which are leading causes of transfusion-related mortality.[1] Like other blood components, the use of convalescent plasma or hyperimmune immunoglobulin requires functional blood transfusion resources and services. During the 2014 Ebola outbreak, attempts to use convalescent plasma revealed the challenges faced by African countries in ensuring transfusion safety.[7]

Compared with the rest of Africa, SA has relatively well developed national blood transfusion policies and services.[7] These existing resources and infrastructure can be leveraged for investigating and implementing plasma transfusion for COVID-19. There are indications that this is already beginning to happen, with the South African National Blood Service currently planning to investigate and use the plasma for the treatment of COVID-19 patients locally.[8] However, doing so may have limited feasibility in provinces where blood transfusion services are less developed, with limited capacity to meet routine blood transfusion demands. Building local capacity of blood transfusion services in donor recruitment, blood collection, adequate blood screening and transfusion safety monitoring will therefore be crucial for the safe and rational use of convalescent plasma in the country.[7]

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