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A RETROSPECTIVE STUDY OF USE OF INTRAVENOUS IMMUNOGLOBULIN IN PEDIATRIC INTENSIVE CARE UNIT IN A TERTIARY CARE CENTRE: AN AUDIT AND REVIEW OF LITERATURE.

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ABSTRACT

Introduction: The use of intravenous immunoglobulin (IVIG) for array of clinical conditions has been ever increasing. The United States Food and Drug Administration (FDA) has approved the use of IVIG in six conditions only. The IVIG is used as a source to replace antibodies at dose of 200–400 mg/kg/month in conditions with primary and secondary antibody deficiencies. At a higher dose of 2 g/kg, IVIG serves as immunomodulatory and anti-inflammatory agent, through mechanisms such as autoantibody neutralization and production of interleukin-12.

Materials And Methods: The study was conducted over a period of 4 years in a tertiary care PICU from January 2015 to December 2018. It is a retrospective chart review of IVIG transfusion received by the children in a 35-bed PICU. The study was conducted after approval of institutional ethics committee. The study included patients who had received one or more doses of IVIG transfusion from the age of 1 month to 18 years. The demographic profile, indication of transfusion of IVIG, dose of IVIG received, length of stay, and outcome of the each patient were collected.

Results: Three hundred and one cases received IVIG therapy during the 4-year study with median age of 5 years and 61.4% (185) children were being males. The patients transfused IVIG under the following clinical categories, 120 cases with neuroimmunologic disorders; 73 cases with cardiology related indications; 65 children with infection and infection related cases; 31 with autoimmune diseases (hematological); seven children with primary immunodeficiency; and five with dermatology related causes.

Conclusion: There is a rise in off label use of IVIG but the quality of evidence is variable for various indications. The use of IVIG may provide benefit in the variety of conditions discussed in this section. Importantly, conditions that are life-threatening and rare do not allow for RCTs. Clinical experience and other, less stringent studies lend support to the use of immunoglobulin in some of these conditions.

KEYWORDS : immunoglobulin, PICU, RCTs, IVIG.

INTRODUCTION

The use of intravenous immunoglobulin (IVIG) for array of clinical conditions has been ever increasing. The United States Food and Drug Administration (FDA) has approved the use of IVIG in six conditions only.[1] The IVIG is used as a source to replace antibodies at dose of 200–400 mg/kg/month in conditions with primary and secondary antibody deficiencies.[2] At a higher dose of 2 g/kg, IVIG serves as immunomodulatory and anti-inflammatory agent, through mechanisms such as autoantibody neutralization and production of interleukin-12.[3] Apart from FDA, the American Academy of Allergy and Immunology, the Canadian Agency for Drugs and Technologies in Health, and Committed evaluation et de diffusion des innovation technologies have scientifically evaluated the available evidence on the use of immunoglobulin and come out with recommendations of its appropriate use.[4,5] The aim of the study is to review the pattern of use IVIG therapy in critically ill children in pediatric intensive care unit (PICU) setting and asses the quality of evidence for off-label indications of transfusion.

OBJECTIVES

To review, use of immunoglobulin (IVIG) for conditions, label and off label, in critically ill children in Pediatric Intensive Care Unit (PICU) setting.

To assess the quality of evidence and strength of recommendation for each indication of transfusion.

MATERIALS AND METHODS

The study was conducted over a period of 4 years in a tertiary care PICU from January 2015 to December 2018. It is a retrospective chart review of IVIG transfusion received by the children in a 35-bed PICU. The study was conducted after approval of institutional ethics committee.

The study included patients who had received one or more doses of IVIG transfusion from the age of 1 month to 18 years. The demographic profile, indication of transfusion of IVIG, dose of IVIG received, length of stay, and outcome of the each patient were collected. If the primary indication was not clearly stated in the medical records, then the final diagnosis or a significant clinical finding that was recorded prior to the administration of IVIG was taken to be primary indication of transfusion of IVIG. The indication of IVIG was categorized as, unknown, if the above mentioned was not observed during the analysis of records.

Statistical Analysis

Categorical was represented as frequencies, proportions, and percentages. The continuous data were analyzed as standard deviation or means or medians or interquartile ranges if data were found to be skewed.

RESULTS

Three hundred and one cases received IVIG therapy during the 4-year study with median age of 5 years and 61.4% (185) children were being males. The patients transfused IVIG under the following clinical categories, 120 cases with neuroimmunologic disorders; 73 cases with cardiology related indications; 65 children with infection and infection related cases; 31 with autoimmune diseases (hematological); seven children with primary immunodeficiency; and five with dermatology related causes.

Fifty six (18.6%) cases who received IVIG were of FDA approved indications which included (primary immune deficiency, idiopathic thrombocytopenic purpura [ITP], and Kawasaki disease).

The diagnosis at admission was ITP in 31 cases, acute myocarditis in 72 cases and one case with dilated cardiomyopathy (DCM). All five cases of dermatological diseases were toxic epidermal necrolysis (TEN). Among infection related diseases, 19 cases with Kawasaki disease, 45 cases with sepsis syndrome, and one case was diagnosed as

toxic shock syndrome. Ninety six cases with Guillain–Barré syndrome (GBS) while other neurological cases were as follows, 10 cases with super-refractory status epilepticus (SRSE), five cases with autoimmune encephalitis, four cases with acute disseminated encephalomyelitis (ADEM), two cases with acute necrotizing encephalopathy (ANEC), and one case each with myasthenia gravis, acute transverse myelitis, and acute flaccid myelitis. Among the primary immunodeficiency disease, two cases with Bruton's Agammaglobulinemia, four cases with severe combined immunodeficiency (SCID), and one case with Selective IgA deficiency were transfused IVIG.

As per the review of evidence by workgroup report of the American Academy of Allergy, Asthma, and Immunology the indications have been classified further. About 50% cases (152 cases) received IVIG with definitely beneficial category, 30% (91 cases) it may provide benefit category, seven in probably beneficial category and two cases in unlikely to provide benefit category which include DCM and Selective IgA deficiency.

DISCUSSION

Adjuvant therapy of IVIG in 45 children with bacterial sepsis or septic shock was given due to possible bactericidal mechanisms such as opsonization of antibodies, stimulation of phagocytosis, and neutralization of toxins of bacteria.[6] A prospective randomized control trial involving IVIG in sepsis syndrome in children in PICU demonstrated a significant reduction in mortality and length of stay.[7] However, a Cochrane review in which 43 trials were included, demonstrated that polyclonal IVIG was not associated with reduced mortality in neonates or adults in sepsis.[8] Other uses of IVIG that had been studied include postoperative sepsis and trauma-associated sepsis. The use of IVIG therapy in setting of sepsis necessitates more specific definition.

The pro-inflammatory cytokine storm caused by endotoxin or super antigen-activated blood cells may be suppressed by IVIG, hence its use in condition such as streptococcal toxic shock, whereas in our study, we observed only one case with toxic shock syndrome that was given IVIG therapy, succumbed to the disease.[9]

Since several multicenter randomized trials demonstrated the efficiency of high-dose IVIG in comparison with systemic steroids in raising platelets in ITP which led to FDA approval as well as its use in prevention and control of bleeding in severe forms, support the rationale of the use of IVIG in 31 children in our PICU.[10]

CONCLUSION

There is a rise in off label use of IVIG but the quality of evidence is variable for various indications. The use of IVIG may provide benefit in the variety of conditions discussed in this section. Importantly, conditions that are life-threatening and rare do not allow for RCTs. Clinical experience and other, less stringent studies lend support to the use of immunoglobulin in some of these conditions.

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