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.

Potential and challenges of serotherapy for severe influenza

We congratulate John Beigel and colleagues[1] in doing the first randomised-controlled, multicentre trial on adjunctive immune plasma for severe influenza, and reported clinical benefits when given before 5 days of illness, compared with neuraminidase inhibitor treatment alone. Our region's experiences with serotherapy (convalescent plasma or serum and hyperimmune intravenous immunoglobulin [IVIG]) in severe acute respiratory syndrome (SARS)-coronavirus infection, avian (A/H5N1 and A/H7N9) virus infections, and pandemic ($A/H1N1_{pdm09}$) influenza virus infection, have suggested probable benefits. Notably, these reports also described an absence of efficacy when serotherapy was given later in the disease course (SARS-coronavirus >10 days; $A/H1N1_{pdm09}$ >5 days).[2] Available evidence suggests that viral replication is most active and viral load is at its peak during the earlier periods, which could have affected the therapeutic time window for antiviral agents (eg, ≤5 days for neuraminidase inhibitors, with highest benefits when given ≤2 days), in these severe infections.[3] Such observations and the futility of non-specific IVIG suggest that the predominant role of serotherapy could be neutralisation and inhibition of the invading virus, although other mechanisms such as immunomodulation might coexist.[2] Viral load reduction was not shown in Beigel and colleagues' main analysis, but sub-analysis of their data according to virus subtype and the respective virus neutralising antibody titre, and future data from the low (haemagglutination inhibition titre ≤1:10) versus high (haemagglutination inhibition titre ≥1:80) antibody concentration plasma trial (NCT02572817) might provide additional insight and help to define the actual effective titre or dose by bodyweight.

If efficacy can be established, it would be important to define the patient group that would benefit most from adjunctive serotherapy in addition to neuraminidase inhibitors, which is currently considered as the standard of care. Several prognostic indexes based on presenting clinical and laboratory parameters (eg, PaO_2 to FIO_2 ratio, Acute Physiology and Chronic Health Evaluation [APACHE] II, and metabolomics) have been proposed, and might assist risk stratification.[4] The magnitude of improvement in outcomes over neuraminidase inhibitor treatment alone, and its risk-to-benefit ratio will need to be further addressed because of several potential safety concerns and practical challenges with this approach (eg, antibody-dependent enhancement, immune-mediated adverse reactions, and blood-borne infections; panel).[2,5] Preliminary safety data from Beigel and colleagues' study and previous studies have been reassuring. Humanised monoclonal antibodies that are broadly neutralising (both group 1 and group 2 influenza viruses) and target the more conservative regions of the virus (eg, anti-haemagglutinin stalk) might circumvent some of the practical issues, such as an emerging virus strain, without evoking adverse host immune responses (eg, complement activation in antibody-dependent enhancement).[6]

***Panel:* Potential safety concerns and practical challenges of serotherapy**

Safety concerns

- Immune-mediated reactions (eg, transfusion reactions, transfusion-related lung injury, or ADE)
- Increased risk of infection (eg, Zika virus infection, cytomegalovirus infection, hepatitis E virus infection, and other blood-borne viral and bacterial pathogen infections)
- Infusion risk (eg, thromboembolism or volume expansion in ARDS)

Practical challenges

- Obtaining convalescent serum or plasma (eg, donor willingness, availability and access issues, timing for collection after recovery from illness, or variation in antibody titre)
- Evolving virological target (eg, seasonal variation or emerging virus strains)

ADE=antibody-dependent enhancement. ARDS=acute respiratory distress syndrome.

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