Reporting of Administration Site Reactions with Parenteral Drugs for the On-Demand Treatment of Hereditary Angioedema Attacks – Analysis of the FAERS Database 2009 to 2022

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Background

- Hereditary angioedema (HAE) is a rare genetic disease associated with recurrent and unpreventable attacks of swelling, which may be life-threatening if involving the airway.
- Treatment guidelines recommend that patients should have access to on-demand therapy to treat attacks as early as possible1-4
- The most common adverse events reported in clinical trials and post-marketing reports for most of the available treatments include injection site reactions, and range from 0% to 7%
- The current research was driven by two objectives: first, to describe reported rates of all administration site adverse drug reactions (AS-ADR) for approved an HAE therapies in the FDA’s Adverse Event Reporting System (FAERS); and second, to detect administration site AS-ADR from clinical trials with higher than expected reporting rates compared to other parenteral drugs in the FDA registry.

Methods

- The FAERS database contains information on spontaneous and medico-legal adverse events reported to the FDA's Adverse Event Reporting System (FAERS). The database includes reports from patients, providers, and others (such as patients, family members, lawyers, and others).
- The database was queried using a variety of search terms to identify administration site AS-ADR.
- The five most frequently reported administration site ADR domains included injection site pain, site swelling, site erythema, site infection, and site bruising.
- The results of the predictive analysis examining the reporting rate of administration site ADRs were compared to other IV ADRs.
- The current results are likely underestimating the real-world burden due to spontaneous reporting; thus, they cannot be used to estimate incidence.

Results

- The average age of HAE patients who reported administration site ADRs was similar across therapies (mean [SD], pdC1-INH, 42.9 [18.7]; icatibant, 42.3 [15.3]; rhC1-INH, 43.4 [17.4]).
- Similar proportions of females across therapies (76% to 83%) had the highest rate of incorrect route of product administration at 3.7 per year.
- The age distribution was much narrower for rhC1-INH (SD=9.4) compared to the other three drugs, with standard deviations ranging from 15.3-18.7.
- These findings support the conclusions from the FDA Patient Voice Summit (2018), which recognized the importance of developing less invasive routes of administration for HAE patients.

Conclusions

- The results of this real-world study suggest that all four FDA-approved on-demand therapies for HAE attacks are associated with administration site ADRs.
- The reported rates in the FAERS database of administration site ADRs are similar for all four therapies, with notable differences for site pain.
- The FDA Patient Voice Summit (2018) recognized the importance of developing less invasive routes of administration for HAE patients.
- Adverse events are significantly underreported in spontaneous reporting systems such as FAERS.

References