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Brief Reports

EFFECT OF INTRANASAL VASOCONSTRICTORS ON BLOOD PRESSURE: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Shawna D. Bellew, MD,*† Katie L. Johnson, MD,‡ Micah D. Nichols,§ and Tobias Kummer, MD||

*Department of Emergency Medicine, Vanderbilt University, Nashville, Tennessee, †VA National Quality Scholars Program, VA Tennessee Valley Healthcare System, Nashville, Tennessee, ‡Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota, §Bethel University, St. Paul, Minnesota, and ||Department of Emergency Medicine, Mayo Clinic, Rochester, Minnesota

Reprint Address: Tobias Kummer, MD, Department of Emergency Medicine, Mayo Clinic, 200 First Street SW, Rochester, MN 55905

☐ **Abstract—Background: Treatment for epistaxis includes application of intranasal vasoconstrictors. These medications have a precaution against use in patients with hypertension. Given that many patients who present with epistaxis are hypertensive, these warnings are commonly overridden by clinical necessity. Objective: Our aim was to determine the effects of intranasal vasoconstrictors on blood pressure. Methods: We conducted a single-center, randomized, double-blind, placebo-controlled trial from November 2014 through July 2016. Adult patients being discharged from the emergency department (ED) at Mayo Clinic (Rochester, Minnesota) were recruited. Patients were ineligible if they had a contraindication to study medications, had a history of hypertension, were currently taking antihypertensive or antidysrhythmic medications, or had nasal abnormalities, such as epistaxis. Subjects were randomized to one of four study arms (phenylephrine 0.25%; oxymetazoline 0.05%; lidocaine 1% with epinephrine 1:100,000; or bacteriostatic 0.9% sodium chloride [saline]). Blood pressure and heart rate were measured every 5 min for 30 min. Results: Sixty-eight patients were enrolled in the study; of these, 63 patients completed the study (oxymetazoline, n = 15; phenylephrine, n = 20; lidocaine with epinephrine, n = 11; saline, n = 17). We did not observe any significant differences in mean arterial pressure over time between phenylephrine and saline, oxymetazoline and saline, or lidocaine with epinephrine and saline. The mean greatest increases from baseline in mean arterial pressure, systolic and diastolic blood pressure, and heart rate for each treatment group were also not significantly different from the saline group. Conclusions: Intranasal vasoconstrictors did not significantly increase blood pressure in patients without a history of hypertension. Our findings reinforce the practice of administering these medications to patients who present to the ED with epistaxis, regardless of high blood pressure.** © **2018 Elsevier Inc. All rights reserved.**

☐ **Keywords—epinephrine; epistaxis; hemodynamics; oxymetazoline; phenylephrine**

INTRODUCTION

Epistaxis is a common reason for presentation to the emergency department (ED), accounting for about 1 in 200 visits (1). Episodes appear to be more common in those younger than 10 years, older than 70 years, and those exposed to dry indoor heating in the winter months (2). Whether a relationship exists between systemic hypertension and epistaxis, and whether that relationship implies causation or correlates with increased severity of bleeding, remains controversial (3–6).

Initial management of epistaxis includes compression and application of topical intranasal vasoconstrictive medications by spray or by packing the nose with soaked pledgets (7–9). Application of these agents facilitates examination by reducing blood flow to the nasal mucosa and, in many cases, bleeding resolves with

Trial Registration: This study was registered at ClinicalTrials.gov (NCT02285634).

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these conservative measures alone (10). Frequently recommended medications for this indication include cocaine, phenylephrine, oxymetazoline, and lidocaine with epinephrine (7–9,11).

The administration of phenylephrine, oxymetazoline, and epinephrine for epistaxis is considered an off-label use, and all three agents have a precaution against use in patients with pre-existing hypertension (12–14). However, strict avoidance of these agents in hypertensive patients with epistaxis would severely limit their applicability, given that patients often have elevated blood pressure during epistaxis and also may have comorbid hypertension. Thus, these warnings are commonly overridden by clinical necessity.

Studies regarding the hemodynamic effects, safety, and efficacy of intranasal vasoconstrictors have been conducted primarily in the operative setting, with the aim of facilitating either otolaryngologic procedures or nasal intubation (15–19). These studies have shown small changes in hemodynamics after administration, and these small effects on blood pressure have been similar when various agents were compared. Instrumentation of the nasal passages itself may limit our ability to apply the results of these studies to other clinical settings, given that such procedures have been independently reported to affect hemodynamics (20).

Therefore, we conducted a randomized, double-blind, placebo-controlled clinical trial to assess the hemodynamic effects of three commonly used medications for epistaxis treatment, lidocaine with epinephrine, phenylephrine, and oxymetazoline, in patients without a history of hypertension who presented to the ED. We hypothesized that these agents would not result in clinically significant increases in blood pressure when compared with a placebo.

METHODS

Study Setting, Design, and Outcomes

A single-center, randomized, double-blind, placebo-controlled trial was conducted in the ED at Mayo Clinic (Rochester, Minnesota), an academic, tertiary care hospital. The study protocol was approved by the Mayo Clinic Institutional Review Board. The trial was registered with ClinicalTrials.gov (identifier NCT02285634). Study reporting adheres to CONSORT (Consolidated Standards of Reporting Trials) guidelines for reporting parallel-group randomized trials (21).

The study statistician used a computerized random-number generator to create a simple randomization schedule, which was then provided to the research pharmacy. Only the study statistician and the research pharmacy had access to the randomization schedule. After a patient was enrolled in the study, a custom order sheet with the patient's study identification number was sent to the research pharmacy. The pharmacy then matched the patient with the randomization schedule, and the patient was allocated to one of four study arms: oxymetazoline 0.05%, phenylephrine 0.25%, lidocaine 1% with epinephrine 1:100,000, or bacteriostatic 0.9% sodium chloride (saline [placebo]). After study enrollment was complete, subject numbers were matched to the randomization schedule to complete the data set.

The primary outcome was the greatest increase from baseline in mean arterial pressure (MAP) after medication administration. Secondary outcomes were the greatest increase from baseline in systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR).

Selection of Participants

We aimed to enroll a convenience sample of patients discharged from the ED after they were evaluated for various conditions. Patients were excluded if they declined research consent, were younger than 18 years, were not fluent in English, or had known allergies to any of the study agents. We also excluded patients if they were currently receiving antihypertensive or antidysrhythmic agents, had clinically significant cardiopulmonary comorbidities (e.g., a history of hypertension, dysrhythmia, coronary artery disease, heart failure), were known to be using a monoamine oxidase inhibitor agent, or had a history of angle-closure glaucoma, benign prostatic hyperplasia, nasal surgery, or nasal abnormalities (including epistaxis).

Patient recruitment commenced on November 12, 2014, and was completed on July 29, 2016. Potentially eligible patients were identified by screening the ED census and by referral from ED staff members who were aware of the study and responsible for patient care. Recruitment was conducted by the investigators and by trained personnel. Patients were recruited from 6:00 AM through 4:00 PM, Monday through Friday, to match the working schedule of the research pharmacy. Written informed consent was obtained by a member of the study team before study enrollment.

Study Protocol

Patients were placed in a supine posture on an ED gurney, with the head elevated by approximately 45°. Patients remained in this position for at least 5 min before measurement of baseline hemodynamic parameters. Standardized, appropriately sized blood pressure cuffs and continuous pulse-oximetry finger probes were applied to the patient for monitoring.

Study drugs were dispensed in 5-mL quantities in unlabeled syringes. All four medications were colorless and visually indistinguishable. After measurement of baseline