Minimizing Adverse Drug Reactions to IVIG in the Home Setting Through Application of an Evidence-Based Clinical Care Management Program

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ABSTRACT

Rationale: Intravenous immunoglobulin (IVIG) infusions are associated with predictable adverse drug reactions (ADRs), some of which are life threatening. The application of a clinical program at the specialty pharmacy (SP) level can decrease both the frequency and severity of reactions.

Methods: A retrospective review of 4,155 patients receiving IVIG over a 10-month period was conducted using the specialty pharmacy electronic medical record. Patients were included if they placed at least one refill of IVIG, age fell between 18 and 89 years, and a refill assessment template was completed and reviewed by a pharmacist for every refill placed. Data included diagnosis, brand, dose and frequency of the IVIG, and history of patient reported problems since the previous infusion. For problems determined to be ADRs, nursing notes were reviewed for premedication regimens, concentration and rate of infusion of the IVIG, and patient tolerability.

Results: 14.1% (4,588/32,537) of assessments revealed a patient reported problem since the previous infusion of IVIG. The majority of these problems were infections (2,897/4,588; 63.1%) or involved the mechanics during administration (1,318/4,588; 28.7%). The number of true ADRs was 373, revealing an adverse event rate associated with the infusion of IVIG in the home of 1.1% (373/32,537). Two of these reactions were considered life threatening (anaphylaxis and pulmonary embolism), while sixteen were classified as severe (potential aseptic meningitis or thromboembolic event).

Conclusions: Our data show that the application of an evidence-based clinical care management program can reduce the incidence of ADRs associated with IVIG below the literature benchmark.

METHODS

Patients were assessed per the Clinical Considerations for IVIG Brand Selection protocol at start of care. This proprietary algorithm was designed to identify patients at increased risk for serious ADRs and offer evidence-based mitigation strategies to decrease the likelihood of occurrence. Figure 1 illustrates the portion of the tool that assesses risk for IVIG associated thromboembolic events (TEE).

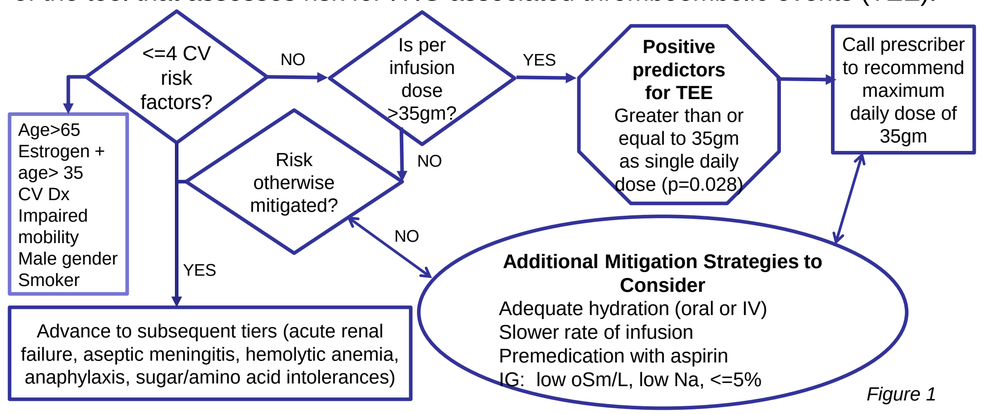

Figure 1

Additionally each regimen was evaluated to assure that the premedication regimen was appropriate to patient age, weight and other comorbidities. If a premedication regimen was not ordered by the prescriber, the pharmacist recommended one.

Patients were matched to a home infusion nurse specializing in the administration of IVIG. Nursing care was delivered using a primary-team model. With each visit, the nurse performed a physical assessment, established IV access and infused the IVIG per prescriber orders. The nurse monitored the patient for the entire infusion, assessing vital signs at pre-defined intervals and making adjustments to the infusion rate as warranted to maintain patient tolerance. As needed, pre-medications were redosed per standing orders.

