

Increased frequency of thromboembolic complications in patients with chronic inflammatory demyelinating polyneuropathy treated with intravenous immunoglobulin through central venous catheters

Ami S. Patel,¹ Billie L. Durn,¹ Sanders Clark,² Tara Grabowsky,³ Rob Curry,² Ann Leon¹

¹CSL Behring, King of Prussia, PA, USA; ²HVH Precision Analytics, Wayne, PA, USA; ³McKinsey Consulting, New York, NY, USA

Introduction

- Intravenous Immunoglobulin (IVIg) is approved for use in chronic inflammatory demyelinating polyneuropathy (CIDP)¹
- However, inflammatory neuropathy patients who use IVIg have an increased risk of thromboembolic events (TEEs)²⁻⁴
 - In two previous studies, the rate of TEEs in inflammatory neuropathy patients following IVIg treatment were 11.3% (n=7) and 10.7% (n=12), respectively^{2,3}
- Central venous access devices (CVADs) offer reliable venous access for IVIg-treated patients, but are also a known risk factor for the development of TEEs⁵

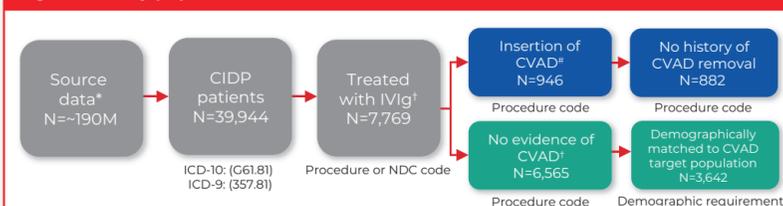
Objective

- To characterize the relationship between CVAD-based IVIg administration and TEE occurrence in CIDP patients

Methods

- This was an observational, retrospective cohort study of IVIg-treated CIDP patients
 - We utilized claims data collected in the United States between January 2006 and May 2018 using the IBM/Truven MarketScan[®] adjudicated claims database
- The study cohort was identified by a CIDP diagnosis claim and a procedure/drug code for IVIg after diagnosis (**Figure 1**)
 - CVAD exposure was defined as having a placement procedure code up to two months prior to initial CIDP diagnosis and without removal before the end of IVIg treatment
- TEE outcomes were composed of arterial, venous, and vascular prostheses-related TEE codes
 - Individual event frequency along with overall presence of TEEs in patients with a CVAD was compared with demographically matched non-CVAD patients throughout the entire study period and p-values determined via difference of proportions tests
 - CVAD patients were individually matched to five non-CVAD patients using: medical insurance type, prescription data availability, sex, age, geographic region and years enrolled in the database by exact matching
- All-cause healthcare resource utilization (inpatient admission and emergency room visit claims) was also assessed

Figure 1: Study population



*Data source: Truven MarketScan[®] (Jan 2006–Jun 2018). *After CIDP diagnosis. *between 2 months prior to CIDP diagnosis and last IVIg code. CIDP: chronic inflammatory demyelinating polyneuropathy; IVIg: intravenous immunoglobulin; CVAD: central venous access device; ICD: international classification of diseases; NDC: national drug code

Results

- A total of 7,769 CIDP patients with ≥1 IVIg claim were identified. Of these, 882 (11.8%) were CVAD patients and 6,565 (88.2%) were non-CVAD patients; other demographic characteristics are shown in **Table 1**
- In terms of comorbidities, in the 12 months prior to IVIg therapy 16.9% vs 10.9% had a prior TEE (P<0.0001), 51.9% vs 45.0% had hypertension (P<0.001), 7.0% vs 5.2% received anticoagulation therapy (P<0.05), 26.9% vs 24.2% had diabetes and 19.1% vs 17.8% had hyperlipidemia (both P>0.05), for CVAD vs matched non-CVAD patients, respectively

Table 1: Patient demographics

Demographic characteristic	CVAD patients (N=882)	Non-CVAD patients (N=6,565)
Male	45%	68%
Median age (years)	58	59
Age group at time of first IVIg dose (years)		
0-17	3%	2%
18-34	7%	6%
35-44	12%	10%
45-54	20%	21%
55-64	33%	34%
65+	25%	27%
Median time in database	6 years	5 years
Type of insurance		
Commercial	66%	66%
Medicare	24%	26%
Medicaid	10%	8%

CVAD: central venous access device; IVIg: intravenous immunoglobulin

Table 2: Most frequent TEEs among IVIg patients with CIDP by CVAD status

Description	CVAD patients N=882, n (%)	Matched non-CVAD patients* N=3,642, n (%)
Total number of patients with at least one TEE complication	224 (25.4)	406 (11.2)
Arterial events		
Total	126 (14.3)	266 (7.3)
Occlusion and stenosis of carotid artery without mention of cerebral infarction	47 (5.3)	101 (2.8)
Cerebral artery occlusion; unspecified with cerebral infarction	37 (4.2)	78 (2.1)
Acute; but ill-defined; cerebrovascular disease	30 (3.4)	65 (1.8)
Occlusion and stenosis of multiple and bilateral precerebral arteries without mention of cerebral infarction	22 (2.5)	33 (0.9)
Venous events		
Total	134 (15.2)	165 (4.5)
Acute venous embolism and thrombosis of unspecified deep vessels of lower extremity	62 (7.0)	64 (1.8)
Other pulmonary embolism and infarction	49 (5.6)	48 (1.3)
Other venous embolism and thrombosis of unspecified site	34 (3.9)	24 (0.7)
Acute venous embolism and thrombosis of deep vessels of proximal lower extremity	24 (2.7)	22 (0.6)
Phlebitis and thrombophlebitis of deep veins of lower extremities; other	19 (2.2)	22 (0.6)
Acute venous embolism and thrombosis of deep vessels of distal lower extremity	16 (1.8)	17 (0.5)

