



Letter

Long-term adherence to self-injectable epinephrine in the veteran population

According to practice parameters, first-line treatment for anaphylaxis, a life-threatening medical emergency that requires prompt recognition and intervention, is intramuscular epinephrine administered in the anterolateral aspect of the thigh.¹ Despite the availability of a lifesaving self-administrable treatment, studies indicate poor prescribing rates by health care professionals and poor adherence rates by patients. Limited data exist for adherence rates of self-injectable epinephrine (SIE) in a clinic setting, particularly during a long-term period. Our study investigated long-term (10-year) adherence to SIE in various clinic settings.

Electronic medical records were retrospectively reviewed for patients who received new SIE prescriptions at the Department of Veterans Affairs (VA) of Greater Los Angeles Medical Center from January 2002 to December 2003 and still had an active prescription in December 2013. Patients who did not actively receive medical care, defined by no health care professional visits or medication refills in 2013, were excluded. Using the Computerized Patient Record System, we obtained patient demographics, clinical setting, health care professional prescribing the SIE, SIE indication, number of SIE refills dispensed, and documented patient educational efforts. Approval was obtained from the institutional review board.

Refill adherence was defined as patients with an active SIE prescription at the end of 2013. Taking into account SIE shelf-life of approximately 18 months, adherence during the 10-year period was categorized as good (7 prescription fills), intermediate (5–6 prescription fills), or poor (≤ 4 prescription fills). Nonadherence was defined as not having an active prescription.

From 2002 to 2003, a total of 173 patients filled a SIE prescription at the VA medical center; by December 2013, only 82 were eligible for study inclusion (mean age, 65.9; age range, 38–91 years; male, 91.5%; white, 53.7%). Reasons for dispensing SIE included insect venom allergy (45.1%), food allergy (26.8%), angioedema (13.4%), immunotherapy (2.4%), urticaria (2.4%), and unknown reason (7.3%).

Of the 82 patients, 37 (45.1%) were considered adherent, whereas 45 (54.9%) were non-adherent. Adherence varied among the indications: venom allergy, 62%; food allergy, 30%; and angioedema, 27%. Adherent patients filled SIE prescriptions 9 times during the 10-year period; nonadherent patients filled their prescriptions less than 3 times. Of the 37 adherent patients, 26 had good, 4 had intermediate, and 7 had poor adherence. Twenty patients (24.4%) only filled their initial SIE prescription, after which they failed to refill their SIE.

Most SIE prescriptions were prescribed in the primary care clinic ($n = 40$ [48.8%]) or allergy and immunology (A&I) clinic ($n = 34$ [41.5%]). The emergency department accounted for 3 patients, whereas other subspecialty clinics and the inpatient ward accounted for 4 patients. Subcategorizing adherence by clinics, 38.1% of A&I patients vs 60.0% of primary care patients remained adherent. Although primary care patients averaged 30 clinic visits, A&I patients averaged 12 visits. Educational efforts were documented for 20% of primary care patients vs 56% of A&I patients.

In this retrospective medical record review study during a 10-year period, only 45.1% of patients had active SIE prescriptions 10 years after receiving initial prescription. Our overall refill rates are lower than those previously reported in short-term studies (54%–56% during 1–2 years),^{2–7} likely a result of the longer follow-up period, but consistent with the only other study, to our knowledge, to have investigated SIE refill rates for greater than 1 year. Kaplan et al⁸ tracked epinephrine refill rates during a 6-year period and found that 46% of patients refilled their SIE at least once and only 11% refilled consistently at all expected refill times. In addition, most epinephrine adherence data exist for management during or after an emergency department visit or hospitalization.^{2,4–6} Our study is the first to look at refill rates of SIE prescription in clinic settings. Primary care patients had greater adherence compared with A&I patients, possibly due to a higher frequency of follow-up visits among primary care patients.

In our study, 24.4% of patients did not refill their prescription beyond their initial prescription. Possible reasons for such high refill failure include lack of education on SIE, lack of awareness of expiration, cost of SIE, fear of using SIE, and discontinuation of prescription by the physician. Another potential explanation for poor adherence is the infrequency of consequences experienced by patients. Hypersensitive patients can go years without having an exposure to the allergen and thus without any adverse events; therefore, asking them to carry a medication could seem impractical. However, because allergies and anaphylaxis could be lifelong conditions, long-term adherence to treatment is just as important as any other chronic disease.

Long-term studies in community settings are needed to confirm our results. Because medications are dispensed in a closed medical system at VA medical centers, long-term adherence for the general population may differ from our study. Limitations of our study also include true use of and adherence to SIE treatment, which can only be implied by the number of refill rates over time. These numbers do not account for frequency of symptoms or actual SIE use. Demographics may have also influenced adherence because older patients may have increased awareness of medical conditions with the convenience of filling their SIE with other medications. Our

Disclosures: Authors have nothing to disclose.

<http://dx.doi.org/10.1016/j.anai.2015.09.011>

1081-1206/Published by Elsevier Inc. on behalf of the American College of Allergy, Asthma & Immunology.

patient population, with a mean age of 66 years, may not be representative of the general population. In addition, the VA exclusively carries EpiPen with a copayment of \$8 to \$12, whereas the copayment in the community could be up to \$100; thus, we assume cost was not a factor in poor refill adherence. However, veterans do not have access to alternative available SIEs (ie, Adrenaclick, Auvi-Q), which may have size and usability advantages.

In conclusion, our study reports that refill rate adherence to SIE remains low and needs further investigation into reasons for non-adherence and actual use of SIE. Many issues remain unanswered. Further investigations should focus on causes and types of non-adherence. Factors that may influence adherence could include severity of patients' reactions, frequency of and comfort level in SIE use, and frequency of referral or discussion of immunotherapy for patients with venom allergy. We plan to address these questions in a follow-up patient survey study.

Acknowledgments

We sincerely thank Jeffrey B. Flores for his contributions in data collection and Sabrina T. Lee for her contributions in facilitating the research project.

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