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Clinical paper

Epinephrine use in older patients with anaphylaxis: Clinical outcomes and cardiovascular complications☆

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ABSTRACT

Background: There is little data describing the differences in epinephrine (epi) administration and cardiac complications among older and younger patients with anaphylaxis.
Methods: This retrospective cohort study was conducted at two urban emergency departments (ED) over a 5 year-period, and included adults who met a pre-specified criteria for anaphylaxis. Patients ≥50 years of age were defined as "older". Univariate logistic regression was performed to compare the difference in frequency of epi administration between the "older" and "younger" groups. Among those who received epi, the proportion of patients who received doses exceeding the recommended maximum and who had pre-specified cardiovascular complications were compared between the two groups, stratified further by route of administration.
Results: Of 2995 allergy-related visits, 492 met criteria for anaphylaxis, including 122 (24.8%) older patients. Older patients were less likely to receive epi injection (36.1% vs. 60.5%). Of those who received epi, older patients were more likely to receive excessive dose of epi (7/44, 15.9% vs 2/225, 0.9%, unadjusted OR 20.7, 95% CI 3.8–211.7). Four (4/44, 9.1%) older patients experienced cardiovascular complications, compared to 1/225 (0.4%) in the younger group (unadjusted OR 22.4, 95% CI 2.1–1129.8). When examining only intra-muscular epinephrine, 1/31 older patients had cardiac complications, compared to 1/186 in the younger group.
Conclusion: Older patients with anaphylaxis were less likely to receive epi injection. Intramuscular epi appears safe in this population; however, the use of intravenous epi should be avoided in older patients due to the potential of developing serious cardiac complications.

Introduction

Anaphylaxis is defined as "a serious allergic reaction that is rapid in onset and may cause death".[1,2] Although the lifetime prevalence is estimated to be low with a range from 0.05 to 2%, the prevalence appears to be rising.[3,4] Allergic reactions and anaphylaxis account for approximately one percent of emergency department (ED) visits.[5]

Older patients have been identified as a vulnerable group for severe or fatal anaphylaxis.[6] Despite this older patients appear less likely to receive epinephrine (epi) injection, possibly due to concern for its side effects.[7,8] It is unclear, however, whether epi use is associated with a higher frequency of side effects in older patients with anaphylaxis.

We conducted a retrospective cohort study at two urban EDs to compare the frequency of epi administration and the subsequent documented cardiovascular complications in patients with

Abbreviations: ED, emergency department; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; sBP, systolic blood pressure; IV, intravenous; IM, intra-muscular; ECG, electrocardiogram; IQR, interquartile range; OR, odds ratio; CI, confidence interval.

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anaphylaxis, and compared patients 50 years and older, with their younger counterparts.

Methods

Design and setting

This retrospective cohort study was conducted at two urban academic teaching hospitals in Vancouver, British Columbia, Canada, affiliated with the University of British Columbia. St. Paul's Hospital is a tertiary care referral center that treated approximately 70,000 ED patients annually during the study period. Mount St. Joseph's Hospital is a community center with nearly 25,000 annual ED visits. The two hospitals share a common comprehensive electronic medical record (Eclipsys sunrise clinical manager, Allscripts Healthcare Solutions Inc., Chicago, IL). All medical treatments, diagnostic investigations, consultations and outpatient prescriptions are recorded with digital time stamps. Emergency physicians complete an electronic summary with at least one diagnosis for every encounter. The study hospitals are located in a region with four additional EDs; all visits are recorded in a unified database, and patient visits can be linked with unique provincial health numbers. This study protocol was approved by the institutional review boards and affiliated ethics committees of Providence Health Care, the University of British Columbia, and Vancouver Coastal Health.

The provincial B.C. Ambulance Service provides prehospital care. Paramedics are licensed to administered intramuscular epi in accordance with provincial guidelines,[9] although corticosteroid administration is not within their scope of practice. In the ED patients were managed at the discretion of the treating physician. ED treatment protocols indicate that all patients who receive epi must have cardiopulmonary monitoring in a nurse-staffed stretcher. Electrocardiograms (ECG's) are ordered by physicians or nurses if patients develop chest pain. In addition, ancillary testing such as chest radiographs and cardiac troponins are also typically ordered in these cases.

