

Original Article

Epinephrine Autoinjector Prescribing Trends: An Outpatient Population-Based Study in Olmsted County, Minnesota

Sangil Lee, MD, MS^a, Erik P. Hess, MD, MSc^b, Christine Lohse, MS^c, Dante Lucas S. Souza^b, and Ronna L. Campbell, MD, PhD^b *Mankato and Rochester, Minn*

What is already known about this topic? The prescription trend of epinephrine autoinjector can be an indicator of the prevalence of patients who have experienced or are at risk of anaphylaxis.

What does this article add to our knowledge? The incidence rate of epinephrine autoinjector prescriptions increased from 2004 to 2010. In childhood, boys were more likely to receive a prescription than girls, but this reversed in later ages.

How does this study impact current management guidelines? Rates of increased epinephrine autoinjector may be related to increased burden of allergic disease, especially food allergy in young patients, increased public awareness, as well as increasing recognition and frequency of diagnosis by health care providers.

BACKGROUND: The prescribing pattern of epinephrine over time is an indicator of the secular trend of anaphylaxis. However, it is not well known in a population level in the United States. **OBJECTIVE:** To evaluate the trend of prescriptions for epinephrine autoinjectors in Olmsted County, Minn, residents. **METHODS:** Outpatient prescriptions for epinephrine were identified among residents of Olmsted County, Minn, between January 1, 2004, and December 31, 2010. We used the first prescription per patient per year, and the first prescription per patient during the study period to calculate incidence rates. Incidence rates per 100,000 person-years were calculated using patients prescribed epinephrine per year as the numerator and age- and sex-specific counts of the population of Olmsted

County as the denominator. The relationships of age group, sex, and year of prescription with incidence rates were assessed by fitting Poisson regression models using the SAS procedure GENMOD.

RESULTS: The overall incidence rate of epinephrine autoinjector prescriptions during the study period was 757 per 100,000 person-years (95% confidence interval: 740-774). The prescription rates per patient per year increased over time, with an annual rate of increase of 8% ($P < .001$), but the rates per patient remained stable ($P = .077$). For each year, incidence rates overall were higher in women compared with men ($P < .001$). From ages 0 to 19, incidence rates were higher in boys compared with girls. At age 20 and above, incidence rates were higher in women compared with men.

CONCLUSIONS: The overall rate of epinephrine autoinjector prescriptions increased, but the rate of first-time prescriptions was stable from 2005 to 2010. In childhood, boys were more likely to receive a prescription than girls, but this reversed in later ages. © 2016 American Academy of Allergy, Asthma & Immunology (*J Allergy Clin Immunol Pract* 2016;■:■-■)

Key words: Anaphylaxis; Epinephrine autoinjector; Epidemiology; Incidence rate

Epinephrine autoinjectors are the first-line therapy for anaphylaxis and can be administered by laypeople or health care providers for the emergency management of anaphylaxis.^{1,2} Because epinephrine autoinjectors are primarily prescribed to treat or prevent anaphylaxis and related allergic reactions, the prescription trends over time can be used as an indicator of the overall prevalence of patients who have experienced or are at risk of experiencing anaphylaxis.³

Trends of epinephrine autoinjector prescriptions in the United States, however, are not well known.⁴ The Rochester Epidemiology Project (REP) is a record linkage system that connects and indexes the records of virtually all providers of

^aDepartment of Emergency Medicine, Mayo Clinic Health System, Mankato, Minn

^bDepartment of Emergency Medicine, Mayo Clinic, Rochester, Minn

^cDivision of Biostatistics and Informatics, Mayo Clinic, Rochester, MN

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Corresponding author: Sangil Lee, MD, MS, Department of Emergency Medicine, Mayo Clinic Health System, 1453 Marsh Street, Mankato, MN 56001. E-mail: lee.sangil@mayo.edu.

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Abbreviations used

REP- Rochester Epidemiology Project

CI- Confidence interval

ED- Emergency department

medical care in Olmsted County, Minn.⁴⁻⁷ Prescription data have become available as a part of the REP since 2003.⁸ Thus, evaluating trends of prescribing for epinephrine autoinjectors within the REP will provide an additional method of estimating the prevalence of patients who have experienced or are at risk of anaphylaxis in Olmsted County, Minn.

