Intravenous Immunoglobulin

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Recommendations

- The COVID-19 Treatment Guidelines Panel (the Panel) recommends against the use of intravenous immunoglobulin (IVIG) for the treatment of acute COVID-19 in adults and children, except in a clinical trial (AIII). This recommendation should not preclude the use of IVIG when otherwise indicated for the treatment of complications that arise during the course of COVID-19.

- The Panel recommends using IVIG in combination with low to moderate dose glucocorticoids in hospitalized patients for the treatment of multisystem inflammatory syndrome in children (MIS-C) (AIIb).

- The Panel recommends against the routine use of IVIG monotherapy for the treatment of MIS-C unless glucocorticoid use is contraindicated (AIIb).

Rationale

It is unknown whether IVIG products derived from pooled donor plasma contain high titers of SARS-CoV-2 neutralizing antibodies. In addition, different lots of IVIG may have different titers of antibodies. Information on antibody titer is not reported in clinical trials that have evaluated IVIG and likely varies based on the dominant circulating variants and when the plasma products were collected. Although IVIG preparations may have general immunomodulatory effects, these theoretical effects do not appear to benefit patients with COVID-19.1

IVIG with or without corticosteroids has been used for the treatment of MIS-C. See Therapeutic Management of Hospitalized Pediatric Patients With Multisystem Inflammatory Syndrome in Children (MIS-C) (With Discussion on Multisystem Inflammatory Syndrome in Adults [MIS-A]) for the Panel’s recommendations.

Clinical Data for COVID-19

A meta-analysis of 6 randomized controlled trials of non-SARS-CoV-2-specific IVIG with 472 patients demonstrated no survival benefit from the use of IVIG in patients with COVID-19 when compared with controls.1 All of the included trials were conducted in 2020, when the presence of SARS-CoV-2 antibodies in blood donors was likely uncommon. None of the studies measured the titers of anti-SARS-CoV-2 antibodies, so the extent that these preparations may have contained SARS-specific antibodies is unknown. Blood supplies collected since that time likely have a higher level of these antibodies, and the IVIG derived from those supplies could be expected to have a higher level of SARS-specific antibodies. Use of non-SARS-CoV-2-specific IVIG for the treatment of COVID-19 should be limited to clinical trials.

Concentrated antibody preparations derived from pooled plasma collected from individuals who have recovered from COVID-19 can be manufactured as SARS-CoV-2 hyperimmunoglobulin (hIVIG). Treatment with SARS-CoV-2 hIVIG did not alter patient outcome in a large randomized controlled trial of hospitalized patients, and it is currently not available for clinical use in the United States.2
Considerations in Pregnancy

IVIG is commonly used in pregnancy for other indications, such as alloimmune thrombocytopenia. However, given the lack of clear evidence of IVIG efficacy for the treatment of acute COVID-19 in nonpregnant adults, the Panel recommends against the use of IVIG for the treatment of acute COVID-19 in pregnant individuals, except in a clinical trial (AIII). This recommendation should not preclude the use of IVIG when otherwise indicated for the treatment of complications that arise during the course of COVID-19.

Considerations in Children

No pediatric comparative studies have evaluated the use of IVIG in patients with acute COVID-19. IVIG is used in pediatric patients for other indications, such as in combination with glucocorticoids for the initial immunomodulatory treatment of MIS-C. However, given the lack of clear evidence of IVIG efficacy for the treatment of acute COVID-19 in adults, the Panel recommends against the use of IVIG for the treatment of acute COVID-19 in children, except in a clinical trial (AIII). This recommendation should not preclude the use of IVIG when otherwise indicated.

For the Panel’s recommendations for children with MIS-C, see Therapeutic Management of Hospitalized Pediatric Patients With Multisystem Inflammatory Syndrome in Children (MIS-C) (With Discussion on Multisystem Inflammatory Syndrome in Adults [MIS-A]).

References