Inclusion and exclusion criteria

All patients from April 1, 2007 to March 31, 2012, with an ED discharge diagnosis of "allergic reaction" (ICD 9 code 995.3), which was the only available allergy-related code for physicians within the electronic medical record, were collected. The following patients were excluded: those younger than 17 years, those with a primary diagnosis of asthma, those who left prior to assessment by a nurse or a physician, those whose allergen was considered to be an angiotensin-converting enzyme (ACE) inhibitor (due to potential misclassification with ACE-induced angioedema), and those who had a past history of non-allergic angioedema. We performed a comprehensive chart review of each patient and applied a definition of anaphylaxis using a previously described, adapted from the National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network criteria (Fig. 1).[1,10,11]

Methods of measurements

Data collection adhered to robust methodologic standards for chart reviews and has been described previously.[10–13] Briefly, three investigators (J.L., T.W.Y., and B.G.) who were unaware of the hypothesis and outcomes of this study, systematically abstracted data using a standardized collection form after training on a set of 50 records. Weekly meetings were held to monitor performance and resolve disagreements. Study investigators collected the following data: demographics, past medical history, characteristics of presentation, treatment with epi injection (self-administered, intra-muscular or intravenous epi, and whether administration occurred in the prehospital setting and ED), length of ED stay, (LOS) and disposition (home, death, or the admission to hospital). The definition of anaphylaxis, severe anaphylaxis, and biphasic reaction were applied to each patient encounter (Fig. 1).[14] LOS was defined as the time period from ED registration to discharge, whether or not the patient was admitted. Overall, five percent of patient charts were randomly identified and reviewed by a second blinded reviewer; inter-observer agreements have been reported previously with all kappa {κ} values >0.9.[10,11] In all cases, missing data were noted in the collection form and undocumented variables were considered not to be applicable to the patient encounter.

An additional investigator (TK) collected data pertaining to cardiac risk factors, prior history of angina, myocardial infarction, and revascularization. Two independent abstractors (TK, FS) reviewed all potential cardiac complications (see below); in cases of disagreement, a third reviewer, blinded to both initial reviews (B.G.), adjudicated.

Outcome measures

The primary outcome of interest was the proportion of patients who were treated with epi. The secondary outcome was the proportion of patients with pre-specified post-epi cardiovascular complications; this was further classified by route of administration; intravenous (IV) or intramuscular (IM). The tertiary outcome was the proportion of patients who received an excessive dose of epi, defined as greater than 0.5 mg for intramuscular, or greater than 100 μg for intravenous administration, respectively.[6,15–17]

Cardiovascular complications after epi injection were defined as follows: (1) new onset of ventricular fibrillation or tachycardia, atrial flutter or fibrillation, or multifocal atrial tachycardia; (2) acute stroke, defined as a new neurologic deficit[18]; (3) elevated cardiac troponin T (above 99th percentile of the upper reference limit (normal sensitivity troponin, Roche Elecsys, Hoffman Laroche, Laval, QC; 99th percentile reference limit > 0.01 ng/ml)); and, (4) the following new ischemic ECG findings: ST-segment elevation greater than 1 mm, ST-segment depression greater than 0.5 mm; left bundle branch block; T-wave inversions, or pathological Q-wave changes.[19]

Seven-day outcomes were obtained by cross-referencing the patient list with the regional ED database to determine subsequent ED visits (classified as allergy-related or unrelated) and the provincial vital statistics database to ascertain mortality.

Statistical analysis

All analyses were performed using STATA version 13.1 (STATA Corp., College Station, TX). Categorical variables are presented as percentages and non-normally distributed continuous variables as medians with interquartile ranges (IQR). In order to demonstrate the linear trend between the proportion of epi treated patients and the age, we divided patients into age categories (17–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years, and 70 years and older), and analyzed with the Cochran–Armitage test.[20]

Study patients were dichotomized by age: older patients were defined as those 50 years of age and older, based on previous literature.[7] We assessed unadjusted associations of each variable between two groups by using Mann–Whitney *U* test, univariate logistic regression, or Fischer exact test, where applicable. To compare the primary outcome between older and younger patients, we conducted univariate logistic regression. For the analysis of the secondary and tertiary outcomes, we conducted univariate exact logistic regression to estimate the odds ratio (OR) with corresponding 95% confidence intervals (CI) for each association. Due to the rarity of events, relative risk calculations were not performed.[18]