Should Intravenous Immunoglobulin G (IVIg) be used in the treatment of COVID-19?

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KEY FINDINGS

There is presently limited evidence on the use of intravenous immunoglobulin G in COVID 19 positive patients.There is an ongoing clinical trial on the use of intravenous immunoglobulin G in COVID 19 patients.

- Intravenous immunoglobulin G (IVIg) is a mixture of polyclonal immunoglobulin G (IgG3, IgG4) antibodies as well as variable amounts of proteins; IgA, IgE, and IgM antibodies isolated and pooled from healthy donors. Immunoglobulin G is involved in viral neutralization. It also modulates the induction of anti-inflammatory cytokines and cytokine antagonists such as interleukin (IL)-1b, IL-1 receptor antagonist and tumour necrosis factor (TNF)-a.
- There were case reports of recovery of three COVID positive patients with severe disease (Wei Cao, 2020) and improvement of ten COVID 19 patients who were given corticosteroids and immunoglobulin G (Zhou ZG 2020).
- There is presently limited evidence on the use of intravenous immunoglobulin G in COVID 19 positive patients.There is an ongoing clinical trial on the use of intravenous immunoglobulin G in COVID 19 patients
- Immediate adverse effects mainly include flu-like syndrome, dermatologic side effects, arrhythmia, hypotension, and transfusion-related acute lung injury (TRALI). Delayed adverse effects can be severe or even lethal and affect less than 1% of patients. These events include thrombotic events, neurological disorders, renal impairment, hematologic disorders, electrolyte disturbance, and transfusion-related infection.
- Surviving sepsis campaign guidelines suggest against the routine use of IVIg in critically ill adults with COVID-19. (Weak recommendation, low-quality evidence) Clinical Practice Guideline for Sepsis and Septic Shock in Adults in the Philippines 2020 also does not recommend the use of standard polyclonal intravenous immunoglobulins in sepsis and septic shock. (Strong recommendation, high quality evidence)

RESULTS

There are presently two case series on the use of intravenous IgG in COVID positive patients. The first case series successfully treated three COVID positive adult patients with severe disease during the early stage of clinical deterioration. (Wei Cao, 2020)

Another case series described the recovery of ten COVID 19 patients who were given short term moderate dose corticosteroids and immunoglobulin G (Zhou ZG 2020).

Surviving sepsis campaign guidelines suggest against the routine use of IVIg in critically ill adults with COVID-19 because of limited efficacy data, absence of adequate antibody titers and possible serious adverse events.(Weak recommendation, low-quality evidence.) (Alhazzani 2020). Clinical Practice Guideline for Sepsis and Septic Shock in Adults in the Philippines 2020 also does not recommend the use of standard polyclonal intravenous immunoglobulins in sepsis and septic shock. (Strong recommendation, high quality evidence) (Clinical Practice Guidelines for Sepsis and Septic Shock Task Force 2020).

CONCLUSION

Evidence on the use of Intravenous Immunoglobulin G on COVID 19 patients with severe disease is presently limited based on case series of adult patients with severe COVID who were successfully treated. There is an ongoing clinical trial on the use of intravenous immunoglobulin G in severe COVID patients. Result of this trial is needed before any recommendation is made. Surviving sepsis campaign guidelines suggest against the routine use of IVIg in critically ill adults with COVID-19.

Declaration of Conflict of Interest

No conflict of interest

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A multicenter study in China led by Peking Union Medical College Hospital, Chinese Academy of Medical Sciences to determine if high dose intravenous immunoglobulin G will reverse the wosening course of COVID 19 patients
https://www.trialsitenews.com/chinese-academy-of-medical-sciences-led-study-reveals-high-dose-ivig-improves-severe-covid-19-cases

Table 1. Characteristics of ongoing clinical trials

No.	Clinical Trial ID / Title	Status	Estimated start date, primary completion date, study completion date	Study design	Country	Population	Intervention Group(s)	Comparison Group(s)	Outcomes
1	NCT04261426 A Randomized, Open-label, Controlled, Single-center Study to Evaluate the Efficacy of Intravenous Immunoglobulin Therapy in Patients With Severe 2019- nCoV Pneumonia	Not yet recruiting	February 10,2020 April 30,2020 June 30,2020	Randomized Open Label Parallel Controlled Clinical Trial	China	COVID 19	IVIg	Standard Care	Clinical Improvement based on the 7 point scale Lower Murray lung injury score 28 day mortality Duration of mechanical ventilation Duration of hospitalization Proportion of patients with negative RT-PCR results Proportion of patients in each category of the 7 point scale Proportion of patient with normalized inflammation factors Frequency of adverse drug events Frequency of serious adverse drug events