Prior to the next scheduled infusion, the patient engaged with a non-clinician by phone to place a refill. During that call the patient was asked a series of non-interpretive questions to screen for potential barriers to successful therapy – including the occurrence of ADRs. Affirmative answers were triaged to a nurse.

- ❑ Are there any problems [(including ADRs or product complaints] to report with your last IVIG infusion?

Since your last reorder of IVIG:

- ❑ Have you had any infections?
- ❑ Have you been seen in an ER or admitted to an inpatient facility?
- ❑ Have you had changes to your medications – including new prescriptions or over-the-counter drugs?

RESULTS

14.1% of assessments (6.4% of patients reordering IVIG [267/4155] – demographics Figures 2 & 3) revealed a patient reported problem since the previous infusion of IVIG; 1.1% (373/32,537) of those were confirmed ADRs (Figure 4).

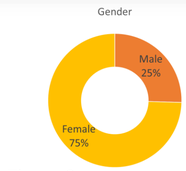

Figure 2

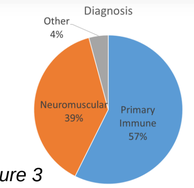

Figure 3

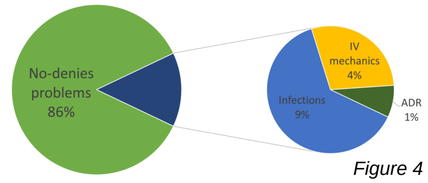

Figure 4

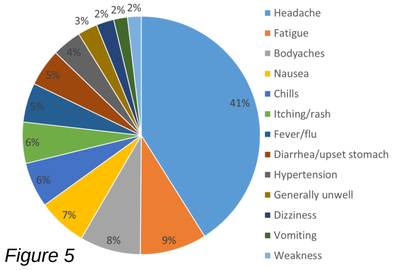

Figure 5

41% of reported ADRs with IVIG were classified as headache. Figure 5 illustrates ADRs which occurred with a frequency of greater than or equal to 2% in our sample.

0.05% (16/32,537) of reported problems were classified as severe ADRs. Two (0.006%) were potentially life-threatening: anaphylaxis/ epinephrine use and pulmonary embolism. Table 1 illustrates the detail around each of these events.

Anaphylaxis/epinephrine use

- Symptoms: rash on right side of body, itching on side of tongue
- Onset immediately after infusion, started to resolve prior to use of epinephrine
- IVIG continued with high dose H1/H2 receptor antagonist premedications

Pulmonary Embolism

- Symptoms: chest pain and dyspnea
- Onset 8 days post IVIG infusion; IVIG ruled out as causative
- Added apixaban 5mg po bid
- IVIG continued with increased hydration and slower rate of infusion

Table 1

141 of 267 (52.8%) patients reporting ADRs were included in a follow-up cohort evaluating the effectiveness of extending the infusion time as a strategy for mitigating the original ADR. Patients were included if they remained on an identical treatment regimen (same IVIG brand, dose, premedication regimen and nursing care provided through the same primary-team at the specialty pharmacy) as the infusion triggering the original ADR. Patients were significantly less likely to report an ADR on a subsequent infusion when the rate of infusion was slowed. Results (analysis was conducted using a paired student's t-test with p-values <5% signaling statistical significance) are summarized in Table 2.

Dose	mg/kg/hr	gm/hr	p value
Reports ADR	163.4	12.6	0.002
Denies ADR	140.8	10.8	0.002

Table 2

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CONCLUSION

Our data show that the application of an evidence-based comprehensive clinical care management program can reduce the incidence of ADRs associated with IVIG below the literature benchmark – an overall rate of 1.1% in this sample. Severe ADRs occurred at a rate of 0.05%, while potentially life threatening events were limited to just 0.006% of the sample. One standard mitigation strategy, reduction of the infusion rate, was shown to significantly reduce the likelihood of recurrence of an ADR. This strategy was successfully driven at the specialty pharmacy through the primary-team home infusion model.