In this study, we used the REP research infrastructure to determine the trends of epinephrine autoinjector prescriptions in Olmsted County residents over a 7-year period, 2004-2010. We hypothesized that the number of prescriptions per year would increase, suggesting an increasing prevalence of anaphylaxis in Olmsted County, Minn.

METHODS**Study population**

All Olmsted County residents identified by REP census between January 1, 2003, and December 31, 2010, who had given permission for their medical records to be used for research were included in the study. A previous study showed that the record linkage system through the REP captures 98.7% of the population of Olmsted County by US census, and the age and sex distributions were nearly identical to US census estimates.⁹ The prescription data capture above 80%-90% from Mayo Clinic and Olmsted Medical Center, 2 large health care organizations in Olmsted County. A previous study suggested that some noncritical medications may be undercounting but still accurately describe trends.⁸ St Sauver et al⁹ reported that age, sex, and ethnic characteristics of Olmsted County were similar to those of the state of Minn and the Upper Midwest; however, Olmsted County was less ethnically diverse than the entire US population, more highly educated, and wealthier. Additional details of REP studies have been published elsewhere.⁹⁻¹² The study was approved by the Institutional Review Boards of both Mayo Clinic and Olmsted Medical Center.

Prescription records

Outpatient prescriptions between January 1, 2003, and December 31, 2010, were obtained from the Mayo Clinic and Olmsted Medical Center in Rochester Minn. These 2 institutions provide nearly all of the health care for Olmsted County residents.^{9,10,12} Both institutions use electronic prescription systems in outpatient settings. Epinephrine autoinjectors were available in 29 prescription formularies. All prescriptions were mutually exclusive, and individuals who received multiple prescriptions within available formularies were counted only once per year for each year during the study period, and first-time prescriptions were also counted once per patient for each year, and once per patient during the study period. We counted each prescription only once whether it was for a single autoinjector or 2-pak. We did not account for refills or duration of medication use.

Statistical analysis

First, we selected the first prescription per patient per year to estimate incidence, and then described first prescription per patient during the study period. Trends for first-time prescriptions were analyzed from 2004 to 2010 to allow for a 1-year washout period to be able to account for patients who had received a prescription the year before. Prescriptions in 2003 were removed to account for a

washout period during the first 12 months of the study. Incidence rates per 100,000 person-years were calculated using patients prescribed epinephrine as the numerator, and age- and sex-specific counts of the population of Olmsted County as the denominator. The denominators were obtained from a complete enumeration of the Olmsted County population provided by the REP.¹³ Because the population of Olmsted County is nearly all white, incidence rates were directly age- and sex-adjusted to the structure of the 2010 US white population. Patients were grouped by age into those 0-9, 10-19, 20-29, 30-39, 40-49, 50-59, and 60+ years old.

The relationships of age group, sex, and year of prescription with incidence rates were assessed by fitting Poisson regression models using the SAS procedure GENMOD. Statistical analyses were performed using version 9.3 of the SAS software package (SAS Institute, Cary, NC). All hypothesis tests were 2-sided, and *P* values < .05 were considered statistically significant.

RESULTS**Overall findings**

A total of 7991 prescriptions among 3801 patients from 2004 to 2010 were identified in Olmsted County. The mean age at the first prescription per year was 31.5 years (median 30 years; interquartile range 11-50; range 0-97). [Table I](#) shows the number of prescriptions each year and the demographics of the

TABLE I. Summary and demographic characteristics of patients receiving epinephrine autoinjector prescriptions in Olmsted County, Minn, from January 1, 2004, to December 31, 2010 (N = 7991)

Feature	N (%)
Age (y)	
0-9	1752 (22)
10-19	1277 (16)
20-29	930 (12)
30-39	952 (12)
40-49	1069 (13)
50-59	1068 (13)
60+	943 (12)
Sex	
Female	4488 (56)
Male	3503 (44)
Race	
Black	213 (3)
Asian	349 (4)
Hawaiian/Pacific Islander	16 (<1)
American Indian	19 (<1)
Other/mixed	358 (4.5)
Undisclosed	98 (1)
White	6938 (87)
Year	
2004	819 (10)
2005	918 (11)
2006	1121 (14)
2007	1168 (15)
2008	1231 (15)
2009	1290 (16)
2010	1444 (18)

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