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Evaluation of infusion reactions associated with intravenous immune globulin (IVIG) in neonatal and pediatric patients

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Evaluation of Infusion Reactions Associated with Intravenous Immune Globulin in Neonatal and Pediatric Patients

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Background

- Intravenous immune globulin (IVIG) is used to treat a variety of conditions such as hemolytic disease of the newborn, Kawasaki disease, toxic shock syndrome, various autoimmune disorders, and infectious processes.
- The current practice for administering IVIG is a titrated approach where initial rates of administration and titration parameters are specific to each IVIG product as recommended by the manufacturer.
- Titration is recommended due to infusion reactions including flushing, fever, changes in pulse rate, and changes in blood pressure—all which are suspected to increase as the infusion rate increases.
- Most infusion reactions are mild and transient, and more severe reactions such as anaphylaxis, aseptic meningitis, and thrombosis are rare.
- Known risk factors for infusion reactions include advanced age and renal failure, but with limited data about infusion reactions in pediatric patients, there may be risk factors not yet shown to have statistical significance.

Purpose

- To investigate possible risk factors influencing the occurrence of IVIG-associated infusion reactions

Objectives

Primary objective

- To assess infusion reactions to conclude whether they were associated with higher infusion rates of IVIG

Secondary objectives

- Rates of discontinuation or interruption of therapy
- Symptoms of infusion reactions
- Use of rescue medications
- Infusion reaction incidence between brands, dose, age, sex, and treatment indication

Methods

Study design

- Single-center, retrospective, observational study at a large tertiary medical center

Statistical analysis

- Fisher's exact test
- $\alpha = 0.05$

Inclusion criteria

- Inpatient neonatal and pediatric patients who received at least one dose of IVIG between January 1, 2017 and December 31, 2021

Exclusion criteria

- Patients >18 years old

Results

Demographic Data

Variables	All patients given IVIG (n=70)	Patients with infusion reactions (n=8)	P-value
Age			**0.005**
≤28 days	34 (49)	0 (0)	
29 days-18 years	36 (51)	8 (100)	
Sex			0.462
Male	33 (47)	5 (63)	
Female	37 (53)	3 (38)	
Max Rate			0.430
≤2 mL/kg/hr	22 (31)	4 (50)	
>2 mL/kg/hr	42 (60)	4 (50)	
Unknown	6 (9)	0 (0)	
Dose			0.113
≤1 g/kg	46 (66)	3 (38)	
>1 g/kg	24 (34)	5 (63)	
Indication			**0.0003**
Hyperbilirubinemia	31 (44)	0 (0)	
Kawasaki	18 (26)	2 (25)	
Autoimmune	7 (10)	0 (0)	
MIS-C	7 (10)	2 (25)	
Infectious	4 (6)	3 (38)	
Other	3 (4)	1 (13)	
Premedication			**0.0002**
Benadryl	6 (9)	1 (13)	
Tylenol	7 (10)	2 (25)	
Both	20 (29)	5 (63)	
None	37 (53)	0 (0)	
Brand			0.464
Gamunex-C	23 (33)	1 (13)	
Gammagard	25 (36)	4 (50)	
Flebogamma	22 (31)	3 (38)	

Infusion Reactions

Time from onset of IVIG to reaction

Time	Frequency (n=8)
0-30 min	0 (0)
31-60 min	0 (0)
61 min-4 hr	7 (88)
5-9 hr	0 (0)
10-15 hr	0 (0)
16-24 hr	0 (0)
25 hr-1 week	1 (13)

Reaction incidence

Reaction	Frequency (n=11)
Hypotension	3 (27)
Tachycardia	2 (18)
Fever	2 (18)
Chills	1 (9)
Aseptic meningitis	1 (9)
Dizzy	1 (9)
Flushing	1 (9)

Prevention and Management

Prevention of infusion reactions

Pre-medications	Frequency (n=8)
Tylenol	2 (25)
Benadryl	1 (13)
Both	5 (63)
None	0 (0)

Management of infusion reactions

Interventions	Frequency (n=8)
Slowing down infusion rate	5 (63)
Temporarily stopping infusion	1 (13)
Rescue medications	1 (13)
No intervention	1 (13)

Discussion

- A total of 70 patients received IVIG infusions.
- Eight patients (11.4%) experienced infusion reactions despite pre-medication, all of which were in pediatric patients between the ages of 29 days and 18 years (p=0.005).
- Administering IVIG at rates greater than 2 mL/kg/hr did not have a significant increase in the number of infusion reactions.
- Additionally, there was no difference in the number of infusion reactions between sex, doses of IVIG greater than 1 g/kg, or among the three IVIG brands (Gammagard, Gamunex-C, Flebogamma).
- There was a significant difference in adverse events between indications, with infectious indications having the highest incidence (p=0.0003).
- The median time from onset of infusion reaction after IVIG initiation was 2 hours.
- The most common reactions were hypotension (27%), tachycardia (18%), and fever (18%).
- Infusion reactions were managed by decreasing the rate of the infusion (63%), temporarily stopping the infusion (13%), or administering rescue medications (13%).
- Among the pediatric subgroup, there was no significant difference in infusion reactions between sex, infusion rate, or dose.

Study Limitations

- Retrospective, non-randomized study
- Select data was pulled from the electronic health record via retrospective chart evaluation by single reviewer
- Small study population with minimal infusion reactions identified

Conclusion

- There was no association between infusion reactions and higher IVIG infusion rates.
- Although patient age was the only variable found to be associated with infusion reactions, findings were potentially limited by the small study sample size.
- Further research is required to evaluate risk factors for infusion reactions and their association with IVIG.

Disclosures

- Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct of indirect interest in the subject matter of this presentation:
- Katie Couch: Nothing to disclose
- Samantha Tatz: Nothing to disclose

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