*Matched by age, sex, geographic region of residence, medical insurance type, prescription drug availability, and length of enrolment in the database. Patients could experience more than one type of TEE event. CVAD: central venous access device; TEE: thromboembolic events; CIDP: chronic inflammatory demyelinating polyneuropathy; IVIg: intravenous immunoglobulin

- The percentage of patients with TEEs was significantly higher for CVAD patients than for non-CVAD patients (25.4% vs. 11.2%; P<0.0001; **Figure 2**)
 - The most frequently observed arterial TEE in both patient groups was occlusion and stenosis of the carotid artery. The most frequently observed venous TEE in both patient groups was acute venous embolism and thrombosis of lower extremity deep vessels (**Table 2**)
- CVAD patients had a higher rate of all-cause inpatient admissions and emergency room visits than non-CVAD patients (**Table 3**)

Figure 2: Percentage of patients with ≥1 TEE complication

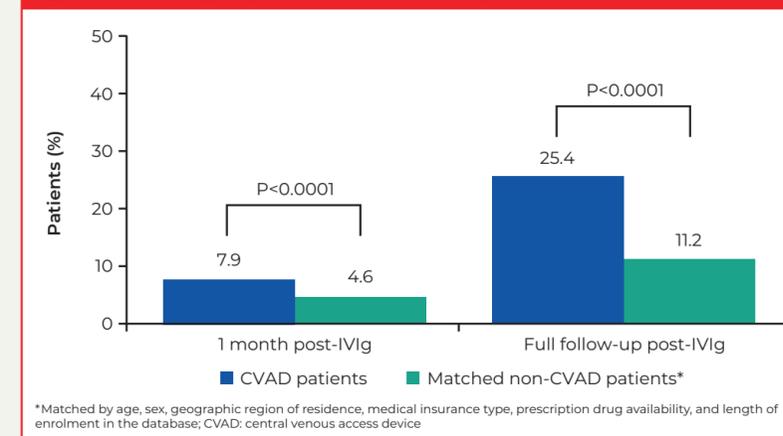


Table 3: Inpatient admissions and emergency room visits

Population	Inpatient admissions (mean ± SEM)		Emergency room visits (mean ± SEM)	
	Distinct months with distinct claim	Inpatient admission frequency (events per month)	Distinct months with ER claim	ER visit frequency (events per month)
CVAD patients (N=882)	1.444 ± 2.28	0.136 ± 0.014	2.01 ± 3.28	0.142 ± 0.013
Matched non-CVAD patients* (N=3,642)	0.405 ± 0.94	0.076 ± 0.006	0.648 ± 1.73	0.087 ± 0.006

Inpatient admissions were determined using both the place of service listed on the claim and a charge for room and board (i.e., claims from an inpatient hospital with a room and board charge were considered admissions). ER visits were determined using outpatient claims with an ER service type listed on the claim
*Matched by age, sex, geographic region of residence, medical insurance type, prescription drug availability, and length of enrolment in the database; CVAD: central venous access device; ER: emergency room; SEM: standard error of the mean

Conclusion

- CIDP patients treated with IVIg using a CVAD may experience TEEs with a greater frequency compared with those that are treated with IVIg without using a CVAD
- CVAD patients have a higher inpatient admission and emergency room visit rate in hospitals than non-CVAD patients
- The rate of TEEs in non-CVAD patients in this study are similar to those reported in previous studies^{2,3}
- Further exploration of confounding variables could aid in clinical decision making regarding choice of Ig treatment or appropriate Ig administration method

References

- Lehmann HC, et al. J Neurol Neurosurg Psychiatry 2019; **90**: 981-987.
- Rajabally YA, Kearney DA. J Neurol Sci. 2011; **308**: 124-7.
- Spillane J et al. J Peripher Nerv Syst. 2017; **22**: 226-414.
- Kapoor, M et al. J Peripher Nerv Syst. 2018; **23**: 249-405.
- Wall C, et al. J Intensive Care Soc. 2016; **17**:160-167.

Author Disclosures

Ami S. Patel: Employment – CSL Behring; Billie L. Durn: Employment – CSL Behring; Sanders Clark: Employment – HVH Precision Analytics; Tara Grabowsky: N/A; Rob Curry: N/A; Ann Leon: Employment – CSL Behring

Editorial assistance was provided by Meridian HealthComms, funded by CSL Behring.